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Intention to split policy

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MINI ABSTRACT:

This is a retrospective study describing the outcomes of split liver transplantation and discussing a strategy for effective use of ex-situ split technique in a combined adult and pediatric liver transplant center

ABSTRACT:

Objective: The primary aim of this study is to evaluate the role of Split liver transplantation (SLT) in a combined paediatric and adult liver transplant (LT) centre. The secondary aim is to reflect on our clinical practice and discuss strategies to build a successful split program using an “intention to split policy”.

Background: SLT is an established procedure to expand the organ pool and reduce wait list mortality, however technical and logistic issues are limiting factors.

Methods: Prospectively collected data and outcomes of SLT procedures performed between November 1992 & March 2014 were analysed retrospectively. To assess the effect of standardisation and learning curve, the experience was divided into two time periods.

Results: Out of 3449 LT procedures performed, 516 (15%) were SLT. The recipients included 266 children (290 grafts; 56%) and 212 adults (226 grafts; 44%). The median donor age was 25 (7-63 years) and the median weight was 70 (22-111 kg). The cold and warm ischemic times improved significantly during the second period (SP) (2001-2014). With experience, there was a significant reduction in the biliary complications for both grafts. The introduction of “intention to split policy” resulted in a significantly increased usage of SLT. There was no mortality on the paediatric wait list for last 4 years. Over the last decade 65% of our paediatric transplants were SLT. The overall 1, 5, 10-year patient and graft survival of left graft recipients was 91%, 90%, 89% and 90%, 87%, 86%. For right grafts it was 87%, 82%, 81% and 82%, 81%, 79% respectively.

Conclusion: SLT is an effective surgical strategy to meet the demands in a combined adult and

paediatric transplant center. Good outcomes can be achieved with a standardised technique.

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Intention to split policy: A successful strategy in a combined pediatric and adult liver transplant center

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Running title: Effective use of split liver transplantation

INTRODUCTION:

Split liver transplantation technique was described in the early 90's as a potential tool to increase the donor organ pool. Early experiences were disappointing due to the use of SLT in extremely unwell recipients combined with the learning curve effect of a new procedure¹. Advances in surgical techniques and a better understanding of recipient selection led to progression of SLT as one of the strategies to cope with the growing demands of liver transplantation. In the pediatric population, SLT was seen as a natural evolution after reduced size liver transplantation, allowing two recipients to benefit and minimising wastage^{2,3}.

Donor livers are a precious resource. Effective utilisation relies on a careful decision making process by the multi-disciplinary teams. In modern clinical practice there is increasing emphasis on achieving good long term outcomes coupled with the increasing pressures to utilise marginal organs⁴. SLT traditionally involves splitting the liver into a smaller left lateral segment (Seg 2&3) ideally suited for a child and the larger right trisegmental remnant for an adult or large child. The size of the pediatric donor pool has decreased over the last decade across Europe (ELTR registry), and the few pediatric donor livers may be better used for children awaiting multivisceral transplantation. SLT has resulted in a reduction of waiting list mortality for pediatric population who are disadvantaged due to lack of size matched donors, and reduces the pressure on parents to become live donors⁵.

The UNOS registry data and few other institutional series demonstrated patient and graft survival outcomes similar to WLT^{6,7}. However, wider practice of SLT is curtailed by a presumed higher vascular and biliary complication rate. Further, strict donor criteria, technical expertise in both liver transplantation and hepatobiliary surgery, logistics and manpower to minimise ischaemia and perform simultaneous transplants of both SLT grafts in

critical volumes are important factors in the delivery of a successful SLT program.

The outcomes of SLT have largely been in favour of pediatric population⁸. First, it had limited impact on the adult waiting list mortality, secondly there were concerns regarding the increased complications and quality of the extended right graft^{9,10}. At the other end of the spectrum, some centers reported acceptable outcomes using split techniques to obtain two hemiliver grafts for two adults, to cope with the increasing demand of adult liver transplantation, but this practice is still very limited¹¹.

The primary aim of this study is to evaluate the effect of SLT on waitlist mortality and delivery of transplant service in a combined pediatric and adult liver transplant center. The secondary aim is to reflect on our clinical practice with standardised split technique and discuss strategies to build a successful split program.

METHODS :

The first SLT was performed at our center in 1992. The use of split grafts was sporadic from 1992 till 1998. In 1998 the pediatric transplant program was moved to the Children's hospital allowing simultaneous SLT procedures. This led to development of an "intention to split policy" to obtain two suitable grafts from any donor that matched the inclusion criteria (**Table 1**). A national policy for splitting was implemented by the UK Liver Advisory Group in 2005. All SLT procedures performed between November 1992 and March 2014 were included in the study. Only donation after brain death (DBD) donors were considered for liver splitting. Data on split surgical technique, donor and graft characteristics, ischemic times, technical complications and survival were collected prospectively and analysed retrospectively.

Technical complications were categorized into biliary and vascular. Hepatic artery thrombosis (HAT) was defined as “*Early*” or E-HAT when this occurred within the first 21 days after transplantation (LAG). Biliary complications diagnosed subsequent to the diagnosis of HAT were not treated as independent events. Biliary tract complications were classed as leak or stricture. Bile leaks were categorized by site of leak as non-anastomotic (liver cut surface) or anastomotic. A non-anastomotic stricture was defined as the diffuse intra-hepatic stricture after liver transplantation in the presence of a patent hepatic artery. The use of duct to duct anastomosis with T-tube drainage or use of a Roux en Y hepaticojejunostomy became routine in RL at our center from June 2001. The end point for patient follow up was the date of last clinic visit or death, and for each graft it was re-transplantation or death. We divided our experience into a first period (FP), from 1992 till 2000 which represents the initial part of our learning curve. The second period (SP), from 2001 till 2014 when the split program was standardised and well established.

Recipient selection: Split grafts were preferred for all pediatric patients and there was no specific selection criteria. However, to minimise ischemic time in adult recipients of RG we favoured recipients who were; stable, no previous upper abdominal surgery, no portal vein thrombus and less severe disease.

Technical details

Almost all of the SLT procedures with few exceptions were performed ex-vivo in an ice cold bath. The SLT technique was either a “classical” split to achieve a right extended graft (segments I, IV-VIII) or variants resecting either segment 1 or IV or both (segments 1,5-8 or segments 5-8) and a left lateral graft (segments II and III). Very rarely, the liver was split along the line of Cantlie resulting in one right (segment V-VIII) and one left (segments I-IV)

hemi-liver to supply either two adult recipients or one adult and one big pediatric recipient³⁹. Our objective was to produce satisfactory grafts for two recipients. Splitting was performed at the Children's Hospital at least an hour after immersion in ice and before the start of recipient procedures to allow the liver to reach cytoprotective temperature of 4°C. After performing routine bench cholangiograms, the structures at porta hepatis were explored, dissected and probed to identify the anatomy of portal vein (PV), hepatic artery (HA), and biliary tree. If the graft anatomy was favourable anatomy for the split, both recipients were sent for transplantation. Otherwise the full graft was used for an adult recipient or rarely reduced for a pediatric recipient. Unfavourable anatomy relates mainly to multiple arteries to both future grafts that would require more than one arterial reconstruction – eg: two left and two right arteries coming off the main hepatic artery, with or without an additional accessory left hepatic artery from left gastric or accessory right hepatic artery from superior mesenteric artery. Anomalies of the hepatic venous system (eg separate segment 2 and 3 hepatic veins) or multiple bile ducts draining segments 2 and 3 were not considered contraindications to splitting.

Hepatic Artery allocation: The diameter of main hepatic arterial branches (left and right) supplying the respective grafts was assessed and the common hepatic artery/cealic axis allocated to the graft bearing smaller hepatic arterial inflow. The main trunk of the HA was usually allocated to the left graft (LG). If a reconstruction was required for the right graft (RG), then the HA proper was cut below gastroduodenal artery and the distal graft common HA was anastomosed on the bench to the right graft hepatic artery..

Portal Vein (PV) Allocation:

The horizontal portion of the left PV was routinely mobilised for length, ligating and dividing small branches to segment 1 and 4, after which it was divided flush to the main portal vein. This was allocated to RG and the left PV orifice was closed transversely with continuous 5/0 or 6/0 prolene.

Hepatic venous outflow allocation:

The suprahepatic IVC was inspected and the hepatic vein orifices were probed to identify anomalous drainage, especially abnormal Segment 3 vein draining into the middle hepatic vein. The IVC was allocated to the RG, the left hepatic vein orifice was closed transversely or with a donor iliac vein patch to prevent outflow stenosis.

Biliary Allocation:

Routine bench cholangiography was performed at the beginning of the procedure after ligating the cystic duct and placing markers at the level of the falciform ligament and at base of the right pedicle(Supplemental data- Figure 1a). Common bile duct was given to the RL and the left duct was divided away from the porta hepatis without any dissection of the main duct from the right hepatic artery.

Parenchymal transection:

The line of parenchymal division was 0.5 to 1cm to the right of the falciform ligament. Hepatic parenchyma was divided using bipolar forceps with crushing technique, all small vessels and bile ducts seen were ligated. In the recent years the integrated bipolar and ultrasonic device was used for parenchymal transection.

Statistical analysis

Mean, median, standard deviation and range summarizes data distribution. All means were expressed as mean \pm standard deviation. Comparisons of continuous measures were assessed by the *t* test for parametric data. Categorical variables were analyzed by the X^2 test. Survivals were estimated by Kaplan-Meier method and compared by Cox regression analysis. Statistical significance is assumed for $p < 0.05$

RESULTS:

During the study period, 2725 adult and 724 pediatric liver transplantation procedures were performed. Of them, 516 were deceased SLT. 219 livers were split at the authors center and 78 grafts were imported from other centers. 66 donors were outside the splitting criteria due to either > 40 years of age or >90 Kg body weight. All but 4 split procedures were ex-situ, the donor characteristics are summarized in the supplemental data as Table 2a. Majority were classical splits producing an extended right lobe for an adult or large pediatric recipient and a left lateral segment for a child. The resultant grafts and their distribution is shown in the supplemental data as Table 3a.

Two hundred and ninety grafts were implanted in children, the median graft-to-recipient body weight ratio (GRWR) was 2.5 (Range 0.89-7.3). Twenty four recipients met criteria for super-urgent transplantation (Status 1A) and the median time waited on the transplant list for acute liver failure was 5 days (0-22) and 59 days (1-636) for chronic liver disease. Twenty four received SLT for re-transplantation, 4 of them were third and one fourth transplant procedure. Two hundred and twenty six grafts were implanted in adult recipients, the median GRWR was 0.93 (Range 0.86-1.9). Five recipients met criteria for super-urgent transplantation. There were 11 retransplant procedures, eight for WLT graft failure and three for failed first SLT graft. One patient received a split graft as a fourth transplant. The mean \pm

SD MELD of the adult recipients was 13 ± 3.5 and the indications for transplantation are listed in the supplemental data as table 4a.

LEFT GRAFTS:

All left graft (LG) recipients, except three were of pediatric age group. The median graft weight was 304 grams (range 178-518 grams). The technical complications between the first and second periods of our experience are summarized in Table 1.

Hepatic artery thrombosis (HAT) (7%) : The majority (n=16) were early, four had successful revascularization. Nine needed retransplant and six (67%) of these retransplants were performed used split grafts. Three children died with acute HAT.

Portal vein complications (4%): Five recipients had early portal vein thrombosis (PVT), they underwent successful thrombectomy and re-anastomosis. One of the three with late PVT had a meso-*rex* shunt for portal hypertension. Three had late portal vein stenosis and were treated by angioplasty.

Venous outflow obstruction (4%) : All were treated successfully by angioplasty.

Biliary complications (21%): Biliary leaks (BL) were encountered in 35 grafts between 2 and 21 days after SLT, majority were cut surface leaks(74%). Seven needed surgical intervention and the rest underwent image guided drainage. Biliary stricture (BS) was diagnosed in 26, the incidence was significantly high during the FP. 16 underwent radiological interventions with resolution of stricture. 10 required biliary reconstruction after unsuccessful Percutaneous transhepatic cholangiogram (PTC) procedures.

Primary non function(PNF) (4%): Seven, underwent retransplantation and a split graft was used in 6 children.

The cold and warm ischemia times were significantly reduced during the second period of

our transplant program.

Retransplant procedure was performed in 24 patients for late graft failure. At a mean follow-up period of 6.2 years (± 4.5 years), there were 39 deaths (13%). The overall recipient survival at 1-, 5-, and 10-years was 91%, 90%, 89%. The graft survival at the same time points was 90%, 87%, 86%, respectively (Figure 1). Cox regression analysis showed no significant difference in graft survival between FP and SP. SLT evolved as the main source of organs for pediatric transplantation at our center over the last 10 years (Figure 3). There was no wait list mortality in chronic children between 2011-2014 (Figure 4).

RIGHT GRAFTS:

Two hundred and twenty six right grafts (RG) were allocated to 14 children and 212 adults (table 6). The median RLG weight was 1046 gm (range 634-1870) The median age and weight of the pediatric recipients was 14 years (range 13-18) and 43 kg (range 23 – 70) respectively. A total of 139 arterial reconstructions were performed using a jump graft for size mismatch or insufficient length. This was significantly higher during the second period of the program. The technical complications are summarised in Table 2.

HAT (8%) : Nine were early, seven of them were retransplanted and 2 had successful revascularisation procedures, six patients died.

PV (3%) : PV thrombus in 5(2%), of them one was early and treated with surgical thrombectomy. Of the four recipients with a late PVT, 1 died 66 days post transplant and the rest are in follow up. Two (1%) patients with PV stricture were treated with balloon angioplasty.

Biliary (21%) : 34 recipients had a BL (15.7%), the bile leak was from the cut surface in 28(83%), anastomotic site in 4(11%) and from T-tube exit site following its removal in

2(6%). Three cases were treated with a hepaticojejunostomy, the others underwent endoscopic or radiological interventions. Biliary strictures were observed in 13 (6%). All of them underwent ERCP/PTC balloon dilatation, three needed biliary reconstruction.

Venous outflow obstruction (2%) : All had successful image guided angioplasty procedure.

PNF (1%) : All underwent retransplantation.

The mean follow-up was 5.4 years (\pm 3.96 years), there were 59(26%) deaths. Overall recipient and graft survival at 1-, 5-, and 10 years was 87%, 82%, 81% and 82%, 81%, 79% respectively (Figure 1). There was a significant improvement in the graft function during the second period ($P=0.04$) (Figure 2). The graft and patient survival of the right lobe grafts was comparable to WLT, these results were shown in our previous published series (Mourad et al).

SUB-GROUP ANALYSIS OF SPLIT LIVER GRAFTS FROM DONOR OUTSIDE

THE STRICT CRITERIA: With increased experience and volume during the second period of the program, we carefully expanded our selection criteria to include donors who were outside criteria for one variable, especially when the appearance of the graft was satisfactory. A total of 66 such donors were identified from the study cohort, of 62 were split during the second period producing 124 grafts. Of these, 117 were transplanted at our institutes and rest were shared with other centers. The demographics and outcomes are presented in Table 3

The overall percentage of SLT grafts used between 92-98 was 7%, following introduction of “intention to split policy” this increased significantly to 18% ($p= 0.0001$). Over the last decade 65% of our pediatric transplants were performed using split livers.

DISCUSSION :

SLT techniques have evolved and overall outcomes have improved but despite an exponential increase in the discrepancy between donor supply and recipient demand, it remains an infrequently performed procedure^{12,13}. The European Liver Transplant Registry data showed that only 6% of the liver transplant procedures performed till 2013 were cadaveric SLT. Further, split right grafts are classed as marginal and were included in the risk stratification model for liver transplantation such as the Donor Risk Index (DRI)¹⁴.

This series of 516 consecutive ex-situ split transplants culminates 2 decades of experience by the authors center and the evolution of techniques to optimize outcomes. Initial graft function and technical complications after SLT have always been under scrutiny, especially in adult recipients¹⁵. Graft volume is paramount to avoid post operative liver dysfunction or failure. A PNF rate of 4% to 5% has been reported in published series¹⁶⁻¹⁸. In our series we observed 14 cases of PNF (3%), 11 of these grafts were transplanted into pediatric recipients. Proponents for in-situ splitting argue that prolonged cold ischemia by ex-situ split liver splitting can potentially increase the risk for PNF¹⁹. Our experience demonstrated that there is no increased risk of graft loss with the ex-situ technique. Arterial complications are a common cause of early graft failure in SLT recipients. The reported incidence of HAT varies widely, in pediatric split transplants it is reported to be up to 10% to 12.5%²⁰⁻²². In pediatric group there aren't any differences in artery reconstruction and complication between FP and SP. This was different in adult recipients, as most adults received a smaller diameter right hepatic artery for anastomoses. During the FP there was a higher percentage of arterial thrombosis (21%). A combination of technical difficulties, lack of a standardised approach to vascular allocation and bench reconstruction are probable causes. In the SP a significantly higher percentage of arterial reconstructions were undertaken using the common hepatic artery stem,

thereby preventing any size mismatch between the right artery and the interposition graft. The rate of HAT reduced significantly (6%) and this was comparable to our incidence of HAT in WLT(7%). Our policy for arterial division is to retain the main hepatic trunk with the smaller diameter vessels, usually the left hepatic artery. To facilitate transplant procedure and increase acceptance of the RL grafts by adult only transplant centers, we use the size matched common hepatic/coeliac trunk for bench reconstruction and lengthening of right artery. To minimise the risk of HAT we aim not perform more than one arterial reconstruction per split procedure. The complications associated with portal and hepatic vein were comparable to the published experience for both RG and LG^{23,24}. There was no significant difference after overcoming the learning curve.

A high incidence of biliary complications are associated with SLT(18-27%). While bile leak is an expected early complication in the early post-operative period, the late course is complicated by strictures^{25,26}. Our biliary complication rate was 21% and there was no difference between right and left grafts. The higher incidence of biliary complications is a result of partial devascularization of the bile duct during hilar dissection or failure to recognise anatomical variants. Our standard policy is to perform a bench cholangiography to accurately plan the parenchymal and hilar transection plane. The hilar plate is divided at the base of segment 4 and to the left of the caudate with a knife to achieve one or more bile ducts to LLS without skeletonisation of the bile duct. The use of T-tubes for DD anastomosis had no significant benefit in reducing the BL rate in the RL grafts, however it probably had an impact on a reduction in the incidence of BS. An overall reduction in BS was noted in both RL and LL grafts during the SP. This probably is a result of improved splitting technique and reduced cold ischemia time.

The right graft survival improved significantly during the SP. This improvement is probably due to recipient selection, improved post operative management, critical volumes and standardised surgical technique.

Since we adopted the “intention to split” policy, there was a significant increase in SLT (7% to 18%). SLT satisfied more than 65% of the needs of our pediatric waiting reducing the need for WLT or reduced grafts in the last decade. There were no deaths on the pediatric wait list over the last 4 years. Split liver transplantation was used in 8% of our total adult transplant recipients and therefore has a limited impact on their wait list mortality, which runs between 15-20%. At our center the adult donor pool expansion strategy includes wide use of “extended criteria” and DCD grafts.

We used SLT for a variety of indications including ALF and re-transplant procedures mainly in pediatric and also in some adult recipients. The results of our RG show that these grafts are not of inferior quality and perhaps we should re-assess the variables in DRI^{27,28}. In 2003, Broering et al used a match pair analysis to demonstrate that the outcomes of extended right lobe grafts are comparable with WLT. A subsequent study by Fruehauf et al using SRTR/OPTN database concluded that RG can be used safely even in patients with high MELD score^{29,30}. The recent Italian multicenter study results further questioned use of the term “extended criteria grafts” for split livers³¹. Split liver grafts can be used for a wide range of indications in both adult and pediatric recipients. Standardisation of techniques and application of a strict policy to split all suitable livers can result in a better service provision without compromising outcomes³²⁻³⁴. The critical learning points from our experience were achieving continuous critical volumes of split grafts, effective co-ordination between donor/splitting/implanting surgeons, improving technical experience with wider use or bench

arterial reconstructions, standardisation of the parenchymal transection phase, and the ability to perform simultaneous implantation of both grafts to minimise ischemic times. The use of in-situ splitting allows for reduction in cold ischemia and facilitates sharing of the two grafts between centers. Adoption of in-situ techniques may allow expansion of the donor criteria currently utilized for ex-situ splitting.

Living donor liver transplantation is a well established technique, however it cannot meet the demands of a pediatric transplant wait list in the West^{35,36}. There is a need for maximum expansion of the split liver program with the use of deceased adult donors. The European Liver Transplant Registry and the data from NHSBT, UK highlighted that the ideal donors for a liver split are becoming a scarce resource^{37,38}. The presented data and also other recent publications have demonstrated that the strict donor selection criteria proposed could be carefully expanded. With a carefully expanded donor criteria, we were able to obtain 26% more grafts since 2000. As shown by a previous study using donors >40 years of age, as long as the graft appears satisfactory it should be possible to consider DBD donors up to their fifth decade^{39,40}. Along with addressing the shortage of pediatric organs, the “Intention to split” strategy also allows all potential pediatric donors referred to our center be first assessed for a combined liver-intestine or multivisceral donation. This helps to pass on the benefit of reducing the wait list mortality for pediatric combined liver-small bowel or multivisceral transplantation. With adequate supply of organs from SLT, large pediatric donors or pediatric donors without a suitable pediatric recipient could be redirected for adult transplantation.

In conclusion, SLT is a significant surgical achievement in the field of liver transplantation. The ex-situ split technique is safe and can generate organs for use in a wide variety of acute and end stage liver disease in adults and children. With outcomes similar to whole organ

transplants, it is safe to use right lobes in adult recipients. SLT has a potential to meet the demands of pediatric liver transplantation and eliminate the wait list mortality. Further expansion of SLT donor criteria should be considered.

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Figure Legends:

- 1) Table 1: The DBD donor criteria to accept a liver for a split procedure
- 2) Table 2: Demographics and complications compared between the two time periods of the split liver program
- 3) Table 3: Demographics and complications data for split livers obtained from donor's beyond our selection criteria
- 4) Figure 1: Split liver graft survival analysis using Kaplan-Meier curves
- 5) Figure 2: Kaplan-Meier curves demonstrating a significant improvement in the graft function during the second period of the program
- 6) Figure 3: Transplant activity graph in pediatric population showing an increase in the use of split liver grafts
- 7) Figure 4: Pediatric wait list data indicating no mortality for four consecutive years

REFERENCES:

1. Azoulay D, Astarcioglu I, Bismuth H, et al. Split-liver transplantation. The Paul Brousse policy. *Ann Surg*. 1996;224:737–746.
2. Broelsch CE, Emond JC, Whittington PF, et al. Application of reduced size liver transplants as split grafts, auxiliary orthotopic grafts, and living related segmental transplants. *Ann Surg* .1990; 212: 368–375.
3. Mirza DF, Achilleos O, Pirenne J, et al. Encouraging results of split-liver transplantation. *Br J Surg*. 1998; 85: 494-497.
4. Alexander J, Zola J. Expanding the donor pool: use of marginal donors for solid organ transplantation. *Clin Transplant*. 1996;10: 1–19.
5. Broelsch CE, Whittington PF, Emond JC, et al. Liver transplantation in children from living related donors. Surgical techniques and results . *Ann Surg*.1991; 214: 428–39.
6. Busuttil RW, Goss JA. Split liver transplantation. Split liver transplantation. *Ann Surg*.1999; 229: 313–321.
7. Rogiers X, Malago M, Gawad K, et al. In situ splitting of cadaveric livers. The ultimate expansion of a limited donor pool. *Ann Surg*. 1996; 224:331–341.
8. Chardot C, Branchereau S, de Dreuzy O, et al. Pediatric liver transplantation with a split graft: experience at Bicetre. *Eur J Pediatr Surg*. 1999; 9:146–152.
9. Burroughs AK, Sabin CA, Rolles K, et al. Three-month and 12-month mortality after first liver transplant in adults in Europe: predictive models for outcome. *Lancet*. 2006; 367:225–232.
10. Collett D, O'Neill J, Neuberger J. Splitting livers – balancing the gain and the pain. *Transpl Int* . 2008; 21:218–222.

11. Humar A, Ramcharan T, Sielaff TD, et al. Split liver transplantation for two adult recipients: an initial experience. *Am J Transplant.* 2001;4:366-72.
12. Deshpande RR, Bowles MJ, Vilca-Melendez H, et al. Results of split liver transplantation in children. *Ann Surg.* 2002; 236:248–253.
13. Renz JF, Emond JC, et al. Split liver transplantation in the United States: Creation of a national registry and preliminary outcomes. *Ann Surg.* 2004 ; 239:172-81.
14. Feng S, Goodrich NP, Bragg-Gresham JL, et al. Characteristics associated with liver graft failure: the concept of a donor risk index. *Am J Transplant.* 2006; 6:783–790.
15. Maggi U1, De Feo TM, Andorno E, et al. Liver Transplantation and Intestine North Italy Transplant Study Group. Fifteen years and 382 extended right grafts from in situ split livers in a multicenter study: Are these still extended criteria liver grafts? *Liver Transpl.* 2015 ;21:500-11
16. Langnas AN, Marujo WC, Inagaki M, et al. The results of reduced-size liver transplantation, including split livers, in patients with endstage liver disease. *Transplantation.* 1992; 53: 387-391.
17. Goss JA, Shackleton CR, McDiarmid SV, et al. Longterm results of pediatric liver transplantation: an analysis of 569 transplants. *Ann Surg.* 1998; 228:411–420.
18. Ghobrial RM, Yersiz H, Farmer DG, et al. Predictors of survival after In vivo split liver transplantation: analysis of 110 consecutive patients. *Ann Surg.* 2000; 232:312–323.
19. Reyes J, Gerber D, Mazariegos GV, et al. Split-liver transplantation: a comparison of ex vivo and in situ techniques. *J Pediatr Surg .* 2000; 35:283–289.
20. Rela M, Muiesan P, Bhatnagar V, et al. Hepatic artery thrombosis after liver transplantation in children under 5 years of age. *Transplantation.* 1996; 15:1355–1357.

21. Rela M, Vougas V, Muiesan P, et al. Split liver transplantation: King's College Hospital experience. *Ann Surg.* 1998; 227:282–288.
22. Renz JF, Emond JC, Yersiz H, et al. Split-liver transplantation in the United States: Outcomes of a national survey. *Ann Surg.* 2004 ;239:172-81
23. Yersiz H, Renz JF, Farmer DG, et al. One hundred in situ split-liver transplantations: a single-center experience. *Ann Surg.* 2003 ; 238: 496-505.
24. Mabrouk Mourad M, Liossis C, Kumar S, et al. Vasculobiliary complications following adult right lobe split liver transplantation from the perspective of reconstruction techniques. *Liver Transpl.* 2015;21:63-71
25. Chardot C, Candinas D, Mirza D, et al. Biliary complications after pediatric liver transplantation: Birmingham's experience. *Transplant Int.* 1995; 8:133–140.
26. Heffron TG, Emond JC, Whittington PF, et al. Biliary complications in pediatric liver transplantation. A comparison of reduced-size and whole grafts. *Transplantation.* 1992; 53:391–395.
27. Hong JC1, Yersiz H, Farmer DG, et al. Longterm outcomes for whole and segmental liver grafts in adult and pediatric liver transplant recipients: a 10-year comparative analysis of 2,988 cases. *J Am Coll Surg.* 2009; 208:682-9.
28. Merion RM, Rush SH, Dykstra DM, et al. Predicted lifetimes for adult and pediatric split liver versus adult whole liver transplant recipients. *Am J Transplant.* 2004; 4:1792–1797.
29. Nadalin S, Schaffer R, Fruehauf N. Split-liver transplantation in the high-MELD adult patient: are we being too cautious? *Transpl Int.* 2009; 22 :702-6
30. Wilms C, Walter J, Kaptein M, et al. Long-term outcome of split liver transplantation using right extended grafts in adulthood: A matched pair analysis. *Ann Surg.* 2006 ;244 :865-72.

31. Cescon M, Spada M, Colledan M, et al. Feasibility and limits of split liver transplantation from pediatric donors: an Italian multicenter experience. *Ann Surg.* 2006 ;244 :805-14
32. Otte JB, de Ville de Goyet J, Alberti D, et al. The concept and technique of the split liver in clinical transplantation. *Surgery* 1990; 107: 605–12.
33. Noujaim HM1, Gunson B, Mayer DA, et al. Worth continuing doing ex situ liver graft splitting? A single-center analysis. *Am J Transplant.* 2003;3:318-23.
34. Cauley RP1, Vakili K, Fullington N, et al. Deceased-donor split-liver transplantation in adult recipients: is the learning curve over? *J Am Coll Surg.* 2013 ;217 :672-684
35. Otte JB. Is it right to develop living related liver transplantation? Do reduced and split livers not suffice to cover the needs? *Transpl Int.* 1995; 8: 69–73.
36. Slooff MJH. Reduced size liver transplantation, split liver transplantation, and living related liver transplantation in relation to the donor organ shortage . *Transpl Int* 1995; 8:65–8.
37. European Liver Transplant Registry – ELTR data- Available at: <http://www.eltr.org/Donor-data.html>
38. NHS Blood and Transplant - UK Transplant Registry Data. Available at : <http://www.odt.nhs.uk/uk-transplant-registry/data/>
39. Cardillo M, De Fazio N, Pedotti P, et al. Liver Transplantation Working Group Split and whole liver transplantation outcomes: a comparative cohort study. *Liver Transpl.* 2006;12 :402-10.
40. Foster R1, Zimmerman M, Trotter JF. Expanding donor options: marginal, living, and split donors. *Clin Liver Dis.* 2007;11:417-29.

Table 1

Donor Criteria
Age < 40 years
Weight > 50kg < 90kg
Liver function tests upto 2-3 times normal
Intensive care stay < 5days
No sepsis
Low dose vasopressors
Satisfactory macroscopic appearance of the graft

Table 2.*a) Left graft recipients:*

	Total	92-00 (FP)	01-14(SP)	P
	n= 290	48	242	
Age (median)	2.5 (0.1-17)	1.7(0.1-13)	2.7(0.1-17.8)	
Gender (male)	53%	49%	52%	
Recipient weight (median) (Kg)	12.7(2.6-62)	11.8 (2.6-44.4)	12.9 (2.8-62)	
Cold ischemia (hr)	10.5±2.6	12.4±3.8	9.9±1.8	0.001
Warm ischemia (min)	40.2±13.7	37.2±11.5	41.1±14.1	0.05
Total ischemia (h)	11.1±2.5	13.0±3.9	10.7±1.9	0.01
Artery reconstruction	62 (21%)	13 (27%)	49 (20%)	
Artery thrombosis	20 (7%)	6 (12%)	14 (6%)	
Portal vein thrombosis	8(3%)	1(2%)	8 (3%)	
Portal vein stenosis	4 (1%)	1(2%)	3(1%)	
IVC stenosis	11 (4%)	2(4%)	9(4%)	
Multiple bile duct	25(8%)	2(4%)	23 (10%)	0.01
Bile Leak	35 (12%)	9(19%)	26(6%)	
Biliary stricture	26(9%)	11(23%)	15(6%)	0.001
PNF	11 (4%)	3 (6%)	8 (3%)	

b) Right graft recipients:

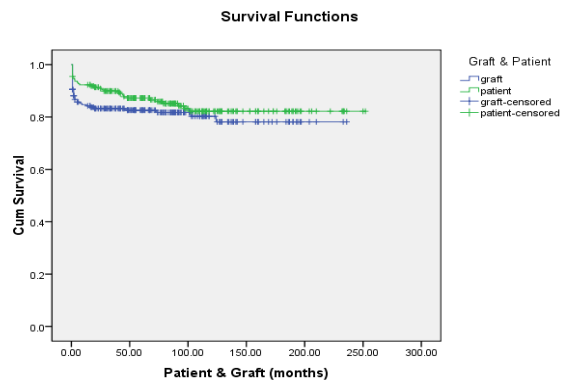
		92-00 (FP)	01-14 (SP)	P
Graft number	226	38	188	
Age median	50(13-69)	45(13-69)	50(13-69)	
Age mean (years)	45.9±16.1	40.5 ±18.6	47.1±15.3	0.01
Gender male	44%	47%	45%	
Recipient weight range (Kg)	66(23-117)	61(23-100)	68(39-117)	
Recipient weight mean (Kg)	68.6±16.6	61.5±15.1	70.2±16.6	0.001
Cold ischemia (h)	9.9±2.2	12.9±3.1	9.6±2	0.001
Warm ischemia (min)	41.6±10.3	49.9±10.1	40.9±10	0.001
Total ischemia (h)	10.5±2.3	13.7±3.1	10.3±2	0.001
Artery reconstruction (graft)	139(62%)	12 (32%)	127 (68%)	0.0001
Artery thrombosis	19 (8%)	8 (21%)	11 (6%)	0.005
Portal vein thrombosis	5(2%)	1 (3%)	4(2%)	
Portal vein stenosis	2(1%)	-	2 (1%)	
Bile Leak	34(15%)	8 (21%)	26 (13%)	
Biliary stricture	13(6%)	7 (18%)	6(3%)	0.008
IVC stenosis	5(2%)	1(3%)	4(2%)	
PNF	3 (1%)	1(3%)	2 (1%)	

Table 3

	Total	Left	Right
	n= 117	n=65	n=52
Donor age years (median)	45 (7-63)		
Donor weight(median)	63(22-111)		
Recipient weight (median) (Kg)		8 (2.6-38)	55(48-117)
Artery thrombosis		5(8%)	1 (2%)
Portal vein thrombosis		-	1 (2%)
Portal vein stenosis		-	3(6%)
IVC stenosis		1(1%)	1(2%)
Bile Leak		6(9%)	7(14%)
Biliary stricture		3(5%)	6(12%)
PNF		0	1(2%)

Figure 1

Right grafts



Left grafts

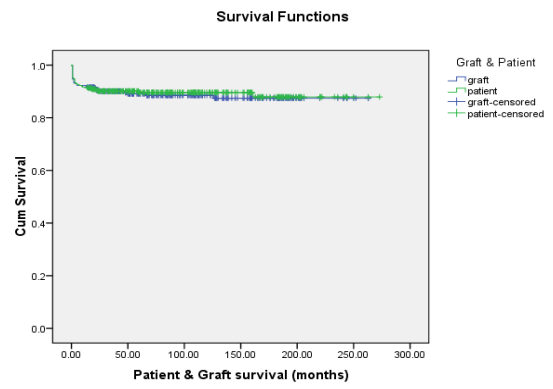


Figure 2

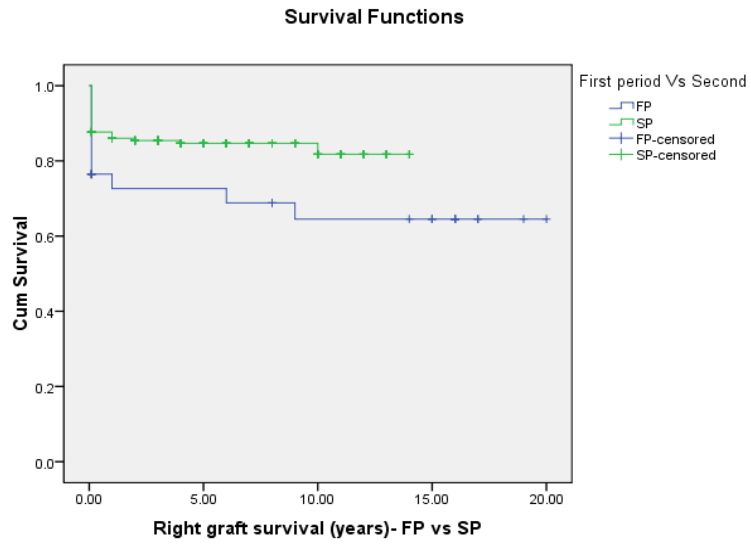


Figure 3

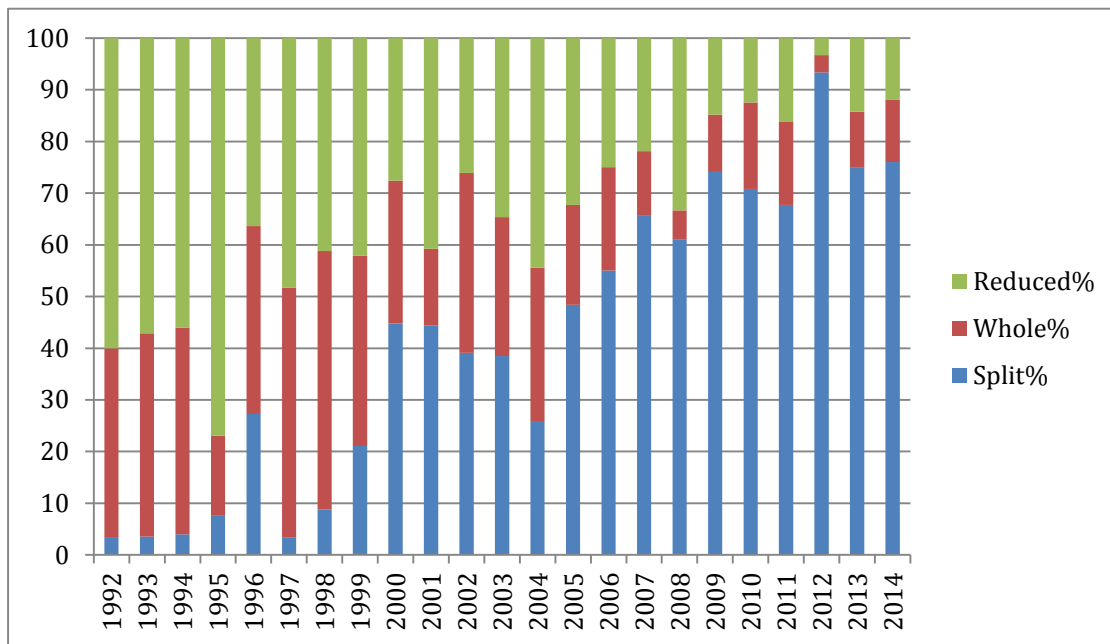
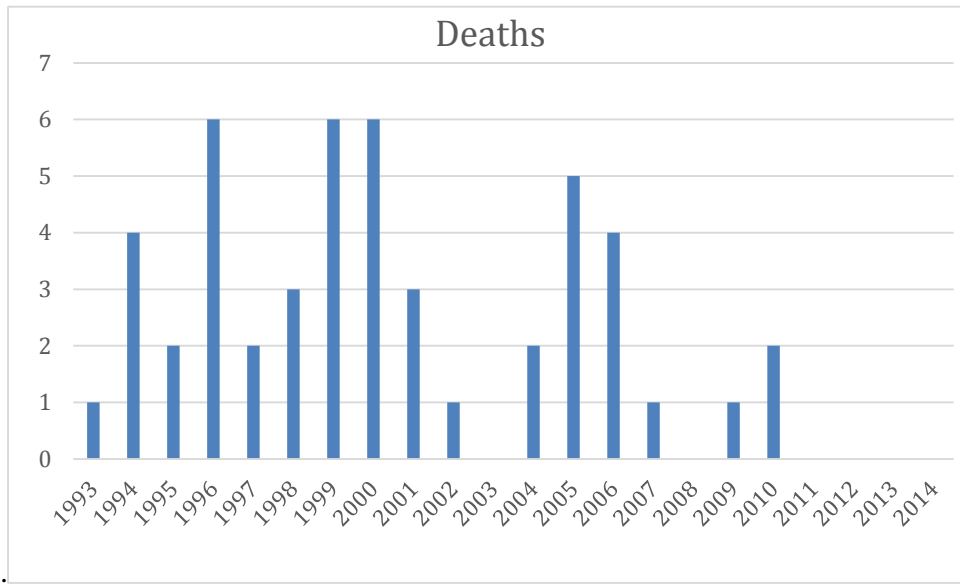


Figure 4



Disclosure:

Author affiliation: Professor Darius Mirza, Mr Thamara Perera and Mr Hynek Mergental are affiliated to National Institute For Health Research (NIHR) Birmingham Liver Biomedical Research Unit (BRU)

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