**Pediatrics**

**by Ashwin Rammohan and Irene Scalera**

**Paediatric Session I: Liver Transplantation for Children in the 21st Century – Right Recipient, Right Donor**

**Expanding Indications for Pediatric LT: How to identify the need?**

 ***John Bucavalas, New York, United States***

The aim of the talk was to highlight the need to develop a framework for pediatric LT indications. The broad framework for indications of PLT are to improve survival, remove future risk and to improve the QOL. There needs to be balance between the potential benefit of transplant being balanced against the risks of transplant and the availability of organs.

**Saving livers whilst saving lives in advanced hepatoblastoma: extended resection vs. liver transplantation**

***Greg Tiao, Cincinnati, United States***

The topic of the talk was changed to include LT in challenging cohorts of hepatoblastoma. Hepatoblastoma have 80-90% survival, and are the most common childhood tumours. 60% of these are unresectable at diagnosis and will need neoadjuvant chemotherapy, of which 20% will remain unresectable. Current transplant indications include: PRETEXT 4 tumours (solitary or multifocal), and central tumours involving the hilum or hepatic veins. Treatment for those with extrahepatic disease include induction chemotherapy followed by resection or transplant in the absence of extrahepatic disease. When pulmonary metastases do not clear with chemotherapy, pulmonary resection is recommended following induction chemotherapy. Navigation surgery based on injection of indocyanin green helps pick out extrahepatic metastatic disease, enabling a thorough resection. As compared to previously available data, which suggested rescue transplant following primary resection had poorer outcomes; the gap is narrowing with 86% survival for primary Tx and 75% for rescue LTx. (Trobaugh Loatrio et al, Semeraro et al.) In the presence of >40% viable tumour cells in post-surgery specimen histopathology, adjuvant chemotherapy has to be altered as it means the tumour has not become resistant to chemotherapy.

**The agelessness of frailty in liver transplantation**

***Binitha Kamath, Toronto, Canada***

Frailty is defined as the biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems and causing vulnerability to adverse outcomes. Sarcopenia remains the biological measure of frailty. There is no data on the effect of frailty in children, most are extrapolated from adult studies. Adult frailty, as objectively measured using the Fried Frailty Index strongly predicts waitlist mortality and post-transplant outcomes. A modified paediatric frailty index has been proposed, to measure frailty in children >5 years of age. Measuring weakness, slowness, exhaustion, shrinkage and diminished physical activity. Ongoing studies are trying to assess if it predicts outcomes in children.

**Expanding the donor pool**

***Paolo Muiesan, New York, Birmingham, United Kingdom***

The donor pool can be expanded in children in many ways. Political ways would include increasing cadaveric donation, promoting splitting of organs, expanding living donations and maximising altruistic donations for children. Technical methods to increase the number of available organs would include expanding and utilising the “marginal donor” pool, domino transplants and utilisation of machine perfusion. According to the ELITA data 2010, the donor age for split grafts can be extended to 50 years of age. Neonatal donors lead to poorer outcomes because of an immature synthetic function, a higher incidence of HAT due to higher resistance, and a higher risk of SFSS.

**O-130 Quantitative immunophenotyping of liver biopsies predicts successful immunosuppression withdrawal in pediatric LT recipients**

***John Bucuvalas, New York, United States***

This was a multicenter (12 centres) clinical trial looking at the efficacy of immunosuppression (IS) withdrawal, defined as operational tolerance (OT) in children. OT was defined as normal liver enzymes, and stable liver histology 1 year after the last dose of IS. Of the 3000 post LT recipients who were screened, 88 met clinical (Normal LFT, no rejection in the past 2 years, non-viral, non-autoimmune etiology) and biopsy (no portal, peri-venular inflammation, absence of bile duct changes, fibrosis or arteriopathy) criteria for withdrawing IS, 33 achieved OT. Baseline demographic, clinical or serological features did not predict outcomes. Presence of mild portal inflammation, lobular MHC II+/CD45+ pairs, MAC387, CD8 patterns and development of de-novo donor specific antibody (DSA) predicted failure of IS withdrawal. Interestingly, those who failed OT, went back on their original dose IS, did not need higher IS. Those who had rejection needed to be pulsed.

**O-131 Next gen sequencing reveals a role of MMP7 in the liver in Biliary atresia**

***Priya Ramachandran, Chennai, India***

At present, 50% of those who undergo Kasai portoenterostomy (KPE) will eventually need a LT. Clinical, biochemical and histological factors do not correlate with outcomes of KPE. Biomarkers – matrix metalloproteinase 7 (MMP7) was noted to be upregulated in failed KPE, and predicted the likelihood of progression of liver disease.

**O-132 Silent allograft fibrosis in 10-year post-transplantation histology of pediatric liver transplantation: is it really silent?**

***Seohee Lee, Seoul, Korea, Republic of***

Korean study of 66 clinically stable children undergoing 10-year protocol biopsy. 47% of the biopsies showed METAVIR fibrosis stage ≥1. Risk factors for long term fibrosis included previous episode of rejection, mean total bilirubin ≥1.0 mg/dl, and > 3 events with aminotransferases >50U/L.

**O-133 - Liver allograft fibrosis after pediatric liver transplantation: risk factors and tools for early detection**

***Roberta Angelico, Rome, Italy***

Italian study of 200 children who underwent periodic protocol biopsies up to 5 years post-transplant. 82% had some form fibrosis (METAVIR stage ≥1) on their biopsy. On multivariate analysis, only risk factor for fibrosis progression was post LT biliary complications.

**O-134 - Paediatric domino liver transplant from paediatric multi visceral transplant recipient**

***Aamir Nawaz, London, United Kingdom***

The recipient was suffering from intestinal neuropathic dysmotility with a normal liver (on appearance, function and histology). This liver was domino transplanted into a cholestatic liver disease recipient.

**O-135 - Pediatric liver transplantation in mainland China**

***Feng Xue, Shanghai, China***

There were 731 re-transplants of the 8188 post-LT children on the SRTR database. Prognostic scoring tool was formulated based on the significant risk factors – age, primary diagnosis, survival time of the first graft, graft type, donor age>40 years. Scoring tool risks were stratified into low (0-4), medium (5-7), high (8+) points and internally validated.

**O-137 - Long-term neurodevelopmental outcomes in children with biliary atresia**

***Lyan Hendrika Rodijk, Groningen, Netherlands***

Forty-six children with a median age of 11 years were included in the study, of whom 78% had undergone a LT. Risk factors for impaired neurodevelopment included intracranial haemorrhage, liver failure, growth failure, surgery and multiple admissions. A higher fraction of school-aged children with biliary atresia had neurodevelopmental impairments compared to the normal population, especially with regards to motor skills. There was no difference in impairment between those who underwent a transplant and those who did not. Neurodevelopmental intervention programs need to assess whether these long term outcomes can be improved.

**O-138 - Study on the risk factors of portal vein stenosis after pediatric liver transplantation**

***Yin Chao, Beijing, China***

Risk factors for PVS on multivariate analysis included a recipient portal vein diameter of ≤4 mm and the use of cold preserved graft veins.

**Paediatric session II: The Journey towards the vision of “one transplant for life”**

**Histological findings in late paediatric post-transplant biopsies: what the pathologist sees that we don’t see**

***Stefan Hübscher, Birmingham, United Kingdom***

During the paediatric session Stefan Hübscher highlighted the presence of histological abnormalities in late post-transplant biopsies in paediatric patients. These are indeed reported even with normal graft function and normal- or near-normal liver function tests. Most common findings are inflammation and fibrosis, the prevalence of which increases with time. Most cases of otherwise unexplained graft inflammation and fibrosis probably reflect alloimmune injury, which may involve both T cell-mediated and antibody-mediated mechanisms. Further studies are required to address the pathogenesis and natural history of graft fibrosis, novel biomarkers of graft injury and treatment strategies to prevent fibrosis progression.

**Subclinical chronic graft injury in very stable pediatric liver transplant recipients: What the clinician has to deal with?**

***Timucin Taner, Rochester, United States***

Timucin Taner in his talk emphasised that an untreated inflammation would ultimately become fibrosis. As there is a correlation between the presence of donor specific antibodies and fibrosis, if the biopsy shows fibrosis, it is necessary increase the immunosuppression (IS) level. The inflammation is reversible with an high level of IS, but fibrosis might be not adjustable. The only way to detect both injuries is a protocol biopsy.

**The challenges with TOO MUCH immunosuppression: Extra-hepatic diseases in liver transplanted children and adolescents – cardiovascular, PTLD, renal**

***Ulrich Baumann, Hannover, Germany***

Increasing immunosuppression is “not the key to open every door”. It is well known that too much immunosuppression can cause toxic effects, and might contribute to morbidity and mortality after paediatric transplantation. As Baumann reminded, renal impairment, cardio vascular disease, PTLD and neurotoxicity are frequent in these patients. Current protocols are mainly based on clinical experience and therapeutic drug monitoring.

**Transition from pediatric to adult care after pediatric liver transplantation: What do adult care teams need from the pediatric teams?**

***Marianne Samyn, London, United Kingdom***

Marianne Samyn drew attention to the transition clinic, speaking about what the adult care teams need from the paediatric team. Transition can be defined as a purposeful, planned process that addresses the medical, psychosocial and educational/vocational needs of adolescents and young adults with chronic disease as they move from child-centred to adult-oriented health care system. For these patients key components are: proactive approach, treating the young person as a young person. Communication should involve not only family, but also friends, and partners. Teenagers are the most misunderstood people as they are treated as a child but they are expected to behave as adults. The service needs to have an holistic approach to address their psychosocial, educational and vocational needs.