Liver Transplantation, Including the Concept of Reduced-size Liver Transplants in Children

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Since the establishment of a clinical program in liver transplantation in 1984, 162 liver transplants have been performed in 131 patients (78 adults, 53 children). The patient mortality rate while waiting for a suitable organ has been 8% for adults and only 4% for children (25–46% reported in the literature). The low pediatric mortality is a result of the use of reduced-size liver transplants. A total of 14 procedures have been performed in recipients whose clinical condition was deteriorating and for whom no full-size graft could be located. Of 14 children, 13 were less than 3 years of age. Patient survival is 50%, comparable to survival of high-risk recipients of full-size livers. Using reduced-size liver grafting in a transplant program can lower mortality for children awaiting a transplant by overcoming size disparity. Reduced-size liver grafting will allow more effective use of donor resources and provide a potential avenue of research for organ splitting and living related donation.

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ORTHOTOPIC LIVER TRANSPLANTATION has received broader application since the National Institutes of Health (NIH) Concensus Conference in 1983.[1,2] A growing number of transplant centers are treating an expanding pool of adult and pediatric candidates with chronic and acute liver failure, and this has led to a relative scarcity of donor organs.[3–5] Because many of these candidates are critically ill, there is also a time constraint to the overall limited donor availability. Although a suitable organ for adult candidates can usually be located through routine mechanisms, small pediatric donors are relatively scarce, and because of this scarcity, 20–50% of infants die while still on the transplant waiting-list.[6–9]

To overcome this size problem, we embraced the concept of reduced-size liver transplants (RLT), primarily for the small child with chronic liver disease. The successful use of RLT was initially reported by Bismuth in 1984[10] and Broelsch et al., also in 1984.[11] This concept is presently applied by several European transplant centers (R. Pichlmayr in Hannover,[12] H. Bismuth in Paris,[10] J.B. Otte in Brussels,[13] and R. Margreiter in Innsbruck), where organ scarcity is even greater. Our early experience has been reported elsewhere.[6]

In this report we present our clinical experience—methods, indications, and results—with 162 liver transplants performed on 131 patients in the 3.25 years since the inception of the liver transplant program at the University of Chicago. Special emphasis is given to our pediatric transplant program, including the concept of reduced-size liver grafting.

Patients and Methods

Patients and Transplants

Between November 1984 and March 1988, 362 patients with liver disease have been evaluated by members of the University of Chicago Liver Transplant program. Of these, 198 patients were adults between 16 and 67 years of age, and 164 were children between 4 months and 16 years of age. One hundred thirty-one patients received 162 liver grafts. Thirty-one retransplants were performed in 25 patients, with 18 patients receiving a total of two livers, 5 patients receiving a total of three, and two patients receiving a total of four. The program has experienced steady growth. Twenty-five transplants were performed in 1985, 53 in 1986 and 84 in 1987 and the first two months of 1988.

Adult Candidates

Forty-one patients were referred for transplantation in 1985; 16 of these patients (39%) died during evaluation,

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TABLE 1. *Growth of Adult Liver Transplant Program in Relation to Number of Patients Referred and Transplants Performed*

	1985	1986	1987–March, 1988
Patients evaluated	41	62	95
Patients transplanted	9 (10 tx)	27 (32 tx)	42 (54 tx)
Pts. died during eval.	16 (39%)	10 (16.2%)	13 (13.6%) n = 39
Pts. died on list	—	2 (7.4%)	3 (7%)
Tx. elective	2 (22%)	13 (48%)	13 (31%)
Tx. urgent	7 (78%)	14 (52%)	29 (69%)

and nine underwent transplantations (Table 1). Seven of these latter nine patients were hospital- or ICU-bound, whereas the remaining two underwent transplantations electively (*i.e.*, called in from home or waiting outside the hospital). In 1986, only ten of 62 patients (16%) referred for transplantation died during evaluation. Still, of the 27 who underwent transplantations, 14 were hospital-bound. In 1987, 13 of 95 (13.6%) died during evaluation, and 29 patients were hospital-bound at the time of transplantation. Thirteen patients were operated on electively. Only four adults (all of whom had chronic liver disease) died while still on the transplant waiting-list.

Pediatric Candidates

The status of pediatric candidates is presented in Table 2. Of 164 patients, 106 were judged transplant candidates. In 1985, 13 patients underwent transplantations, nine of whom were hospital- or ICU-bound and four of whom were elective. In 1986, 15 patients underwent transplantations, six patients of whom were elective. Twenty-five children received transplants in 1987. Thirteen were elective, and twelve were hospital-bound. Overall, seven children who were potential transplant candidates died during evaluation. Only four of 106 (4%) died before a donor could be located.

Indications

The indications for transplantation in adult and pediatric recipients are presented in Tables 3 and 4. In adults, chronic active hepatitis with cirrhosis was the most frequent diagnosis (n = 34; 44%), whereas in children, the diagnosis of biliary atresia was the most frequent (n = 33; 67%). Fulminant hepatic failure (n = 18) was somewhat over-represented in our series. Six children received transplants for fulminant hepatic failure from non-A non-B hepatitis. (Tables 5 and 6).

TABLE 2. *Pediatric Candidates for Liver Transplantation*

Patient Status as of April 1988	Number	%
Patients evaluated with liver disease	164	
Potential transplant candidates	106	100
Transplanted	53	50
Transplant not yet indicated	42	40
Died during evaluation	7	6
Died while on waiting-list	4	4

TABLE 3. *Liver Transplantation Indications in 78 Adults*

	Number	%
Chronic active hepatitis with cirrhosis	34	44
Cryptogenic cirrhosis	9	12
Fulminant hepatic failure	12	16
Primary biliary cirrhosis	6	7
Primary hepatic cancer	5	6
Sclerosing cholangitis	5	6
Secondary biliary cirrhosis	3	4
Other	4	5
Totals	78	100

Reduced Liver Transplant Indications

Of a total of 66 transplants in 53 patients, 14 children have received RLT grafts. RLT was performed when expected survival was less than 48 hours (n = 6) and on children with chronic liver disease who were on the waiting list on high priority for at least 1 month and who experienced progressive deterioration despite maximal in-patient medical support (n = 7). Recently, a 6-year-old boy weighing 18 kg underwent transplantation electively with an RLT from a 17-year-old donor weighing 64 kg. Ten children received a RLT as a primary graft, and four as a retransplant. The indications for grafting in these 14 cases are presented in Tables 5 and 6.

Surgical Techniques of RLT

Three different types of hepatic reductions were used to create a transplantable lobe of the liver, where liver mass was the appropriate size for the recipient's abdominal space. The right lobe was used in three cases, the left lobe in nine cases, and the left lateral segment in two cases. Up to 6.5 times the weight of that of the recipient was accepted as maximum weight difference between donor

TABLE 4. *Liver Transplantation Indications in 53 Children*

	Number	%
Biliary atresia	33	67
Fulminant hepatic failure	6	11
Metabolic disorders	5	9
Progressive intrahepatic cholestasis	4	8
Alagille's syndrome	2	4
Other	3	6
Total	53	100

(U of C 3/88)

TABLE 5. *Primary Grafts Preoperative Clinical Status*

Patient No.	Age (mos)	Weight (kg)	Diagnosis	Indication for RLT	Encephalopathy (0–4)	ICU (0, 1)
1	11	9	Bil. atresia	Deterioration (5 wk†)	2	0
2	15 y	61	FHF‡	Coma	4	1*
4	48	16	FHF	Coma	4	1*
6	4	6	Bil. atresia	Deterioration (5 wks)	1	0
7	6	7	Bil. atresia	Deterioration (4 wks)	0	0
8	24	15	Bil. atresia	Deterioration (8 wks)	0	0
9	36	18	Bil. atresia	Deterioration (12 wks)	1	0
11	24	12	Bil. atresia	Deterioration (8 wks)	2	0
13	7	5.5	Bil. atresia	Deterioration (4 wks)	2	1
14	6 y	18	SC§	Elective	0	0

* On ventilator.
† Weeks spent on transplant list (inpatient status).
‡ Fulminant hepatic failure.
§ Sclerosing cholangitis.

and recipient. The average weight difference was 3.4 times the recipient weight.

Donor and recipient operations were performed using conventional techniques.[14] The donor liver was perfused *in situ* with limited preliminary dissection and was transported to the recipient operating room. The size reduction was performed after recipient laparotomy and assessment of the abdominal space, distance between the supra- and infrahepatic vena cava and the size of the portal vein. The *ex vivo* hepatectomy was then performed while a second surgical team completed the recipient hepatectomy.

Right Lobe Graft

Preparing the right lobe consisted of an anatomical left hepatectomy (Fig. 1). First, a cholecystectomy and ligation of cystic artery and cystic duct was performed. The common bile duct was dissected into the hilum, up to the junction of the left and right duct, and the left hepatic duct was ligated. Attention was given to the small vessels surrounding the common duct. The hepatic artery was then dissected, beginning at the celiac trunk, followed along the common hepatic artery and the proper hepatic artery to the bifurcation, and the left hepatic artery was ligated. The portal vein was then isolated until the left portal branch was identified and excised. The site of the excision was closed with a 6-0 running suture to maximize the length of the vessel. Once the hilum was dissected, the vena cava (IVC) was isolated from the caudate lobe by sharp dissection with ligation of individual small hepatic veins entering the IVC. With the IVC stretched out, its anterior wall was separated from the hepatic parenchyma by sharp dissection until the major hepatic veins were isolated. The left and median left hepatic veins were divided, and the cava was rotated to the right to reveal the space between the hepatic veins and the posterior surface of the liver that provides the anatomical division between the right and left lobes.

The transection of the parenchyma started at the gallbladder fossa and was directed toward the hilum. On the liver surface, the line was parallel to the falciform ligament toward the left hepatic vein. The parenchyma was bluntly dissected with the tip of the scissor, and each vascular or biliary structure to the right side was suture-ligated. The cut surface was inspected by flushing the portal vein and individually suturing each site of leakage. Irrigation was performed through the hepatic artery and the bile duct, as well.

Mattress sutures with 3-0 Surgilene® (American Cyanamid Company, Danbury, CT) were used to reduce the raw surface and to apply moderate pressure to the rim of parenchyma along the line of dissection. No glue or adhesive was used to seal the surface. After revascularization, parenchymal bleeding was controlled with an infrared light coagulator (Lumed, Medizintechnik GmbH, Muenchen, F.R.G.).

TABLE 6. *Retransplants Preoperative Clinical Status*

N	Age ICU (mos)	Weight (kg)	Diagnosis	Indication for RLT	Encephalopathy (0–4)	Encephalopathy (0, 1)
3	15	10	Bil. atresia	Acute art. thrombosis	4	1*
5	6	7	Bil. atresia	Acute art. thrombosis	4	1*
10	9	10	Bil. atresia	Rejection (8 wks)	0	1
12	24	10.5	Bil. atresia	Primary non-function	4	1*

* On ventilator.

Left Lobe Graft

Preparation of the left lobe was done similarly, following the steps of the previously described procedure exactly by performing a cholecystectomy, ligating the cystic duct, dissecting bile duct, and ligating the right hepatic duct (Fig. 2). After the isolation of the hepatic artery (including the celiac trunk, the common hepatic artery, and the proper hepatic artery), the right hepatic artery was ligated and divided. Finally, the portal vein was isolated, the right portal vein was divided, and the site of bifurcation oversewn with 6-0 running Surgilene suture. Along the vena cava, the caudate lobe did not have to be removed, but several small hepatic veins entering the vena cava from the right side were ligated. The right hepatic vein was divided, and the site was closed with 4-0 Surgilene running suture. The parenchymal dissection was identical and all vascular structures on the transected surface were suture-ligated. Again, the margin was gently compressed by mattress sutures using the falciform ligament as a pledget.

Left Lateral Segment Graft

The third method used was the construction of a left lateral segment (Fig. 3). Ordinarily, this segment comprises less than 25% of the mass of the liver and is the smallest anatomically independent segment to have its own hepatic venous outflow and vascular supply. The procedure basically consists of a hepatic trisegmentectomy.

The preparation was begun at the common duct that was followed to the junction of the left and right duct, where the right duct is openly divided. The duct was followed toward the left lobe, and the branches to the caudate lobe and the median hepatic left lobe (Segment 4), were ligated and divided. The hepatic artery was isolated as previously described, and, after being divided from the right hepatic artery, was followed toward the left lobe, with the branch to the left median lobe ligated and divided. The portal vein was dissected next, and the right portal vein branches, as well as the median left portal vein branch and the branch to the caudate lobe, were divided. As always, all orifices were closed with 6-0 Surgilene running suture. The inferior vena cava was dissected completely free of its attachments to the liver, and all hepatic veins were divided until the outlets of the median left hepatic vein and the left lateral hepatic vein were reached.

The transection of the parenchyma followed the falciform ligament, beginning with careful ligation of all branches within the round ligament until the hilum of

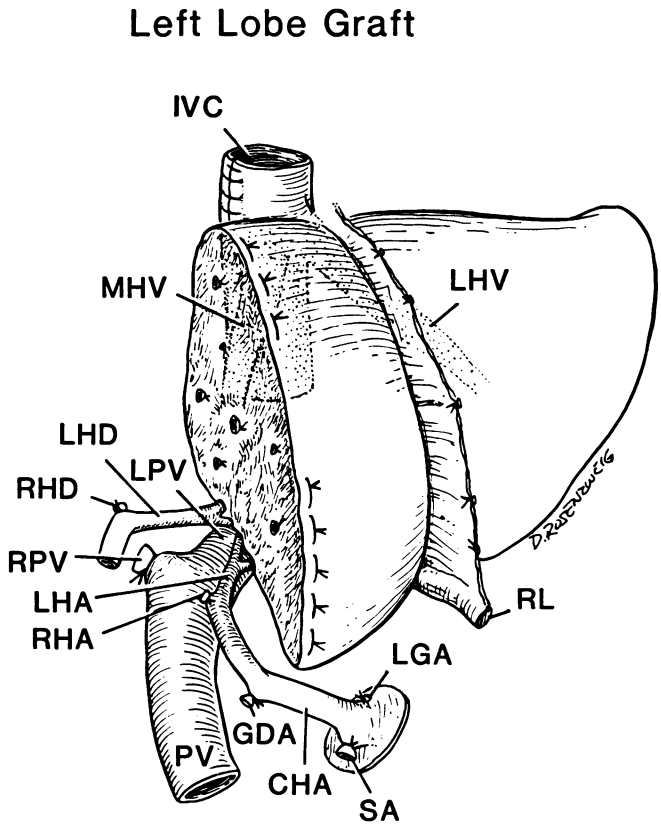

FIG. 2. A left lobe graft using the entire parenchyma of the left liver. Abbreviations are as in Figure 1 with the following exceptions: LHD = left hepatic duct; LPV = left portal vein; RL = round ligament.

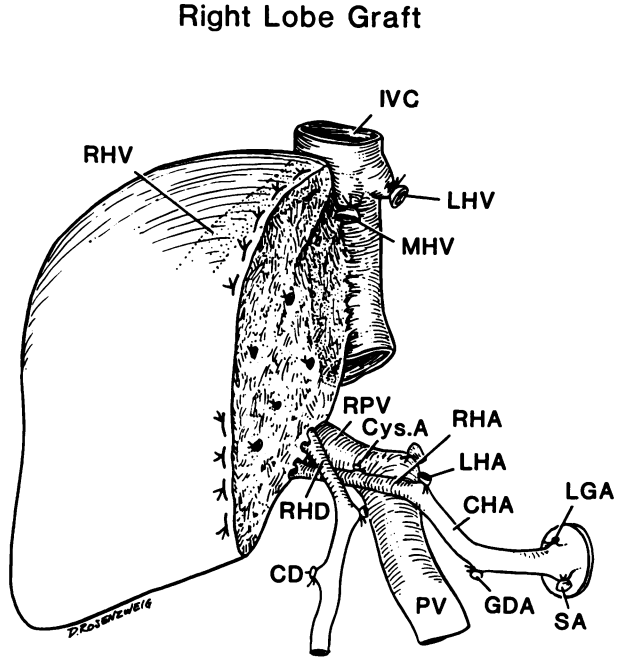

FIG. 1. A completed right lobe graft. The following abbreviations are used: IVC = Inferior vena cava; RHV = right hepatic vein; LHV = left hepatic vein; MHV = middle hepatic vein; RPV = right portal vein; CYs.A = cystic artery; RHA = right hepatic artery; LHA = left hepatic artery; CHA = common hepatic artery; GDA = gastroduodenal artery; SA = splenic artery; LGA = left gastric artery; RHD = right hepatic duct; CD = common duct; PV = portal vein.

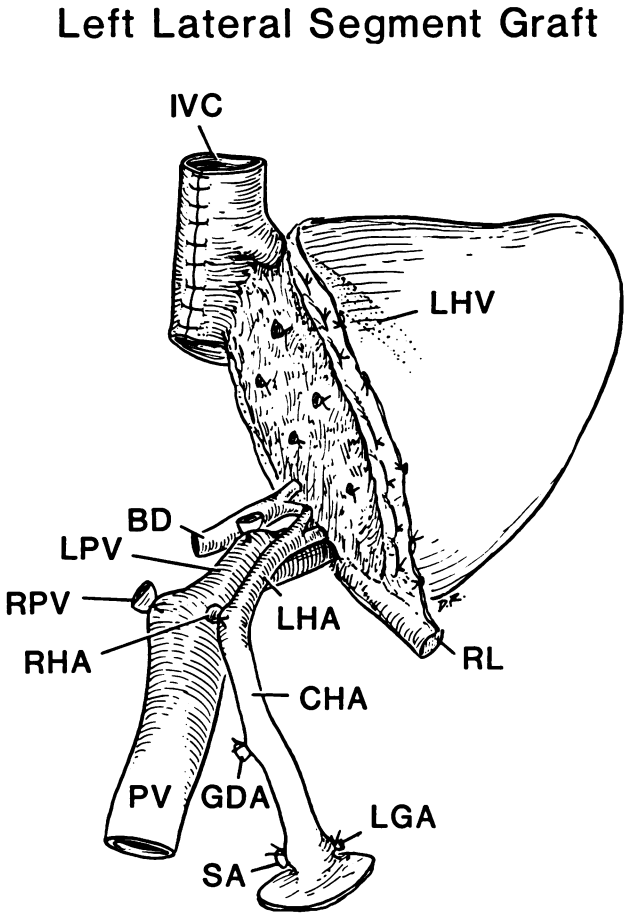

FIG. 3. The completed left lateral segment graft, including the parenchyma of segments 2 and 3 of Couinaud. Abbreviations are as in previous figures.

the liver was reached. In fact, the cut surface tends to be relatively small and requires only careful suture ligation of all visible vascular or biliary structures. Perfusion was then carried out through the portal vein, hepatic artery, and bile duct to detect leakage. While dissection through the parenchyma was taking place, a segment of the left median hepatic vein was preserved to serve as the vascular interposition for the recipient vena cava. Several orifices of hepatic veins had to be suture-ligated. The diameter of the suprahepatic vena cava was reduced to half its original size, or about 20–25 mm. Its diameter was merely adapted to that of the recipient suprahepatic and infrahepatic vena cavae, and its length to the distance between them (about 5–6 cm). During implantation, the graft was slightly rotated counterclockwise to allow the segment to fill the space of the right subdiaphragmatic area.

Implantation

All RLT grafts were transplanted orthotopically. The portal vein was anastomosed end-to-end, and the arterial anastomosis was accomplished either end-to-end between the common hepatic arteries of the recipient and donor, or by anastomosis between the aorta of the recipient and a Carrel patch of the celiac trunk of the donor. The bile duct was drained with a hepaticojejunostomy. Primary abdominal closure was possible in 12 to 14 cases. In two cases, temporary closure was accomplished with a Goretex (W. L. Gore & Associates, Inc., Elkton, MD) or reinforced Silastic patch.

After surgery, patients were managed using our standard postoperative protocols, as reported previously.[3] Rejection episodes were treated with bolus steroids in all cases, and, in cases of steroid resistance, with monoclonal OKT3 (Orthoclone OKT-3, Ortho Pharmaceutical Co., Raritan, NJ).[3]

Results

Overall patient survival rates, calculated by the life table method, have increased from 49% (n = 24 patients) during the first year, 63% (n = 53) transplants during the second year, to 70% (n = 67 transplants) during the last year (Fig. 4). Candidate criteria have not changed, nor has the relative distribution of high-risk candidates *versus* elective candidates. Elective candidates accounted for 27% of the transplants in 1985, 33% in 1986, and 26% in 1987.

Thirty-one retransplants have been performed in 25 patients. The causes for retransplantation in the adult population were nonviable grafts (n = 11), acute artery thrombosis (n = 1), and chronic rejection (n = 7). In children, the causes were primary malfunction (n = 4), arterial thrombosis (n = 4), and rejection (n = 5); the survival of patients requiring retransplant was 40% (4 of 10 patients).

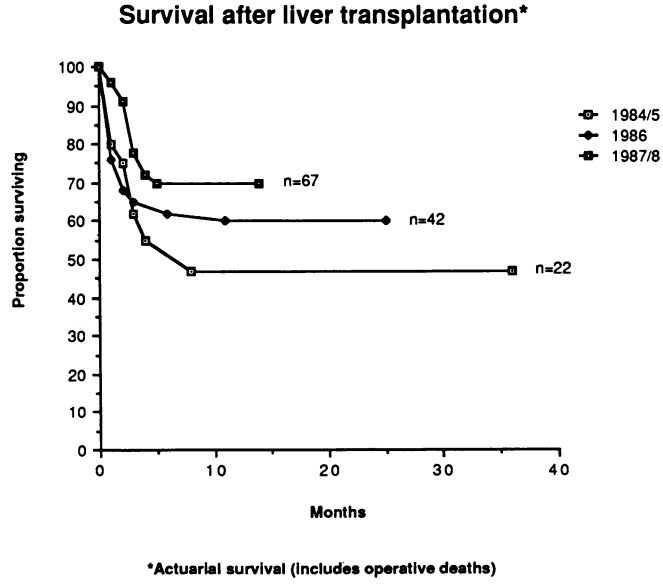

FIG. 4. Actuarial survival in three time periods.

TABLE 7. *Patient Outcome for Primary Transplants*

Patient No.	Follow-up	Alive (0, 1)	Cause of Death
1	5 days	0	Intracranial hemorrhage
2	5 days	0	Nonviable graft
4	6 mos	0	Systemic CMV G.I. bleeding
6	18 mos	1	
7	12 mos	1	
8	10 mos	1	
9	14 days	0	Intracranial hemorrhage
11	7 mos	1	
13	5 mos	1	Retransplant with full size graft
14	1 mos	1	

Survival times and causes of death in the pediatric group receiving RLT are presented in Tables 7 and 8. In all, six of ten patients who received their RLT as a primary graft (60%), are alive between 1 and 18 months after surgery. Patients 1 and 9 died of intracranial hemorrhage on postoperative Days 5 and 14, when liver function was acceptable. Patient 4 died 6 months after transplantation with severe CMV infection, recurrent gastrointestinal (G.I.) bleeding, multiple intestinal fistulas and a B-cell lymphoma. Patient 2 received a nonviable graft and died of coagulopathy and hemoperitoneum. Patient 13 received a RLT that failed because of acute hepatic artery thrombosis. This patient is alive after retransplantation, although with neurological deficiencies from shock due to acute sepsis and brain edema.

Patient survival after retransplantation with a RLT is poor, with one patient out of four surviving after 11 months (Table 8). The survivor, Patient 5, was initially transplanted electively and was retransplanted for acute rejection and hepatic artery thrombosis. The second liver was a full-sized, nonfunctioning graft from a hypoxic, newborn donor. The RLT was the third graft and served as a life-sustaining, temporary support. The graft was too large and any attempt to close the abdomen resulted in ventilatory insufficiency. Finally, this infant (weighing 7 kg) underwent retransplantation a fourth time with a whole liver, and is alive and well 15 months later. In the three other attempts, retransplant with RLT failed, with one intraoperative death and two patients dying of sepsis after 1 month.

TABLE 8. *Patient Outcome for Retransplants*

Patient No.	Follow-up (mos)	Alive	Cause of Death
3	0	0	Intraoperative death
5	9	1	(Retransplanted with full-size graft after 10 days)
10	1	0	Sepsis
12	1	0	Sepsis

TABLE 9. *Donor/recipient Size Match in Primary Grafts*

Patient No. Used)	Recipient Age/Weight (kg)	Donor Age/Weight (kg)	Weight Ratio (D:R)	Graft (lobe)
1	11 mos/9	12 yrs/33	3.6:1	Left
2	15 yrs/61	37 yrs/90	1.5:1	Left
4	4 yrs/19	45 yrs/70	3.7:1	L lateral
6	4 mos/6	7 mos/11	2:1	Right + 4
7	8 mos/8	15 yrs/25	3.1:1	Left
8	3 yrs/17	18 yrs/60	3.5:1	Left
9	30 mos/15	30 yrs/50	3.3:1	Left
11	24 mos/10.4	13 yrs/35	3.4:1	Left
13	7 mos/5.5	7 mos/15	2.7:1	Left
14	6 yrs/18	17 yrs/64	3.5:1	Right

Donor-Recipient Size Match

The relationships between the donors and the recipients of RLT grafts, their ages and weights, and the type of graft that was prepared are presented in Tables 9 and 10. In the group receiving RLT as a primary graft, our aim was not to exceed four times the weight difference between donor and recipient. In retrospect, it was difficult to predict the relationship between donor and recipient age and weight and the segment eventually used. This is because the relative size and shape of the hepatic segments vary greatly with respect to overall size of the liver. Left lateral segment grafts were used to overcome the largest size disparities; three pediatric donors were used for recipients weighing less than 10 kg. For the retransplant group, the donor recipient weight ratio exceeded once, but the lobe chosen was too large for abdominal closure. Within the donor-recipient weight range of two to four times their weight difference, the left lobe was used in nine instances. When the donor was less than twice as large as the recipient, a right lobe could be used.

Complications

Graft complications were encountered in ten of 14 recipients of RLT (Tables 11 and 12). Severe ischemia damage (n = 5) and acute vascular occlusions (n = 2) were most common. One graft was nonviable (Patient 2). Four others suffered severe ischemia damage that resulted in one intraoperative death and that may also have com-

TABLE 10. *Donor-Recipient Size Match in Retransplants*

Patient No.	Recipient Age/Weight (kg)	Donor Age/Weight (kg)	Weight Ratio (D:R)	Graft (lobe)
3	15 mos/10	22 yrs/64	6.5:1	L lateral
7	6 mos/7	2 yrs/13	2:1	Right
10	12 mos/12	15 yrs/30	2.5:1	Left
12	24 mos/10.5	8 yrs/20	1.9:1	Left

TABLE 11. *Complications in Patients Receiving RLT as a Primary Graft*

Patient No.	Graft Complication	Extrahepatic Complication	Outcome
1	Ischemic injury	Intracranial hemorrhage (Day 3)	Death
2	Ischemic injury Primary nonfunction		Death
4	Graft too large Bile duct necrosis	CMV-G.I. hemorrhage B-cell lymphoma	Death
6	Ischemic injury		Resolved
7	None	Pulmonary failure	Resolved
8	Portal vein thrombosis G.I. bleeding		Resolved
9	Ischemic injury	Intracranial hemorrhage	Death
11	Cholangitis (6 mos post-transplant)	Recurrent pleural effusion	Resolved
13	Arterial thrombosis	Ischemic neurologic injury	Retransplant, alive with neuro deficit
14	None	None	Alive

plicated the postoperative course of two children who died of intracranial bleeding. Ischemic damage resolved in one case. Two patients had portal vein thrombosis and hepatic arterial thrombosis, respectively, the first being successfully treated by declotting and patching the anastomosis. One patient was retransplanted successfully with a RLT. Other complications such as cholangitis (n = 1) and bile duct necrosis (n = 1) were treated with antibiotics or with a Roux-Y biliary reconstruction. In two instances, the graft was too large, necessitating retransplantation in one case and delayed closure in the other.

Extrahepatic complications occurred in virtually every patient receiving RLT except the elective recipient (Patient 14). In seven patients, extrahepatic problems did not affect the transplant function. One patient (Patient 7) required ventilatory support for more than 1 month without its having any significant effect on the transplant function. Two patients with sepsis who received a RLT retransplant showed normal liver function until their final decompensation. CMV infection resolved upon treatment in one patient (Patient 15), but led to severe intestinal bleeding in another patient, who subsequently died.[15] Rejection episodes occurred in eight patients and responded to bolus steroid therapy in all.

Discussion

The series reported here includes the first 162 transplants performed at the University of Chicago. The program was established as a joint effort among the Departments of Surgery, Medicine, and Pediatrics, because we recognized the complex needs of liver patients. We have continued to function with the team concept and have solicited active participation from anesthesiologists, intensive care specialists,[10] psychiatrists, and infectious disease personnel, in addition to the surgeons and hepatologists originally involved.[16–18]

TABLE 12. *Complications in Patients Receiving RLT as a Retransplant*

Patient No.	Graft Complication	Extrahepatic Complication	Outcome
3	Ischemic injury		Intraop death
5	Graft too large	CMV (resolved)	Retransplant alive
10	None	Sepsis	Death
12	None	Sepsis	Death

In the initial stages of development, most patients were referred from the Chicago area, and included a large percentage of decompensated patients who required intensive medical workup and treatment. Many of these adult candidates died before an operation could be considered (Table 1). The pattern of referral has changed because of communication with our professional colleagues and programs of continued medical education. The broader acceptance and understanding of transplantation has resulted in a patient population that has increased during the past year, yet many patients are still being referred late in the course of disease. However, fewer adults have died before transplantation could be considered (13.6% in 1987 *vs.* 39% in 1985), perhaps because of improved medical management and donor referral (Table 1).

Because of regional organ sharing, sharing within the national pool of donors through the UNOS system, and the acceptance of crossing ABO blood groups, the death of an adult who is still on the transplant waiting-list has become something of an exception. However, it is still a major problem for pediatric transplantation, with 25–50% of candidates dying before a donor becomes available.[7,11,13,19,20] It is estimated that children less than 2 years of age are at an even greater risk of death before transplantation can occur, because availability of small donors is more scarce than it is for larger children.[4,8,9] The estimated waiting time for small pediatric recipients has increased with increasing demand,[8] and this nearly precludes treating children with acute liver failure.[21]

The concept of RLT has been developed to overcome this shortage of donor organs and to include in the group

of transplant candidates children with acute liver failure. Bismuth first reported the use of RLT in 1983.[10,11] It was developed on the basis of two precepts. First, the technical feasibility results from the segmental anatomy of the liver[22–25] as it is encountered by routine hepatic surgery.[18,26,27] Second, relative to infants' organs, adult or larger pediatric donor organs have become more available.

This results from there being a larger population pool in which more head injuries caused by accidents are likely to occur, causing maldistribution of liver donors. For example, in the Illinois procurement area, in 1986 only 40% of 143 cadaveric renal donors were also liver donors.* Other reports confirm these figures and reveal a wastage of procurable livers due to a lack of size-matched recipients.[28]

Pediatric donor organs, however, will always be scarce, particularly for the smaller recipients. There is a bimodal distribution of end-stage liver disease in children. Uncorrectable biliary atresia, which accounts for the majority of infants who require transplantation, and several metabolic disorders account for a peak near the end of the first year.[8,9] Later, near the end of the first decade and increasing into adolescence, a second peak is observed to result from progressive cirrhosis in patients with biliary atresia and successful Kasai procedure, alpha-1-antitrypsin deficiency and chronic active hepatitis. In the latter group, organ availability is not the problem that it is in the former.

Many small infants (*i.e.,* weighing less than 10 kg) die before a whole infant organ becomes available. Indeed, referrals from two major pediatric surgical groups for orthotopic liver transplantation (OLT) were more apt to die before transplant than after.[8] RLT provides a flexibility in using available cadaveric donor organs to match size disparities and in using all available organs to reduce the loss of infants waiting on the transplant list.

Partly as a result of this strategy, at the University of Chicago, the loss of pediatric patients on the list was as little as 4% (Table 2).

Fulminant liver failure (FHF) has a high mortality rate with medical therapy.[29,30] Results of liver transplantation in adults with FHF have been encouraging, with a 1-year survival rate of more than 60% in our own experience, as well as that of others.[17,21] OLT is less of an option in children because of the size of the recipient, which is aggravated by the absence of abdominal distention from chronic ascites, and the urgency of the need. Therefore, in children and even in small adults with acute liver failure, RLT increases the treatment options dramatically.

The role of RLT in retransplantation for acute graft failure due to primary nonfunctioning graft or hepatic artery thrombosis is difficult to assess.[21,31] Survival of patients in Stage 4 coma and multiorgan failure at the time of retransplantation has not been reported, and, if possible, this setting should be avoided for retransplantation to be successful. Hence, a suitable organ procured in a timely fashion would provide survival for the child with acute graft failure.

It is important to recognize that RLT improves the use of donor organs and does not deprive another patient who needs a graft. Organs from elementary school-aged children are most useful in transplanting infants through RLT. In this same age group, liver disease is at an ebb and accident rates are high, producing a donor-recipient mismatch. Although greater usage of childrens' and adults' organs may be realized as referrals increase, they will always be more available than infants' organs. Also, the logical extension of RLT is "split-grafting," where two RLTs are performed with one organ, which will further improve usage of organs.[32] A recent analysis from our center involving the ethical issues surrounding RLT indicates that a strategy involving RLT will be to the advantage of the pediatric liver transplant candidate.[33]

Two technical problems remain important to RLT: adequate size reduction and the control of hemorrhage or leaking from the resected surface.

Preparing a RLT is dependent on the size and shape of the donor liver, which is not predictably related to the body weight, size or abdominal circumference of the donor. To avoid the possibility of wasting the organ, a backup size-matched recipient should be prepared for transplant. The size reduction is generally feasible if the donor is no more than 4–6 times the weight of the recipient. The donor liver should be delivered intact into the recipient operating room, and, with the recipient's abdomen open, the choice of the lobe should be made. In general, the right lobe is the largest usable segment, although in one instance a disproportionately large left lobe was used. With regard to special arrangement and vascular anastomoses, the right lobe best fits into the right upper quadrant with a vena cava, hilar structures and the cut surface being easily accessible.

Alternatively, the entire left lobe provides a prostheses of similar size if the AP diameter of the graft is small enough to allow closure of the abdomen. Occasionally, the vena cava has to be reduced in diameter through a longitudinal incision and resection of part of the back wall. The portal vein requires some more length because the hilum is leaning more toward the right side. With the celiac trunk attached to the hepatic artery there is enough length to reach the recipient's common hepatic artery or suprahepatic aorta.

A left lateral lobe has been used twice in this series (three in personal series).[11] It is the smallest functional unit to which the liver can be reduced and was performed when donor-recipient weight ratio exceeded the factor of

* Illinois Transplant Society, 1986 (unpublished data).

6. The dissection is technically easier than the other two methods described because there is sufficient length of the portal vein and the hepatic artery can be achieved by dissection of the left median segment. Furthermore, the cut surface is relatively small in diameter and anatomically follows the falciform ligament. Reconstruction of the hepatic vein outflow can be accomplished in two. First, a vascular interposition for the recipient vena cava with a segment of the median left hepatic vein attached can be used by adapting the diameter of the vena cava outflow to the suprahepatic vena cava of the recipient.[11] Secondly, the recipient vena cava can be preserved during the recipient hepatectomy, and a direct anastomoses between the donor left lateral hepatic vein and the vena cava orifice of the recipient left hepatic vein can be performed.[12]

Biliary reconstruction is usually accomplished by hepatico-enterostomy in all RLT. It is important to note that the bile duct must be short when a left lobe or left lateral segment is being used because the blood supply of the duct usually originates from the right hepatic artery and is cut off when those lobes are used.

Occasionally, the anterior-posterior dimension of the left lateral segment can be too large to allow comfortable abdominal closure at the time of transplant, although the abdomen needs only to be decompressed above the liver surface. Secondary closure can be attempted, but failure to do so can lead to infection. In one case, a retransplantation became necessary to overcome this complication.

Bleeding from the resected surface has been minimal, and occurred only in cases with diffuse coagulopathy. Meticulous suturing during the bench procedure, mattress sutures of the parenchyma, and infrared light coagulation have been sufficient to control bleeding or bile leakage. The use of tissue glue or polyacrylic surface spray has been reported by other groups to seal off the surface,[7,13,20,34] but was not used in our series.

Other details of the procedure, blood loss, operating time, ischemia time, and early functional assessments have been reported elsewhere.[6] Since ischemia damage accounted for three instances of severe malfunction of the graft, the advent of improved organ preservation, using solution originating from the University of Wisconsin, should avoid these complications and allow a more leisurely dissection. In addition, by extending the indication of RLT for more elective candidates, results are expected to improve simply because the candidates have more reserve to overcome complications.

In conclusion, our initial clinical series demonstrates that long-term survival with RLT is possible. The procedure could also serve as a temporary support measure in cases of fulminant hepatic failure or graft failure until an optimal donor can be located. Our group and others have had sufficient experience to find that this operative technique is developed to the degree that the operative risk is comparable to that of whole liver grafting. By overcoming size limitations, RLT can increase use of available donors without competition with adult recipients who are likewise awaiting transplants. Further experience with planning and execution of size reduction is mandatory to optimize the application of RLT.

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Discussion

DR. RONALD W. BUSUTTIL (Los Angeles, California): Dr. Broelsch and his colleagues have focused their attention on the dire problem of the existing shortage of pediatric donors for critically ill children with end-stage liver disease. In this presentation they have reported their experience with reduced size organ transplantation in a group of 14 children urgently in need of liver replacement. These pediatric patients had the usual indications for urgent liver grafting, including retransplantation, fulminant hepatic failure, and rapidly aggressive chronic liver disease. The technique used has been previously described and is based on the anatomic removal of hepatic segments to allow a suitable fit into a small recipient. The use of the left lobe is most appealing, in that it requires minimal tailoring of the vena cava and avoids the potential problem of bile duct necrosis that can occur when a left lateral segment is used alone.

Using a reduced liver graft, six of ten patients who underwent primary transplantation survived. However, only one of four patients who were retransplanted with a reduced graft survived. This is discouraging, because it seems that retransplantation would be the Number One indication for a reduced size organ graft.

What is of further concern is that the reduced organ is fraught with a 70% incidence of graft complications. These range from global graft ischemic damage to both hepatic artery and portal vein thrombosis. To put this into perspective, I have looked at our own experience with pediatric liver transplantation at UCLA, and specifically, at that subgroup of patients who we would consider to be potential candidates for reduced size livers—namely, those pediatric patients who were in urgent need of retransplantation.

(Slide) Two hundred fifty-nine liver transplants were performed at UCLA between February 1, 1984 and April 15, 1988. Of these 259 cases, 109 pediatric liver transplants were performed on 91 children. These children ranged in age from 5 months to 15 years, with a mean of 5 years. Our overall 4-year actuarial survival rate of these 91 patients is currently 80%. Eighteen of these children required retransplantation and make up the group shown on the bottom curve. Indications for retransplantation included hepatic artery thrombosis (seven patients), primary nonfunction (four patients), and liver rejection (seven patients). For none of the patients who required retransplantation were we unable to find a donor. We mismatched blood groups in eleven cases and generally accepted even the so-called "bad donor."

What is clear is that these children did not do as well as those with primary grafts. However, their rate of survival is still significant, underscoring the benefits of an aggressive policy at retransplantation using only whole organs. Four-year actuarial survival of this group of 18 patients who underwent retransplantation is 61%. The reduced organ size graft technique is a novel one, and I commend Dr. Broelsch on his pioneering efforts. However, I would caution against its widespread acceptance until more experience is accumulated to properly define its role in pediatric liver transplantation.

I would like to conclude by asking three questions.

If one looks at the donor age and weight, which were used for reduced size organs, eight organs were of pediatric size, which we would prefer to use for a recipient of that size. Thus, isn't this technique potentially reducing the pool of grafts that might be more appropriately suited for those pediatric recipients who would have a more favorable prognosis?

There seems to be a higher incidence of infection and intracranial hemorrhage in these patients than one would anticipate with those having whole organ grafts. Dr. Broelsch, do you believe that this is due to greater graft ischemia or to the poor quality of the host in whom you are implanting the organ?

If one takes this technique one step further, do you feel that it is applicable to living related partial hepatic grafts?

DR. ROBERT J. CORRY (Iowa City, Iowa): I would like to compliment Dr. Broelsch and the other authors on this outstanding presentation, and I commend them on their application of a partial donor liver graft in overcoming the size disproportion of some children who, because of the limited number of pediatric donors, might not otherwise receive a liver graft.

Several years ago, Dr. Ron Malt of the Massachusetts General Hospital and I used partial liver grafts for heterotopic auxiliary transplantation in dogs, primates, and in one human. We believed that this procedure could be used as a bridge for those patients who might be able to recover their own liver function, and perhaps also be used as a permanent graft in high-risk patients.

As you are aware, at that time (20 years ago), the success rate of this technique as well as that of even the orthotopic technique was not good, and the heterotopic liver transplant procedure was abandoned in humans. However, as you know, auxiliary grafting has recently been applied in a few of the European programs with some long-term success, particularly in reoperative patients and other high-risk patients.

So my question, Chris, is whether or not you plan to extend this unique technique of transplanting a portion of the donor liver as either a bridge for patients who might recover their own liver function or possibly even as a permanent graft in high-risk patients.

DR. CHRISTOPH E. BROELSCH (Closing discussion): Thank you, Dr. Busuttil and Dr. Corry for your remarks. I believe that Dr. Busuttil pointed in the right direction regarding the application of this procedure; at the present time, urgent retransplantation is where the scarcity of donor organs in children is preeminent.

In most instances, the success of retransplantation relies on the immediate availability of organs. I haven't presented our data yet on the retransplanted children with full-size organs. When you get a full-size organ within 24 hours after the decision for retransplant has been made, the results certainly will be better.

In the past, we would wait 24 hours or even 48 hours to get a full-size graft first, and when this didn't succeed, we would increase the weight range of the donor to get any piece of liver in order to attempt the