**Anesthesia / Critical Care / Quality Assurance in LT**

**By Michael Spiro and Ryan Chadha**

Three special Sessions dedicated to Anaesthesia and Critical Care on Perioperative Challenges, Current Controversies, and Optimizing Outcomes in ICU, respectively were the feature of this years Anesthesia and Critical Care Scientific Programme, in addition to an Oral abstract Session.

**O-115 - Feasibility and safety of the mild hypothermia and acute kidney injury in liver transplantation (MHALT) trial.**

***Bokoch M.P., UCSF, San Francisco, United States.***

AKI is associated with negative outcomes post OLT including worsened 30 days and 1 year graft and patient survival. One year survival is reduced to 45% for stage 3 AKI post operatively. Mild hypothermia may have benefits on the kidneys. In rodent models local or systemic cooling is protective for IRI. In humans, induced mild hypothermia in DBD renal transplant donors resulted in a reduction in delayed graft function. Bokoch et al. reported the initial results of an on going single blind trial inducing mild hypothermia in the OLT recipient prior to reperfusion. Control patients were maintained as normothermic throughout transplantation. The hypothermia group were systemically cooled during the dissection and anhepatic phases using an esophageal cooling device. Local cooling of the right kidney was also performed by ice packing. Patients were rewarmed post reperfusion with the aim of extubating the patients at conclusion of surgery. The primary endpoint was AKI at 72 hours. DCD donors and patients who received pre-operative RRT were excluded. There was no difference in blood loss, product usage or ICU LOS. Core temperatures were significantly lower in the intervention group (34.5 +/- 0.3 vs. 36.5 +/-0.6 degrees Centigrade). The authors concluded that the trial is feasible and safe. Enrollment is ongoing and we look forward to the results of this study.

**O-116 - Liver transplant for patients with grade 3 acute on chronic liver failure: pre-transplant factors of post transplant mortality in a multicenter study.**

***Francois Faitot, Strasbourg, France***

One year survival in ACLF grade 3 is 84%. They represent a heterogenous group and it can be difficult to decide on who should be transplanted. The authors reported the post transplant results, and tried to identify pre OLT criteria to help predict outcome. A retrospective analysis of 5 transplant centers between 2007-2017 was performed following division into a determination or a validation cohort. A predictive model was produced. They identified 4 pre OLT factors that were associated with 1 year mortality. These were: Age >53; Lactate >4; Respiratory failure requiring mechanical ventilation; pre operative low leukocyte count (White cell count <10,000). They suggested that patients with >2 variables had a 1 year survival of <10% (64% with a score of 2; 79% with 1 variable).They recognize that this is a retrospective cohort vulnerable to pre-screening bias. The aim of the score is to identify patients who represent futility.

**O-117 - An individualized, in hospital pre-habilitation program for patients with cirrhotic liver disease awaiting transplantation surgery: a single center feasibility study.**

***Clare Morkane, London, United Kingdom***

It is well established that sarcopenia and frailty are independent risk factors for morbidity and mortality in end stage liver disease. The aim is to maximize function preoperatively to help the patient to withstand the stress of surgery. There is currently no consensus on quantity of necessary exercise to achieve this. Patients with cirrhosis on the waiting list were enrolled into a structured exercise arm tailored to their initial physical fitness based on their baseline CPET. They underwent three 40 minute exercise episodes per week for 6 weeks. A repeat CPET was performed at 3 weeks, again at week 6 and then another 6 weeks after stopping exercise. These patients were compared with matched standard care patients. Study aims were to recruit 30 patients and to demonstrate feasibility (ability to recruit >40% of patients approached for the study). Actual recruitment was 54%. There was a large drop out in both groups, with no drop out due to complication of exercise. The exercise group increased their VO2 peak after 6 weeks (from 16.2 to 18.5 ml/kg/min P=0.02) and demonstrated a deterioration after cessation of exercise. The control group showed deterioration in VO2 peak whilst on the waiting list. Structured exercise in OLT wait-list patients is safe and feasible. Sessions were well attended (94%) with signal toward improved exercise capacity in intervention group.

**O-118 - Pre transplant metabolic syndrome (MS) associated with major adverse cardiovascular events (MACE) after liver transplant surgery**

***Victor Xia, Los Angeles, United States***

Cardiovascular events are the leading cause of non-graft related death post liver transplantation with an incidence of 12.8%. Pre transplant metabolic syndrome is a major risk factor for MACE. The speaker presents a retrospective study of adult liver transplant recipients (excluding redo transplantation and acute liver failure). 858 patients were included with 243 (28%) diagnosed with pre transplant MS. MS was defined by: raised BMI, raised triglycerides, low HDL, hypertension and raised fasting glucose. Primary outcome was the incidence of MACE at 30 days post OLT. MACE was defined as: myocardial infarction, heart failure, atrial fibrillation (AF), cardiac arrest, pulmonary emboli and stroke. Patients with MS were matched to those without MS giving 241 pairs overall. The MS group had a significantly increased risk of MACE (25.7%vs 17.8% p=0.035). New onset AF was the most common complication. When modeled including intraoperative factors pre-transplant MS remained an independent risk factor for MACE. MS is common in transplant patients. Pre transplant MS is associated with major adverse cardiac events.

**O-119: Living donor liver transplantation in recipients with left ventricular dysfunction**

***Pooja Bhangui, Delhi NCR, India***

Data on outcomes of living donor liver transplantation (LDLT) in patients with left ventricular dysfunction (LVD) is scarce. A single center review of close to 2000 LDLTs revealed a total of 12 patients with severe LVD (EF < 50%) Twelve male patients had LVD during work up. Etiology of liver disease was due to alcohol (6), Hepatitis C (2), nonalcoholic steatohepatitis (2) and cryptogenic (2). Two recipients were post CABG, one was post PTCA, five had a history of myocardial infarction, 2 had dilated cardiomyopathy and 4 had cirrhotic cardiomyopathy. The EF of the patients ranged from 25%-45%. Intraoperative course was uneventful in all recipients, with arrythmia’s in 4 patients. One patient required an IABP post procedure. Three patients developed stress cardiomyopathy. 2 improved, while 1 needed continued IABP support (EF was 25%), and died of multi-organ failure on POD 20. Another patient died on POD30 due to septic shock. Mean LOS was 22 days. In the remaining 10 that survived, there were no long term cardiac morbidities or mortalities.

**O-120: The cardiac output optimization following liver transplant (COLT) trial: a feasibility randomized controlled trial**

***Clare M Morkane, London (UK)***

Goal directed fluid therapy (GDFT) reduces morbidity following major surgery but has not been assessed after liver transplantation. A prospective trial was performed to assess feasibility of delivering GDFT following liver transplantation. Patients with liver cirrhosis were recruited to either 12 hours of GDFT using a non-invasive cardiac output monitor or standard care (SC) guided by attending clinicians with the primary outcome being feasibility and the secondary outcomes being postoperative complications. 60 patients were enrolled into the trial during the study period. Median crystalloid administered during the intervention period was 3500 ml in the GDFT group versus 2225 ml in the SC group. There were an increased number of Clavien Dindo grade 3 complications in the GDFT group at discharge from hospital (63.3%) versus the SC group (20.0%). This feasibility study has demonstrated that it is possible to recruit patients to a study of GDFT following liver transplantation and deliver the intervention in a critical care setting.

**O-121: Perioperative fluid management strategies and postoperative outcomes in liver transplantation: a systematic review.**

***Francois Carrier, Montreal, Canada***

Liver transplant (LT) recipients suffer many complications and fluid management is an important aspect of perioperative care. A systematic review was performed to assess the effects of restrictive perioperative fluid management strategies compared to liberal ones on postoperative outcomes.The primary outcome was the incidence of acute kidney injury (AKI), with secondary outcomes being bleeding, mortality and other postoperative complications. 7 RCTs and 29 observational studies were included. Data from RCTs and cohort studies suggested that the use of restrictive fluid management strategies did not affect the incidence of AKI or mortality. In restricted fluid patients, fewer pulmonary complications reduced duration of mechanical ventilation (mean difference = -13.04 hours) and reduced blood loss (-1.29 liters) This finding was observed with a low or very low level of certainty. No effect on graft or non-pulmonary infectious complications was observed. More research is required in this area regarding optimal fluid manangement in LT.

**O-122: Thromboelastography demonstrates significant hypercoagulability in patients undergoing right donor hepatectomy-a prospective single center analysis.**

***Anupam Raj, New Delhi, India***

Lack ofavailability of deceased donors has led to a rise in living donor liver transplantation (LDLT). Preventing post-operative complications for donors is a major concern in LDLT, specifically DVT. This study attempted to show that TEG done on liver donors would demonstrate hypercoagulability. 80 patients were enrolled in the study. TEG analysis was done a day prior to surgery and POD #1,3,5 and 7.. Postoperative blood counts, liver function tests, and INR were also analyzed. All patients were hypercoagulable at postoperative day POD #1 and 3. 98.8 % of patients were hypercoagulable in POD# 5 and 6. These TEG findings were despite anincreased PT INR and decreased platelet counts.There were no DVTs noted in alll patients. TEG monitoring showed significant hypercoagulability in all patients who underwent right donor hepatectomies in the study, so thromboprophylaxis is recommended.

***O*-123: Predicting acute kidney injury after orthotopic liver transplantation using machine learning.**

***Andrew Bishara, San Francisco, United States***

In patients undergoing orthotopic liver transplantation (OLT), the incidence of acute kidney injury (AKI) is up to 60%. A Gradient Boosting Machine (GBM) is a form of machine learning that uses ensemble decision trees and builds a model. The aim of this project was to evaluate the use of GBMs to accurately predict AKI after OLT. 745 adult patients' records who underwent OLT at UCSF were retrospectively reviewed with 904 variables assessed. Data was included until the end of surgery defined as “anesthesia stop.” AKI was defined as either stage 2 or 3 kidney injury according to the International Club of Ascites 2015 criteria modified to 48 hours postoperatively. The data were normalized and separated into training (64%), validation (16%), and test sets (20%). The GBM performed better than logistic regression, random forest, and fully connected deep neural network on the validation set. Overall incidence of AKI ≥ Stage 2 was 33.7%. We achieved a test accuracy of 75.84% of predicting AKI ≥ Stage 2 and a ROC-AUC of 0.800 on the test set. Machine learning can be used on perioperative data to predict postoperative outcomes.

**LB O-014 - Increasing trans-hepatic caval pressure gradient is associated with acute kidney injury after liver transplantation, irrespective of surgical technique**

***Michael Spiro, Royal Free Hospital, United Kingdom***

Despite many years of research there remains no consensus regarding the optimal surgical implantation technique to reduce postoperative AKI. The piggyback technique has multiple attractive theoretical physiological benefits due to improved anhepatic caval blood flow, better hemodynamic stability and reduced distal venous engorgement , yet renal benefits have not been consistently demonstrated in trials. This study approached this question from a different angle, looking at the hemodynamic disturbance caused by the clamp rather than just by surgical technique. They measured the trans-caval anhepatic venous gradient [inferior vena caval pressure (as measured via a femoral line) minus central venous pressure (measured via a right internal jugular line)], and explored the influence on postoperative renal failure. 115 patients were enrolled, with a primary outcome of Acute Kidney Injury Network (AKIN) grade ≥2 AKI at 72 hours post transplant. Mean anhepatic caval pressure gradients were measured. They found a straight line correlation showing that increased venous pressure was associated with an increased incidence of renal failure at 72 hours post OLT in an almost linear fashion, with higher pressures increasing the risk of severe renal failure (OR 1.11, p=0.01).They expected a high trans-caval pressure gradient in cava replacement group, but interestingly they observed a huge range of pressure gradients in the piggyback group, frequently not dissimilar to a full caval cross clamp. This demonstrates the great heterogeneity of venous obstruction depending on positioning of the Satinsky clamp. They proposed that this a potentially modifiable risk factor for AKI. Measuring the gradient allows feedback to the surgeon of the degree of venous obstruction caused and potentially could lead to clamp repositioning. Anhepatic trans-caval pressure gradient correlated linearly with severe (AKIN ≥2 at 72 hours) AKI post transplant.

**Parallel Session: Anaesthesia and Critical Care I/II**: Perioperative Challenges and Current Controversies

**NASH – potential perioperative problems**

***Dmitri Bezinover, Hershey, United States***

Liver transplantation related to NASH is increasing rapidly and is expected to be a leading indication within next 5 years. NAFLD is the hepatic manifestation of the metabolic syndrome characterized by liver steatosis with mild inflammation and the absence of fibrosis. There are multiple factors involved in the etiology, not just obesity. NAFLD may progress to biopsy proven NASH in approximately 10-20% of cases, with 26% of these progressing on to cirrhosis. To progress to NASH requires another trigger other than just inflammation, which is yet to be fully understood. NASH is associated with a higher level of inflammation and steatosis with accompanying fibrosis and scarring. Patients with NASH frequently represent a cohort who may be older, female, diabetic and have renal dysfunction. It is associated with increased perioperative cardiac events due to ischaemic heart disease, left ventricular hypertrophy and arrhythmias. Patients with NASH are particularly prone to atrial fibrillation and ventricular tachycardia, possibly due to autonomic dysfunction associated with this syndrome. In general the 1, 3 and 5 year survival in NASH is similar to other transplant indications, but with more frequent cardiac events than observed in other etiologies. Patients with NASH were more likely to wait longer for a transplant or die on the waiting list. There is currently no consensus regarding different screening for cardiovascular disease or specific anaesthetic management techniques of these patients intra-operatively. There is a subset of patients with particular risk: Age >60, BMI >30, hypertension and diabetes who may have a 1 year mortality of 50%. Patients with high risk NASH were 24% more likely to die awaiting transplant and 14% more likely to die post operatively. NASH is associated with an increased risk of venous thromboembolism and portal vein thrombosis. This hypercoagulability may cause inflammation with can help drive NASH to NASH cirrhosis. NASH is related to HCC in up to 29% of cases due to similar risk factors, including the metabolic syndrome. NASH is also associated with renal dysfunction and occasionally require a simultaneous liver-kidney transplant. There is an increased prevalence of steatotic grafts. A fatty donor organ is associated with primary non-function, delayed function, increased ICU and hospital length of stay. It is important to balance the risk of a steatotic graft with those of recipient (using the UNOS BAR score). The various machine perfusion techniques, cold or normothermic, may improve quality of steatotic grafts, allow evaluation of the graft and potentially expand the donor pool. NASH is an independent risk factor for cardiovascular events and arrhythmias. High risk NASH may need more in depth work up and cautious perioperative management.

**An evidence-based review of TEG/ROTEM guided coagulation management**

***Antoni Sabate, Barcelona, Spain***

It is well established in the literature that cirrhosis is a state of rebalanced coagulation. Coagulation management is a key determinant in transfusion amounts in liver transplantation. The concept of viscoelastic-guided blood product management involves several important components: 1) correct hemostatic drug/product, 2) product given at the right time, 3) avoiding inappropriate transfusion, 4) exclude reasons for bleeding. Some limitations of ROTEM include: 1) late fibrinolysis takes 30 minutes to be detected, 2) platelet and thrombomodulin function is not adequately assessed, 3) there will be no clot formation in hyperfibrinolysis and hypofibrinogenemia. There is significant data that ROTEM can be utilized as a predictor of bleeding during liver transplantation, as well as show degree of hypercoagulability.

**Extracorporeal liver support in ALF and ACLF**

***Constantine Karvellas, Edmonton, Canada***

It has been described that liver injury pathologically varies in between acute on chronic liver failure (ACLF) and acute liver injury (ALI). The rational for the usage of extracorporeal liver support (ELS) includes reversal of hepatic encephalopathy as well cerebral edema, improvement in hemodynamics and hepatorenal syndrome, and being a bridge to liver transplantation or recovery. Common forms of ELS include albumin dialysis via the MARS circuit, plasma separation/exchange via the Prometheus circuit, or ELAD/bioartificial liver. Only plasma exchange in acute liver failure has been shown to show a survival benefit. [[1]](#footnote-1) While significant uncertainty exists on patient selection and timing, ELS devices will continue to play a prominent role in the future.

**Transplanting a DCD-liver: perioperative challenges**

***Annabel Blasi, Barcelona (Spain****)*

DCD liver transplants are traditionally at higher risk for PNF and biliary complications. DCD liver grafts can either be uncontrolled or controlled, with both being suboptimal grafts due to the degree of warm ischemia. In the presenter's center, the graft is placed on a NECMO circuit for evaluation for potential normothermic regional perfusion. (NRP) NRP is essential in uncontrolled DCD (uDCD), and is optional, but useful in controlled DCD. Data comparing uDCD and DBD shows higher transfusion requirements and higher incidence of postreperfusion syndrome in uDCD recipients.[[2]](#footnote-2) However, in controlled DCD with NRP versus DBD grafts, the transfusion requirements and incidence of PRS was similar at the same center. It is felt that NRP may facilitate the management of DCD grafts, however further research is needed.

**Treatment and prophylaxis of pre- and postoperative thrombosis**

***Marco Senzolo, Padua, Italy***

Spontaneous bleeding and thrombotic complications have different incidence rates depending on the severity of liver disease. When looking at deep vein thrombosis and venous thromboembolism, studies have shown PTT and hypoalbuminemia to be predictive, as well as the presence of HCC. The Padua score has been shown to be predictive of DVT events in cirrhotics, and several studies looking at thromboprophylaxis in this patient population have shown its benefit, however patient selection is difficult. There is no consensus on the optimal anticoagulation regiment for the treatment of DVT in cirrhotic patients. When looking at portal vein thrombosis (PVT), the incidence ranges from 7.4% to 27%. PVT has been associated with worse outcomes after liver transplantation. Various regiments in preoperative management of PVT have been described and anticoagulation in some form is recommended for a period of time. For these patients, the incidence of major bleeding complications is low. Patients with PVT preoperatively should be considered for postoperative anticoagulation, as well.

**Quality Assurance and Performance in Liver Transplantation**

**Beyond patient and graft survival: How do we know that we are any good?**

***Ryutaro Hirose, San Francisco, USA***

"Without data, your just another person with an opinion," was the quote by W. Edwards Deming that defined this lecture. Quality measures are a critical portion to any surgical program and in terms of liver transplant, must cover the entire spectrum of transplant care. (Pre-transplant, organ offers accepted/declined, waitlist mortality, intraoperative phase, postoperative phase, early post-discharge, and long term outcomes) The TRANSIP/NSQIP Transplant program will hopefully create a means for programs to assess outcomes in real time and to keep improving over the long-term.

**ERAS for Liver Transplantation**

***Stuart McCluskey, Toronto, Canada***

Enhanced Recovery after Surgery is a well-supported concept for various surgical subspecialties, however it has not been studied in liver transplantation. (ERAL) When looking for evidence based recommendations, the conclusions that have been drawn include that preoperative assessments are similar and defined at most institutions; in intraoperative management, the only area that has some degree of consensus in studies is coagulation management, and in postoperative care, early extubation is supported significantly by numerous papers. ERAL can also be adapted to research in liver transplantation, specifically when looking at AKI. The key to an effective ERAS protocol is ensuring it is evidence based, always attempting to improve, and that it is reviewed by content experts.

**Re-weight the value of transplantation- the recipient benefit**

***Giuliano Testa, Dallas, USA***

Today the true benefit to the patient is not short-term survival. Organ shortages can be ameliorated by the use of extended criteria organs, DCD livers (although the safe limits for the usage of these organs is unclear) and live donor transplantation. Listing must be done for the patient’s benefit rather than the benefits of the institution and we must list the patients who will really benefit from the transplant, listing early where possible. Consideration should be given to “liberate from the list” with organs being allocated to the center. This talk highlighted the need to go beyond MELD to identify the patients who will really benefit from liver transplantation. Consideration should be given to additional factors, such as extra-hepatic organ failures, frailty, futility and donor risk index. There is a need to align the patient’s needs and the transplantation system. Outcome metrics should trump the patient’s request for liver transplantation. It is important, when possible, to list and transplant patients earlier and avoid transplantation of patients with a poor or “hopeless” prognosis. There are prediction tools that can assist with this: a score >8 on “The futility Risk Score” indicates a less than 50% chance of long-term graft survival. The true benefit is a combination of short waiting list time, a complication free procedure with rapid recovery and resumption of normal QOL and long-term survival without secondary organ failure. We should be aiming for long-term survival >10 years. This goal is limited by organ shortages as well as listing and allocation practices.

**Re-weight the value of transplantation- the donor benefit**

***Hiroto Egawa, Tokyo, Japan***

This presentation summarized how to increase live donation benefits. For patients worked up as donors, there is a psychological benefit in those that go on to donate. A detailed assessment must be made to ensure patient safety. To increase success we should be less invasive and expand the donor acceptability rate as well as caring for the patient’s physical and psychological health. Barriers to donation include, donor comorbidities, psychological, immunological and ethical considerations along with the risk of disease transmission in some settings (for example hepatitis C). The barriers to maximizing successful donor benefit include size mismatch and the invasiveness of surgery. Left lobe donation reduces donor stress and if possible procurement should be via a small incision facilitated by laparoscopic surgery. Less invasive surgery results in less pain, early recovery and return to work. A thorough risk assessment must be performed to increase donor safety. Absolute contraindications include malignancy, active infection, asthma, ischemic heart disease and pulmonary fibrosis. Relative contraindications include hypertension, diabetes and mental health issues. The donor must understand the risks and benefits and make an informed decision. Careful assessment of the residual volume for donors must be made and this varies with age. Liver function deteriorates with age, however several studies show age of donor did not alter outcome, but this view is changing. The conservative safe zone is >30% residual volume for donors aged <50, and >35% for aged 50-60 year donors undergoing right hepatectomy. A clinical case was discussed to highlight complexities of decision-making in LDLT and the need for a robust plan. The donor was a patient with multiple relative contraindications, including hypertension, mild steatosis, raised BMI and preoperative anemia. Intraoperatively there was a change of surgical plan to harvest the graft along with the middle hepatic vein and a lower residual volume (26% - lower than the planned 37% without the MHV). Post operatively on the ICU the donor developed reverse portal vein flow, severe liver dysfunction requiring liver transplantation from which the patient failed to recover. A diagnosis of NASH was made on the explanted graft, which was an uncommon diagnosis in Japan at the time. Key questions to ask yourself include: Is this transplant necessary? Is the donor safe? Are you sure of safety for the entire life of the patients? Are you ready for any comorbidity of the donor? Is this transplant for the patient and not your reputation?

**The role of multidisciplinary care**

***Kyung-Suk Suh, Seoul, Republic of Korea***

It has been shown that multidisciplinary teams improve outcomes in various medical and surgical subspecialties. At this center that has performed over 2,000 liver transplants, their multidisciplinary approach is described. There is a standardized preoperative protocol, pre-liver transplant conference meeting, donor evaluation with the radiologist for assessment of biliary system and liver fat quanitifcation, psychiatric evaluation, immunologist consult, and hepatology evaluation with focus on HCC. In the postoperative period, there is multidisciplinary care in the ICU with the intensivist, rehab specialist, and nutrition, as well availability of GI and pathology for immediate management of biliary complications, and assessment for rejection, respectively. This approach has allowed the most optimal management of patients.

1. [↑](#footnote-ref-1)
2. [↑](#footnote-ref-2)