TRANSPLANT INTERNATIONAL

ELITA POSTER PRESENTATIONS

EP - 01 EFFECT OF PORTAL VEIN THROMBOSIS (PVT) ON SURVIVAL AFTER LIVER TRANSPLANTATION (LT): A METANALYSIS

*A. Zanetto, K.I. Rodriguez-Castro, A. Ferrarese, E. Nadal, G. Germani, F.P. Russo, P. Burra, M. Senzolo
Multivisceral Transplant Unit, Department of Surgery, Oncology, and Gastroenterology, Padua University Hospital, Padua, Italy
Email: alberto.zanetto@yahoo.it

Keywords: liver transplant, portal vein thrombosis

Background: PVT is a common complication in patients with liver cirrhosis undergoing LT. Although PVT is no longer considered an absolute controindication to LT, published data of its effect on mortality after the surgery are heterogeneous and discordant. The aim of the present study was to systematically review the current literature on the role of PVT in LT recipients in term of outcome.
Methods: A systematic review of the English and non English literature was performed by analyzing studies that report on PVT in LT recipients and were published between January 1986 and January 2013. We performed a meta-analysis using the 30-day and 1-year mortality as endpoints in all the studies, using random effect model.
Results: Twenty six studies among the total of 426 articles initially retrieved were considered. Of 25,753 LT, 2004 were performed in patients with PVT (7.78%), and approximately half had complete thrombosis (according to Yerdel's classification) at the time of LT. Seven studies report on 30-day mortality in both patients with PVT and without PVT, for a pooled mortality rate of 10.5% vs 7.7% ($P = 0.01$) respectively with OR equal to 2.29 (95%, CI 1.43–3.68). Nineteen studies report on 1-year mortality after LT in both patients with and without PVT, for a pooled mortality rate of 18.8% vs 15.3% ($P = 0.001$). The OR for 1 year mortality in patient with PVT was 1.39 (95%, CI 1.18–1.64). Four studies report on 30-day mortality in both patients with partial and complete PVT, for a pooled mortality rate of 5.9% vs 17.5% ($P = 0.001$) respectively, with OR equal to 5.65 (95%, CI 2.00–15.96). There wasn't heterogeneity between studies both for the 30-day and 1-year mortality.
Conclusion: Presence of PVT in liver transplant recipients increases 30-day and 1-year mortality, therefore screening and treatment of this complication in patient awaiting LT seems essential.

EP - 02 EFFECTS OF NON-SELECTIVE β-BLOCKERS ON HEMODYNAMICS AFTER LARGE VOLUME PARACENTESIS IN PATIENTS WITH CIRRHOSIS LISTED FOR LIVER TRANSPLANTATION: A PRELIMINARY REPORT

A. Ferrarese[1], A. Zanetto[1], P. Angeli[2], E. Casiglia[2], S. Fasolato[2], G. Boschetti[2], K.I. Rodriguez-Castro[1], E. Nadal[1], I. Bortoluzzi[1], F.P. Russo[1], G. Germani[1], **P. Burra**[1], *M. Senzolo[1]
[1]Multivisceral Transplant Unit, Department of Surgery, Oncology, Gastroenterology, Padua University Hospital, Padua, Italy; [2]Department of Medicine (DIMED), Padua University Hospital, Padua, Italy
Email: marcosenzolo@hotmail.com

Background and aims: Non-Selective β-Blockers (NSBBs) have been associated with increased incidence of Paracentesis Induced Circulatory Dysfunction (PICD) and reduced survival in patients with cirrhosis and refractory ascites. We have prospectively evaluate intra-individual central and peripheral hemodynamic effects produced by NSBBs and incidence of PICD in patients undergoing large volume paracentesis (LVP).
Methods: Patients with cirrhosis and refractory ascites, listed for liver transplantation, having indication to initiate or discontinue NSBBs were enrolled. During two consecutive LVP (while been respectively on and off NSBBs therapy), Cardiac Output (CO), Systemic Vascular Resistances (SVR), Peripheral Vascular Resistances (PVR), and Plasma Renin Activity (PRA) before and after LVP were recorded.
Results: Eleven patients were enrolled, six completed the study; all the patients did have new indication to introduce NSBBs. Before NSBBs introduction, SVR (1808 ± 358.3 vs. 1398 ± 332.4 dyn s cm^{-5}; $P = 0.02$) and PVR (45.9 ± 7.0 vs. 27.7 ± 5.9 mmHg·min·dl·ml^{-1}; $P = 0.04$) significantly decreased after LVP; CO consequently showed an increasing trend (3.8 ± 0.67 vs 4.4 ± 1.14 l/min; $P = 0.06$). PICD was diagnosed in 2/6 patients. After NSBBs introduction, CO did not increase after LVP (3.3 ± 0.9 vs 3.6 ± 1.0 l/min; $P = 0.1$), but this was counterbalanced by a smaller decrease of SVR (1981.12 ± 314.2 vs. 1763.29 ± 555.05 dyn·s·cm^{-5}; $P = 0.1$) and PVR (44.17 ± 12.2 vs. 32.1 ± 7.86 mmHg·min·dl·ml^{-1}; $P = 0.2$). PICD was diagnosed in three patients. One year survival was 83%, one patient underwent liver transplantation, one dropped out the waiting list.
Conclusions: In patients listed for liver transplantation with refractory ascites, the inotropic negative effect of NSBBs seems to be counterbalanced by a smaller decrease of vascular resistances, due to splanchnic β_2-blockade. Therefore, incidence of PICD was not increased by introduction of NSBBs, which may be void of detrimental effects in these patients.

EP - 03 HYPERCOAGULABILITY IN CIRRHOTIC PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCC) AND PORTAL VEIN THROMBOSIS (PVT)

*A. Zanetto[1], A. Ferrarese[1], K. Rodriguez[1], M. Fadin[2], S. Gavasso[2], C. Radu[2], P. Zerbinati[2], A. Vitale[3], U. Cillo[3], F. Farinati[4], F.P. Russo[1], G. Germani[1], P. Simioni[2], P. Burra[1], M. Senzolo[1]
[1]Multivisceral Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy; [2]Department of Cardiologic, Thoracic, and Vascular Sciences, Padua University Hospital, Padua, Italy; [3]Hepatobiliary Surgery and Liver Transplantation Unit, Padua University Hospital, Padua, Italy; [4]Gastroenterology, Department of Surgical, Oncological and Gastroenterological Sciences, Padua University Hospital, Padua, Italy
Email: alberto.zanetto@yahoo.it

Background and aim: Studies which explore the hypercoagulable state associated with neoplastic disease and its correlation with the risk of developing PVT in patients with HCC are lacking even if PVT is a common complication in patients with liver cirrhosis and hepatocellular undergoing LT. The aim of the present study was to evaluate the thrombophilic role of HCC in cirrhotics with and without HCC and in controls and to correlate the presence of HCC and the coagulation profile with the incidence of PVT.
Methods: Cirrhotic patients with and without HCC were prospectively enrolled in the study. Age- and sex-matched healthy individuals constituted the control group for thromboelastometry (ROTEM). All cirrhotic patients with and without HCC underwent: ROTEM, platelet count, determination of prothrombin time and of levels of pro and anticoagulation factors. During follow-up, PVT onset in both patients with and without HCC was recorded.
Results: Seventy-six cirrhotics, 41 with HCC and 35 without HCC, were included. Forty-eight healthy volunteers were included as the control group. Volume of active HCC was >5 cm^3 in 18 patients. Levels of pro and anticoagulation factors were similar between patients with and without HCC, but fibrinogen was increased in HCC patients with active volume >5 cm^3 HCC compared to those with ≤5 cm^3 HCC bulk (348.72 ± 124.06 mg/dL vs 237.64 ± 99.18 mg/dL) and to cirrhotics without HCC (260.57 ± 126.07 mg/dL) ($P = 0.006$). Platelet count was significantly increased in HCC patients compared to non-HCC patients, and this was especially true in Child Class A subjects. Patients with HCC showed significantly lower clotting formation time (CFT) and maximum clot formation (MCF) at ROTEM compared to healthy controls. The hypercoagulable state was present even when HCC patients were compared to cirrhotics without HCC, and was more evident when performing a subgroup analysis of Child Class A patients, with statistically significant differences in MCF EXTEM, MCF NATEM e CFT NATEM. During the 12 months follow-up there were 14 PVT episodes (10 in HCC and 4 in non HCC group). At Cox multivariate analysis HCC and fibrinogen test of ROTEM were independently associated with risk of developing PVT. In the HCC group, 5/10 PVT occurred in patients in Child Class A. At FIBTEM test of ROTEM, MCF and AUC were statistically greater in HCC patients who later developed PVT.
Conclusions: Cirrhotics with HCC demonstrate a prothrombotic hemostatic balance resulting in an increased risk of PVT development. Since the presence of PVT in liver transplant recipients increases 30-day and 1-year mortality, screening and treatment of this complication in patient awaiting LT seems essential. In this scenario, ROTEM seems to be a sensitive method to identify hypercoagulability, that would otherwise be undetected by routine laboratory testing. Moreover, ROTEM seems to be identify those patients who could benefit from thromboprophylaxis.

EP - 04 COMPARING PREDICTIVE MODELS OF SHORT-TERM MORTALITY AFTER LIVING DONOR LIVER TRANSPLANTATION DUE TO ACUTE LIVER FAILURE

*H.S. Chung, J.H. Choi, J. Lee, Y.S. Kim, C.S. Park
Department of Anaesthesiology and Pain Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seocho-gu, Seoul, Republic of Korea
Email: anesthe@catholic.ac.kr

Keywords: acute liver failure, liver transplantation, living donors, mortality, prognosis

Background: Acute liver failure (ALF) is a rapidly progressing and fatal disease. Various predictive models of ALF outcome have been developed, but none provided the definitive predictive accuracy. We investigated which predictive model is most suitable, and suggested new predictive model in patients undergoing living donor liver transplantation (LDLT) due to ALF.
Methods: Preoperative data from 85 patients who had undergone LDLT due to ALF were reviewed using King's College Hospital criteria (KCH), the Child-Turcotte-Pugh (CTP) classification, the model for end-stage liver disease (MELD) score, serum phosphate and serum lactate. After multivariate adjustment process with preoperative indicators of ALF prognosis, MELD conjugated serum phosphate model (MELD-p) as new predictive model suggested by resulting from a logistic regression analysis. The relationships of KCH, CTP, MELD, serum phosphate and lactate, and MELD-p with 3-month post-transplant mortality were respectively analyzed. The area under the receiver operating characteristic curve (AUC) was used to evaluate the diagnostic accuracies of individual models in predicting 3-month mortality.
Results: The MELD-p and MELD score was highly predictive (AUC > 0.9). KCH and serum phosphate showed acceptable predictive abilities (AUC > 0.7), while CTP failed to show discriminative powers in predicting 3-month mortality (Table 1).
Conclusions: The MELD-p score system can predict short term mortality better after LDLT due to ALF.

Table 1 Comparison of the predictive value, sensitivity, specificity, and the diagnostic accuracy of the King's College Criteria, CTP, serum phosphate, MELD and MELD-p for prediction of 3 month mortality after Living Donor Liver Transplantation due to Acute Liver Failure

Prognostic test	Threshold score	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
CTP	C	0.0	100.0		91.0	0.606
KCH	Fullfilled criteria	0.0	100.0		91.0	0.702
Serum phosphate	>4.08	66.67	95.38	57.1	96.9	0.754
MELD	>30	100.0	67.61	23.3	100.0	0.908
MELD-p	>0.3181	83.33	95.38	83.3	98.5	0.956

References:
Botta F., Giannini E., Romagnoli P., Fasoli A., Malfatti F., Chiarbonello B., Testa E., Risso D., Colla G., Testa R., (2003). MELD scoring system is useful for predicting prognosis in patients with liver cirrhosis and is correlated with residual liver function: a European study. Gut., 52, 134–9.
Cholongitas E., Marelli L., Shusang V., Senzolo M., Rolles K., Patch D., Burroughs AK., (2006). A systematic review of the performance of the model for end-stage liver disease (MELD) in the setting of liver transplantation. Liver Transpl., 12, 1049–6.

EP - 05 CONFIDENCE INTERVALS FOR THE RADIOLOGICAL MEASUREMENT OF TUMOR SIZE IN HEPATOCELLULAR CARCINOMA

K. Milto[1], J. Bradley[1], *I. Currie[1,2]
[1]Department of Clinical Surgery, University of Edinburgh, United Kingdom; [2]Scottish Liver Transplant Unit, Royal Infirmary of Edinburgh, United Kingdom

Introduction: Liver transplantation for hepatocellular carcinoma (HCC) is currently indicated based on size and number of lesions. Milan and UCSF criteria are used in many countries, and in the UK, modified Milan criteria are in use. Nonetheless, tumour size is critically important in all scoring systems. In contrast to quantitative medical techniques used in all hospitals across the world, the measurement of HCC is not subject to quality assurance. Neither is the variability between different operators recognised by way of confidence intervals or similar statistical indicators of variability.
Aims: We hypothesised that there would be variability in the radiological measurements of hepatocellular carcinoma tumours between different liver transplantation radiologists and set out to quantify this variation.
Materials and methods: Full abdominal Computed Tomography and Magnetic Resonance Imaging scans of two anonymised patients with hepatocellular carcinoma were selected. The scans contained five tumours of different sizes. These scans were transferred onto discs and distributed to UK transplant radiologists. Results were recorded using a data collection sheet which indicated the size, site and number of tumours observed by the radiologist. The means, standard deviations (SD), standard errors (SE) and 95% confidence intervals (CI) of tumour size for each tumour were calculated.
Results: There are approximately 20-30 liver transplant radiologists performing HCC measurement in the UK in seven centres. Radiologists were approached in six out of seven UK centres. Data were obtained from five radiologists between two centres. Mean tumour sizes (±95% CI) were 42.0 ± 6.9, 9.6 ± 1.6, 16.2 ± 4.7, 24.0 ± 4.0 and 38.2 ± 2.2 mm (for tumours 1–5 respectively). The SD of each tumour size was 7.9, 1.8, 5.4, 4.5 and 2.5 mm (for tumours 1–5 respectively). The SE of each tumour size was 3.5, 0.8, 2.4, 2.0 and 1.1 mm (for tumours 1–5 respectively).
Conclusions: Variation in measurements of HCCs was observed between different radiologists, as expected for any observer-dependent size estimation. The magnitude of this variation was sufficient to suggest that patients exceeding listing criteria should have scans assessed by more than one radiologist on an independent basis. A larger group of study radiologists would be required before specific recommendations regarding confidence intervals and tumour size could be made.

EP - 06 THERAPEUTIC MONITORING OF TACROLIMUS FOLLOWING ADULT LIVER TRANSPLANTS: DOES PERCEIVED SUB-OPTIMAL MONITORING PRACTICE AFFECT THE OUTCOMES?

*B. Dasari[1], J. Hodson[2], A. Nassir[1], S. Bramhall[1], J. Issac[1], P. Muiesan[1], H. Mergentel[1], D. Mirza[1], T. Perera[1]
[1]The Liver Unit, Queen Elizabeth Hospital Birmingham, Edgbaston, Birmingham, United Kingdom; [2]Wolfson Computer Laboratory, Queen Elizabeth Hospital Birmingham, Edgbaston, Birmingham, United Kingdom
Email: bobby.dasari@yahoo.com

Key words: Tacrolimus, therapeutic drug monitoring, outcomes

Introduction: Owing to the narrow therapeutic index of Tacrolimus, careful monitoring of trough levels and dose adjustments are recommended. The objective of this study is to assess the current practice of drug monitoring of Tacrolimus in the early post operative period following liver transplantation (LT), and its impact on outcomes.
Methods: Patients exposed *de-novo* to Tacrolimus following LT between January-2011 and January-2013 were included. Duration to trough levels (DTT) were calculated from the time of administration of last prescribed dose of Tacrolimus to the time blood taken for measurement of the trough levels. Data was collated retrospectively from the electronic database that precisely records the dosing and sampling times. All measurements of Tacrolimus and creatinine were Log^2-transformed prior to analysis and data were analysed using Generalised Estimating Equations, with an autoregressive correlation structure. Finally a statistical model was built as a dose/drug level estimation tool based on these data and validated prospectively.
Results: Two thousand nine hundered and forty-six events of Tacrolimus monitoring in 275 patients were evaluated. The median DTT was 7:19 h (range: 27 min–19:38 h). DTT was ≤6, 6–8, 8–10 and ≥10 h in 18%, 55%, 7% and 20% of the measurements respectively. A significant association was found between DTT and Tacrolimus levels ($P = 0.022$). However, the average creatinine levels were found to be similar and there was no significant difference in the rejection rates between different groups of DTT. The predicted Tacrolimus measurements from the dose estimation tool were reasonable estimates of the actual tacrolimus levels (R^2 value of 0.522).
Conclusion: There is a significant variation in the 'real world' practice of therapeutic monitoring of Tacrolimus. The majority of therapeutic measurements performed with DTT falling below manufacturer recommendations however this did not lead to adverse transplant sequalae.

Reference:
Jorgensen K, Povlsen J, Madsen S, et al (2002). C2 (2-h) levels are not superior to trough levels as estimates of the area under the curve in tacrolimus-treated renal-transplant patients. Nephrol Dial Transplant 17(8):1487–90.

EP - 07 THE QUANTITATIVE ASSESSMENT OF HEPATIC ARTERY RECONSTRUCTION IN LIVING DONOR LIVER TRANSPLANTATION

***M. Dayangac**, R. Killi, L. Yalcin, Y. Tokat*
Liver Transplantation Unit, Florence Nightingale Hospital, Istanbul, Turkey
Email: dayangac@florence.com.tr

Keywords: hepatic artery, living donor liver transplantation

In living donor liver transplantation (LDLT), intraoperative ultrasound (IOUS) is indispensable for evaluating the vascular anastomoses and the blood flow. In this prospective cohort study, our objective was to investigate the impact of quantitative Doppler US assessment on the outcome of hepatic artery (HA) reconstruction in LDLT.

Between January 2013 and January 2014, 77 adult patients who underwent right lobe LDLT were included. Under the operating microscope, HA reconstruction was performed in end-to-end fashion using interrupted sutures and an immediate IOUS was performed with 9-MHz linear transducer upon the completion of anastomosis.

Quantitative sonographic evaluation included luminal diameter of the graft and recipient arteries and the anastomosis, peak systolic velocity (Vs), systolic acceleration time (SAT), and resistive index (RI). A qualitative evaluation was also performed for both graft and recipient arteries to detect intimal thickening, occurrence of thrombus, and dissection. A surveillance Doppler US was performed selectively in patients with suboptimal HA flows in IOUS, and all other recipients were followed clinically without routine radiologic examination.

A single HA anastomosis was performed in all cases. The median luminal diameter of the graft and the recipient HA and the anastomosis were 3.4 (3.0–3.8), 3.5 (2.9–4.2), and (1.8 (1.5–2.1) mm, respectively. The median peak systolic velocity and RI were 62.5 (37.2–86.7) cm/sec and 0.64 (0.57–0.63), respectively. In 17 (22.0%) patients, IOUS showed pathological findings, which were corrected by immediate surgical revision. In patients with anastomotic revision, the mean diameter of the arterial anastomosis was significantly lower (1.9 ± 0.44 vs. 1.6 ± 0.46, $P = 0.01$).

In a median follow-up of 7.0 (4.0–10.0) months, only one (1.2%) patient developed HA thrombosis. After anastomotic revision and celiac artery decompression for significant arcuate ligament compression, the final quantitative IOUS assessment was optimal. However, he developed HA thrombosis 2 weeks after the primary transplant and underwent successful re-transplantation.

In LDLT, the use of IOUS provides instant diagnosis and correction of vascular problems. In patients with satisfactory quantitative IOUS assessment, the outcome of HA reconstruction is excellent.

EP - 08 CAVAL REPLACEMENT LIVING-DONOR LIVER TRANSPLANT: FIRST ARAB WORLD CASE REPORT

***F.Z. Eldeen**, M.R. Abdelfattah, Y. Elsheikh, Y. Saleh, B. ALqahtani, H.M. Al-bahili, M. Al-sebayel, D.C. Broering*
King Faisal Specialist Hospital and Research Hospital; Department of Liver and Small Bowel Transplantation and Hepatobiliary and Pancreatic Surgery
Email: firaszahreldeen@yahoo.ca

Introduction: LDLT with total hepatectomy including the retro-hepatic vena cava with reconstruction of the inferior vena cava (IVC) for hepatocellular carcinoma (HCC) for located on hepato-caval confluence or in contact with Inferior Vena Cava (IVC) is technically challenging [1,2]. Additionally it poses considerable risk for tumor recurrence and risk of thrombosis related to IVC reconstruction.
Methods: We report the first case of LDLT in Arab world combined with IVC reconstruction using cryo-preserved iliac vein graft (CPIVG) after en bloc resection of the liver with a part of retrohepatic IVC for hepatocellular carcinoma. A 59 year old female patient underwent LDLT one year ago for HBV related cirrhosis and 5 cm HCC on top at segment VII abutting IVC (Fig. 1). Total hepatectomy was performed along with partial resection of IVC (7 cm in length and around 50% of IVC circumference). Reconstruction of IVC was done utilizing CPIVG (Fig. 2).
Results: Postoperative course was uneventful. Patency and no evidence of tumor recurrence were demonstrated one year postoperative.
Conclusions: Caval replacement using CPIVG during LDLT is safe and feasible for treatment group of patients with tumors abutting IVC. However, long term follow up results should be reported.

References:

1. Chardot C, Saint Martin C, Gilles A, et al. Living-related liver transplantation and vena cava reconstruction after total hepatectomy including the vena cava for hepatoblastoma. Transplantation. 2002;73(1):90–92.
2. Matsuda H, Sadamori H, Shinoura S, et al. Aggressive combined resection of hepatic inferior vena cava, with replacement by a ringed expanded polytetrafluoroethylene graft, in living-donor liver transplantation for hepatocellular carcinoma beyond the Milan criteria. J HepatobiliaryPancreat Sci. 2010;17(5):719–724.

EP - 09 IMPACT OF BRIDGING STRATEGIES ON SURVIVAL IN PATIENTS WITH HEPATOCELLULAR CARCINOMA LISTED FOR LIVER TRANSPLANTATION

***D.M. Felsenreich**[1], G. Györi[1], G. Silberhumer[1], F. Wolf[2], W. Sieghart[3], F. Mühlbacher[1], T. Soliman[1], G.A. Berlakovich[1]*
[1]Department of Surgery, Division of Transplantation, Medical University of Vienna, Austria; [2]Department of Radiology and Nuclearmedicin, Division of Cardiovascular and Interventional Radiology, Medical University of Vienna, Austria; [3]Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Medical University of Vienna, Austria
Email: Moritz.felsenreich@meduniwien.ac.at

Keywords: HCC; OLT; locoregional therapy; TACE; bridging therapy.

Background: Disease progression of hepatocellular carcinoma (HCC) in patients eligible for liver transplantation (LT) occurs in up to 30–50% of patients, resulting in withdrawal from the LT waiting list. Therefore, multiple bridging strategies have been implemented over the last decade. Aim of this study was to review the response rate of these bridging modalities by mRECIST and the impact of successful down-staging on outcome.
Methods: We performed a retrospective review of prospectively collected data on all HCC patients listed for LT at our center between 2005 and 2011. Standard baseline parameters, pre- and post-treatment CTscans, as well as histological evaluation of the explanted liver were analyzed. Patient survival and tumor-recurrence-rate were compared in patients in- vs. outside Milan criteria at time of listing.
Results: 146 patients suffering from HCC were listed for LT, out of these 102 patients (70%) were within Milan and 64 (63%) received LT. 38 patients (37%) were removed from the waiting list (11 died, 20 tumor progression, seven other reasons).

Out of the 44 patients outside Milan at time of listing 28 patients (64%) were transplanted. The drop-out rate was comparable to patients within Milan (overall drop-out 16 patients (36%): two died, 10 tumor progression, four other reasons).

Overall, 262 bridging treatments were performed. According to mRECIST 18% of patients had complete response, 22% partial response, 50% stable disease and 10% showed tumor progression. The correlation with histology of the explanted liver indicated in 28% overestimation and in 12% underestimation of mRECIST.

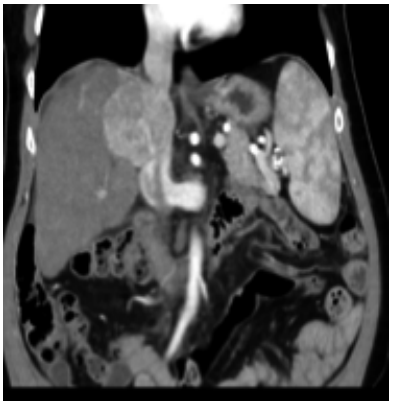


Figure 1

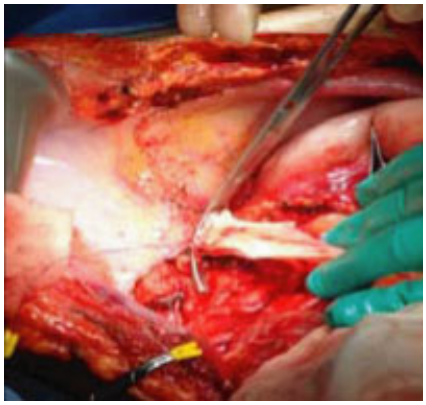


Figure 2

Down-staging was successful in 15 patients (34%) outside Milan. One- and 3-year patient survival after LT was 95% and 71% in patients within Milan at time of listing and 89% and 73% in patients outside Milan ($P = 0.56$).
Conclusion: Sucessful down-staging of patients outside Milan at time of listing results in post-LT survival comparable to patients inside Milan. Local ablative therapies appear more effective than indicated by mRECIST as demonstrated by an underestimation of the therapeutic success.

EP - 10 ROLE OF COLOR DOPPLER ULTRASOUND IN THE MANAGMENT AND FOLLOW UP OF HEPATIC ARTERY COMPLICATIONS AFTER LIVER TRANSPLANTATION

***F. Frongillo**, M.C. Lirosi, E. Nure, G. Bianco, N. Silvestrini, A. De Gaetano, R. Inchingolo, A. Cina, C. Di Stasi, S. Agnes*
Institution: Institute of Surgery, Faculty of Medicine, Liver Transplant Unit, Catholic University,Rome, Italy
Email: ffrongillo@yahoo.it

Keywords: Hepatic artery; stenosis; thrombosis; liver transplantation; Doppler ultrasonography, Peri – operative management topics

Purpose: We assessed the usefulness of color Doppler imaging in diagnosis and monitoring hepatic artery complications after liver transplantation.
Methods: Subjects were 423 liver transplant recipients who underwent serial US Color-Doppler evaluations of the hepatic arteries after surgery. Patients with abnormal findings underwent subsequent angiography.
Results: We experienced 41 hepatic arterial complications (7 thromboses, 30 stenosis, three dissection, one kinking). In six of the seven thrombosis incidents, hepatic arterial obstruction occurred within one month after transplantation and was diagnosed with absence of Doppler signals; angiography confirmed the lack of hepatic arterial perfusion in these cases. In the other case, the thrombosis developed 3 or more months after surgery and was suspected for the absence of Color-Doppler signals in the site of the main arterial trunk and the presence of intraparenchymal "tardus-parvus" waveforms. In these cases, angiography showed obstruction of the main arterial trunk and the development of compensatory collateral circles. In 17 of the 30 cases of stenosis, high flow velocities were recorded at the site of the narrowing, and intrahepatic tardus-parvus waveforms were present. In the other stenosis cases, the site of stenosis could not be identified, but intraparenchymal tardus-parvus waveforms were recorded.
Conclusion: The use of US Color-Doppler examination allows the early diagnosis of hepatic arterial complications after liver transplantation. "Tardus-parvus" waveforms, indicated severe impairment of hepatic arterial perfusion, from either thrombosis or severe stenosis. The presence of these indirect signs enhanced the accuracy of Color-Doppler diagnosis (100% positive predictive value), and their detection should prompt angiography.

References:

1. Bekker J, Ploemb S and de Jonga KP. Early Hepatic Artery Thrombosis after Liver Transplantation: A Systematic Review of the Incidence, Outcome and Risk Factors. Am J Transpant 2009; 9: 746–757.
2. Warner P, Fusai G, Glantzounis GK, et al. Risk factors associated with early hepatic artery thrombosis after orthotopic liver transplantation - univariable and multivariable analysis. Transpl Int 2011; 24:401–8.
3. Vivarelli M, Cucchetti A, La Barba G, et al. Ischemic arterial complications after liver transplantation in the adult: multivariate analysis of risk factors. Arch Surg 2004; 139: 1069–74.
4. Valente JF, Alonso MH, Weber FL, et al. Late hepatic artery thrombosis in liver allograft recipients is associated with intrahepatic biliary necrosis. Transplantation 1996; 61:61–5.
5. Pastacaldi S, Teixeira R, Montalto P, et al. Hepatic artery thrombosis after orthotopic liver transplantation: a review of nonsurgical causes. Liver Transpl 2001; 7:75–81.
6. Fouzas I, Sklavos A, Bismpa K et al. Hepatic Artery Thrombosis After Orthotopic Liver Transplantation: 3 Patients With Collateral Formation and Conservative Treatment. Transplant Proc 2012;, 44: 2741–2744.
7. Grodzicki M, Anysz-Grodzicka A, Remiszewski P, et al. Treatment of Early Hepatic Artery Thrombosis After Liver Transplantation. Transplant Proc 2011; 43: 3039–3042.
8. Pareja E, Cortes M, Navarro R, et al. Vascular Complications After Orthotopic Liver Transplantation: Hepatic Artery Thrombosis. Transplant Proc 2010; 42: 2970–2972.

EP - 11 SAFETY OF DUCT TO DUCT BILIARY RECONSTRUCTION IN PEDIATRIC PARTIAL LIVER TRANSPLANTATION

***T. Gelas**[1], A. Lachaux[2], C. Rivet[2], C. Boucaud[3], E. Javouhey[4], O. Boillot[5]
[1]Department of Pediatric Surgery, Hôpital Femme Mère Enfant, Hospices Civils de Lyon and Claude Bernard University, Lyon, France; [2]Department od Pediatric Hepatology, Hôpital Femme Mère Enfant, HCL and UCBL, Lyon, France; [3]Department of Pediatric Anesthesiology, Hôpital Femme Mère Enfant, HCL and UCBL, Lyon, France; [4]Pediatric Intensive Care Unit, Hôpital Femme Mère Enfant, HCL and UCBL, Lyon, France; [5]Liver Transplant Unit, Hôpital Edouard Herriot, HCL and UCBL, Lyon, France
Email: thomas.gelas@chu-lyon.fr

Keywords: pediatric, living donor, biliary anastomosis

Background: In pediatric liver transplantation (LT) Roux-en-Y hepatico-jejunostomy (HJ) is the most common method for biliary reconstruction and duct-to-duct biliary anastomosis (DD) is still controversial, especially when a partial graft is used. There are some advantages to perform DD when possible: it is simpler to achieve without intestinal manipulation, permit an earlier food intake and endoscopic treatment is facilitated in case of biliary stenosis. Our aim was to show the safety of DD reconstruction compared to HJ.
Methods: Sixty-nine children received living related or split LT between 2000 and 2013, and their database was reviewed. Six patients with graft lost within 2 weeks after LT were excluded from the study.
Results: The recipient age and weight at transplantation were 27.5 months (range: 7–166) and 11.9 kg (range: 6–50 kg) respectively. The main indications for LT were biliary atresia ($n = 39$), acute liver failure ($n = 7$) and PFIC ($n = 6$). The mean follow-up period was 76 months. There were 39 split LT and 24 LRLT, mainly with left lateral segment grafts (90%, $n = 57$). Biliary reconstruction was achieved with DD in 14 and with RY in 49 patients. Biliary stents were used in 93% of DD and 63% of HJ. The operative time was shorter in DD compared to HJ (285 vs 382 min, $P = 0.08$). The incidence of biliary leakage in the DD and RY groups was 14.3% and 16.3% and that of stricture 14.3% and 30.6%, respectively; but the differences were not statistically. Biliary complications in the DD group tended to require more revision surgery compared with that in the RY group. There was no mortality related to biliary complications.
Conclusion: Our results suggest that DD biliary reconstruction is a safe alternative to HJ with satisfactory outcome in terms of biliary complications, including leakage and stricture.

EP - 12 STEATOSIS AFTER LIVER TRANSPLANTATION: PREVALENCE, RISK FACTORS AND OUTCOME

***I. Hejlova**[1], E. Honsova[2], E. Sticova[2], V. Lanska[3], T. Hucl[1], J. Spicak[1], P. Trunecka[4]*
[1]Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [2]Department of Clinical and Transplant Pathology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [3]Department of Biostatistics, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [4]Transplant Centre, Institute for Clinical and Experimental Medicine, Prague, Czech Republic
Email: irhe@ikem.cz

Keywords: liver transplantation, steatosis, NAFLD

Background and Aims: Steatosis after liver transplantation (LT) is a frequent biopsy finding of uncertain significance. We aimed to determine the prevalence of posttransplant steatosis in our population of LT recipients and its impact on patient/graft survival and to identify risk factors for significant (>33%) steatosis.
Methods: A single centre analysis of 752 LT in 715 recipients was performed. Steatosis was evaluated on 2507 posttransplant biopsies in 575 patients, the impact of steatosis on patient/graft survival was analyzed. In a matched case-control study, clinical, laboratory, and histological factors of 80 patients with significant steatosis were compared to 160 controls without steatosis, fibrosis progression was compared in both groups.
Results: Posttransplant steatosis was found in 320 (55.7%) patients, significant steatosis in 94 (16.4%) patients and steatohepatitis (NAS≥5) in 57 (9.9%) patients. The prevalence of steatosis increased over time from LT. Significant steatosis was associated with worse patient survival after the third posttransplant year but was not an independent mortality risk factor. Graft survival and liver related mortality were not influenced by steatosis grade. Alcoholic cirrhosis and pretransplant BMI were independent pretransplant predictors and mycophenolate mofetil in initial immunosuppression an independent negative predictor of significant steatosis. Posttransplant BMI, serum triglycerides, AST and cyclosporin administration were independent posttransplant predictors of significant steatosis. Significant steatosis was not associated with faster fibrosis progression.
Conclusions: Posttransplant steatosis affected more than a half of LT recipients and its prevalence increased over time from LT. Significant steatosis was associated with worse long-term patient survival from non-liver related disease. Recipient factors and type of immunosuppression influenced steatosis development.

EP - 13 EVALUATING THE EFFECT OF RECIPIENT AGE ON OUTCOME AFTER LIVER TRANSPLANTATION FOR ACUTE LIVER FAILURE: POPULATION-BASED RETROSPECTIVE COHORT STUDY

***S.R. Knight**, A. Roebuck, G.C. Oniscu, K. J Simpson, S. J Wigmore, E.M. Harrison*
Scottish Liver Transplant Unit, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom
Email: stephenknight@doctors.org.uk

Keywords: age, survival, acute liver failure

Background & Aims: Increasing recipient age is known to significantly worsen prognosis in liver transplantation for acute liver failure (ALF). However most studies have small power or more recent data is now available.
Methods: A retrospective analysis of the UK Transplant Registry was performed (1 January 2001 – 31 December 2011) with recipients categorised into three equal groups by age (18–34, 35–49 and 50–70 year old groups). Kaplain–Meier methods were used to determine graft and patient survival. A Cox proportional hazards model was used in a multivariate analysis to control for other statistically or clinically important variables and included Monte Carlo simulation of outcomes at given ages.
Results: In 925 transplants performed for ALF, the median recipient age was 40 (range 18–70). Three year patient survival were 82.7%, 82.3% and 70.3% (log-rank test, $P < 0.001$) while for graft survival were 75.7%, 75.2% and 65.0% (log-rank test, $P = 0.002$) for age groups 18–34, 35–49 and 50–70 years respectively. In a Cox proportional hazards model, recipient age was a predictor of patient death (hazard ratio (HR) 1.32, 95% CI 1.17–1.49, $P \leq 0.001$) for every 10 year increase, but not graft loss (HR 1.10, 1.00–1.20, $P = 0.051$). Compared to a 20 year old recipient, risk of death for those aged 30 (HR 1.30, 1.15–1.46), 50 (2.22, 1.51–3.09) and 70 years old (2.03–7.07) increased in a step-wise fashion. Donor age did not affect patient or graft survival.
Conclusions: In a large national population-based retrospective cohort study, recipient age is a key determinant of patient survival following super-urgent liver transplantation for ALF, however there is a weaker relationship with graft survival. While age is a negative outcome, it should not be a contraindication to transplantation as good outcome is possible with careful selection of older recipients.

EP - 14 RENAL REPLACEMENT THERAPY AND LIVER TRANSPLANTATION FOR ACUTE LIVER FAILURE: INSIGHTS FROM A UK POPULATION-BASED RETROSPECTIVE COHORT STUDY

***S.R. Knight**, A. Roebuck, G.C. Oniscu, K.J. Simpson, S.J. Wigmore, E.M. Harrison*
Scottish Liver Transplant Unit, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom
Email: stephenknight@doctors.org.uk

Background and aims: Acute kidney injury is associated with a poor prognosis in acute liver failure (ALF) but little is known about the outcomes of patients undergoing transplantation for ALF who require renal replacement therapy (RRT).
Methods: A retrospective analysis of the UK Transplant Registry was performed (1 January 2001 – 31 December 2011) with graft and patient survival determined using Kaplan-Meier methods. A Cox proportional hazards model was used in a multivariate analysis and included Monte Carlo simulation of outcomes at given covariate levels.
Results: In 922 transplants performed for ALF, 3 year patient and graft survival for patients receiving RRT were 74.6% and 66.5% compared with 85.1% and 78.6% for those not requiring RRT (log-rank test, $P < 0.001$). In a Cox proportional hazards model, RRT was the single best predictor of both patient death (hazard ratio (HR) 2.24, 95% CI 1.13–4.46, $P = 0.021$) and graft loss (HR 2.59, 1.50–4.48, $P < 0.001$). Patients with a pre-operative serum creatinine >120 μmol/l in the absence of RRT had a similar risk of death as those receiving RRT. A non-significant trend towards a higher risk of death in those not on RRT but with a high creatinine compared with those on RRT was seen (HR 1.50 (0.81–2.55) at creatinine (no RRT) = 300 μmol/l).
Conclusions: In patients being transplanted for ALF, use of RRT is the strongest predictor of patient death and graft loss. Serum creatinine concentration independently predicts mortality and although RRT was not associated with better outcome for those with renal failure, consideration should be given to its timing and indications prior to transplantation.

EP - 15 IS LIVER PROGENITOR CELLS TRANSPLANTATION ONLY MELD-SCORE BRIDGE FOR LIVER TRANSPLANTATION OR MORE?

***O. Kukharchuk**, A.B. Padma Priya*
EmProCell Clinical Research Pvt. Ltd., Mumbai, India
Email: professorgeneral@gmail.com

Keywords: liver cirrhosis, transplantation, progenitor cells

Progression of liver cirrhosis inevitably brings to the last chance of patient in life – liver transplantation. Unfortunately lack of liver donors is the cause for many such patients' death. Alternative of liver transplantation could be transplantation of fetal liver progenitor cells.

Khan A.A. et al. (2010) demonstrated the efficacy of fetal hepatic progenitor cells. There was decrease in mean MELD score observed in 6 months follow-up in all patients.

In present study we used progenitor liver cells (fetal hepatoblasts, FH) and fetal liver hematopoietic progenitor cells (FL-HPC), and fetal liver extracts (FLE) injections. Objective: safety and efficacy of the intra-vein introduction of FL-HPC and FH, and FLE (from 6 till 20 weeks of gestation) injections. One hundered and forty-three patients were examined with liver cirrhosis. Age of patients: from 35 to 55 years. Disease span: 7.10 ± 0.25 years. Modified Child-Pugh Classification: Grade C: 12.6 ± 2.1. Life expectancy: 1–3 years. Abdominal surgery peri-operative mortality: 82%. MELD score: 21.7 ± 2.1. Transient elastography (FibroScan): 57.4 ± 6.5 kPa. The Ishak Modified HAI Grading: Necroinflammatory Scores: 15.3 ± 1.8.

Results after 48 months follow-up: died 18 patients, 15 out of them after treatment continued alcohol consumption; restoration of normal liver architecture – 35 patients; reduction of fibrosis – 90 patients (transient elastography: 18.7 ± 3.0 kPa; Ishak Scores: 4.6 ± 0.9).

Adverse Events: transient thrombocytopenia – 52, post transplantation arrhythmia – 11, abdominal pain – 34, pain in bones – 41, hypertension – 7, hypotension – 10 patients, severe adverse events – 0. The most effective transplantation of FL-HPC/FH showed in alcoholic liver cirrhosis, ineffective – in liver cirrhosis caused by hepatitis C virus.

Thus, human fetal liver progenitor cells transplantation offers a supportive modality to organ transplantation in the management of liver diseases and in cases of alcoholic liver cirrhosis can be mono therapy treatment.

EP - 16 INTERVENTIONAL RADIOLOGY: A GOOD SOLUTION FOR TOTAL REPARATION OF CELIAC TRUNK ANEURYSMS IN THE LIVER TRANSPLANT

***S. Mambrilla**[1], B.P. Saborido[1], H. Calero[2], M. Rodriguez[1], M. Gonzalo[1], R. Velasco[1], M. Bailón[1], P. Rodriguez[1], E. Asensio[1], P. Pinto[1], J.C. Sarmentero[1], A. Barrera[1], D. Pacheco[1]*
[1]Liver Transplantation Unit, General and digestive Surgery Department, Rio Hortega University Hospital, Valladolid, Spain; [2]Radiology Department, Rio Hortega University Hospital, Valladolid, Spain
Email: Smambrilla@gmail.com

Keywords: Celiac Trunk, aneurysm, embolization, liver transplant.

The Celiac trunk (CT) aneurysm is an infrequent abnormality (4% of visceral aneurysms). There is an increased risk of spontaneous rupture in post-transplant period. Surgical treatment is a useful option for these patients but its association with interventional radiology is very valuable.

A 45 years old man with alcoholic liver cirrhosis with esophageal varicose veins, ascites and encephalophaty (grade II) was admitted for a pre-transplant study. Chronic hepatophaty signs and an aneurysmatic CT dilatation with origin in the aorta were founded in abdominal imagining. Pre-transplant intravascular treatment was no feasible due to aneurysm location. During transplantation procedure only a partial, repairing surgery of the aneurysm was feasible due to the fragility of the artery wall and no vascular recontruction was requiered. Proper blood flow to the liver was observed through the gastroduodenal artery, what allowed ligature of spleenic and common hepatic arteries. The e left gastric vein, the splenic and common hepatic artery were ligated.

The donor celiac trunk and the recipient gastroduodenal artery were anastomosed. On the 20th day, a selective micro-catheterism and embolization with coils were done for total reparation of the aneurysm. The procedure was completed with a liquid agent that was placed between the coils. A correct embolization of the aneurism was checked with left gastric and phrenic artery permeability.

The election of the best treatment for CTA is controversial due to the limited reports of aneurysms of celiac trunk in the liver transplant published to date. We performed endovascular techniques to complete the treatment ought to the fragility of the aneurysm wall and the vascular abnormalities typical of portal hypertension. The association of surgical and endovascular techniques in the celiac axis aneurysms reparation can optimize the treatment.

References:

1. Sachdev-Ost. U. Visceral artery aneurysms: review of current management options. Mt. Sinai J Med 77(3), 296–303.
2. Stone WM, Abbas MA, Gloviczki P, Fowl RJ, Cherry KJ (2002). Celiac arterial aneurysms: a critical reappraisal of a rare entity. Arch surg;137, 670–6.

EP - 17 PROGNOSTIC VALUE OF 18F-FDG PET-CT IN LIVER TRANSPLANTATION FOR HEPATOCARCINOMA

*N. Meurisse[1], O. Detry[1], L. Govaerts[2], A. Deroover[1], M. Vandermeulen[1], S. Malenga[3], N. Bletard[4], C. Mbendi[5], A. Lamproye[5], P. Honoré[1], P. Meunier[3], J. Delwaide[5], R. Hustinx[2]
[1]Department of Abdominal Surgery and Transplantation, University of Liege, Liege, Belgium; [2]Department of Nuclear Medicine, University of Liege, Liege, Belgium; [3]Department of Radiology, University of Liege, Liege, Belgium; [4]Department of Pathology, University of Liege, Liege, Belgium; [5]Department of Hepato-Gastroenterology, University of Liege, Liege, Belgium
Email: Nicolas.Meurisse@chu.ulg.ac.be

Keywords: Cancer, hepatoma, hepatocellular cancer, liver transplantation

Aim: The aim of this study was to evaluate the prognostic value of pretreatment 18f-fdg PET-CT in patients with hepatocarcinoma treated by liver transplantation.
Methods: The authors retrospectively analyzed the data of 27 patients (mean age 58 ± 9 years) who underwent FDG PET-CT before liver transplantation for hepatocarcinoma. Mean follow-up was 26 ± 18 months. The FDG PET/CT was performed according to a standard clinical protocol: 4 MBqFDG/kg body weight, uptake 60 min, low-dose non-enhanced CT. The authors measured the SUVmax and SUVmean of the tumor and the normal liver. The tumor/liver activity ratios (RSUVmax and RSUVmean) were tested as prognostic factors and compared to the following conventional prognostic factors: MILAN, CLIP, OKUDA, TNM stage, alphafoetoprotein level, portal thrombosis, size of the largest nodule, tumor differentiation, microvascular invasion, underlying cirrhosis and liver function.
Results: Overall and recurrence free survivals were 80.7% and 67.4% at 3 years, and 77.4% and 67.4% at 5 years, respectively. According to a multivariate Cox model, only 18f-fdg PET-CT RSUVmax predicted recurrence free survival. Even though the MILAN criteria alone were not predictive, it is worth noting that none of the patients outside the MILAN criteria and with RSUVmax < 1.15 relapsed.
Conclusions: FDG PET/CT with a cut-off value of 1.15 is a strong prognostic factor for recurrence and death in patients with HCC treated by liver transplantation. Further prospective studies should test whether the metabolic index should be systematically included in the preoperative assessment.

EP - 18 PREDICTORS OF OUTCOME OF LIVER TRANSPLANTATION IN RECIPIENTS OVER 60 YEARS OF AGE

*D. Mikulic, S. Jadrijevic, M. Poljak, I. Kocman, B. Kocman
Department of Surgery, University Hospital Merkur, Zagreb, Croatia
Email: danko.mikulic@zg.t-com.hr

Keywords: Liver Transplantation, Outcome, Elderly.

Introduction: As the population of elderly patients with liver disease expands, we are facing increasing numbers of transplant recipients from older age groups. In this retrospective study we aimed to identify donor and recipient factors associated with graft failure and patient mortality following liver transplantation in recipients over 60 years of age.
Patients and methods: A retrospective study of prospectively collected data was performed. Analyzed patients included first time, cadaveric liver-only recipients aged over 60 years at the time of the transplant. The patients (n = 138) were transplanted at a single center, between May 2007 and May 2013. Mean age of the patients in this group was 64 years of age (range 60–77). After an average follow up of 34 months (range 12–72) from the transplant, 101 patients (73.2%) were alive with a functioning graft, 5 patients (3.6%) were retransplanted and 37 patients (26.8%) died. Univariate and multivariate analyses were performed to search for predictors of graft failure and patient mortality.
Results: Recipient MELD over 25, male sex, acute liver failure and HCV positivity were predictive of patient mortality, while increased incidence of graft failure was seen in patients transplanted with livers from older donors.
Conclusion: In times of organ scarcity, optimal organ utilization is of utmost importance. We believe our results can be used for better recipient selection and improved graft to recipient matching in this challenging group of patients.
References:
1. Keswani RN, Ahmed A, Keeffe EB. (2004) Older age and liver transplantation: a review. 10:957–967.
2. Aloia TA, Knight R, Gaber AO, Ghobrial RM, Goss JA. (2010) Analysis of liver transplant outcomes for United Network for Organ Sharing recipients 60 years old or older identifies multiple model for end-stage liver disease-independent prognostic factors. 16:950–959.

EP - 19 CD14S AS NEW BIOMARKER OF BACTERIAL INFECTION IN LIVER TRANSPLANT RECIPIENTS

*V. Morabito[1], G. Ferretti[2], L. Poli[1], F. Ruberto[3], P.B. Berloco[1], G. Novelli[1]
[1]Department "Paride Stefanini" General Surgery and Organ Transplant, Sapienza University, Rome, Italy; [2]Department of Infectous Disease, Sapienza University, Rome, Italy; [3]Department of Intensive Care and Anesthesia, Sapienza University, Rome, Italy
Email: vemorabito@gmail.com

Keywords: bacterial infection, liver transplant, Presepsin, antibiotic therapy.

Introduction: CD14s (Presepsin) has been identified as a protein whose levels increase specifically in the blood of patients with bacterial infection. Pathfast Assay System (PAS) is able to detect the levels of sCD14. In this study, we evaluated the clinical performance of PAS and its usefulness in the early diagnosis of bacterial infection in liver transplant (LT) recipients.
Materials: Twenty-five patients were enrolled in this study. Mean age of patients was 52.5 years, 12 female and 13 male. The heparinized whole blood for PAS was used in the evaluation of bacterial infection after 48 h of liver transplant [T0]. The PAS was repeated after 48 h [T1]; at 96 h [T2]; at 144 h [T3] than at 15 days [T4] for monitoring the clinical responses to therapeutic interventions. Blood cultures were performed in all patients at moment that PAS test was performed. The assay time was 15 min using a sample volume of 100 μL. A value >377 pg/mL was considered positive as indicated by manufacturers.
Results: Twelve patients resulted positive to PAS. The mean sCD14 level was 1045 ± 977 pg/mL. Microbiological findings confirmed the presence of bacterial infections within 81 ± 3.2 h from enrolment in all 12 positive patients. Presepsin level increased in five patients at [T1] and [T2]. These five patients (31%) did not respond to empiric antibiotic treatment and the antibiotic therapy was modified. When the PAS was performed, 41% of patients no showed signs or symptoms of bacterial infection. At 30th day of follow up, the survival was 100% with a good graft function.
Conclusions: Early diagnosis is essential to improving the results of treatment of infections in particular in LT recipients where infection represents one of the primary barrier to success of transplant. PAS test highlighted a significant performance, showing the presence of infection in a very short time (15 min). A greater number of patients is necessary to confirm these data.

EP - 20 ANGIOSARCOMA AS SHOCKING HISTOLOGICAL DIAGNOSIS AFTER LIVER TRANSPLANTATION DUE TO BUDD-CHIARI SYNDROME

*M. Rodriguez Lopez, D. Pacheco, A. Barrera, J.C. Sarmentero, B. Perez-Saborido, P. Pinto, E. Asensio, P. Rodríguez-Vielba, M. Gonzalo, R. Velasco, S. Mambrilla, M. Bailon
Liver Transplantation Unit, General and Digestive Surgery Department, Rio Hortega University Hospital, Valladolid, Spain
Email: mariorodriguezlopez@yahoo.es

Keywords: angiosarcoma, Budd-Chiari syndrome, Liver Transplantation

Liver angiosarcoma (AS) is a high-malignant tumor, presenting usually at advanced stages, what implies poor outcomes after conventional treatments (surgical resection, chemotherapy) and also after liver transplantation (LT) (1). Consequently, the latter is currently a contraindication, as quoted in an article from the ELTR (2).

A 23-year-old man, with neither prior diseases nor toxic intake, presented with sudden jaundice and hepatic decompensation. A complete study was conducted in our LT Unit: contrast-enhanced CT, liver biopsy and viral and tumor markers (both negative). Results were plausible with Budd-Chiari Syndrome (BCS), severe abnormal liver function (MELD: 20). Consequently, the patient was included in LT wait-list and one month later he was operated on. Histopathology of the explant liver showed a primary diffuse AS (CD31 and CD34 positive) with paediatric features (kaposiform cells), no extra-hepatic extension. Post-transplant period was uneventful except for early acute renal failure. Seven months after LT, the patient presented metastases in several locations and graft dysfunction, which led to his death.

Diffuse AS has been exceptionally reported to mimick BCS (1,3). Due to this, LT would be performed and it would only be possible to diagnose the tumor during explant histological study, as occurred in our patient. Besides, AS is uncommon among children and the early age of our patient was a factor not suggesting this neoplasm. In fact, to the best of our knowledge, histological paediatric form of AS in a 24 year-old patient has never been reported to date.

References:
1. Bonaccorsi-Riani E et al (2010). Liver transplantation and vascular tumours. *Transpl Int* 23(7), 686–691.
2. Orlando G et al (2013). Hepatic hemangiosarcoma: an absolute contra-indication to liver transplantation – the European Liver Transplant Registry experience. *Transplantation* 95(6), 872–877.
3. Schluger LK et al (1995). Unexplained Budd-Chiari Syndrome in a Young Man. *Hepatology* 21(2), 584–588.

EP - 21 RENAL IMPAIRMENT POST MULTIVISCERAL AND SMALL INTESTINAL TRANSPLANTATION

*C.S. Rutter[1], L.M. Sharkey[1], N. Russell[2], S.J. Middleton[1], A.J. Butler[2]
[1]Department of Gastroenterology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [2]Department of Transplant Surgery, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom
Email: crutter@nhs.net

Keywords: renal impairment, multivisceral, intestinal transplantation

The cumulative incidence of chronic renal impairment in intestinal transplantation is 0.25 at 72 months. It is the highest of all non-renal grafts and is associated with an increase in mortality by a factor of more than four[1]. It is multifactorial and calcineurin inhibitors may play a role.

We conducted a retrospective review of renal function in all patients who underwent small intestine (SBT), liver/small intestine (LSBT), modified multivisceral (MMVT) and multivisceral transplantation (MVT) in our unit between 2003 and 2013. Renal impairment was defined as creatinine above the upper limit of normal (>125 μmol/l). Early sustained renal impairment was defined as occurring at ≥2 months post transplant without recovery to within the normal range. Late renal impairment was defined as occurring at ≥6 months post transplant without recovery to within the normal range.

Forty transplants were undertaken. Fifteen were excluded because of death ≤6 months post transplant (6), re-transplant within 6 months of index surgery (2), transplanted kidney at index operation (6) and explant of small bowel graft (1). Three patients (12%) had early sustained renal impairment and 14 (56%) had late renal impairment post transplant. The 2 patients who died had late renal impairment. In total 68% of patients had renal impairment post transplant and it was more prevalent in the MVT group (Table 1).

Seven patients were switched from Tacrolimus to Sirolimus. Fifty-seven percent showed improvement in creatinine but only 1 had a sustained response. One patient required re-transplant for acute rejection which did not respond to medical therapy. Two patients needed long-term renal replacement therapy - one was re-transplanted with a kidney containing graft, the second remains on long-term haemodialysis.

Although small numbers, 68% of our patients had chronic renal impairment, higher than in published sutdies Further analysis of mortality and contributing factors is needed.

Table 1 Patients with renal impairment depending on organs transplanted.

	Number	% (n = 25)
SBT with early (≥2 m) sustained renal impairment	1	4
SBT with late (≥6 m) renal impairment	3	12
LSBT with early (≥2 m) sustained renal impairment	0	0
LSBT with late (≥6 m) renal impairment	2	8
MMVT with early (≥2 m) sustained renal impairment	1	4
MMVT with late (≥6 m) renal impairment	3	12
MVT with early (≥2 m) sustained renal impairment	1	4
MVT with late (≥6 m) renal impairment	6	24
	17	68

Reference:
1. Ojo AO, Held PJ, Port FK, Wolfe RA, Leichtman AB, Young EW, Arndorfer J, Christensen L and Merion RM (2003). Chronic renal failure after transplantation of a nonrenal organ. New England Journal of Medicine 2003;349:931–40.

EP - 22 SURVIVAL FOLLOWING INTESTINAL AND MULTIVISCERAL TRANSPLANTATION AT ADDENBROOKE'S HOSPITAL, CAMBRIDGE, UK

*C.S. Rutter[1], L.M. Sharkey[1], T. Ambrose[1], N. Russell[2], J. Green[1], S. Duncan[1], D. Massey[1], S.J. Middleton[1], A.J. Butler[2]
[1]Department of Gastroenterology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, United Kingdom; [2]Department of Transplant Surgery, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, United Kingdom
Email: crutter@nhs.net

Keywords: survival, multivisceral, intestinal transplantation

Small intestinal transplantation was first undertaken in the UK, in Cambridge, in 1991. The introduction of new immunosuppressive agents around the millennium has resulted in improved outcomes and we present our experience over the last 10 years. Cambridge is the only UK centre offering multivisceral transplantation in adults.

Since 2003, 47 transplants were performed on 42 patients with the following organs included in the graft: isolated small bowel (SB), liver and small bowel (LSB), modified multivisceral (stomach, pancreas, small bowel, no liver - MMVT) and multivisceral (stomach, pancreas, liver, small bowel - MVT). Colon is now routinely included to aid fluid balance and does not preclude regular endoscopic surveillance for rejection.

We reviewed all patients who underwent SB and MVT at Addenbrooke's Hospital between 2003 and 2013.

Five-year survival in patients transplanted is 100% for SB, 64.3% for MMVT and 56.6% for MVT/LSB (Figure 1); this is compared with international registry survival figures of 59% (SB) and 22% (MVT). Five-year survival for all patients transplanted in our unit is 66%.

Over the past 2 years we have experienced an increase in the number of transplants for patients with widespread mesenteric arterial insufficiency, who are often critically ill at the time of surgery. Our centre undertakes a relatively large number of procedures (16 in 2013). It is possible that our favourable survival figures are due to a particular focus on preoperative assessment and optimization of patients, coupled with an emphasis on multidisciplinary team working.

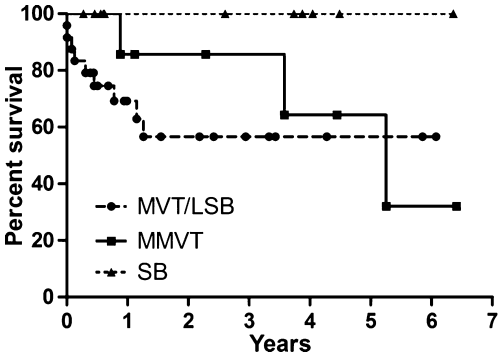


Figure 1: Addenbrooke's Transplant Survival.

EP - 23 TO DRAIN OR NOT TO DRAIN AFTER LIVER TRANSPLANTATION

*C. Schwarz, T. Soliman, G. Györi, G. Silberhumer, S.F. Schoppmann, F. Mühlbacher, G.A. Berlakovich
Department of Surgery, Division of Transplantation; Medical University of Vienna, Austria
Email: christoph.a.schwarz@meduniwien.ac.at

Keywords: abdominal drainage, outcome, infections

An abdominal drain (AD) is routinely inserted to drain ascites and identify postoperative hemorrhage or bile leakage in patients who have undergone liver transplantation (LT). However, the benefit of this surgical practice is debated in regard of potential drainage-associated morbidities. In a retrospective pair-matched analysis, 116 patients who underwent LT were divided into a drain and a no-drain group, and assessed in regard of the benefits and risks of abdominal drainage, taking MELD, age and gender into account. A higher rate of early bile leaks was noted in patients with AD (13.8% vs. 1.7%; P = 0.03). A significantly higher frequency of infections requiring antibiotic therapy was observed in the drain group (63.8% vs. 39.7%, P = 0.015). The contribution of the drain as a diagnostic tool was marginal: in the drain group, other diagnostic tools apart from the drain itself confirmed 50% of early bile leaks and 60% of postoperative hemorrhages. Overall, we registered no difference in the duration of hospitalization (P = 0.22), and one- and five-year patient (P = 0.98) and graft survival

rates ($P = 0.09$). We conclude that the use or non-use of an AD is associated with equivalent outcomes in recipients with whole-liver grafts. The benefit of AD as a diagnostic tool was also not remarkable.

EP - 24 INCIDENTAL HEPATOCELLULAR CARCINOMA: RISK FACTORS AND LONG-TERM OUTCOME AFTER LIVER TRANSPLANTATION

***R. Senkerikova**[1], S. Frankova[1], J. Sperl[1], M. Oliverius[2], E. Kieslichova[3], H. Filipova[4], D. Kautznerova[4], E. Honsova[5], P. Trunecka[6], J. Spicak[1]*

[1]Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [2]Department of Transplant Surgery, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [3]Department of Anesthesiology and Resuscitation, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [4]Department of Radiodiagnostic and Interventional Radiology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [5]Department of Clinical and Transplant Pathology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [6]Transplantacenter, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Email: renata.senkerikova@ikem.cz

Keywords: liver transplantation, incidental hepatocellular carcinoma, risk factor, outcome

Orthotopic liver transplantation (OLT) currently represents the treatment of choice for early hepatocellular carcinoma (HCC). Preoperatively known HCC (pkHCC) is diagnosed via imaging methods prior to OLT or HCC, denoted as incidental HCC (iHCC), is found postoperatively in the liver explant. The aim of our study was a comprehensive analysisof post-transplant survival of patients with iHCC and identification of risk factors of iHCC occurrence in cirrhotic liver.

We retrospectively reviewed 33 adult cirrhotic patients with incidentally found HCC comparing them with 606 tumor-free adult cirrhotic patients with end-stage liver disease (group Ci) who underwent OLT in our center betweenJanuary 1995 and August 2012. Within the same period, a total of84 patients were transplanted for pkHCC. We compared post-transplant survival of iHCC, Ci group and pkHCC patients. In the group of cirrhotic patients (Ci + iHCC) we searched for risk factors of iHCC occurrence.

There was no difference in sex, MELD score and time spent on the waiting list in either group.

In the multivariate analysis we identified the age>57 years (OR 3.37, 95% confidence interval (CI) 1.75–8.14, $P < 0.001$), HCV or alcoholic liver disease (ALD) (OR 3.89, 95% CI 1.42–10.7, $P < 0.001$) and alpha-fetoprotein (AFP) level>6.4 μg/l (OR 6.65, 95% CI 2.82–15.7, $P = 0.002$) to be independent predictors of iHCC occurrence. 1-, 3- and 5-year overall survival differed in iHCC patients compared with Ci group (iHCC: 79%, 72% and 68%, respectively vs. Ci group: 93%, 94% and 87%, respectively; $P < 0.001$).

We conclude that the survival of iHCC patients is worse than in tumor-free cirrhotic patients, but comparable with survival of pkHCC patients. Independent risk factors for iHCC occurrence in cirrhotic liver are age, HCV or ALD etiology of liver cirrhosis and AFP level.

The study was supported by the project (Ministry of Health, Czech Republic) for development of research organization 00023001 (IKEM, Prague, Czech Republic) – Institutional support.

References:

Sotiropoulos GC, Malago M, Molmenti EP, et al. Liver transplantation and incidentally found hepatocellular carcinoma in liver explants: need for a new definition? Transplantation. 2006;81(4):531–535.

Raphe R, Felicio HC, Rocha MF, et al. Histopathologic characteristics of incidental hepatocellular carcinoma after liver transplantation. Transplant Proc. 2010;42(2):505–506.

Chui AKK, Wong J, Rao ARN, et al. High incidence of incidental hepatocellular carcinoma exists among hepatitic explanted livers. Transplant Proc. 2003;35(1):350–351.

Castillo E, Pelletier S, Kumer S, et al. Incidental hepatocellular carcinoma after liver transplantation: population characteristics and outcomes. Transplant Proc. 2009;41(1):219–221.

Klintmalm GB. Liver transplantation for hepatocellular carcinoma: a registry report of the impact of tumor characteristics on outcome. Ann Surg. 1998;228 (4):479–490.

EP - 25 GENETIC VARIATION IN *TNFA* PREDICTS PROTECTION FROM SEVERE BACTERIAL INFECTIONS IN PATIENTS WITH END-STAGE LIVER DISEASE AWAITING LIVER TRANSPLANTATION

***R. Senkerikova**[1], E. de Mare-Bredemeijer[3], S. Frankova[1], D. Roelen[4], T. Visseren[3], P. Trunecka[1], J. Spicak[1], H. Metselaar[3], M. Jirsa[2], J. Kwekkeboom[3], J. Sperl[1]*

[1]Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [2]Laboratory of Experimental Hepatology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [3]Department of Gastroenterology and Hepatology, Erasmus MC – University Medical Centre, Rotterdam, The Netherlands; [4]Department of Immunohematology and Blood Transfusion, University Medical Centre, Leiden, The Netherlands

Email: renata.senkerikova@ikem.cz

Keywords: liver cirrhosis, inflammatory signalling, toll-like receptor 4, innate immune cells, neutrophil exhaustion

Augmented susceptibility to infections increases mortality in patients with end-stage liver disease (ESLD). We sought to determine the contribution of selected genetic variants involved in inflammatory signalling downstream of the Toll-like receptor 4 (TLR4) to severe bacterial infections (SBIs) in patients with ESLD.

We retrospectively assessed incidence of SBIs in 336 adult ESLD patients enlisted for orthotopic liver transplantation (OLT) and genotyped them for *TLR4* c.+1196C/T, *CD14* c.-159C/T, *TNFA* c.−238G/A, *TNFA* c.−863C/A, *IL1B* c.−31C/T and *IL1RN* variable number of tandem repeats allelic variants. Principal findings were validated in an independent cohort of 332 ESLD patients.

Thirty-four percent of patients from the identification cohort and 40% of patients from the validation cohort presented with SBI while enlisted for OLT. The presence of the variant allele *TNFA* c.−238A (rs361525) was associated with lower serum levels of TNF-α, and with significantly decreased risk of SBI in both cohorts. Multivariate analysis showed that the relative protection from SBI associated with this allele almost completely negated the increased susceptibility to SBI owed to advanced ESLD. Although not predictive of overall mortality, the presence of the *TNFA* c.−238A allele was associated with a complete prevention of SBI-related pre-transplant deaths.

Our results suggest that genetic variability in inflammatory signalling is associated with the development of SBI in patients with ESLD. Specifically, we identified the importance of the *TNFA* c.−238A allele as a strong predictor of protection from SBI, and as a genetic marker associated with significantly improved pre-transplant survival in patients with SBI.

The study was supported by the project (Ministry of Health, Czech Republic) for development of research organization 00023001 (IKEM, Prague, Czech Republic) – Institutional support.

References:

Stadlbauer V, Mookerjee RP, Hodges S, Wright GA, Davies NA, Jalan R. Effect of probiotic treatment on deranged neutrophil function and cytokine responses in patients with compensated alcoholic cirrhosis. J Hepatol 2008; 48:945–951.

Lin RS, Lee FY, Lee SD, Tsai YT, Lin HC, Lu RH, et al. Endotoxemia in patients with chronic liver diseases: relationship to severity of liver diseases, presence of esophageal varices, and hyperdynamic circulation. J Hepatol 1995; 22:165–172.

Opal SM, Huber CE. Bench-to-bedside review: toll-like receptors and their role in septic shock. Critical care 2002; 6:125–136.

Tritto G, Bechlis Z, Stadlbauer V, Davies N, Francés R, Shah N, et al. Evidence of neutrophil functional defect despite inflammation in stable cirrhosis. J Hepatol 2011; 55:574–581.

Ono Y, Watanabe T, Matsumoto K, Ito T, Kunii O, Goldstein E. Opsono-phagocytic dysfunction in patients with liver cirrhosis and low responses to tumor necrosis factor-alpha and lipopolysaccharide in patients' blood. J Infect Chemother 2004; 10:200–207.

Kawai T, Akira S. The role of pattern-recognition receptors in innate immunity: update on toll-like receptors. Nat Immunol 2010; 11:373–384.

EP - 26 DISCORDANCE BETWEEN SMALL BOWEL AND COLONIC BIOPSIES POST INTESTINAL TRANSPLANT

*M. Crowson[1], ***L.M. Sharkey**[2], C.S. Rutter[2], S.J. Middleton[2], A.J. Butler[1]*
[1]Department of Transplant surgery, Cambridge University Hospitals NHS Trust, Cambridge, United Kingdom; [2]Department of Gastroenterology, Cambridge University Hospitals NHS Trust, Cambridge, United Kingdom
Email: lisa.sharkey@addenbrookes.nhs.uk

Keywords: Intestinal, histology, concordance, rejection

Small bowel (SB) transplant has been modified to include the ileocaecal valve and colon to improve quality of life by improving fluid balance and reducing stoma output. Endoscopic biopsy remains the method of choice for diagnosing acute cellular rejection (ACR). Accessing the small bowel via colonoscopy can often be challenging post intestinal transplantation and standardized histological criteria for rejection in colonic grafts have not yet been established. We present our concordance data of small bowel and colonic biopsy assessing for ACR.

We conducted a retrospective study of all patients receiving both a small bowel and colon transplant (including as part of a multivisceral graft) at our institution between January 2012 and December 2013, comparing paired biopsy results. The VIII international small bowel transplant symposium criteria are used when reporting biopsy results. The categories used were: no ACR (Including borderline or indeterminate), mild ACR, moderate ACR and severe ACR.

Twelve patients received a colon-containing graft during the study period. Sixty-six sets of paired ileal and colonic biopsies were examined. The majority, 57/66 (86%), did not show any evidence of rejection. Nine biopsy sets in three patients did show some degree of ACR. Four out of these (44%) were concordant with regards to the severity of rejection with 56% therefore being discordant. Two of the five biopsy sets showed more severe rejection in the ileum compared to colon and interestingly, three of the five had more severe changes in the colon compared to the ileum.

The histopathological severity of rejection in ileal and colonic biopsies following transplantation is discordant in over half the cases. Clinicians should continue to biopsy both the small bowel and colonic grafts to assess for acute cellular rejection.

Table 1 Histopathological grading of nine paired biopsies with ACR

Ileum	Colon
Mild	Borderline
Severe	Mild-moderate
Borderline	Moderate
Normal	Mild
Borderline	Mild
Mild	Mild
Severe	Severe
Severe	Severe
Moderate	Moderate

References:

Ruiz P, Bagni A, Brown R, Cortina G, Harpaz N, Magid MS, Reyes J. Histological criteria for the identifications of acute cellular rejection in human small bowel allografts: results of the pathology workshop at the VIII International Small Bowel Transplant Symposium. Transplant Proc 2004;36(2):335–7.

LICAGE ORAL PRESENTATIONS

LO - 01 IMPROVEMENT IN OUTCOME FOLLOWING IMPLEMENTATION OF CARDIOPULMONARY EXERCISE TESTING IN LIVER TRANSPLANT RECIPIENTS

*J. Prentis, ***E. Bonner**, C. Snowden*
Department of Perioperative and Critical Care medicine, Freeman Hospital, Newcastle upon Tyne, United Kingdom
Email: Emily.bonner@nuth.nhs.uk

Keywords: cardiopulmonary exercise testing, mortality, transplantation

Introduction: Accurate risk assessment of liver transplant candidates will allow for better perioperative and longer term outcomes. This study aimed to assess the impact of CPeT on a transplant programme, looking particularly at mortality rates in the transplant population following implementation of a CPeT service.
Methods: Patients attending liver transplant assessment were asked to perform a CPeT prior to listing for transplantation. Results were used in the risk assessment process in a single centre and were available at the time of listing and when an offer of an organ was made to aid in matching organs to recipients.

Consecutive patients from 2006 until 2013 were split into an early or late cohort depending on whether they were assessed pre or post implementation of the CPeT programme. Follow up assessed whether they were listed; the number deemed unfit for transplantation; and mortality rates for all groups.
Results: Early cohort mean AT 11.5 mls/Kg/min (10% with AT < 9.1 mls/Kg/min) versus 12.4 mls/Kg/min (6% with AT < 9.1 mls/Kg/min) in late cohort. On-list 50% survival in early cohort 2.5 years versus 3.3 years in late ($P = 0.002$). MELD score at transplantation early cohort 16 versus 19 late cohort. Mean donor age increased from 44 to 47 between the early and late cohorts respectively.
Discussion: Implementation of CPeT in this centre has led to improvement in the fitness of recipients listed. Despite worsening MELD scores at transplantation and increasing donor age there has been a significant decrease in both on-list and transplant mortality. This association with implementation of CPeT has been seen at a time when there have been no other changes in the transplantation pathway.

LO - 02 THE EDINBURGH LIVER FUNCTION (ELF) SCORE OBJECTIVELY QUANTIFIES GRAFT DYSFUNCTION AFTER LIVER TRANSPLANTATION

***I.S. Currie**[1,2], J.H. Ong[2], W. Ho[2], A. Lee[1], A.J. Lee[3]*
[1]Scottish Liver Transplant Unit, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; [2]Department of Clinical Surgery, University of Edinburgh, Edinburgh, United Kingdom; [3]Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, United Kingdom
Email: ian.currie@ed.ac.uk

Keywords: liver, dysfunction, severity, PNF, score

Introduction: Primary graft dysfunction (PGD) after liver transplantation is becoming more common as a result of increasingly marginal donor organs. Severe dysfunction requires early recognition and multiple organ support to ensure patient survival. By contrast, Primary Graft Non-Function (PNF) is rare, but invariably fatal without urgent re-transplantation. In clinical practice, the diagnosis of PNF as opposed to PGD is difficult in the first 48 hours, as intensive care support may mask key indicators of PNF. Delaying re-transplant in favour of diagnostic certainty increases the risk of death in PNF patients, whereas the scarcity of donor organs and operative risk precludes re-transplant unless the diagnosis is well established. Currently, there are no reliable scoring systems for early and objective scoring of graft dysfunction and non-function based on routinely available clinical data.
Aim: To derive a statistical model describing the normal distribution of liver function in the first 48 hours after liver transplantation.
Materials and Methods: Routine clinical data were recorded prospectively and analysed retrospectively in 169 control patients and 10 patients with PNF in the Scottish Liver Transplant Unit. Regression techniques were used to construct a predictive model describing post-operative liver function, derived from indices identified from correlational analyses. As the model was developed retrospectively, scores were not available to clinical teams.
Results: Post-operative trends in bilirubin, lactate and prothrombin time comprised the model. Z scores for these analytes at different time points were combined to give the Edinburgh Liver Function (ELF) Score. ROC curves every 6 h at 0 – 48 h post-transplant showed an Area Under the Curve (AUC) of 0.5 and 0.88 at zero and six hours respectively; AUC from 12 hours was 0.95 or greater. 11/179 patients developed an ELF score >1.96 at 12 h or later post-transplant. Of these, one died after rapid deterioration, and nine were listed for super-urgent re-transplantation. One subsequently improved and was de-listed with a falling ELF score (ELF < 1.96 at 48 hours). The remaining eight were re-transplanted. The 11th patient had undergone split liver transplantation and had severe graft dysfunction (ELF >4.5). Re-listing was considered, however, the patient fortunately improved after 48 hours. No PNF cases were missed by the ELF score. An ELF score >1.96 had a positive predictive value for PNF of 90.9% and a negative predictive value of 99.4%.
Conclusions: The ELF score is a simple and rapid technique which appears to give an accurate index of graft dysfunction after liver transplantation. Statistical refinement is in progress, however, the ELF score may identify severe liver dysfunction objectively, allowing targeted intervention and the earliest possible re-transplantation.

LO - 03 LIVING DONOR LIVER TRANSPLANTATION IN HIGH MODEL FOR END-STAGE LIVER DISEASE SCORE

***M. Dayangac**, M. Akyildiz, G. Gungor, Y. Erdogan, Y. Tokat*
Liver Transplantation Unit, Florence Nightingale Hospital, Istanbul, Turkey

Keywords: MELD, living donor liver transplantation

Statistical models suggest that the sickest patients are those who derive the highest benefit from living donor liver transplantation (LDLT).[1] However, multivariate analyses have shown that model for end-stage liver disease (MELD) score >20 was independently associated with reduced graft survival[2], and a MELD score of ≥25 was an independent adverse prognostic factor for in-hospital mortality.[3]

In this retrospective analysis of 450 adult patients, who underwent right lobe LDLT between August 2004 and May 2013, we examined the impact of pre-transplant MELD score on post-transplant outcome. Patients were divided into three MELD categories: MELD<15 ($n = 193$), MELD between 15 and 25 ($n = 215$), and MELD>25 ($n = 42$) (Table 1).

The median follow-up was 30 (15–58) months. There was a significant difference between the groups in terms of perioperative mortality (6.2%, 9.3%, and 31.0%, respectively; $P < 0.001$), which showed a significant positive correlation with the MELD score ($P < 0.001$, Spearman's correlation coefficient = 0.188).

A similar 1- and 3-year patient survival was found between the MELD < 15 and MELD 15–25 groups, which was significantly higher than that of the MELD > 25 group (Wilcoxon test, $P = 0.007$; 88%, 86%, and 64% at 1 year and 82%, 78%, and 64% at 3 years, respectively).

In the MELD>25 group, the only statistically significant difference between patients with and without perioperative mortality was graft-to-recipient weight ratio (1.12 ± 0.24 vs. 1.35 ± 0.42, respectively; $P = 0.03$).

In LDLT, disease severity is the most significant factor that determines recipient outcomes. Our results indicate that LDLT being performed for candidates with high MELD scores have a significantly higher risk of dying from the procedure. To justify the risk incurred by the donor, the timing of LDLT should be done to avoid high pre-transplant MELD scores.

Table 1 Clinical features of 450 adult LDLT recipients

	MELD groups			
Variables	<15 ($n = 193$)	15–25 ($n = 215$)	>25 ($n = 42$)	*P*
Recipient age	52.6 ± 9.9	50.5 ± 10.9	44.4 ± 13.3	**<0.001**
MELD score	10.9 ± 2.4	18.7 ± 2.8	30.2 ± 5.2	**<0.001**
Donor age	34.0 ± 10.2	34.4 ± 10.3	34.4 ± 8.9	0.9
Graft weight (g)	870 ± 149	869 ± 171	878 ± 150	0.9
Graft-to-recipient weight ratio (GRWR)	1.15 ± 0.2	1.19 ± 0.6	1.19 ± 0.3	0.6
Graft ischemia time (min)	145.7 ± 51.4	141.2 ± 43.6	134.7 ± 35.9	0.5
Recipient hospital stay	19.7 ± 23.8	20.9 ± 12.3	20.7 ± 9.5	0.8
Perioperative mortality	12 (6.2%)	20 (9.3%)	13 (31.0%)	**<0.001**

References:
1. Durand F, Belghiti J, Troisi R, et al. Living donor liver transplantation in high-risk vs. low-risk patients: optimization using statistical models. Liver Transpl. 2006; 12(2): 231–9.
2. Ikegami T, Imai D, et al. D-MELD as a predictor of early graft mortality in adult-to-adult living-donor liver transplantation. Transplantation. 2014; 97(4): 457–62.

3. Kaido T, Egawa H, Tsuji H, Ashihara E, Maekawa T, Uemoto S. In-hospital mortality in adult recipients of living donor liver transplantation: experience of 576 consecutive cases at a single center. Liver Transpl. 2009; 15 (11): 1420–5.

LO - 04 OBESITY

L. De Baerdemaeker

Introduction: The extremes of BMI (malnutrition versus obesity) both have the potential to influence the perioperative course and outcome in patients undergoing a liver transplantation or major hepatic surgery.

Which of these extremes has the biggest impact on outcome and can we undertake measures to alter these outcomes?

Malnutrition is a frequent complication in cirrhotic patients. In particular sarcopenia (loss of muscle mass) is an important factor in the state of malnutrition with an adverse effect on outcome. If malnutrition and sarcopenia are related to poorer outcome in patients with liver disease, the assumption is made that improving malnutrition will improve outcome. There are no established therapies to reverse or prevent this condition. Nutritional interventions with leucine enriched amino acid mixtures, myostatin antagonists and physical activity might hold the promise to reverse sarcopenia. Macronutrient replacement combined with micronutrient supplementation, specifically vitamin D, is expected to improve outcomes.

Oral nutrition is preferred, but tube feeding with the offering of nocturnal meals is a new strategy.

It is hard to realize that 30% of the world's population is obese. There is a spectrum of obesity-induced changes in the liver: from steatosis over non-alcoholic steatohepatitis (NASH) to cirrhosis and eventually hepatocellular carcinoma. 84–96% of morbidly obese have NAFLD, with NASH being prevalent in 25–55% of morbidly obese.

Gradually, NASH is on the trajectory to become the third most common indication for LTX (after HCV and alcohol) in the USA.

Should morbidly obese patients be excluded for liver transplant? Obesity makes access to transplantation more difficult due to: increased surgical risk, graft loss, wound complications, new onset of diabetes following LTX, Recurrent NASH in transplanted graft and last but not least greater risk of death.

Can we make morbidly obese patients allegeable for liver transplantation by performing bariatric surgery? Bariatric surgery is both safe and effective in patients with chronic kidney disease and end-stage renal disease, and helps patients become eligible for transplant based on BMI.

Nevertheless, Morbidly obese patients remain a high-risk population. Bariatric surgery in these patients can be dangerous in the setting of portal hypertension. Bariatric surgery in unsuspected NASH cirrhosis can precipitate hepatic decompensation.

Is bariatric surgery in liver transplant candidates feasible?:

- In Cirrhotic and liver failure: surgery should be performed before significant portal hypertension or liver synthetic dysfunction sets in.
- More aggressive weight control in NASH without portal hypertension.
- Once patient develop portal hypertension and varices: bariatric surgery is prohibited.

Consider TIPSS, reassess bariatric surgery.

- Sleeve gastrectomy may become increasingly utilized in pre and post transplant obese patients.

Does obesity affect outcome after LTX? The opinions on this topic differ between USA and Europe. There are reports from Germany and the UK that demonstrate a worse outcome in the obese livertransplant patients.

Conclusions:

- Malnutrition and sarcopenia worsen outcome of liver transplantation
- With the increase in morbidly obese patients, more hepatic complications of obesity will lead to liver disease
- NASH as an indication for liver transplant is likely to become the most common one!
- It is highly imperative that we develop more specific guidelines to preoperatively optimize and postoperatively reduce morbidity in overweight and obese recipients undergoing liver transplantation

References:

Dasarathy S. et al. Curr Treat Options Gastroenterol. 2014 Jun;12(2): 242–55.

Surg Today. 2014 Jan 29. Perioperative nutritional therapy in liver transplantation.

Curr Opin Clin Nutr Metab Care. 2010 Sep;13(5):554–61.

Curr Opin Gastroenterol. 2014 Mar;30(2):208–14. The evidence for the use of nutritional support in liver disease.

Charlton et al. Outcomes of livertransplantation for NASH in the united states gastroenterology 2011;41:1249–53.

Heuer et al. LTX in NASH is associated with high mortality and post transplant complications: single German centre Digestion 2012;86:107–13.

Hakeem et al. Increased Morbidity in Overweight and Obese Liver Transplant Recipients: A Single-Center Experience of 1325 Patients From the United Kingdom.

LIVER TRANSPLANTATION 19:551–562, 2013.

LO - 05 MASSIVE BLOOD TRANSFUSION INDEPENDENTLY COMPROMISES OUTCOME AFTER LIVER TRANSPLANTATION

***N. Gilbo**[1], L. Ceulemans[1], I. Jochmans[1], M. Verhaegen[2], F. Nevens[3], W. Laleman[3], J. Van Pelt[3], R. Aerts[1], D. Monbaliu[1], J. Pirenne[1]*

[1]Abdominal Transplant Surgery, University Hospitals of Leuven (KUL), Leuven, Belgium; [2]Anaesthesiology, University Hospitals of Leuven (KUL), Leuven, Belgium; [3]Hepatology, University Hospitals of Leuven (KUL), Leuven, Belgium

Email: nicholas.gilbo@hotmail.it

Keywords: massive blood transfusion, liver transplantation

Massive Blood Transfusion (MBT) can still occur during Liver Transplantation (LTx) and has been reported to compromise outcome. However, risk factors for MBT have not been clearly identified.

We retrospectively reviewed 552 LTx (45 ReTx) performed in our center (2000–2010). Median (IQR) transfusion rate was 3 (1–6) U of packed cells. MBT was defined as transfusion >6 U. LTx with or without MBT were compared (MBT+: 132 vs. MBT-: 398). Donor (age, sex, ECD, DCD/DBD), recipient (age, sex, indication, Child, MELD, portal hypertension, cell-count, previous surgery, TIPSS) and surgery variables (ReTx, surgery duration, CIT/WIT, plasma transfusion) were compared. Uni- and multivariate analyses were used to identify risk factors. Graft/recipient survival were analyzed by Cox regression analysis.

No differences in donor variables were observed between the two groups. Compared to MBT-, MBT+ recipients were sicker (MELD 21 vs. 14, $P < 0.001$), had lower preTx Hb (9.3 g/dl vs.11.7 g/dl, $P < 0.001$) and PLT-count (76.10^9 vs. 103.10^9, $P < 0.001$), more frequent portal hypertension (84.8% vs. 76.8%, $P = 0.05$) and TIPSS (21.5% vs. 9%, $P < 0.001$). MBT+ LTx were more complex procedures, often ReTx (15.9% vs. 6%, $P < 0.001$), with longer surgery, WIT/CIT, and more frequent revision for bleeding (11.6% vs. 4.3%, $P < 0.001$). Independent risk factors for MBT were surgery duration (OR:1.55, CI:1.13–2.12, $P < 0.01$), plasma transfusion (OR:1.5, CI:1.31–1.72, $P < 0.001$), and preTx Hb (OR: 0.65, CI: 0.54–0.79, $P < 0.001$). MBT worsened 5 year graft (61% vs. 75%, $P < 0.001$) and recipient survival (67% vs. 77%, $P < 0.001$) and remained an independent risk factor in the Cox analysis (HR:1.85 CI:1.11–3.08, $P < 0.05$).

In conclusion, these data show that MBT during LTx independently worsens outcome (85% increase in risk of death), and they suggest that -in order to prevent MBT and improve survival- attempts should be made to i) optimize preTx Hb; ii) reduce the use of plasma periLTx; and iii) shorten surgery duration.

LO - 06 MALNUTRITION

P. Kohout

Department of Internal Medicine and Center of Nutrition, Thomayer' s Hospital, Prague, Czech Republic

Keywords: Malnutrition, End stage liver disease, Liver transplantation, Sarcopenia, Artificial nutrition

End stage liver disease (ESLD) is closely associated with malnutrition. The liver is the main organ of metabolism responsible for protein synthesis and metabolism of all nutrients including vitamins and trace elements Prevalence of malnutrition in liver cirrhosis is 35%, in patients with decompensated liver cirrhosis about 85%. Malnutrition worsens the results of liver transplantation and survival of patients on waiting list.

Treatment of malnutrition in liver disease is associated with two key problems, the first one is the diagnosis of malnutrition, the second issue is its solution – nutritional treatment.

The insufficient markers of poor nutrition status in ESLD are: Subjective global assessment (SGA), body weight, body mass index (BMI), serum level of albumin and other serological markers, even mid-arm circumference (MAC) and/or bioimpedance are not good nutritional markers. The biggest problem in patients with ESLD is muscle loss (sarcopenia), the best marker of nutritional status is its examination using hand-grip measurement and/or step tests. Survival of patients with ESLD before and after liver transplantation depends also on cardio-respiratory capacity

Treatment of malnutrition is based on the supply of sufficient quantities of energy substrates and in particular proteins, together with an aerobic training, that increases muscle mass, exercise capacity and leads to increased survival. Nocturnal home enteral nutrition via nasojejunal tube together with guided exercise is the best method of improvement of nutritional status.

References:

Alvares da Silva MR, Reverbel da Silveira T (2005) Comparison between handgrip strength, subjective global assessment and prognosis nutritional index in assessing malnutrition and predicting clinical outcome in cirrhotic outpatients. Nutrition, 21, 113–117.

Peng S, Plank LD, McCall JL, et al. (2007) Body composition, muscle function, and energy expenditure in patients with liver cirrhosis: a comprehensive study. Am J Clin Nutr; 85:1257–1263.

Plauth M, Cabré E, Riggio O, et al. (2006) ESPEN Guidelines on Enteral Nutrition: Liver disease. Clin Nutr; 25:285–292.

Sanchez J., Aranda-Michel J, (2006) Nutrition for the Liver Transplant Patient. Liver Transpl 12:1310–1316.

LO - 07 CANDIDIASIS COMPLICATIONS IN LIVER-TRANSPLANT RECIPIENTS DUE TO YEAST PRESERVATION FLUID CONTAMINATION

Z. Noorah[1], *C. Paugam-Burtz*[2], **E. Levesque*[1], *F. Saliba*[3], *L. Khoy-Ear*[2], *J.C. Merle*[1], *B. Jung*[4], *L. Stecken*[5], *M. Ferrandiere*[6], *L. Mihaila*[7], *F. Botterel*[8]
[1]*Réanimation digestive et transplantation hépatique, GH Henri Mondor, Créteil, France;* [2]*Service d'anesthésie et Réanimation Hôpital Beaujon, Clichy, France;* [3]*Centre Hépato-Biliaire, Hôpital Paul Brousse, Villejuif, France;* [4]*Service d'anesthésie et Réanimation CHU Montpellier, Montpellier, France;* [5]*Service d'anesthésie et Réanimation CHU Bordeaux, Bordeaux, France;* [6]*Service d'Anesthésie et Réanimation et SAMU, CHU Tours, Tours, France;* [7]*Service de Parasitologie, G.H. Kremlin-Bicètre, Kremlin-Bicètre, France;* [8]*Unité de Parasitologie-Mycologie, DHU VIC, GH Henri Mondor, Créteil, France*
Email: eric.levesque@hmn.aphp.fr

Keywords: liver transplantation, preservation fluid, candida, complications

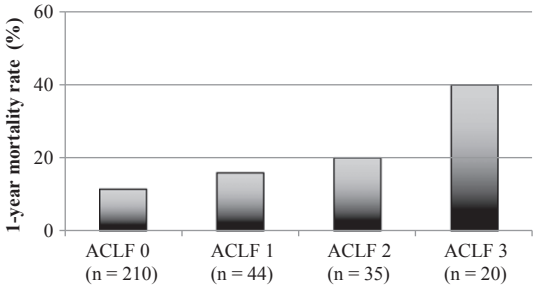
Introduction: Donor-derived fungal infections can be associated with serious complications in transplant recipients. Most cases of donor-derived candidiasis occurred in kidney transplant recipients in whom contamination of the preservation fluid is a commonly proposed source. The aim of this study was to determine the incidence and clinical relevance of *Candida* contamination of preservation fluid (PF) in liver transplantation.
Patients and methods: A 5-year (2008–2012) retrospective study involving six French liver transplantation centers was designed to determine the incidence of *Candida* PF contamination and its postoperative clinical features and outcomes in recipients after liver transplantation.
Results: *Candida* were isolated from 28 out of 2107 PF (1.33%). *Candida albicans* was the most common yeast found ($n = 18$, 64% of cases). An antifungal treatment was administered at 22 patients with duration of treatment going from 7 to 37 days. Fourteen patients (50%) developed major postoperative complication, among which eight developed yeast related complications (28.6%) including hepatic artery aneurysms ($n = 6$) and *Candida* peritonitis ($n = 2$). Among these eight patients, six had received an antifungal treatment. The mortality at one-year, in patients which developed a yeast related complication, was 62.5%.
Conclusion: The incidence of *Candida* PF contamination is low, but is associated with dramatic postoperative complications with a higher morbidity. In this context, an angiographic monitoring of the hepatic artery seems necessary in the courses of LT but must be estimated in a large-scale study.

LO - 08 CIRRHOTIC PATIENTS AND LIVER TRANSPLANTATION: EVALUATION OF THE CLIF-SOFA SCORE FOR PREDICTING POST-OPERATIVE MORTALITY

Z. Noorah[1], **E. Levesque*[1], *P. Compagnon*[2], *J.C. Merle*[1], *G. Dhonneur*[1], *C. Feray*[3], *D. Azoulay*[2]
[1]*Hôpitaux de Paris, CHU Henri Mondor, Réanimation Digestive et Transplantation Hépatique, Créteil, France;* [2]*Hôpitaux de Paris, CHU Henri Mondor, Service de Chirurgie Digestive et Transplantation Hépatique, Créteil, France;* [3]*Hôpitaux de Paris, CHU Henri Mondor, Service d'Hépatologie, Créteil, France*
Email: eric.levesque@hmn.aphp.fr

Keywords: Liver Transplantation, cirrhotic patients, outcomes

Introduction: Cirrhotic patients undergoing liver transplantation (LT) have a good prognostic, with a 1-year survival exceeding 85%. Among these patients, some present an acute decompensation with organ failure at time of liver transplantation. The aim of this study was to identify patients at higher risk of mortality at 1-year in relation with their severity at time of transplantation.
Patients and methods: Three hundred nine cirrhotic patients admitted to our Liver ICU between January 2008 and April 2013, and who underwent liver transplantation were enrolled in this study. Mean age was 55.5 ± 9.2 years. Main indications for liver transplantation were end-stage cirrhosis ($n = 147$, 47%) and cirrhosis with hepatocellular carcinoma ($n = 142$, 46%). Cirrhosis was mostly related to alcohol (52%) and chronic viral hepatitis (34%). From criteria for Acute-On-Chronic Failure (ACLF) based on Clif-SOFA score, we focused our analysis on futile outcome (one-year mortality) and long-term post-transplant outcome.
Results: Overall mortality at 1-year was 14.8% (46/309 patients). A correlation between the number of organ failures (defined by the grade of ACLF) and the mortality at one-year was observed: cirrhotic patients without ACLF at the time of LT had a 1-year mortality of 11.4%, whereas grade 3 ACLF patients had a mortality of 40%. Univariate analysis showed that ACLF grade ($P = 0.02$), neurologic failure, defined by encephalopathy grade 3 or 4, (15% vs. 5%, $P = 0.02$), hemodynamic failure (30% vs. 2%, $P < 0.001$), and serum creatinine (109 ± 79 vs. 88 ± 61, $P = 0.04$) at the time of liver transplantation were associated with higher 1-year mortality rate.
Conclusion: Our findings clearly show that cirrhotic patients with ACLF have a higher 1-year post-transplant mortality risk, especially in those with three or more organ failures.



LO - 09 BLEEDING – IS IT STILL AN ISSUE?

****D. Tomescu***
Fundeni Clinical Institute, Bucharest, Romania
Email: danatomescu@gmail.com

Bleeding is and will always be an issue because it can be fatal. Other major (and minor) complications in the perioperative setting are attributed to bleeding and to transfusion respectively, being major determinants of the patient outcome (mortality, morbidity), aswell as on duration of stay in the postanesthesia care unit, duration of hospital stay and cost.

One of the main problems of the perioperative management is to predict and treat bleeding. A correct strategy in order to manage bleeding must or should lead to a better patient outcome – which means less complication, better survival, shorter duration of hospital stay and a lower overall cost.

Liver transplantation (LT) has emerged as an increasingly successful treatment for patients with end-stage liver disease (ESLD) but the procedure is extensive, complex, and technically challenging, with multiple vascular transections and anastomoses. In addition, the liver is an extremely vascular organ and extensive bleeding can occur in patients with portal hypertension due to ESLD.

Historically, significant blood loss at the time of liver transplantation has been treated with large autologous transfusions of packed red blood cells (PRBCs), fresh frozen plasma (FFP), platelets, and cryoprecipitate. Drugs are given along with the blood products, to help correct metabolic and coagulation abnormalities.

The literature includes cases of orthotopic liver transplantation (OLT) performed without transfusion of any blood products and OLT performed safely without additional blood products if blood loss is limited to 1600–3400 mL, but most studies showing conflicting results and an enormous variability in transfusional practice.

Because of many transfusion-related complications, especially those from large-volume transfusions, alternative therapies and approaches to transfusion are being investigated in transplantation and other surgical fields.
Bleeding during liver transplantation: Contributing factors to blood loss during liver transplantation can be categorized as preoperative, intraoperative, or postoperative.
***Preoperative factors*:** Preoperative factors associated with blood loss during liver transplantation include liver failure, cirrhosis, cholestasis, and splenomegaly. Many complex derangements of hemostasis are associated with ESLD (impaired synthesis of coagulation factors, increased fibrinolytic activity with a low-grade disseminated intravascular coagulation–like picture, thrombocytopenia). The important change lately is understanding the complex rebalanced coagulation profile of the patient with ESLD. Recent evidence has shown that the haemostatic process requires more than platelets and coagulation cascade in order to generate an effective clot and stop the bleeding. Novel theories suggest that coagulation is cell based; i.e. that a cell surface is necessary to promote coagulation. In this model, vascular endothelium, platelets and coagulation factors interact in precise order to initiate, amplify and propagate clotting.[1]

Some underlying conditions that explain the bleeding tendency in patients with end-stage liver disease (ESLD) are listed in Table 1.

Table 1 Underlying Conditions That Explain the Bleeding Tendency in Patients with Decompensated Chronic Liver Disease.[2]

Underlying Conditions That Explain the Bleeding Tendency in Patients with ESLD
1.Hemodynamic alterations owing to portal hypertension
2.Endothelial dysfunction
3.Development of endogenous heparin-like substances owing to bacterial infection
4.Renal failure

***Intraoperative factors*:** Bleeding during the liver transplantion procedure occurs il all phases (preanhepatic, anhepatic phase and reperfusion and postreperfusion period).

In the preanhepatic phase bleeding is mostly due to surgical resection, portal hypertension and can be enhanced by the preexisting abnormalities of clotting, platelets, and fibrinolysis.

Transplantation of a healthy liver usually restores the patient's clotting function in the operating room. However, a dysfunctional graft may not immediately produce clotting factors. In severe cases, this may lead to nonfunction of the primary graft, which mandates retransplantation. However, in some patients this is temporary and the graft recovers and function improves.

During the anhepatic or postanhepatic phase, fibrinolysis can occur.

Bleeding during the postanhepatic phase also may be related to disseminated intravascular coagulation (DIC) and platelet trapping., as well to the release of heparinlike factors from the allograft, release of preservative solution into the systemic circulation, and dysfunction of the graft.

***Postoperative factors*:** Postoperative bleeding is not common, and is mainly related to clot lysis or technical failures, or- less commonly, due to thrombocytopenia.

An acute graft disfunction or primary graft non-function can be another cause of postoperative bleeding.

Transfusion requirements in LT: Historically, LT was associated with massive blood loss. More recent reports show a trend toward decreased mean blood loss, and several reports describe liver transplantation without the use of blood products. In the past, the volume of blood loss has been inversely associated with favorable outcome; therefore, efforts have been made to determine predictors of transfusion requirements.

Transfusion practice in similar established economies is highly variable, lacks evidence, and is independently associated with adverse events in cancer surgery, cardiac surgery, and noncardiac surgery;although, causality as historically defined remains to be established in most settingsof multi-centric randomized control trials**.**

Predictors of transfusion requirements: Some authors have shown that there are some factors that affect transfusion requirements: severity of disease (MELD score and Child classification), preoperative PT, previous abdominal surgery, and factor V levels. Other factors identified as independent predictors of transfusion include the preoperative hematocrit value, thrombocytopenia, use of the piggyback technique, and duration of surgery.[2] Other studies found that age, hepatocarcinoma, renal dysfunction, graft quality (donor age, expanded criteria) and the surgical team are predictors of transfusion requirements.

In conclusion, blood loss and transfusion during LT remains difficult to predict because of patient variability (low vs. high MELD/MELD-Na score, deceased-donor vs. living-donor, co-morbidities), variability in surgical technique, unstandardized transfusion protocols, inter-institutional variability, inter-individual variability, scarsed resources (prothrombin complex, fibrinogen etc. . .).[3–6]

Another issue is to choose the best and most accurate laboratory test which might help to asses haemostasis and to predict bleeding. But there are some questions too:

***How "classical" are classical coagulation tests?*:** aPTT was developed as a diagnostic test for patients exhibiting features consistent with hemophilia, PT/INR were developed for monitoring warfarin anticoagulation BUT standard coagulation tests (INR and PT) are part of liver cirrhosis assesment (MELD, MELD-Na,[5] Child-Pugh scores).

Another tests were developed to asses hemostasis and to diagnose coagulopathy (trombelastometry, trombelastography), but there are not yet standard of care because lack of studies.

The thromboelastogram is used to monitor clot formation until an endpoint of clot lysis or retraction is determined. The thromboelastogram, which is performed using whole blood, analyzes the interactions of plasma coagulation proteins with platelets and fibrinogen and its findings correlate with intraoperative hemorrhage and coagulopathy and can assist the anesthesiologist in treating intraoperative bleeding by helping identify the cause.

A debate is the choice between standard coagulation tests vs. Point-of-Care Devices.

Standard coagulation tests have a delayed availability, do not asses hyperfibrinolysis and are *In vitro* tests.

Point – of – care devices are time efficient, clinically efficacious, cost-effective, permit goal-directed therapy and a selective drug use.

We can speak about a concept "Time is Blood": Standard coagulation tests are available after a median of *53 min* (IQR 45–63), whereas 10 min values of ROTEM® are available after *23 min* (IQR 21–24 min).[7]

The question shifted from **"why does this patient bleed?"** to **"will this patient bleed?"**.[8]

Preoperative correction of coagulation tests with blood products *may not be necessary* and may even *have harmful side-effects*.

Fluid overload, by administration of FFP, resulting in *exacerbation of portal hypertension* may in fact *promote bleeding*.

Things we often forget in order to minimize bleeding are[9,10]: correction of hypothermia: mild hypothermia (<35.5°C) increases blood loss by 16% and the relative risk of transfusion by 22%, correction of hypocalcemia, of acidosis.[10]

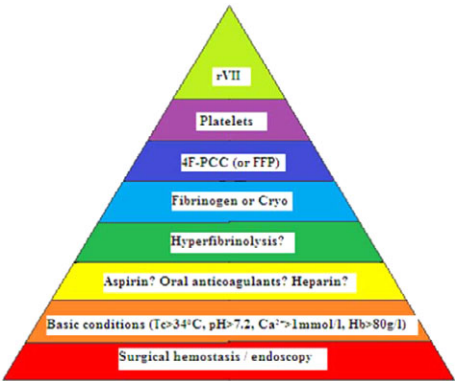


Figure 1 Delicate Balance of Bleeding and Thrombosis in End-Stage Liver Disease and Liver Transplantation.[11]

There are some principles in order to minimize bleeding and its consequences:

1. Treat disease/clinical situations not test results
2. Observe, assess and treat bleeding
3. "If you don't measure it, you cannot manage it!"
4. Think interdisciplinary – surgeon, transfusion therapist ?
5. Treat individualized: act fast & targeted & pathophysiology oriented
6. The volemic approach: *"neither wet nor dry"*
7. Survival benefits?[12,13]
8. The 1:1:1 ratio[14]
9. Benefits in correction of *trauma-induced coagulopathy*[15]
10. Use of fresh whole blood in large-volume hemorrhage may be superior to whole blood reconstituted from multiple components. Multicomponent apheresis can overcome logistical difficulties in matching patient needs with fresh component availability and can deliver the benefits of fresh whole blood.[13–17]
11. The use of the cell salvage system! (**NO** recommendation could be made and used as a safety precaution, in "stand-by mode"
12. Goal-directed therapy – A return to physiology

"A – 1 – 2"
Antifibinolytic drug
Coagulation factor **1** (Fibrinogen)
Coagulation factor **2** (Thrombin)

The final conclusion may result in a vicious circle: the higher the blood loss – the more you transfuse **and** the more you transfuse the higher the blood loss. . . and the more you transfuse the more likely seems to develop postoperative complications (respiratory distress, acute kidney injury, graft disfunction etc).[18,19]

References:

1. Lisman, T.,Porte, R.J. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences Blood 2010; 116(6):878–885.
2. Tripodi, A., Mannucci, P. M. The coagulopathy of chronic liver disease. New England Journal of Medicine 2011; 365(2): 147–156.
3. Feltracco, Paolo, et al. "Blood loss, predictors of bleeding, transfusion practice and strategies of blood cell salvaging during liver transplantation." World journal of hepatology 5.1 (2013): 1–15.
4. Cywinski, Jacek B., et al. "Prediction of Intraoperative Transfusion Requirements During Orthotopic Liver Transplantation and the Influence on Postoperative Patient Survival." Anesthesia & Analgesia 118.2 (2014): 428–437.
5. Tomescu D., Popescu M., Droc G., Fota R., Ungureanu D., Brasoveanu V. Intraoperative blood loss and blood transfusion during liver transplantation. A national single center experience, J Rom Anest Terap Int 2014; 21(1): 27–34.
6. Massicotte, Luc, et al. "Transfusion rate for 500 consecutive liver transplantations: experience of one liver transplantation center." Transplantation 93.12 (2012): 1276–1281.
7. Kitchens, C. S. "To bleed or not to bleed? Is that the question for the PTT?." Journal of Thrombosis and Haemostasis 3.12 (2005): 2607–2611.
8. Haas, T., et al. Comparison of thromboelastometry (ROTEM®) with standard plasmatic coagulation testing in paediatric surgery. British journal of anaesthesia 108.1 (2012): 36–41.
9. Westerkamp, Andrie C., Ton Lisman, and Robert J. Porte. How to minimize blood loss during liver surgery in patients with cirrhosis. HPB 2009; 11 (6): 453–458.
10. Kozek-Langenecker, Sibylle A., et al. "Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology." European Journal of Anaesthesiology (EJA) 30.6 (2013): 270–382.

11. Saner, F. H., Gieseler, R. K., Akız, H., Canbay, A., Görlinger, K. Delicate Balance of Bleeding and Thrombosis in End-Stage Liver Disease and Liver Transplantation. Digestion 2013; 88(3): 135–144.
12. Hess JR; Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Scientific problems in the regulation of red blood cell products. Transfusion. 2012;52(8):1827–1835.
13. Young P.P., Cotton B. A., Goodnough L.T. Massive Transfusion Protocols for Patients With Substantial Hemorrhage Transfus Med Rev. 2011; 25(4): 293–303;
14. Kashuk, Jeffry L., et al. "Postinjury life threatening coagulopathy: is 1:1 fresh frozen plasma: packed red blood cells the answer?" J Trauma and Acute Care Surgery 65.2 (2008): 261–271.
15. Zehtabchi, Shahriar, and Daniel K. Nishijima. "Impact of Transfusion of Fresh-frozen Plasma and Packed Red Blood Cells in a 1:1 Ratio on Survival of Emergency Department Patients with Severe Trauma." Academic Emergency Medicine 16.5 (2009): 371–378.
16. Dries D.J. The contemporary role of blood products and components used in trauma resuscitation Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2010, 18:63.
17. Spinella PC: Warm fresh whole blood transfusion for severe hemorrhage: U.S. military and potential civilian applications. Crit Care Med 2008, 36 (Suppl7): S340–S345.
18. Schuster KM, Davis KA, Lui FY, Maerz LL, Kaplan LJ: The status of massive transfusion protocols in United States trauma centers: massive transfusion or massive confusion? Transfusion 2010, 50:1545–1551.
19. Glance LG, Dick AW, Mukamel DB, et al. Association between intraoperative blood transfusion and mortality and morbidity in patients undergoing noncardiac surgery. Anesthesiology. 2011;114(2): 283–29.

LICAGE POSTER PRESENTATIONS

LP - 01 CARDIOVASCULAR COMPLICATIONS AFTER ORTHOTOPIC LIVER TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

*E.D. Kosmacheva[1], ***A.E. Babich**[2]*

[1]Regional Clinical Hospital No.1 Ministry of Healthcare, Kuban State Medical University of Ministry of Health of the Russian Federation, Krasnodar, Russian Federation; [2]Department of Surgery, Regional Clinical Hospital No.1 Named after Prof. S.V. Ochapovsky Ministry of Healthcare, Krasnodar, Russian Federation

Email: anna-babich1@yandex.ru

Keywords: liver transplantation, cardiac complications

Aim: The aim of this study was to document the frequency and management of cardiovascular complications after liver transplantation.
Method: We retrospectively analysed 88 patients who had undergone LT between May, 2010 and December, 2014 at the Regional Clinical Hospital №1, seeking to evaluate the incidences of postoperative cardiovascular complications and the incidences of de novo of cardiovascular diseases.
Results: Genders were male in 59% and female in 41%, aged from 13 to 64 years (mean age 47), patients older than 50 years – 36.4%. There were early arterial vascular complications: thrombosis of the hepatic artery and its branches (2%) and thrombosis of the hepatic artery and celiac trunk (3%). Venous vascular complications were portal vein thrombosis (1%) and mural thrombosis of the portal vein (1%). Causes of early cardiovascular postoperative mortality were massive pulmonary embolism (1.1%) and portal vein thrombosis (1.1%). Long-term cardiovascular diseases analysis after LT has been shown the incidences of de novo arterial hypertension – 35.2%, chronic heart failure -14.8%, coronary artery disease – 3.4%. There was significant difference for the development of arterial hypertension, which seemed to be more related to cyclosporine (43.5%) than to tacrolimus (26.2%). The most of cardiovascular diseases were in patients older than fifty years old.
Conclusion: The development of new cardiovascular diseases arising after liver transplantation. Calcineurin inhibitors are associated with arterial hypertension. We suggest that it should be possible to reduce the risk of transplant-related cardiovascular diseases by evaluation of individual risk factors, new therapeutic scheme and by close monitoring after transplantation especially in elderly.

LP - 02 FIBRINOGEN REPLACEMENT IN THE SCOTTISH LIVER TRANSPLANT UNIT

*V. McMullan[1], ***C. Beattie**[1], E. Thomson[1], S. Zahra[2]*

[1]Scottish Liver Transplant Unit, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; [2]Scottish National Blood Transfusion Service, Edinburgh, United Kingdom

Email: Craig.Beattie@luht.scot.nhs.uk

Keywords: fibrinogen concentrate, liver transplantation, cryoprecipitate

Introduction: Liver transplantation (LT) may be associated with bleeding and coagulopathy.[1,2] In the UK, acquired hypofibrinogenaemia is treated with fresh frozen plasma (FFP) and cryoprecipitate. In many European countries fibrinogen concentrate (FC) is used.[3,4] In LT, units of red blood cells (RBCs), FFP and cryoprecipitate transfused correlate negatively with patient survival (and graft survival for RBCs).[5,6,7]

Audit aims were to:

- Describe preoperative fibrinogen levels and perioperative replacement
- Examine the cost implications of changing practice in the Scottish Liver Transplant Unit (SLTU)

Methods: We reviewed 283 consecutive LT cases (Jan 2011-April 2014) from our prospectively maintained database. The amount of fibrinogen given in cryoprecipitate was calculated from the mean fibrinogen in cryoprecipitate (1576 mg/pool).[8] Costs were calculated using the NHS Blood and Transplant price list (£195.53/pool)[9] and FC cost in our institution (£340/g).
Results: Results are shown in Table 1. All patients with a preoperative fibrinogen <0.9 g/l received cryoprecipitate. Based on *average* fibrinogen content of cryoprecipitate this amounts to ~761.2 g of fibrinogen costing £93,474.99. The same dose of fibrinogen administered as FC would cost £258,810.72 (€318,258.71).
Discussion: Low fibrinogen is common in SLTU patients with over 50% receiving cryoprecipitate to treat bleeding. Costs would increase if FC were used to replace fibrinogen. This additional financial burden needs to be offset against proposed benefits of FC including reduced pathogen transmission, standardised fibrinogen content, improved efficacy, no thawing requirement and potential for improved outcomes with reduced transfusion of blood and products.[3,5,6,7,10,11]

The authors believe that, with the body of evidence regarding safety and efficacy of FC, the licensing issue in the UK should be addressed. The cost of its introduction in our patient group is justified in the face of its proposed benefits.

References:

1. Tripodi A, Mannucci PM, The coagulopathy of chronic liver disease. NEJM 2011;365: 147–56.
2. Ozier Y, Tsou M. The changing trends in transfusion practice in liver transplantation. Current Opinion in Organ Transplantation 2008; 13: 304–309.
3. Wikkelso A, Lunde J, Johansen M, et al.. Fibrinogen concentrate in bleeding patients. Cochrane Database Syst Rev 2013; 8: CD008864.
4. Kozek-Langenecker SA, Afshari A, Albaladejo P, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol 2013; 30: 270–382.
5. Boyd SD, Stenard F, Lee DK, et al. Alloimmunization to red blood cell antigens affects clinical outcomes in liver transplant patients. Liver Transpl 2007; 13: 1654–1661.
6. Massicotte L, Sassine MP, Lenis S, et al. Survival rate changes with transfusion of blood products during liver transplantation. Can J Anaesth 2005; 52: 148–155.
7. Cacciarelli TV, Keeffe EB, Moore DH, Burns W, Busque S, Concepcion W, So SK, Esquivel CO. Effect of intraoperative blood transfusion on patient outcome in hepatic transplantation. Arch Surg. 1999; 134:25–9.
8. Kosmirak L. NHSBT Portfolio of Blood Components and Guidance for their Clinical Use. Specification SPN223/6. p35.
9. NHS Blood and Transplant. Price List 2013/2014. p1.
10. Franchini M, Lippi G. Fibrinogen replacement therapy: a critical review of the literature. Blood Transfus. 2012; 10(1): 23–27.
11. de Boer MT, Christensen MC, Asmussen M, et al. The impact of intraoperative transfusion of platelets and red blood cells on survival after liver transplantation. Anesth Analg 2008; 106: 32–44.

LP - 03 PROCEDURE-RELATED BLEEDING IN LIVER TRANSPLANT CANDIDATES WITH AND WITHOUT PREEMPTIVE HAEMATOLOGICAL THERAPY BASED ON CLASSICAL HAEMOCOAGULATION TESTS

***L. Skladaný[1],** *J. Šváč[1], P. Molčan[1], E. Čellárová[2]*

[1]HEGITO – Hepatology, gastroenterology and liver transplant unit of Dept. Internal medicine II., Slovak Medical University, F.D.Roosevelt Univ Hospital, Banská Bystrica; [2]Department of Haematology, F.D.Roosevelt Univ Hospital, Banská Bystrica

Introduction: Procedure-related bleeding (PRB) is a serious problem in liver transplant (LTx) candidates. Standard protocol (SP) concerning PRB at the institution of authors included: (1) consultation of haematologist before the procedure; (2) standard panel of *in vitro* haemocoagulation tests (HT); (3) preemptive haematological therapy based on results of HT. Step 3 consisted

Table 1 Preoperative fibrinogen levels (g/l), blood loss and cryoprecipitate administration in LT patients in SLTU. Values expressed as median and interquartile range

	Number of patients (*n*)	Pre-operative fibrinogen concentration (g/l)	Estimated blood loss (ml)	Number of patients receiving cryoprecipitate (*n*, %)	Cryoprecipitate received per patient transfused (pools)
All LT	283	2.0 (1.2–2.9)	4000 (2000–6963)	157 (55%)	1 (0–2)
MELD ≥ 25	64	1.0 (0.9–2.0)	4673 (1800–9850)	52 (81%)	2 (1–4)

mostly of supplementation of the deficient haemocoagulation factors (HF); the dose of HF was calculated by haematologist according to the results of HT.

But the understanding of haemostasis in ESLD is changing lately*:* (i) the role of HT in guiding PRB prevention is being questioned; (ii) there is higher focus on the risk of thrombotic events; as well as on (iii) the cost effectiveness of SP.

Hypothesis: Leaving out step 3 from SP (=modified protocol, MP) will not lead to increase in the rate of PRB in: (i) potential LTx candidates without the history of bleeding, (ii) undergoing procedures with invasiveness grade 1-2/3. In MP-group, HF were prepared for acute use but administered only when bleeding occured.

Aims: To compare the rates of PRB and consumption of HF between SP-group and MP-group.

Patients (Pts) and methods: The LTx programme was established in May 2008 with SP being standard of care until September 2012 (retrospective part of the study); thereafter, MP was adopted (prospective follow up – for the purpose of this analysis until December 2012). Consecutive patients, potential LTx candidates ($N = 77$). Female/male 55/22, mean age 50.8 years (y) (21–66 y). ESLD etiology: alcoholic liver disease 38 patients, viral hepatitis B or C 10 patients, nonalcoholic steatohepatitis nine patients, other etiologies 20 patients. Fifty-eight patients were included in SP and 19 patients in MP group. There were no differences between the SP group and MP group in baseline characteristics (i.e. Child-Pugh, MELD, HT).

Results: Procedure-related bleeding has been recorded in 22% of patients from SP and in 21% from MP, respectively (n.s.); HF consumption in SP and MP groups, respectively, were as follows (in packages): fresh frozen plasma 9.8 *vs.* 5.23; prothrombine complex 0.82 *vs.* 0.41; antithrombine III 0.13 *vs.* 0. Costs of HFs in SP a MP groups, respectively, were (per patient) 702€ *vs.* 379€. No PRB-related death was recorded.

Conclusion: The modified protocol appears to be as safe in regard to PRB as the SP; while being less costly.

LP - 04 INFLUENCE OF THROMBELASTOMETRY (TEM) CONTROLLED PRESCRIPTION OVER FUNCTION OF LIVER ALLOGRAFT AFTER LIVER TRANSPLANTATION (LTX) IN EARLY POSTOPERATIVE PERIOD

M. Uhliar

Department of Anesthesiology, Division of Transplant, Hospital F.D.Roosevelta, Banská Bystrica, Slovakia

Email: marceluhliar@gmail.com

Keywords: thrombelastometry, liver transplantation, allograft

Background: Coagulation disorders and massive bleeding are common problems during major visceral surgery like liver resection and liver transplantation (LTx). Thromboelastometry (TEM) is point of care examination relying on detection of mechanical clot characteristic. TEM results are available sooner than those of conventional laboratory coagulation tests and they provide more information regarding cooagulation strength, platelet function and fibrinolysis.

Aim: Evaluate influence of TEM controlled prescription over function of liver allograft after LTx in early postoperative period. Study: We have performed a retrospective study of liver transplant recipients. All patients since may 2008 until may 2014 have been reviewed and divided into two cohorts either with use of TEM during LTx or without its use. We compared both of groups using a single center electronics database. We evaluated following parameters of early postoperative period (72 hours after LTx): consumption of blood products, application of vasopressor therapy, hypotension occurence, massive bleeding, increase of PT, decrease of fibrinolysis.

Results: There were 99 patients who underwent LTx in Transplant center (TC) Banská Bystrica, Slovakia. Fifty-one recipients (51.51%) were transplantated with intraoperative use of TEM and 48 recipients (48.48%) without TEM. Consumption of blood products (red blood cells, fresh frozen plasma), use of vasopressor therapy, hypotension episodes and massive bleeding were increased in group without use of TEM and there was longer period of lower PT and higher fibrinolysis after LTx as well. In second group (cohort with TEM) we used antifibrinolytic therapy (fibrinolysis diagnostics by TEM) less frequently and drug eliminating influence of heparin more frequently.

Conclusion: LTx procedures and severe multifactorial coagulopathy detectable by TEM provide additional information in more aspects than conventional coagulation parameters. The use of TEM controlled prescription in perioperative period has influence over better liver allograft function in early postoperative period.

References:

Charvát J., Vychodil P., Kieslichová E. et al.:Trombelastograf při transplantaci jater, porovnaní s konvenčními koagulačními testy. Časopis Lékčes., 2004, 143, 697–699.

Nardo B., Bertelli R., Montalti R. et al.: Red blood cell transfusion in liver transplantation: A case-control study. Transplantation Proceedings, 2005, 37, 4389–4392.

Steib A., Freys G., Lehmann C. et al.: Intraoperative blood loss and transfusion requirements during adult liver transplantation remain difficult to predict. Can J Anaesth, 2001, 48, 1075–1079.