Size Reduction of the Donor Liver Is a Safe Way to Alleviate the Shortage of Size-Matched Organs in Pediatric Liver Transplantation

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The development of pediatric liver transplantation is considerably hampered by the dire shortage of small donor organs. This is a very sad situation because in most experienced centers, liver replacement can offer a long-term hope of survival of more than 70% in a growing variety of pediatric liver disorders. The reported experience with 54 reduced-size grafts on a total of 141 transplants performed in 117 children between 1984 and 1988 demonstrates that the technique of reduced-size liver transplantation not only allows long-term survival but, in fact, offers the same survival hope with the same quality of liver function, regardless of the child's age and clinical condition. The prominent feature of our experience with the reduced liver concerns its deliberate use for elective cases. Seventy-seven per cent of the 30 children who electively received a reduced liver were alive 1 year after transplantation, as were 85% of the 62 children who received a full-size graft. There is no difference in the long-term survival rate of patients who received elective grafts, which is in the range of 75% with both techniques.

THE FIRST CHILD to receive a reduced-size liver (RSL) harvested from a non–size-matched donor was operated in August 1984.[1] She was 18 months old and suffered from terminal liver failure secondary to biliary atresia. The respective weights of the donor and recipient were 35 kg and 8.5 kg. She did very well and is fully rehabilitated 4.5 years later. After this early successful experience, we became progressively confident with this technique, which we have used for 54 of the 141 grafts (39.4%) performed in 117 children who were less than 15 years old between 1984 and 1988. Initially we reserved this technique for urgent cases; recently, however, we have started to use it confidently for the elective cases and have formed our present policy of accepting any available donor for any potential candidate regardless of size unmatching (within limits defined on the basis of our growing experience). This policy allows us to keep the mortality rate of children on the waiting list relatively low at 14%.

In this report we present a detailed account of our experience with RSL transplantation with a description of the technique, its limits, and its long-term results in a series of 117 children transplanted between 1984 and 1988. In the long term, there is no difference between the results obtained by transplanting either a full-size liver or a reduced-size graft, both in elective and urgent cases. This technique is safe and reliable and should become part of the armamentarium of every surgeon involved in pediatric liver transplantation.

Both in America and in Europe, 25% to 30% of the children on liver transplant waiting lists die before they can be treated because of the lack of size-matched donor organs.[2] The scarcity of small pediatric donors is even greater in Europe. This is a very sad situation because in most experienced centers liver replacement can offer a long-term hope of survival of more than 70% in a growing variety of pediatric liver disorders.[2–8]

From the start of our pediatric liver transplantation program in 1984, the prospect of children dying while on donor waiting lists was troublesome because two thirds of the potential recipients referred to our center are younger than 3 years of age and weigh less than 12 kilograms.[3] There is heavy ethical pressure to find a surgical alternative so that these children benefit from the larger pool of teenager and adult potential donors, the latter being offered by Eurotransplant in numbers exceeding the demand.[9]

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A videofilm describing the technique of RSL transplantation can be obtained at the cost of BF 5000. Address the order with a bank check to J.B. Otte, M.D., Department of Pediatric Surgery, University Hospital St-Luc, Avenue Hippocrate 10, B-1200 Brussels.

Description of the Procedure

Credit should be given to Bax and coworkers[10] for the first experimental study performed in the dog on the orthotopic transplantation of part of the liver and to Bismuth and Houssin[11] for the first published clinical application. Broelsch and coworkers[12] recently presented their experience with 14 children (13 urgent, 1 elective). Our own initial experience was reported in 1986[1]; several progress reports have followed,[3,13–15] including a detailed description of the technique,[16] which since has been modified on a few points. In each case the decision to perform a RSL transplantation initially is based on the donor–recipient body weight ratio and is confirmed or abrogated on the basis of visual comparison of the respective sizes of the diseased and donor livers.

Initial Preparation of the Graft

Harvesting of the donor liver is performed according to the well-standardized technique of multiorgan procurement. Preservation fluid was initially the Collins solution, although it was recently replaced by University of Wisconsin solution when this was made available to us in August 1988 for a collaborative trial within Eurotransplant. Undoubtedly the latter solution gives more flexibility due to the 2 hours of extra time needed to perform the reduction.

The work on the back table starts, as usual, with trimming of the diaphragm and dissection of the liver pedicle after proper identification of the hilar structures. Traction sutures are placed on both ends of the vena cava before its dissection away from the right liver. Constant attention should be paid to avoid untoward rewarming of the graft by keeping it immersed in the ice-cold preservation fluid during the lengthy procedure, the graft being partly elevated above the fluid only as much as needed.

Anatomical Landmarks and Extent of Reduction

The technique consists of a transparenchymal *ex vivo* right hepatectomy or lobectomy according to the Couinaud terminology (right bisegmentectomy or trisegmentectomy in the American terminology).[17] A choice is made between the two variants according to the amount of liver tissue to be removed to have a reduced liver of appropriate size to fit to the recipient liver fossa.

In both cases we detach the whole retrohepatic vena cava from the liver substance up to the outlet of the hepatic veins. This is needed for later resection of the prominent part of the caudate lobe, which reduces the sagittal diameter of the graft, and it helps to perform the portal anastomosis and the tailoring of the lower end of the vena cava when needed to approximate the size of the recipient infrahepatic vena cava (see below).

The next step is the dissection of the right hepatic vein, which is encircled close to the vena cava and then divided; the orifice in the vena cava is closed by a double running monofilament suture. The water tightness of this suture is carefully checked; additional sutures are placed when needed on the orifices of the accessory hepatic veins.

For bisegmentectomy, the resection line on the inferior surface of the liver (Fig. 1) starts just medial to the orifice of the divided right hepatic vein, runs on the right side of the IVC groove and of the caudate lobe to the right of the hilum and on the gallbladder fossa anteriorly. Over the incisure of Ganz where the posterior branch of the right Glisson's pedicle lies, transection is slightly displaced laterally to preserve the anterior branch that supplies the medial part of segment VIII (see below).

On the superior surface of the liver (Fig. 2), the line of resection is marked again from the orifice of the divided right hepatic vein to the gallbladder fossa, curving to the

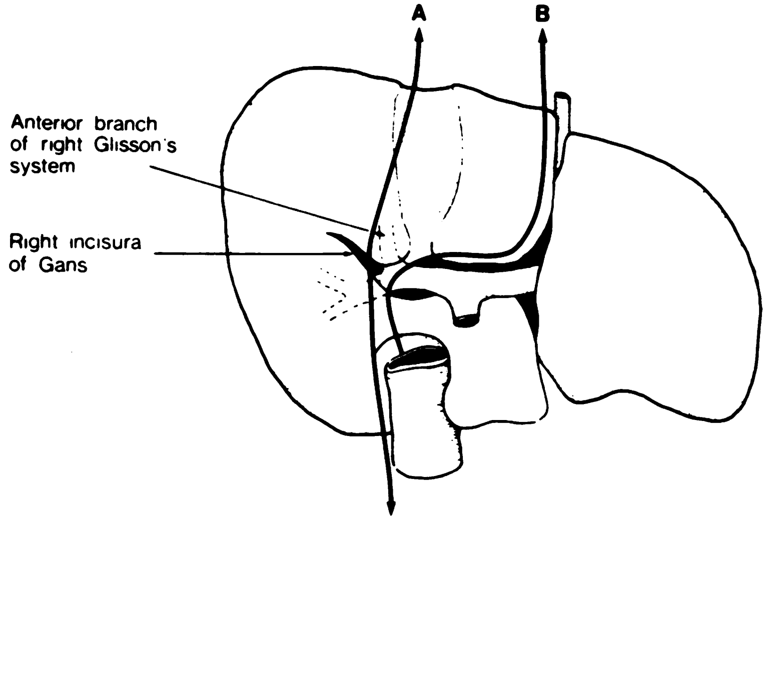

FIG. 1. Resection line on the inferior surface of the liver. (A) In case of bisegmentectomy; (B) in case of trisegmentectomy.

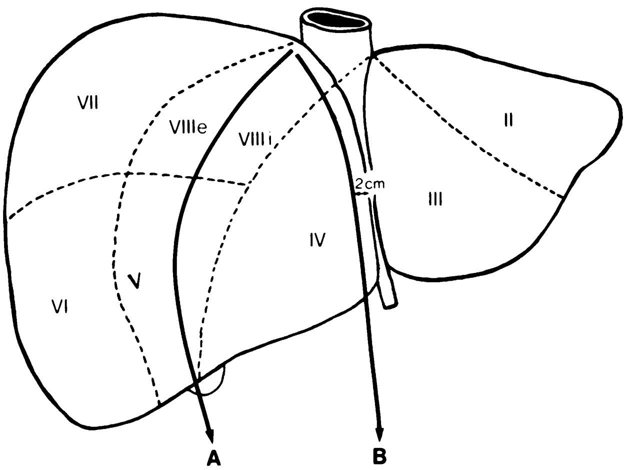

FIG. 2. Resection line on the superior surface of the liver. (A) In case of bisegmentectomy (with preservation of the internal part of segment VIII); (B) in case of trisegmentectomy. Liver segmentation according to Couinaud (see text).

right to preserve the medial part of Couinaud's segment VIII.

For trisegmentectomy the line of transection on the inferior surface follows the umbilical fissure with a margin of ± 2 cm to the right, across segment IV (quadrate lobe or medial left segment). The line of transection on the superior surface of the liver starts on the right side of the medial hepatic vein to preserve its last portion. It extends along the falciform ligament with a margin of ± 2 cm to the right to preserve the Glisson branches to segments II and III (lateral left segment)

In both technical variants the prominent part of the caudate lobe (segment I) is resected with transparenchymal division and ligation of the encountered vascular and biliary structures. The raw surface of the resected caudate lobe is then covered by approximating the edges of the liver capsule.

At the completion of the procedure, the reduced liver will comprise segments II, III, IV (left lateral and medial segments in the American terminology), and the medial part of segment VIII in the case of bisegmentectomy, and segments II and III (left lateral segment) in the case of trisegmentectomy.

Technique of Transection and Transparenchymal Division of the Glissonian Branches (Figure 3)

The liver capsule is incised with the knife over both the superior and the inferior surface as described earlier. Starting from the anterior edge, the liver is gradually divided by crushing the liver substance with a mosquito clamp. Vascular and biliary structures that resist this crushing are grasped with mosquito clamps and ligated. All glissonian branches are approached transparenchymally. The first ones to be encountered in the case of bisegmentectomy are anterior branches leading to segment V; next the posterior branches to segments VI and VII are approached through the incisura of Ganz and are divided. The last branch to be divided is the one going to the outer part of segment VIII. In the case of trisegmentectomy, the anterior and the posterior branches of the right glissonian pedicle are divided separately while the glissonian branches going to segment IV are approached while dividing the parenchyma on the right side of the falciform ligament. The medial hepatic vein is transected at some distance of its outlet in the vena cava. The major branches are closed with double running 4/0 polydioxanone (PDS) sutures.

After the liver reduction is completed, cold preservation solution is infused through the portal vein, the hepatic artery, and the common duct under appropriate pressure to check for vascular and biliary leakage. Leaks are oversewn with fine sutures of PDS. The raw surface is dried with a piece of gauze and covered with fibrin sealant (clottable protein-aprotinin-thrombin-calcium chloride solution*) that has been warmed to 37 C a few minutes before use to seal the small leaks left behind during the section of the liver substance. We apply two layers of Tissucol at 5 mL per layer.

We must stress again that throughout the entire procedure the liver must be kept immersed in the ice-cold preservation solution, except for the raw surface when it has to be exposed for sealant application.

Transplantation Technique

The reduced liver is transplanted orthotopically with slight modifications of the standard technique (Fig. 4).

The reduced graft must be rotated between 60 and 90 degrees counterclockwise around the axis of the vena cava to fill the right hepatic fossa and keep the raw surface against the posterolateral abdominal wall.

To rotate the graft on its vertical axis, the corner sutures of the suprahepatic caval anastomosis are shifted. The left corner suture is placed on the posterior margin of the vena cava at the junction between the left hepatic vein and the posterior wall. The right corner suture is placed opposite on the anterior wall. The rest of the suprahepatic caval anastomosis is done in a routine fashion, taking special care to identify the posterior wall of the donor IVC while doing the posterior suture.

The infrahepatic caval anastomosis is done next. To overcome the size discrepancy with the recipient vena cava, the donor vena cava is tailored to the appropriate size by removing a triangular portion of its anterior wall and closing the defect with a running suture; the previous

*Tissucol, Immuno AG, Austria.

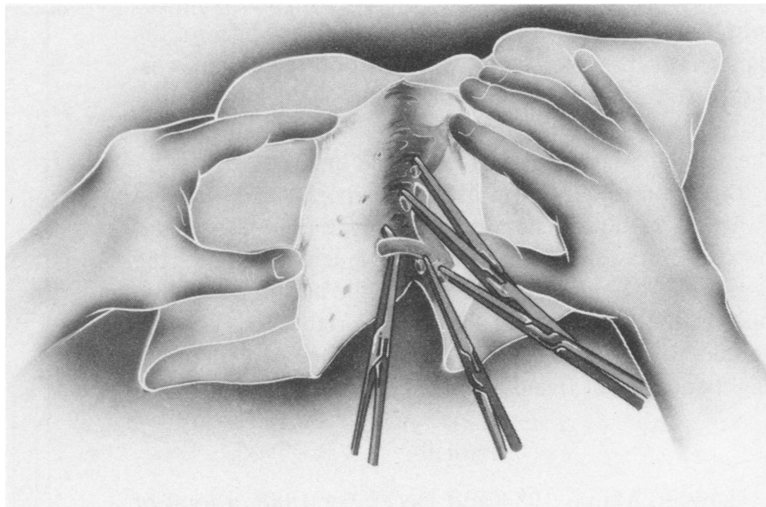

FIG. 3. Transparenchymal resection in case of bisegmentectomy: branches going to segments V and VI have been divided; pedicle of segment VII encircled by forceps; pedicle to outer part of segment VIII still intact (upper part).

full mobilization of the retrohepatic vena cava makes this tailoring much easier. The portal vein anastomosis is done in a routine fashion; size discrepancy can be overcome by resecting the recipient portal vein up to the splenomesenteric junction.

All three venous clamps are then released, allowing for portal reperfusion of the graft. Residual leaking points from the raw surface can be temporarily controlled by compression and later by extra sutures if needed.

The arterial anastomosis is performed end-to-end between the common hepatic artery or the celiac axis of the donor and the recipient proper hepatic artery at the takeoff of the gastroduodenal artery or the common hepatic artery. Alternatively, when the discrepancy is too great,

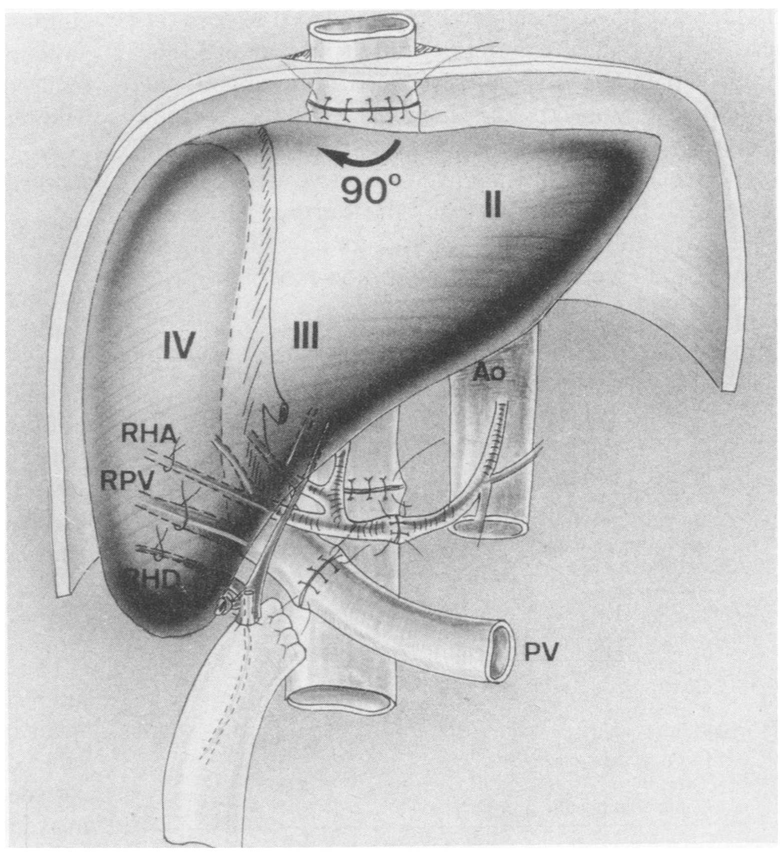

FIG. 4. Technique of orthotopic transplantation of the reduced liver (artist view). Counterclockwise rotation of the graft with transparenchymally divided pedicles of the right liver (RHA: right hepatic artery; RPV: right portal view; RHD: right hepatic duct). Most often the reduced liver comprises Couinaud segments II, III and IV (left lateral and medial segments).

the donor celiac axis is anastomosed with the recipient infrarenal aorta approached from behind the head of the pancreas, occasionally with interposition of an iliac prosthesis harvested from the same donor.[18] When it is anticipated that the portal vein will obstruct access to the artery, the arterial anastomosis can be done first.

Biliary reconstruction is always performed using a Roux-en-Y choledochojejunostomy with an internal stent brought to the skin either through the jejunal loop or the donor cystic duct. Drains are left in the peritoneal cavity, one on the left side and two on the right side, in close contact with the raw surface; the latter ones are kept under slight suction for five days to collect oozing blood.

Patients

Between March 1984 and December 1988, a total of 141 transplants were performed in 117 children. The indications for liver replacement were cholestatic diseases in 92 (biliary atresia in 86), metabolic diseases in 18, and miscellaneous in 7 (Table 1).

The age of the recipients was between 0 and 3 years in 73, (10 aged less than 1 year), between 3 and 6 years in 21, and between 6 and 14 years in 23 (Fig. 5).

Full-Size Liver and Technical Variants

Of the 141 grafts, 83 were full-size livers (59%) while 58 (41%) were technical variants : a reduced liver in 54, a partial or segmental graft in 1, and a split liver in 3. The only segmental graft was performed according to the technique described by the Hannover[19] and the Brisbane groups.[20]

The technique of the split liver, which we used for three children, is reported separately;[21] the fourth half liver obtained with this technique was used for an adult patient.

With the exception of two cases, the experience with the technical variants has been gained from 1986 to 1988 (Table 2). Tables 3 and 4 give the repartition for the first and the second orthotopic liver transplants (OLT) and for the age categories respectively; a similar proportion of children of every age group benefited from the technical variants. The data presented below are restricted to the reduced livers, excluding, for clarity, the four children who received either a segmental or a split liver.

TABLE 1. *Indications in 117 Children*

Indication	No. of Children (%)
Cholestatic diseases	92 (79)
Biliary atresia	86
Ductular paucity	4*
Sclerosing cholangitis	2
Metabolic diseases	18 (15)
Byler disease	6
Wilson	4
α-1-antitrypsin deficiency	2
Crigler-Najjar	2
Glycogenosis	2
Tyrosinemia	2
Miscellaneous	7 (6)
Cryptogenetic cirrhosis	3
Tumors	3
Congenital hepatic fibrosis	1*

* Two children received a combined liver and kidney transplant.

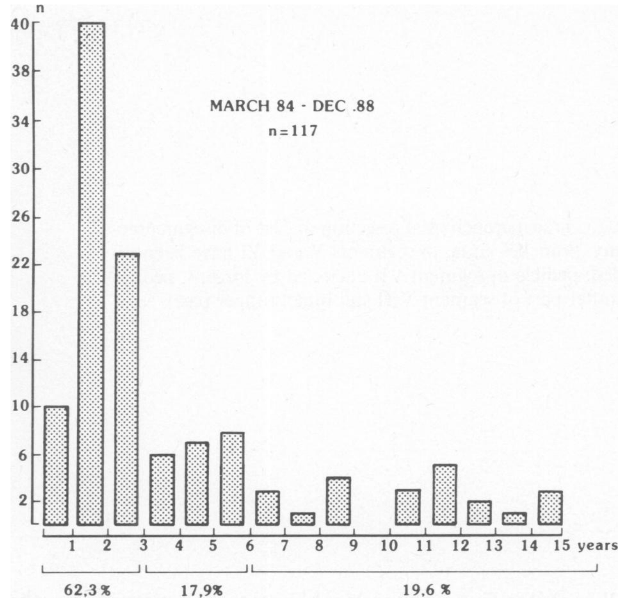

FIG. 5. Age distribution of 117 recipients.

Reduced Livers

Of a total of 137 grafts performed in 113 children, 54 (39.4%) were livers reduced in size on the back table using the technique described above (Table 5).

The proportion of reduced livers was 32.6% and 62% of the elective OLT and the urgent OLT, respectively, and 37% and 50% of the first grafts and the secondary grafts, respectively.

The proportion of reduced livers was similar regarding the indications: 37.7%, 37.2%, and 33.3% of the children transplanted for cholestatic, metabolic, and miscellaneous diseases, respectively (Table 6).

Donor–Recipient Weight Ratio

The difference between the respective weights of donors and recipients can best be expressed as a weight ratio. The mean ratio was 3.5 (1.5:7.7) for the entire series of 54 reduced livers, which means that the weight of the donors exceeded the weight of the corresponding recipients by an average 250%. The mean weight ratio increased slightly over the years due to increased experience and confidence

TABLE 2. *Experience with Technical Variants According to the Years*

Year	Whole Graft	Reduced	Partial	Split Liver	Total	Recipients
1984	3	1			4	4
1985	11	1			12	11
1986	14	16			30	27
1987	32	15			47	34
1988	23	21	1	3	48	42
Total	83 (59%)	54	1	3	141	117
		41% (Reduced + Partial + Split Liver)				

with the technique (Table 7). It was lower in elective cases (3.3; range, 1.5 to 5.6) than in urgent cases (5.4; range, 4.1 to 7.7), which is explained by the greater difficulty to rapidly find a donor of appropriate size in urgent situations (Table 8). On the basis of our initial experience, we recommended not to exceed a weight ratio of 4 (300%); however we went beyond that ratio on 11 occasions, and the highest figure was 7.7 (670%) in an urgent retransplantation.

Results

Actuarial survival rates of patients and grafts were calculated according to the Kaplan–Meier method.[22] For statistical analysis, the children who were retransplanted were allocated to the group of the first graft they received (full-size or reduced graft) and survival was calculated from the time of the first transplant. The survival curves were compared by the Mantel-Haenszel test.[23]

Patient Survival

The 1-year survival rates are 77% for the entire series (N = 113), 82% and 68% of the children grafted with full-size livers (n = 71) and reduced livers (n = 42), respectively (Fig. 6).For the elective patients, the 1-year survival rates are 83%, 85%, and 77% for the entire series (N = 92), the full-size livers (n = 62), and the reduced livers (n = 30), respectively. For patients undergoing urgent procedures, the rates are 52%, 67%, and 43% for the entire series (N = 21), the full size livers (n = 9), and the reduced livers (n = 12), respectively (Fig. 7).

Graft Survival

The 1-year survival rates are 64% for the entire series (N = 137), 69% and 54% for the full size livers (n = 83) and the reduced livers (n = 54), respectively (Fig. 8). For the elective grafts, the 1-year survival rates are 75%, 79%, and 68% for the entire series (N = 93), the full-size livers (n = 63), and the reduced livers (n = 30), respectively (Fig. 9). For the urgent grafts, the rates are 38%, 40%, and 35% for the entire series (N = 44), the full-size livers (n = 20), and the reduced livers (n = 24), respectively (Fig. 10). Sixty-nine per cent of the first grafts (N = 113) were functional at 1 year (73% and 61% of the full-size livers (n = 71) and the reduced livers (n = 42), respectively). Forty per cent of the second grafts (N = 24) were functional at 1 year (50% and 29% of the full-size livers (n = 12) and the reduced livers (n = 12), respectively).

Graft Loss

Twenty-six of the 83 full-size livers were lost (31%), 17 from hepatic causes (9 instances of hepatic artery thrombosis and 6 instances of PNF) and 9 from nonhepatic causes.

Twenty-four of the 54 reduced livers were lost (44%), 12 from hepatic causes (3 instances of hepatic artery thrombosis and 3 instances of PNF) and 12 from nonhepatic causes (mostly operative deaths and infections

TABLE 3. *Experience with Technical Variants in First Grafts and Retransplantations*

	Whole Graft	Reduced	Partial	Split Liver	Total
1st OLT	71	42	1	3	117
2nd OLT	8	10			18
3rd OLT	4	1			5
4th OLT		1			1
Total	83 (59%)	54	1	3	141 (100%)
		41% (Reduced + Partial + Split Liver)			

TABLE 4. *Experience with Technical Variants According to the Age of the Children*

Age of Recipients	Whole Graft	Reduced	Partial	Split	
Less than 3 years n = 88 (62%)	55 (62%)	32	1	—	33 (38%)
3–5 years n = 26 (18%)	12 (46%)	11	—	3	14 (54%)
6–14 years n = 27 (20%)	16 (59%)	11	—	—	11 (41%)

TABLE 5. *Distribution of Grafts according to Circumstances of Transplantation*

Type of Graft	Whole Liver (%)	Reduced Liver (%)
Elective OLT n = 92	62 (67.3)	30 (32.6)
Urgent OLT n = 21	8 (38)	13 (62)
Primary graft n = 113	71 (62.8)	42 (37)
Secondary graft n = 24	12 (50)	12 (50)
Total n = 137	83 (60.6)	54 (39.4)

TABLE 7. *Donor-Recipient Weight Ratio*

	1984	1985	1986	1987	1988
Number of grafts	1	1	16	15	21
Mean ratio	4	2.3	3.25	3	4
Range	—	—	1.6–5.6	1.5–7.7	1.8–6.5
Ratio >4	—	—	2	3	6

Reduced livers, n = 54.
X = 3.5 (1.5:7.7).

observed in urgent cases and in retransplantations; Tables 9 to 11).

In addition to the 12 grafts lost due to hepatic artery thrombosis, there were six more instances of this complication in young children who remained alive without retransplantation at the cost of a biliary stricture that had to be surgically repaired. Thus the total incidence of hepatic artery thrombosis was 17% (14 of 83) for the full-size livers and 7% (4 of 54) for the reduced livers (Table 12).

Liver Function

Of 74 patients bearing functional grafts 6 months after transplantation, 67% had completely normal liver tests (serum glutamic pyruvic transaminase [SGPT], gamma-glutanyl-transferase [GGT], and bilirubin) and 14% had slightly abnormal liver tests (SGPT and gamma-GT less than twice the normal values but normal bilirubin). The corresponding figures were 63% and 20% for the full-size livers, and 76% and 4% for the reduced livers (Table 13).

Discussion

Long-term survival in the range of 70% to 80% can now be obtained in children in a growing number of liver transplant centers. Pediatric donor organs, however, are scarce, leading to deaths of a major proportion of the pediatric candidates on waiting lists before a donor of appropriate size becomes available. This shortage is particularly dire in two groups: infants and children younger than 3 years, and those needing urgent transplantations. The first category includes a large number of children referred because of unrelieved biliary atresia (representing more than two thirds of the children referred with this indication to our center[24]) or metabolic diseases leading to liver failure in early life (such as tyrosinemia and familial cholestasis).

The discrepancy between the increasing waiting list and the limited donor pool leads to an unacceptable lengthening of the waiting time which, in our center, averages 1 year for small children with blood type O and B. Meanwhile many of them suffer worsening of their condition, which leads to death on the waiting list or to anticipated transplantation in a semiurgent situation with by-passing of other children whose conditions are more elective, and attrition of the survival rates.

The second category includes the urgent liver grafting for either graft failure (due to primary nonfunction or, infrequently, at least in our experience, hepatic artery thrombosis[18] and uncontrollable acute rejection) or fulminant hepatitis; in all these circumstances, the chance of success sharply decreases when the waiting time for an appropriate donor exceeds 24 hours because of multiorgan failure and irreversible brain damage.

It is consistent with medical ethics to try new surgical techniques in desperate situations that can not be solved by standard methods if it can benefit the patient. In this context it was natural that the technique of RSL transplantation was first applied to urgent situations for which a size-matched donor could not be found; this was our experience, as well as Broelsch's,[12] because we are not as fortunate as some of our American colleagues to find easily appropriate pediatric donors for urgent grafting or re-

TABLE 6. *Reduced Livers According to Indications*

Indications	Total	Whole Liver				Reduced Liver			
		Elective	Urgent	Total	%	Elective	Urgent	Total	%
Cholestatic diseases	90	50	6	56	62.2	26	8	34	37.7
Metabolic diseases	17	8	3	11	64.7	2	4	6	35.2
Miscellaneous	6	4	—	4	66.6	2	—	2	33.3
Total	113			71					42

TABLE 8. *Donor–Recipient Weight Ratio*

	Elective (code 2)	Urgent (code 0, 1)
Number of grafts	30	24
Mean ratio	3.3	5.4
Range	1.5–5.6	4.1–7.7
Ratio >4	3	8

Reduced livers, n = 54.
X = 3.5 (1.5:7.7).

transplantation.[25] The results we have obtained in these urgent situations are in the range of 50% for long-term patient survival; the 1-year survival rate was 67% for the children transplanted in emergency situations with a full-size graft and 43% for the children who received a RSL. However up to 6 months (Fig. 6) the survival rates were very similar (67% *vs.* 64%); the increased difference between the two survival curves over 6 months was due to late deaths of children transplanted with reduced-size grafts that were unrelated to the technique (mostly infections). Moreover statistical analysis showed no significant difference between the two survival curves.

Of 13 children transplanted by Broelsch and coworkers[12] with the RSL in emergency situations, five were reported to be long-term survivors with the reduced liver, while two more had to be retransplanted with a full-size graft.

The use of a RSL for urgent transplantation seems to be validated by these data; it may be anticipated from our own experience that resorting to this technique more aggressively when a full-size graft cannot be found will improve the results. In our opinion an aggressive policy of retransplantation should include this surgical variant if the liver is not size matched.

The prominent feature of our experience with the reduced liver concerns its deliberate use for the elective cases. Seventy-seven per cent of the 30 children who received electively a reduced liver were alive 1 year after transplantation, as were 85% of the 62 children who received a full-size graft. The corresponding rates were 83% and 89% at 3 months and 83% and 87% at 6 months (Fig. 7). The increased difference between the two survival curves over 6 months was due to late deaths unrelated to the technique. Moreover statistical analysis showed no significant difference between the two survival curves. There is no statistically significant difference in the long-term survival rates of the elective grafts for either the full-size or the reduced livers.

Statistical analysis of the survival curves was also performed by allocating the retransplanted children to the group of the last graft they received (either full-size or reduced); once again no statistically significant difference was found.

We had a slightly greater graft loss for the reduced livers (44%) than for the full size grafts (31%) (Table 9), but the number of grafts lost from hepatic causes (Table 10) was similar (22% *vs.* 20%). The two cases of poorly preserved reduced livers were experienced when the Collins solution was used, which gave a too-short margin of safety in view of the two hours extra work needed by the reduction whenever there was a long-distance procurement. In this regard the UW solution undoubtedly increases the flexibility.

The relatively high incidence of operative deaths among children transplanted with a reduced liver is related to their very precarious condition at the time of transplantation or retransplantation but not to the technique.

Finally there is no difference in the long term regarding

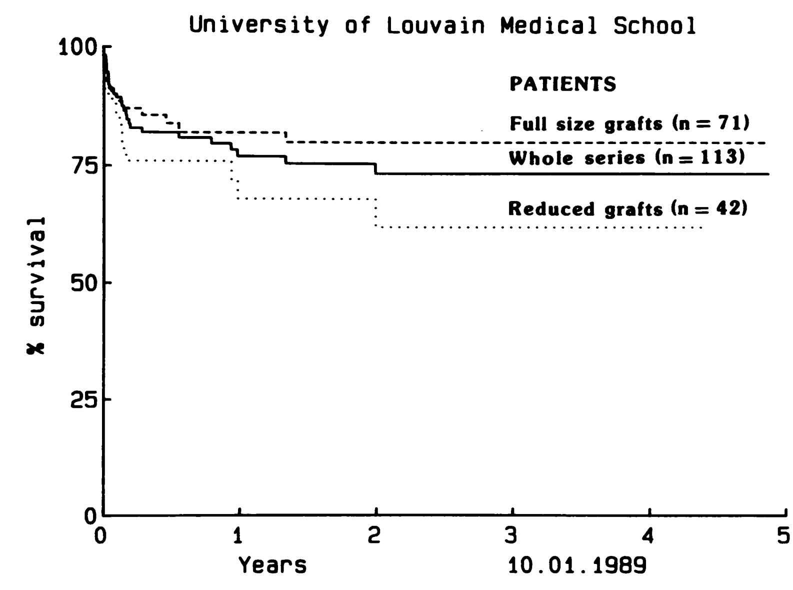

FIG. 6. Patient survival curves according to the technique used. The 1-year survival rate is 77% for the whole series, 82%, and 68% for the children grafted with full-size livers, and the reduced-size livers, respectively.

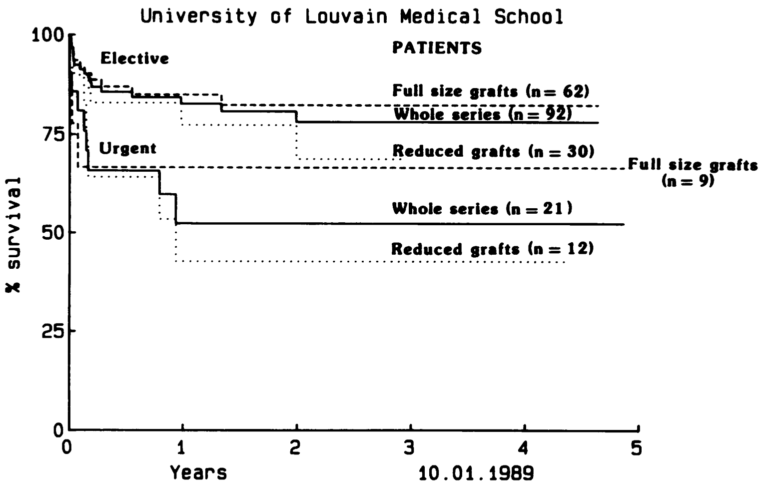

FIG. 7. Patient survival curves according to the circumstances of the transplant. For the elective patients, the 1-year survival rates are 83%, 85%, and 77% for the whole series, the full-size livers, and the reduced-size livers, respectively. For the urgent patients, the respective rates are 52%, 67%, and 43%.

the quality of the liver function (Table 13). Of the 49 children bearing a functional full-size graft 6 months after transplantation, 63% and 20% had completely normal or slightly abnormal liver tests, respectively; the corresponding rates for the 25 children bearing a reduced liver are 76% and 4%. These data show clearly that full rehabilitation is provided equally by the transplantation of a reduced-size liver.

Proceeding by errors and trials, we refined the method. Now we would like to offer the following comments regarding the technique and the possible extent of its application.

When a donor liver has to be reduced in size, it seems logical to discard the bigger part and preserve the smaller one. For this reason we have always used the left lobe, thus preserving the maximal amount of liver tissue that could fit into the liver fossa while allowing an easy closure of the abdominal wall. Depending on the visual comparison of the size and the shape of the two livers, we decide, case by case, how much to resect; the largest reduced liver includes the anatomical left lobe (Couinaud's segments II, III, and IV) and the medial part of segment VIII (this latter detail also gives the raw surface a curved shape, fitting best to the posterior wall of the right liver fossa), while the smallest reduced liver includes only the lateral segment of the left lobe (Couinaud's segments II and III). In between, depending on the available space, we may resect also the medial part of segment VIII and even some part of segment IV (left medial segment), giving the technique maximal flexibility. Proceeding that way and rotating the graft counterclockwise, we never had any serious problem with abdominal closure.

In our first cases we followed the description given by Bismuth and Houssin,[11] placing the reduced liver in its anatomical position in the midepigastric area. The resulting drawbacks were a dead space in the right hypochondrium, which was prone to accumulate blood oozing from the raw surface and the operative field, occasional

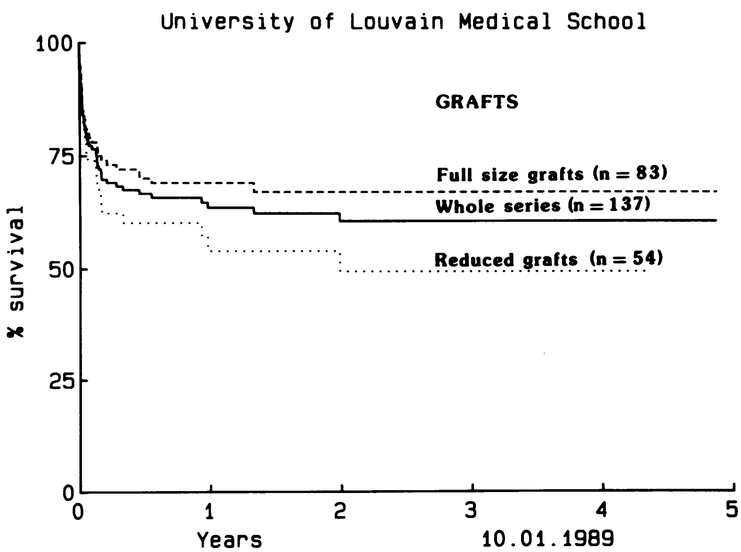

FIG. 8. Graft survival curves according to the technique used. The 1-year survival rates are 64%, 69%, and 54% for the entire series, the full-size grafts, and the reduced-size grafts, respectively.

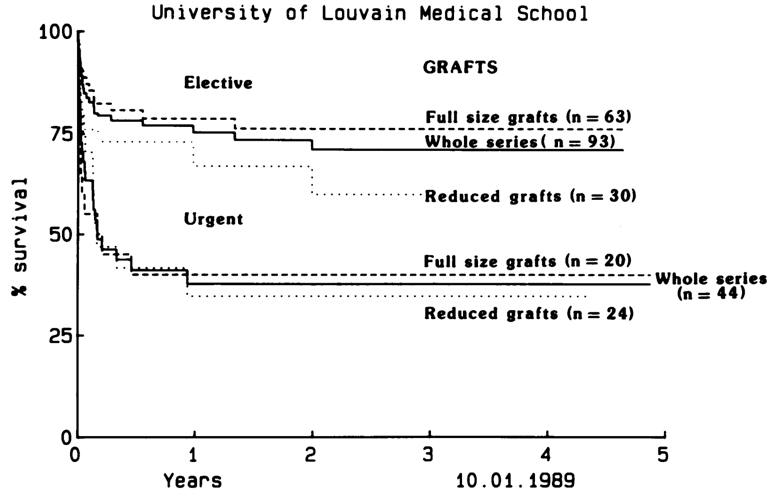

FIG. 9. Graft survival curves according to the circumstances of the transplant. For the elective grafts, 1-year survival rates are 75%, 79%, and 68% for the whole series, the full-size grafts, and the reduced-size grafts, respectively. For the urgent grafts, the respective rates are 38%, 40%, and 35%.

difficulties in the closure of the abdomen due to the bulky shape and size of the reduced graft, and possible twisting of the vascular inflow and outflow caused by the displacement of the graft to the empty right liver fossa occurring during the closure under tension of the abdominal wall.

All these drawbacks can be easily prevented by rotating the graft counterclockwise to the right by 60 to 90 degrees around the axis of the vena cava. As described earlier, this rotation is simply obtained by shifting the corner sutures of the suprahepatic caval anastomosis. Since we have adopted these details, which have soon become a routine part of our current technique, the incidence of blood collection close to the raw surface, which is sometimes secondarily infected, has been eliminated.

Hepatic artery thrombosis is a well-know complication of pediatric liver transplantation, with reported incidence varying between 6%[2] and 40%.[18,26-28] Our own incidence in the present series of 137 grafts was 13%. There was a much lower incidence in children who received a RSL (7%) than a full-size graft (17%). The explanation for this impressive difference is not univocal. Undoubtedly the size of the vascular supply plays a role, as suggested by the higher incidence of thrombosis in children younger than 1 year who receive a size-matched liver, which was observed both in Pittsburgh[29] and in our center.[18] The bigger size of the arterial supply of the reduced liver offers some protection, but also, we believe, the lesser increase in the abdominal pressure resulting from the closure of the wall. Houssin,[30] using implantable doppler probes, has proved that closure of the abdomen resulted in a significant drop of the arterial flow, even after transplantation of a size-matched liver. Due to the shortage of small pediatric donors, we have often transplanted full-size livers, despite the fact that the difference between the donor and recipient weights was more than 20%, which is considered by Shaw and coworkers to be the safe limit.[2] Another complication that might result from this situation is a pressure necrosis of the right lobe, as we have experienced in two children who required a secondary right lobectomy.

During the most recent part of our experience, we have

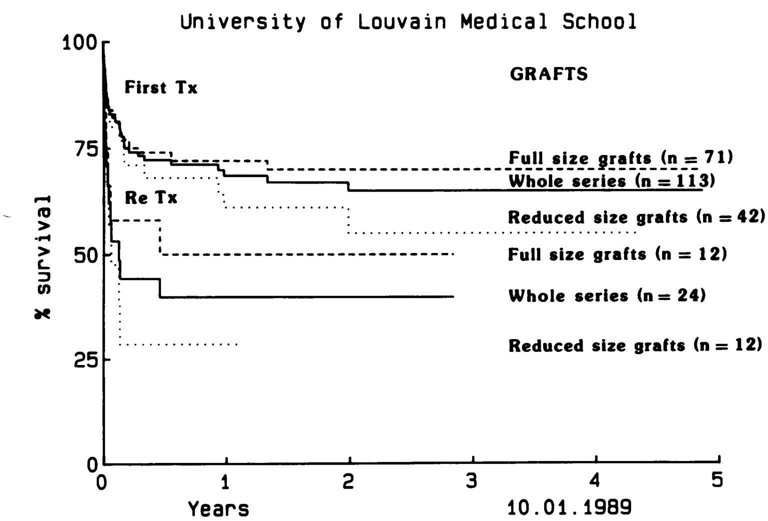

FIG. 10. Graft survival curves of the first grafts and retransplants (re Tx). In the first category, the 1-year survival rates are 69%, 73%, and 61% for the whole series, the full-size grafts, and the reduced-size grafts, respectively. The corresponding figures for the retransplants are 44%, 50%, and 29%.

TABLE 9. *Graft Loss*

Causes of Graft Loss	Full-Size Livers 26/83 (31%)	Reduced Livers 24/54 (44%)
Hepatic	17 (20%)	12 (22%)
Nonhepatic	9 (11%)	12 (22%)

reduced the graft size more and more liberally; this policy, combined with technical refinements including routine use of magnification with 5.5 × loupes and early use within the first 24 hours of antiaggregant substances (Dipyramidol 7 mg/kg and aspirin 3 mg/kg per day), led to a drastic decrease of the arterial thrombosis rate: among 44 transplants performed in 1988 in 35 children with either a full-size graft or a reduced liver, only 4 (9%) were complicated by arterial thrombosis (2 of 23 full-size grafts and 2 of 21 reduced grafts).

To identify the vascular and the biliary structures to be divided, we prefer the transparenchymal approach, but the hilar approach used by Broelsch[12] is undoubtedly of equivalent value; both are commonly used in resection for hepatic masses. The transparenchymal approach is safer, allows more flexibility in tailoring the liver mass to a size fit for use in each individual case, and protects the vascular supply of the common bile duct originating from the right hepatic artery. We have never observed any ischemic necrosis of the common bile duct of a reduced liver with a patent hepatic artery.

Some guidelines are needed regarding the acceptable difference between the potential donor and recipient weights before embarking on a RSL transplantation. We reported earlier that a weight ratio of 4 was the safe limit not to be exceeded.[3] However with increasing experience we have recently exceeded this ratio in 11 occasions, both in urgent retransplantations for graft failure and in elective cases. Such was the case in 2 of 16 reduced livers grafted in 1986, 3 of 15 in 1987, and 6 of 21 in 1988 (Table 7). The highest weight ratio was 7.7 and we would agree with Broelsch[12] that surgeons having extended experience with the technique can go up to a weight ratio of 6, although we would recommend that less experienced surgeons not exceed a weight ratio of 3 or 4.

Some authors such as Busutill[25] and Burdelski[31] have argued that the technique might potentially reduce the pool of grafts that might be more appropriately suited for those older pediatric recipients who would have a more favorable prognosis; we believe that this is specious and conservative reasoning. First the pool of donors in the adolescent age group is larger than that of infants and small children, whereas the need for liver replacement is the highest in young children because of the age distribution of pediatric liver diseases; moreover in Eurotransplant[9] the pool of adult donors exceeds the demand. Second the technique can be used in any age group; we have used it for 38% of the children younger than 3 years, 54% of the children between 3 and 6 years, and in 41% of the children between 6 and 14 years (Table 4). We also used it in adult patients of small size. Taking into account the age distribution of both the donor and recipient pools and the reliable safety of the RSL technique as demonstrated by the present report, we believe that this technique allows a more even access to and a more fair distribution of the donor organs. The technical barriers having been taken down, it is logical and ethically justified to systematically organize a shift of the donor organs down the age scale.

Mastering the technique of RSL transplantation has already led to new technical developments such as the segmental graft and opens new avenues of experimental and clinical research. The segmental graft technique (partial liver) differs from the reduced liver in one main point: the retrohepatic vena cava of the recipient is preserved during hepatectomy and a direct anastomosis between the donor left hepatic vein and the vena cava orifice of the recipient hepatic veins is performed.[19,20] This technical modification allows transplantation into small children of segments of adult livers up to a weight ratio of 8 to 9.

Future avenues of research include segmental grafts removed from adult related living donors; experimental work in progress in several laboratories, including our own, and extended clinical experience with liver resection as well as with the technical variants of liver transplantation, of which the reduced liver is only one, will likely allow future clinical application. However ethical problems remain to be solved. A first case, although unsuc-

TABLE 10. *Hepatic Causes of Graft Loss*

Causes of Graft Loss	Full-Size Livers	Reduced Livers
HA thrombosis	9	3
Low portal flow	—	1
PNF	6	3
Poor preservation	—	2
Nonvascular necrosis	1	—
Rejection	—	2
Hepatitis	—	1
Tumor recurrence	1	—

TABLE 11. *Nonhepatic Causes of Graft Loss*

Causes of Graft Loss	Full-Size Livers	Reduced Livers
Operative death	1	4
Heart failure (glyc. stor. dis. IV)	—	1
Iatrogenic	2	—
Infection	6	6
CVA	—	1

TABLE 12. *Hepatic Artery Thrombosis*

Type of Graft	Number with Thrombosis
Full-size livers	14/83 (17%)
Reduced-size livers	4/54 (7%)
Total	18/137 (13%)

TABLE 13. *Liver Tests—6 Months After Transplantation*

Liver Tests	Normal	Slightly Abnormal	Severely Abnormal
SGPT (Iu/L)	<32	32–60	>60
GT (Iu/L)	<45	45–90	>90
Bilirubin (mg%)	<1	<1	>1
Full-size livers (n = 49)	31	10	8
Reduced livers (n = 25)	19	1	5

SGPT, serum glutamic pyruvic transaminase.
GGT, gamma-glutamyl-transferase.

cessful, was already tried in Brazil. Another very attractive field is represented by some metabolic diseases not affecting the liver, such as Crigler-Najjar syndrome, oxalosis, and hemophilia in which an *in situ* auxiliary left segmental graft replacing the removed native left lobe of the recipient would be a more clever and less disturbing (for the surgeon) procedure than the total removal of a perfectly functioning liver but for a single enzyme.

Another procedure worthy of careful exploration by surgeons experienced with the reduced liver technique is the split liver. In this technique the liver parenchyma of the donor liver is divided into two parts with partition of the liver pedicle to obtain two viable grafts fit for use. We have recently transplanted three children and one adult with the grafts obtained from two such split livers with two successes.[21] Other cases have been performed in Hannover, Paris, and Chicago by surgeons extensively experienced with the reduced liver technique.

The experience reported here, which is now the largest worldwide, demonstrates that the technique of RSL transplantation not only allows long-term survival but, in fact, offers the same survival hope with the same quality of liver function, whatever the age and clinical condition of the child. The technique is safe and reliable and we recommend it as the definitive treatment in urgent and elective cases. It allows a more flexible use of the donor organ resources and is a valuable way to overcome the shortage of pediatric liver donors. This technological improvement will undoubtedly booster the development of pediatric liver transplantation if these children are allowed to benefit from the larger pool of teenager and adult donor livers, as is done in several European liver transplant centers.

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