ANNALS OF SURGERY
Vol. 227, No. 2, 282–288

Split Liver Transplantation

King's College Hospital Experience

Mohamed Rela, F.R.C.S., Vassilis Vougas, M.D., Paolo Muiesan, M.D., Hector Vilca-Melendez, M.D., Vassilis Smyrniotis, M.D., Paul Gibbs, F.R.C.S., John Karani, F.R.C.R.*, Roger Williams, F.R.C.P.†, Nigel Heaton, F.R.C.S.

*From the Liver Transplantation Surgical Service, Department of Radiology * and the Institute of Liver Studies †, King's College Hospital, London, UK*

Background
The purpose of split liver transplantation is to increase the source of pediatric grafts without compromising the adult donor pool. Early results have been discouraging because of technical complications and selection of poor risk patients.

Methods
The results of a single center experience of 41 split liver transplantations were analyzed. Patient and graft survival and complications related to the technique were analyzed.

Results
Patient and graft survival for the whole group was 90% and 88% respectively at a median follow up of 12 months (range 6–70 months). Patient and graft survival for the right lobe graft was 95% and the left lateral segment 86% and 82% respectively. Four patients died, of which two of the patients were first two splits following technical complications. Two others died, one from cerebral lymphoma and the other of multiorgan failure secondary to sepsis. One patient has been retransplanted for chronic biliary sepsis.

Conclusion
Split liver transplantation has now become an acceptable treatment option for both adult and pediatric recipients with end stage liver disease. Right lobe recipients are not disadvantaged by the procedure. Good results can be achieved with better patient selection and by the use of good quality organs.

Liver reduction techniques were developed to overcome the shortage of size matched grafts for children and the results are comparable to whole liver transplantation. In reduced size liver transplantation an adult liver is cut down to a left lobe or left lateral segment (LLS), is then used to transplant a child, and the remaining liver is discarded. Although these techniques reduced the mortality of children on the waiting list[1], they place adult recipients at a relative disadvantage because these livers are withdrawn from the adult donor pool. The current graft shortage has prompted the development of split liver transplantation (SpLT) where one donor liver is split into two grafts thereby increasing the number of grafts available for both adult and pediatric recipients. Early reports of

Correspondence and reprint requests to: Mr. Mohamed Rela, Consultant Surgeon, Liver Transplant Surgical Service, Kings College Hospital, London SE5 9RS, UK.
Accepted for publication August 22, 1997.

SpLT showed discouraging results because of technical complications and the selection of poor risk recipients.[2–4] More recently, encouraging results have been collected from several European centers.[5] We report our experience of 41 SpLT performed in a single center. This experience includes our early experience where the first two splits resulted in the deaths of two pediatric recipients from technical complications.

PATIENTS AND METHODS

Between October 1989 and October 1996, 975 liver transplants were performed in the King's College Hospital Liver Transplant Programme. Of these, 774 (79.6%) were performed on adults and 201 (20.4%) on children. One hundred and twenty two (61%) pediatric liver transplants were performed with a reduced size graft. During this period, 22 donor livers were split and 41 patients were transplanted within our center and 3 right lobe (RL) grafts were exported to other centers. All of the donors were young, with a median age of 21 years (range 8–47) and a median weight of 70 kg (range 30–95). The median period in the Intensive Care Unit before organ donation was 2 days (range 1–4). All but three livers were retrieved by our own surgical retrieval team and the procedure was uneventful in all cases. In one case where a donor liver was sent from another center, a split was performed and the RL was returned to the retrieving center for transplantation.

Technical Details

Bench Surgery

Our primary objective was to produce a satisfactory LLS graft for transplanting a child and to use the RL only if it was anatomically feasible. The split procedure started 1 hour before the start of the pediatric transplant and usually immediately after the donor team returned to avoid prolonged cold ischemic time for the second transplant. The donor liver was cleaned and the anatomy of the hepatic veins determined. The structures in the porta hepatis were gently probed to identify the anatomy of the portal vein (PV), hepatic artery (HA), and bile duct. The main trunk of the HA and the PV were allocated to the LLS graft leaving the RL with short vessels to be reconstructed later. However the common bile duct was given to the RL graft and the left duct was divided away from the porta hepatis without any dissection of the main duct. Segment IV was resected in all but one case and the RL graft was confined to segments V to VIII. The hepatic parenchyma was divided using the forceps crushing technique. The cut surface was covered with a fibrin sealant (Tisseel Kit, Immuno AG, Vienna, Austria). The PV to RL graft usually required no further lengthening but a short right HA was always lengthened by using a short segment of donor splenic or superior mesenteric artery (SMA). The RL graft was packed and replaced into the icebox until required for implantation.

A PV bifurcation was present in all but one graft where there was a trifurcation that resulted in two branches to the right lobe. The main PV trunk was kept with LLS graft in 20 cases. In two patients with low division of the PV and long extrahepatic left portal veins the main PV was given to the RL graft. Of the 19 RL grafts transplanted in our center, 15 had sufficient length of PV for end-to-end anastomosis with the recipient PV. Of the remaining four, two with very short right PV and another transplanted for Crigler-Najjar Type 1 syndrome with right auxiliary graft, required lengthening of the right PV using donor iliac vein. A fourth patient had a PV trifurcation that resulted in two veins to the right liver that was reconstructed using a Y patch of the junction of donor common iliac vein and the external and internal iliac veins.

There was a single common HA from coeliac axis in 13 livers, of which 12 were kept with LLS. The right HA branch from these cases was lengthened by using donor splenic artery in eight cases and SMA in four cases. In one liver, the common HA remained with the RL and the left HA to LLS was anastomosed directly to recipient's common HA. No reconstruction was required in three right lobe grafts with a replaced HA from SMA and in six LLS with a left accessory HA from left gastric artery because of a common origin with the CHA from the coeliac trunk, which was kept with the left graft. The common bile duct remained with the RL graft in all cases. Routine cholangiography was not performed during the split procedure and no obvious biliary anomalies were identified.

Left Lateral Segment Recipients

Twenty-two pediatric patients (15 boys; median age 5 years, range 1–14) received a LLS graft. Median donor to recipient body weight ratio was 3.3:1. The majority of the children who received LLS were transplanted for chronic liver disease, of which extra hepatic biliary atresia being the most common diagnosis (Table 1). Four of the children in this group were transplanted as an emergency. Veno-venous by-pass was not used in this group and the median blood requirement during surgery was 1.4 liters (range 0.2–7.5). The median graft cold ischemic time was 9 hours (range 6.5–15).

Two children with Crigler-Najjar Type 1 syndrome had auxiliary orthotopic liver transplants using the LLS. One of these was a retransplant for chronic rejection and graft atrophy. All LLS were implanted as "piggy back" trans-

Table 1. LEFT LATERAL SEGMENT RECIPIENTS

Split No.	Diagnosis	Age	Complications	Outcome
1	Budd chiari/HAT (Emerg Tx)	11	Outflow obstruction	died
2	Extrahepatic biliary atresia	14	Poor graft function/ICB	died
3	Wilson's disease (Emerg Tx)	10	Wound dehiscence	alive
4	Extrahepatic biliary atresia	2	Chronic biliary sepsis	alive (ReTx)
5	Alpha 1 antitrypsin deficiency	4		alive
6	Extrahepatic biliary atresia	1		alive
7	Crigler-Najjar type 1 (AUX)	11	Lymphoma	died
8	Cryptogenic cirrhosis	8		alive
9	Extrahepatic biliary atresia	11		alive
10	Cystic fibrosis	7		alive
11	Crigler-Najjar type 1 (AUX)	7		alive
12	Caroli's disease	3	Bowel perforation	alive
13	Fatty oxidation defect (Emerg Tx)	2	Anastomotic bile leak	alive
14	Familial Intrahepatic Cholestasis	8	Bowel perforation/HAT	alive
15	Extrahepatic biliary atresia	5		alive
16	Alpha 1 antitrypsin deficiency	3	Bile leak from cut surface	alive
17	Extrahepatic biliary atresia	11		alive
18	Extrahepatic biliary atresia	2		alive
19	NANB hepatitis (Emerg Tx)	1, 8		alive
20	Alpha 1 Antitrypsin deficiency	11		alive
21	Familial intrahepatic cholestasis	4		alive
22	Rabdomyosarcoma	1	Laparotomy for bleeding	alive

HAT = Hepatic artery thrombosis; ICB = Intracranial bleed; AUX = Auxiliary liver transplant; ReTx = Retransplanted; Emerg Tx = Emergency Liver Transplant.

plants with replacement of native inferior vena cava in one case. Arterial revascularisation was achieved with an infrarenal iliac conduit in all but two recipients who had direct anastomosis to the recipient common HA. Biliary reconstruction was achieved by hepatico-jejunostomy using a Roux-en-Y loop. Nine patients had a Roux loop from previous surgery for extrahepatic biliary atresia (7) or liver transplant (2).

Right Lobe Recipients

Nineteen patients (9 male, median age 40 years, range 7–61) received a right lobe. Median donor to recipient body weight was 1.1:1. All of the patients in this group except for the first RL recipient were transplanted for chronic liver disease (Table 2). Veno-venous by-pass was used in 12 adult recipients. Three adults and four children were not by-passed. Median blood requirement during surgery was 5.8 liters (range 1.8–10.3) and graft median cold ischemic time was 18 hours (range 12–21).

Of the 19 right lobe grafts 18 were implanted by the standard orthotopic replacement technique. One pediatric recipient had an auxiliary transplant using a right lobe graft that was implanted by the "piggy back" technique after resection of the native RL. In the 15 RL grafts that required no PV lengthening, there was no difficulty in opposing the recipient main PV to the donor right PV. End-to-end (3) and end-to-side (1) anastomosis was performed with recipient PV in the the four grafts that had previously been lengthened with iliac vein.

Arterial revascularization was performed using donor iliac artery as a conduit between the donor right HA and recipient's infrarenal aorta in 10 out of 19 cases. The biliary reconstruction was achieved by a Roux-en-Y hepatico-jejunostomy in 6 cases and an end-to-end bile duct anastomosis in the remaining 12 cases. A T-tube was not routinely used for direct duct to duct anastomosis in the earlier part of the series, however it was used in the last seven cases.

RESULTS

At a median follow up of 12 months (range 6–70) the overall patient and graft survival is 90% and 88% respectively. Four patients have died and one has been retransplanted. Three of the four deaths were in recipients of LLS and two were from the first two splits performed (Table 1). Patient and graft survival for the LLS recipients was 86% and 82% respectively. There was one death with no graft loss in the right lobe recipients which gave a patient and graft survival of 95%.

Venous outflow obstruction associated with an ascitic

Table 2. RIGHT LOBE RECIPIENTS

Split No.	Diagnosis	Age	Complications	Outcome
1	NANB hepatitis (Emerg Tx)	30		alive
2	Alpha 1 Antitrypsin deficiency	14		alive
3	Secondary sclerosing cholangitis	61	Segment 4 necrosis	alive
4	Exported			
5	HBV related cirrhosis	55		alive
6	Exported			
7	Extrahepatic biliary atresia	11		alive
8	Hepatocellular carcinoma	40		alive
9	Primary sclerosing cholangitis	37	Roux loop perforation	died
10	HCV related cirrhosis	47	Bile leak from cut surface	alive
11	Crigler-Najjar type 1	11	Bile leak from cut surface/stricture	alive
12	Cryptogenic cirrhosis	57	Laparotomy for bleeding	alive
13	Alcoholic liver disease	47		alive
14	Exported			
15	Chronic rejection	24		alive
16	Amyloid disease	35		alive
17	HBV related cirrhosis	52	Bile leak	alive
18	Hepatocellular carcinoma	19		alive
19	HBV related cirrhosis	40		alive
20	Alcoholic liver disease	56		alive
21	Chronic rejection	9		alive
22	Autoimmune hepatitis	18		alive

Emerg Tx = Emergency Liver Transplant.

loss of 9 to 10 liters/day was the cause of death in the first LLS recipient who died 17 days after being transplanted. The second child died of poor graft function because of partial venous outflow obstruction which resulted in intracranial hemorrhage 8 days after the transplant. The child had a similar event 3 months before surgery. A third child died of disseminated lymphoma 6 months after a retransplant with a split graft. An adult patient died of chest sepsis 7 weeks after a transplant. Two weeks before this incident she was explored for hypovolemic shock due to HA rupture secondary to a localized Roux loop perforation. The perforation was oversewn and the HA was reconstructed by using a donor iliac artery.

Other complications included a superficial wound dehiscence in a child whose deep muscle was not closed at transplant and laparotomy for bleeding in two patients. Segment IV infarction was seen in one patient who underwent laparotomy and excision of segment IV. Peritonitis secondary to multiple small bowel perforation occurred in two children with biliary atresia and these were oversewn. One child who received a LLS graft developed late HA thrombosis 5 months after the transplant and after an episode of severe gastro-enteritis. This has been managed conservatively and graft function remains satisfactory.

Six biliary complications occurred: 3 each in right and left graft recipients (14.6%). There have been two bile leaks: one from the cut surface and the other from the anastomosis in the LLS recipients. Both required laparotomy and drainage. A third child had recurrent episodes of ascending cholangitis which was thought to be a result of rotation of the LLS and obstruction to the flow of bile. Refashioning of the hepatico-jejunostomy did not resolve the problem and he was retransplanted 6 months later for chronic biliary sepsis with a cadaveric left lobe graft. He is now well. Three RL recipients (a child and two adults) had bile leaks from the cut surface confirmed by cholangiography and ultrasound guided needle aspiration and "pigtail" catheter drainage led to resolution in the two adults. The child had an associated anastomotic stricture and underwent laparotomy and revision of the hepatico-jejunostomy.

DISCUSSION

Liver division offers a potential solution to the shortage of donor organs by transplanting two recipients from one donor liver. Increased experience acquired from transplantation with reduced size grafts in combination with a shortage of donor organs for children has

Table 3. REVIEW OF PUBLISHED DATA FROM CENTRES WHICH HAVE PERFORMED >10 SpLT

Author	Year	No.	Patient Survival %	Graft Survival %
Emond	1990	18	67	50
Broelsh	1990	30	60	42
Langnas	1992	10	50	50
Houssin	1993	16	75	69
Slooff	1995	15	73	67
Otte	1995	29	71	67
De Ville (combined European)	1995	98	68	62
Rogiers (ex situ)	1996	19	63	58
Rogiers (in situ)	1996	14	93	86
Kalayoglu	1996	12	91	75
Rela (present series)	1997	41	90	88

led to a reawakening of interest in SpLT.[6–8] Initial results with SpLT were disappointing in comparison to those obtained with whole and reduced size grafts. This is possibly because of poor patient selection and a high incidence of technical complications that resulted in graft loss. Many centers reported a patient survival of 50% to 65%[6–8] (Table 3) and these results were considered unacceptable for use of the technique in elective patients. However, collective European experience[5] and later reports from centers with greater experience have shown more favorable results.[9–11] In the early series a number of patients had fulminant hepatic failure and if urgency code was taken into consideration the survival figures became more acceptable. A recent American report of experience with splitting 6 livers resulting in 12 SpLT[12] has shown excellent results with patient and graft survival of 91.6% and 75% respectively.

Data from the split liver transplant registry (JB Otte - personal communication) shows good results from centers that have performed more than 30 SpLT. However graft and patient survival of patients requiring ICU care before the transplant, particularly for the RL recipients, was poor (15% and 21% respectively). Our policy is not to split a liver for an ICU based adult patient, but to give a full size graft. Split liver techniques should be used to create a LLS graft for a child (urgent or routine) when there is no urgent adult patient waiting and the use the RL should be restricted to elective cases. The only situation where surgeons may be tempted to split in unfavorable circumstances is when there are two urgent patients one adult and one pediatric. Fortunately such situations are rare. In our series all of the RL, except for the first split, were used for elective transplants. However, 4 out of the 22 children who received a LLS were transplanted as an emergency.

A number of parameters should be taken into account when considering SpLT including donor selection, anatomical variations, techniques, and complications.[9,13] Median donor age in our series was 21 years. All donors were hemodynamically stable and on very low doses of inotropes before and during organ retrieval. Very small livers (<20 kg donors) or donors older than 50 years of age have not been considered for splitting until now, but such constraints are arbitrary.[7,13] Absolute contraindications to splitting are the absence of a PV bifurcation and atrophy of left lobe. Absence of PV bifurcation occurs in 1% to 4% of potential grafts.[14–16] Experience so far has shown that preservation of segment IV to the right graft causes ischemia or necrosis.[8,9] Following the episode of ischemia in one patient we have always resected segment IV on the back table. The incidence of PV thrombosis varies in several reported series from 4% to 12.5% and most of these were in small children.[5,9] In the present series there were no PV complications.

Back table angiography to identify HA anomalies has been suggested particularly when the left HA arises from the left gastric artery or the right HA arises from the SMA to determine whether it is the sole arterial supply to left or RL.[14,16,17] Only two angiograms were performed in our series to confirm the presence of a replaced right HA from SMA. In our experience the ideal HA anatomy for SpLT is simple division of the common HA that is present in 50% to 60% of organs. As the left HA is smaller in caliber than the right, and as our primary aim is to create a standard LLS graft the main HA is kept in continually with the left graft. The right HA can always be lengthened using donor arteries such as the splenic or SMA. The reported incidence of HA thrombosis from SpLT is 9% to 25%.[5,8,9] In our series of 41 split liver transplants there has been one case of late HA thrombosis in a child with a LLS graft. There have been no thrombotic complications in the RL grafts. The retransplantation rate in this series with a relatively short follow up (median 12 months) is 2.4%.

Cholangiography has been recommended to detect biliary duplications.[9,13] A reported high incidence of biliary complications during SpLT (18%–27%) reflects the technical and anatomical problems which produce anastomotic and cut surface bile leaks, and anastomotic and nonanastomotic strictures.[5,9] We report a 14.6% biliary complication rate resulting in 4 laparotomies and one retransplantation. In the child who required retransplantation, biliary drainage was against gravity due to the positioning of the graft. This child had polysplenia syndrome with absent IVC and the left hepatic vein instead of being piggy backed on to the IVC was anastomosed on to the recipient

confluence of suprahepatic veins which drained directly into the right atrium. The graft therefore appeared to rotate along a horizontal axis with nondependent drainage to the bile duct. This complication was a result of the wrong choice of graft for the child and is unrelated to the split procedure itself. Such children should preferably be transplanted with a whole graft or a reduced graft with an intact donor vena cava in order to avoid this complication.

The prolonged cold ischemic time for the RL recipient was due to logistical problems and the lack of a second operating theater. The export of one of the two grafts to other institutions is a potential solution and with improving results being reported, should become more common place. Although a primary nonfunction (PNF) rate of 4% to 5% has been reported in other series,[5,8] there were no instances of primary nonfunction in our series despite a median cold ischemic time of 18 hours and 3 cases with a cold ischemic time of 21 hours.

Centers with extensive experience in SpLT in Europe are now developing the technique of insitu splitting.[18] The main advantages proposed for this procedure are that it avoids prolonged bench surgery which may lead to ischemic injury of the graft and that perfect hemostasis can be achieved during the donor operation reducing the blood loss during the recipient operation. However, the major disadvantage of this procedure is that it increases the operation time in the donor hospital by a further 2 to 3 hours. The transplant community in general has worked over the years to minimize the inconvenience caused to donor hospitals by modifying techniques to shorten donor operating time.[19] We believe that such extended operations in donor hospitals would have a negative effect on organ donation thereby defeating the purpose of the split procedure. Our experience has shown that if good quality organs are selected, satisfactory results can be achieved without primary nonfunction despite prolonged cold ischemic time to the second graft. The incidence of biliary complications is relatively high in our series (14.6%). However, the majority have been bile leaks from the cut surface, which may be avoidable by meticulous ligation of bile duct radicles on the cut surface, the routine use of T-tubes for the right liver grafts, and possibly by increasing use of bench cholangiography to identify anomalous biliary anatomy.

Measures to alleviate donor shortage will take time to implement but SpLT represents one way forward and merits further development. The advantage of this technique over living related liver transplantation is that it expands the existing donor pool without placing otherwise healthy people at risk of complications from the donation procedure. The success of SpLT has significantly altered clinical practice within our own institution. Although we have a living related liver transplant program in our institution only 14 have been performed over the past 3 years with 1 year survival of 93% and no donor mortality. Our policy has been to place these children on a cadaveric waiting list during the assessment period for living related liver transplantation. Over the past year, five such children were transplanted with a split liver graft before the assessment was completed and our waiting time for pediatric recipients has reduced dramatically.

Split liver transplantation represents a significant source of pediatric liver grafts without compromising the adult donor pool, and the right lobe graft should be used in good risk patients with grafts from optimal donors in order to obtain the best possible results. There is a difficult learning curve as shown by the fact that two of the four deaths in our series occurred in the first two SpLTs. It remains a demanding and complex surgical procedure that should be performed in centers with extensive experience in liver anatomy, major liver resections, and reduced size liver transplantation.

References

1. Ville de Goyet J de, Hausleithner V, Reding R, Lerut J, Janssen M, Otte JB. Impact of innovative techniques on the waiting list and results in pediatric liver transplantation. Transplantation 1993;56: 1130–1136.
2. Pichlmayr R, Ringe B, Gubernatis G, et al. Transplantation einer Spenderleber auf zwei Empfanger (Splitting-Transplantation): Eine neue Methode in der Weiterentwicklung der Lebersegmenttransplantation. Langenbecks Arch Chir 1988;373:127–130.
3. Bismuth H, Morino M, Castaing D, et al. Emergency orthotopic liver transplantation in two patients using one donor liver. Br J Surg 1989;76:722–724.
4. Langnas AN, Marujo WC, Inogaki M, et al. The results of reduced size liver transplantation including split livers in patients with end-stage liver disease. Transplantation 1992;53:387–391.
5. De Ville de Goyet J. Split liver transplantation in Europe-1988 to 1993. Transplantation 1995;59:1371–1376.
6. Otte JB, de Ville de Goyet J, Alberti D, et al. The concept and technique of the split liver in clinical transplantation. Surgery 1990;107:605–612.
7. Broelsch CE, Emond JC, Whitington PF, et al. Application of reduced size liver transplants as split grafts, auxiliary orthotopic grafts and living related segmental transplants. Ann Surg 1990;214:368–377.
8. Emond JC, Whitington PF, Thistlethwaite JR. Transplantation of two patients with one liver. Ann Surg 1990;212:14–22.
9. Houssin D, Boillot O, Soubrane O, et al. Controlled liver splitting for transplantation in two recipients: technique, results and perspectives. Br J Surg 1993;80:65–68.
10. 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.

11. Slooff MJH. Reduced size liver transplantation, split liver transplantation and living related liver transplantation in relation to donor organ shortage. Transpl Int 1995;8:65–68.
12. Kalayoglu M, D'Alessandro AM, Knechtle JS, et al. Preliminary experience with split liver transplantation. J Am Col Surg 1996; 182:381–387.
13. Heaton ND, Corbally MT, Rela M, et al. In: Williams R, Portmann B, Tan KC, ed. Surgical techniques of segmental reduction, split and auxiliary liver transplantation. The practice of liver transplantation. 1st ed. London: Churchill-Livingstone 1995:143–151.
14. Couinaud C, Houssin D. In: Couinaud C, Houssin D pers. ed. Controlled partition of the liver for transplantation. Anatomical limitations. Paris 1991:1–80.
15. Bismuth H. Surgical anatomy and anatomical surgery of the liver. World J Surg 1982;6:3–6.
16. Rat P, Paris P, Friedman S, et al. Split liver orthotopic liver transplantation: How to divide the portal pedicle. Surgery 1992;112: 522–526.
17. Daseler EH, Anson BJ, Hambley WC, Reiman AF. The cystic artery and the constituents of the hepatic pedicle. Surg Gynecol Obstet 1947;85:47–50.
18. 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.
19. Starzl TE, Miller C, Bronznick B, et al. An improved technique for multiple organ harvesting. Surg, Gynecol Obstet 1987;165:343–346.