Original communications

Small remnant liver volume after right lobe living donor hepatectomy

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Background. *Right lobe living donor liver transplantation has become a viable option for adult patients with end-stage liver disease, however, the safety of the donor is of paramount importance. One of the key factors in donor safety is ensuring adequate donor remnant liver volume.*
Methods. *We retrospectively examined donors who had less than 30% remnant liver volume after right graft procurement. Eighty-six right lobe living donor transplants were carried out in Chang Gung Memorial Hospital, Kaohsiung Medical Center, from January 1999 to December 2004.*
Results. *Eight donors had less than 30% remnant liver volume (Group 1) after graft procurement and 78 donors had remnant liver volume greater than 30% (Group 2). There were no differences in donor characteristics, types of graft, operative parameters, and post-operative liver and renal function as well as liver volume at 6 months post-donation between the 2 groups. The graft weight obtained in Group 1 donors was significantly greater compared with that from Group 2 ($P < .005$). The overall donor complication rate was 6.98%, and all the complications occurred among group 2 donors.*
Conclusions. *The judicious use of donors with less than 30% remnant liver volume is safe as a last resort. (Surgery 2006;140:749-55.)*

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Living donor liver transplantation (LDLT) was used initially in pediatric patients using the left lateral segments to alleviate the demand for deceased donor liver in this age group. The use of this technique in terms of donor safety is well established.[1-3] The success of pediatric LDLT, combined with a worsening shortage of deceased organs, has led to the growth of LDLT in the adult population. However, the left lateral segment and left lobe do not provide sufficient hepatic mass for most adults.[4-6] The right lobe is usually of adequate size to meet the demands of an adult. Right lobectomy is technically more challenging and the surgical literature has suggested a morbidity of 35% and a mortality of 5% associated with this procedure.[7] Healthy donors, however, have fared much better.[8,9]

It is imperative that the safety of the donor is ensured after donor hepatectomy. The remnant liver volume must be sufficient so that the donor is not at risk of developing liver failure post-donation. Previous authors have shown that a remnant liver volume of 27% in a normal liver after a major hepatectomy is sufficient to prevent liver failure.[10] Fan et al[11] have suggested that the lowest limit of remnant liver volume should be 30%. Some other centers apply a more conservative benchmark to ensure greater donor safety.[12]

At our center, we routinely aim to ensure a minimum of 30% remnant liver volume to ensure donor safety. We have retrospectively examined the remnant liver volume in our donors and analyzed those donors with less than 30% remnant liver volume, compared with those with greater remnant liver volume, in terms of donor outcome to reach a reasonable conclusion on whether it is safe to leave

Supported in part by grant NHRI-EX 93-228SP from the National Health Research Institutes, Taiwan.

Accepted for publication February 3, 2006.

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0039-6060/$ - see front matter

doi:10.1016/j.surg.2006.02.019

less than 30% remnant liver volume after right lobe living donor hepatectomy.

PATIENTS AND METHODS

Donor evaluation. The selection criteria and evaluation of potential donors in our institution has been specified previously.[13] Since 2000, non-invasive computed tomographic angiography (CTA) has replaced invasive catheter angiography for vascular imaging. Multiple detector computed tomography (CT) that allows high-speed high-resolution helical scanning and image processing with three-dimensional multiplanar reconstruction is now used to produce images of superior quality. Computed tomography volumetry is calculated from 10-mm cut slices and this gives an accurate volume with an error of ±10%. The remnant liver volume is calculated from this volumetry study and expressed as a percentage of the total liver volume by volumetry. When a donor is found to have less than 30% remnant liver volume at evaluation and there is no other suitable donor, we repeat the volumetric studies. Routine biopsy of the donor liver is not carried out unless the imaging studies show the possibility of steatosis[14] or other pathologies, and the donor's body mass index is greater than 25.

Anesthetic management. The anesthetic management for living donor liver resection is conducted using the protocol set in this institution[15]. A central venous catheter is inserted and arterial pressure is measured by radial artery catheter and non-invasive blood pressure monitoring. The patient is maintained on minimal intravenous fluids (1 to 1.5 ml/kg per hour) during extrahepatic dissection and parenchymal transection with a target central venous pressure (CVP) between 5 and 10 cmH_2O. If the CVP remains greater than 10 cmH_2O despite diuresis induced with furosemide, then no further attempt is made to reduce the CVP either with intravenous nitroglycerin or morphine. No Swan-Ganz catheter is inserted. The cumulative fluid deficit is immediately replaced after the completion of parenchymal transection to expand the intravascular volume and to preserve renal function.

Right graft procurement. The donor is placed supine and catheterized; all pressure points are protected to prevent injury. A supra-umbilical midline incision with right lateral extension is made. A thorough laparotomy is carried out and the liver is inspected. If there is a suspicion of unexpected steatosis or other pathologies, a biopsy is taken and a frozen section examined.

The right liver is mobilized by freeing its ligamentary attachments to expose the suprahepatic vena cava. The liver is dissected from the ventral surface of the vena cava by careful individual ligation and division of the small retrohepatic veins. Retrohepatic veins that are greater than 5 mm in diameter are preserved for reconstruction directly to the recipient inferior vena cava. The right hepatic vein is isolated and encircled extraparenchymally.

After detachment of the gallbladder, right-sided hilar dissection is carried out. The right portal vein and hepatic artery are isolated. The right portal vein is dissected to confluence but the hepatic artery is not dissected to its bifurcation. Instead, during bulldog clamping of the right hepatic artery, intraoperative Doppler ultrasound is used to confirm the presence of adequate arterial supply to the remnant liver. After simultaneous bulldog clamping of the right hepatic artery and portal vein, the line of demarcation is noted and marked on the liver surface. Intraoperative Doppler ultrasound is also used to map out the course of the middle hepatic vein (MHV).

Our principle on whether the MHV is procured with the graft is explained in another article.[16] Since then we have developed further refinements. Routine use of the MHV with the donor graft is not practiced in our center. The MHV is taken with the graft if there are multiple large segment V and VIII veins (V8) draining into it and the remnant left lobe volume is larger than 30%. However, if there is only a single large V8 draining into the MHV, it is our policy to reconstruct the V8 via direct anastomosis to the recipient's MHV or with an interposition vein graft. At times, a venoplasty of the V8 together with the right hepatic vein is carried out to create a single outflow tract. Similarly, if pre-operative CTA shows that the drainage of segment IV is predominantly into the MHV, the MHV is not taken with the graft. This is to prevent congestion in the donor's segment IV that could compromise the safety of the donor. Once the proximal end of the MHV is encountered during the parenchymal transection, bulldog clamping of the MHV and right hepatic artery is carried out and the area of congestion noted. If the size of the proximal MHV is larger than 5 mm in diameter and the area of congestion is large, reconstruction of the proximal MHV with an interposition vein graft (explanted left portal vein, recipient saphenous vein or umbilical vein) is carried out. This is especially important if the graft size is marginally larger than 40% of the recipient's estimated standard liver volume and the recipient is ill as evident from a high MELD score and intractable large volume ascites.

For right lobe grafts with MHV, the line of parenchymal transection is at the line of demarcation.

Previously, our line of transection was about 1 cm left of the MHV to leave a cuff of liver parenchyma around the MHV to protect it. However, our current practice is to transect the parenchyma close to the MHV as we found it unnecessary to leave any parenchyma around the MHV.

Parenchymal transection is carried out using a combination of the clamp fracture technique and the Cavitron Ultrasonic Surgical Aspirator (CUSA System 200, Valleylab Inc, Boulder, Colo). No vascular inflow control is used. All vessels less than 2 mm in diameter are coagulated with bipolar electrocautery, with an outlet for dripping water, and divided. Larger vessels are cut between ligatures. When approximately two-thirds of the parenchymal transection is done, we routinely perform an intraoperative cholangiogram (IOC) for right-sided graft procurement. A Phycon cholangio-catheter (Fuji Systems Corp, Tokyo, Japan) is inserted via the cystic duct opening for an IOC. A radio-opaque string, removed from standard surgical gauze, is used to mark the point of biliary transection. Scissors, instead of electrocautery, are used to cut the bile duct so as not to cause thermal injury to the cut ends of the bile duct. Fibrous connective tissues are not dissected off the ends of the right hepatic duct so as to preserve the blood supply to the ducts. The right hepatic duct stump(s) are closed with sutures using 6-0 polyprolene (Prolene). Although we try to obtain a single ductal opening for biliary reconstruction, this is not done at the expense of the remnant liver biliary system.

Once the bile ducts are cut and parenchymal transection is completed, the graft is attached only by its vasculature. For the first 34 LDLT cases, cold Ringers lactate infusion was started through the portal vein but we have subsequently stopped this in situ infusion. The graft is detached and ex situ perfusion is started with cold Ringers lactate solution followed by University of Wisconsin solution (Viaspan; Dupont, Wilmington, Del).

The raw surface of the donor's liver is inspected carefully for bile leak and areas showing possible leak are suture-ligated. All bleeding points are suture-ligated. The ligated small retrohepatic vein stumps have been individually reenforced with suture-ligation from the 174th LDLT. The abdominal cavity is washed and a collagen fleece coated with fibrin glue (Tachocomb, Hafslund Nycomen, Linz, Austria) is placed on the raw area. A routine Doppler ultrasound is done again to ensure that the remnant liver vasculature is intact.

The abdomen is closed in layers using interrupted Polyglactin (Vicryl 0) sutures and at each stage of closure, the wound is constantly irrigated.

Graft procurement for donors with remnant liver volume less than 30%. For donors with left lobe liver volume less than 30% by pre-operative CT volumetric study, procurement is similar to the above except for the following precautions:

1. The segment 4 artery is identified pre-operatively by CT angiography and if present, the vessel is preserved during procurement. This is done for all right graft procurements but is especially important in donors with small remnant liver volume.
2. If taking the MHV is deemed necessary, segment 4b venous drainage is not disrupted and is kept with the donor. If there are multiple large segment 4b veins draining into the MHV and the donor has marginal remnant liver volume, the donor is rejected.
3. If the MHV is not taken, the line of parenchymal transection is skewed more to the right.
4. If the donor liver appears fatty, a frozen section is taken before procurement and if the level is greater than 10%, the procurement is abandoned.

All donors are monitored in the intensive care unit immediately after hepatectomy. They are discharged to the general ward when they are absolutely stable. Blood investigations are carried out on every other post-operative day. Routine use of total parenteral nutrition is not practiced and oral feeding is encouraged as soon as bowel function returns. Antibiotics are only given at induction and not continued unless there are complications. The donors are started on chest therapy early and they are mobilized as soon as possible. They are discharged when they are well and blood investigations are near normal. They are seen in the outpatient department and followed up for 2 years. At 6 months post-donation, a CT volumetric study is carried out as well as complete blood count, liver and renal function tests.

Statistical analysis. All values are expressed as mean ± standard deviation. The Mann-Whitney *U* test was used for non-parametric variables and Fisher's exact test was used to compare the proportion of donors with fatty liver and to compare complication rates between the 2 groups of donors. A *P* value of less than .05 was considered significant. Statistical analyses were done using SPSS computer software (SPSS version 13 for Windows, SPSS Inc, Chicago, Ill).

Table I. Donor characteristics, operative, and post-operative parameters

	Group 1 (n = 8)	*Group 2 (n = 78)*	P *value*
Age (years)	39 ± 7.93	33.09 ± 9.56	.074
Gender (M/F)	4/4	38/40	.617
Donor body weight (kg)	61.86 ± 10.27	65.45 ± 11.63	.308
Mean blood loss (ml)	97 ± 164	118 ± 81	.192
Mean CVP (cmH_2O)	7.84 ± 2.26	8.47 ± 11.68	.829
Duration of operation (min)	868 ± 149	849 ± 145.91	.650
Transection time (min)	165 ± 42	165 ± 37	.682
Graft weight (g)	847.25 ± 82.76	702.65 ± 96.52	<.005
Peak AST (U/l)	277.25 ± 102.35	311.04 ± 155.93	.699
Peak ALT (U/l)	279.13 ± 163.86	304.16 ± 174.55	.749
Peak TB (mg%)	3.45 ± 1.53	3.44 ± 1.85	.841
Peak creatinine (mg%)	0.75 ± 0.21	0.79 ± 0.86	.570
ICU stay (days)	2.3 ± 1.5	2.5 ± 1.0	.556
Hospital stay (days)	8.5 ± 2.5	9.5 ± 1.5	.645

ALT, alanine aminotransferase; *AST*, aspartate aminotransferase; *TB*, total bilirubin.

RESULTS

There were 86 RLDLT from January 1999 to December 2004 in Chang Gung Memorial Hospital, Kaohsiung Medical Center. Eight donors had less than 30% remnant liver volume (Group 1) after graft procurement and 78 donors had remnant liver volume greater than 30% (Group 2). Therefore 9.3% of donors had less than 30% remnant liver volume in this series.

Donor characteristics. The average remnant liver volume in Group 1 was 28% ± 1.19% (range, 26% to 29%) and 43% ± 5.61% (range, 32% to 57%) in Group 2. The average age of the donors in Group 1 was 39 ± 7.93 years (range, 25 to 48 years) and 34 ± 9.56 years (range, 19 to 55 years) in Group 2. The average body weight was 61.86 kg ± 10.27 kg in Group 1 and 65.45 kg ± 11.63 kg in Group 2. There were 4 female and 4 male donors in Group 1 and 38 males and 40 female donors in Group 2. There were no differences between the 2 groups in terms of donor characteristics.

Operative parameters. The operative parameters are given in Table I.

Post-operative liver function test. The results of the post-operative liver function tests are listed in Table I. There was no significant difference between the 2 groups in terms of the post-operative parameters.

Length of intensive care unit stay and hospital stay. The average length of stay in the intensive care unit (ICU) for was 2.5 ± 1.5 days for Group 1 donors and 2.5 ± 1.0 days for Group 2 donors. The length of hospital stay was 8.5 ± 2.5 days for Group 1 donors and 9.5 ± 1.5 days for Group 2 donors. There were no differences between the 2 groups.

Table II. Overall complications in the series

Morbidity	*No. of donors**
Biloma†	2
Bile leak‡	1
Post-op bleeding§	2
Drain site infection‖	1

*No donors experienced the complications of pleural effusion, transient ascites or deep venous thrombosis in the series (N = 86; 6.98%).
†Includes all bilious collections that are detected via imaging; they may be treated percutaneously, conservatively, or surgically.
‡Defined as effluent bilious contents from intra-abdominal drains, regardless of the amount or duration of flow. This is confirmed by biochemistry studies that validate the bile salt content.
§Includes all forms of hemorrhage, regardless of intervention required.
‖Proven by culture study.

Type of graft. There were 4 right lobe grafts with MHV and 4 right lobe grafts without MHV in Group 1. In Group 2, there were 15 right lobe grafts with MHV and 63 right lobe grafts without MHV. There were no differences in terms of type of grafts between the 2 groups ($P = .068$).

Donors with fatty liver. There were 4 donors with mild fatty liver (<10%) in Group 1 and 23 donors with mild fatty liver in Group 2. There was no difference between the 2 groups in terms of proportion of donors with fatty liver ($P = .211$).

Actual graft weight obtained versus that using CT volumetry studies. The mean graft weight obtained in the whole series was 716.12 ± 80.25 g and the mean value of CT volumetric calculations was 770.15 ± 65.65 g. There was a difference of 54.03 g that equates to a 7% difference between the two.

Donor complications. The donor complications are summarized in Table II. There were no donor deaths in this series. The overall complication rate

was 6.98% for this series of donors. There were no complications among the donors in Group 1 and 6 complications in donors of Group 2. Two donors (LDLT 116 and 43) had biloma that required interventional radiologic drainage and antibiotic treatment. One donor (LDLT 130) had bile leak post-operatively through the abdominal drain that resolved conservatively without intervention. Another donor (LDLT 202) had infection at his drain site that required only prolonged antibiotic usage. Two donors (LDLT 173 and 194) had post-operative hemorrhage that required re-operation for hemostasis. At laparotomy, the bleeding was found to be from a retrohepatic vein that was suture-ligated. All donors remain well to date and have had no further complications. In terms of complication rates, there was no significance difference between the 2 groups ($P = .546$).

During the study period, only 1 donor surgery was abandoned due to hemodynamic instability of the donor at the start of anesthesia. The cause of the instability was unknown but the donor has recovered well with no further problems.

Liver volume at 6 months post-donation. Sixty-three of the 86 donors have returned for their 6-month post-donation blood investigations and CT volumetric studies. The remaining 15 donors have not yet reached their 6-month post-donation date. Two donors underwent ultrasound examination because they had a history of allergic reaction during the pre-donation scans. Two donors are from overseas and their follow-up was carried out in their native country. Three donors did turn up for their 6-month review in the outpatient clinic but did not perform the CT volumetric study. The mean liver volume at 6 months was 93.96% ± 20.68% of the original liver volume in Group 1 ($n = 8$) and 89.28% ± 11.53% in Group 2 ($n = 55$). There was no significant difference between the 2 groups ($P = .645$).

In this institution, the minimum volume required in the recipient is an arbitrary 40% of the estimated recipient's liver volume. The overall 1-year survival rate for the recipients was 97.1% and the 5-year survival rate was 90.5%.

DISCUSSION

Donor safety must be the predominant focus of all discussions concerning LDLT, and primum non cocere ("first do no harm") must be the principle for all involved in donor selection. One of the key factors in donor safety in RLDLT is to ensure a sufficient, functioning liver remnant in the donor after procurement of the right lobe. In animal studies, it has been shown that 10% of viable liver mass is adequate for spontaneous recovery after major hepatectomy.[17] In humans, many patients survive major liver resection for large tumors mainly because of hypertrophy of the contralateral side, and the tumor does not contribute to significant liver function.[11] Before the era of CT volumetry, Stone et al[10] estimated that the removal of 70% of the total liver volume was well tolerated in patients with normal liver. Fan et al[11] indicated that a residual liver volume of 27% is the lowest limit that can support survival in a non-fatty liver, but to increase donor safety, a residual liver volume of 30% of the total liver volume is recommended. In another review, Fan et al[18] cited 17 of 178 donors who had left lobe residual volume less than 30% and found no statistical difference in post-operative liver function as measured by the international normalized ratio (INR) between this group of donors and those with a larger residual liver volume.

In another series, Sakamoto et al[19] examined the post-operative bilirubin levels of donors who had liver remnant less than 40%, compared them with those who had more than 40% remnant liver volume, and found that the bilirubin clearance was slower in those with less than 40% remnant liver volume.

Yigitler et al[20] examined the occurrence of small remnant liver volume (defined as <30% of the original liver volume) after major liver resection and its relevance. In that study, there was no correlation between the remnant liver volume and the occurrence of complications. However, the post-operative course was more difficult as the remnant liver volume got smaller.

Moon et al,[21] in a review of their LDLT program, reported that the lowest remnant liver volume in one of their donors after right graft procurement was 27% of the original total liver volume and the donor's serum total bilirubin was elevated to 9.0 mg/dl. They went on to comment that if the remnant liver volume of the donor after right graft procurement was less than 30%, intraportal glucose and insulin infusion were given until the 7th post-operative day to accelerate regeneration of the liver.

The absolute remnant liver volume is not the only issue that needs to be addressed when considering adequate liver function in the donor. The level of steatosis is also important. In partial hepatectomy a trend toward increased mortality was reported for patients with moderate to severe steatosis (>30%).[22] A fatty liver is more vulnerable to injury by general anesthesia and ischemia-reperfusion episodes.[23,24] Therefore, the calculation of remnant liver volume must take into account the

level of fatty change.[11] In a recent report of a donor death, the residual liver volume was 28% but the donor was later discovered to have non-alcoholic steatohepatitis (NASH).[25]

In this series, we have retrospectively looked at right lobe donors who had less than 30% of liver remnant. We found that 9.3% of donors had less than 30% remnant liver volume. There were no differences between the 2 groups in terms of donor characteristics, type of grafts and donors with fatty liver. The post-operative peak liver enzymes and peak total bilirubin were not different between the 2 groups, although the mean values were lower in patients in Group 1 that was surprising. The peak creatinine level was not different between the 2 groups. There was also no difference between the 2 groups in terms of complications and all complications occurred among Group 2 donors. The liver volume attained at 6 months post-donation was also similar in the 2 groups. The graft weight obtained in Group 1 was significantly higher compared with Group 2. This is not surprising as the donors in Group 1 were a highly selected group who had greater than 70% of their liver volume in the right lobe. In this series, although the donors with less than 30% remnant liver volume have done well compared with the other donors, we must emphasize 2 important points. The mean remnant liver volume in these donors was 28% and only 1 donor had a liver remnant volume less than 27%. This is a retrospective analysis and there could be other confounding factors that could skew the results. One such confounder would be the presence of Type II statistical errors due to our small sample size. Moreover, there could be errors in the CT volumetric studies (up to $\pm$10% difference) and this thus could also skew the results. In this series, there was a difference of 7% between the weight obtained via CT volumetry versus the actual right graft weight obtained. This difference could be due to the fact that the right graft obtained no longer possesses the blood or bile that would have been measured during CT volumetric calculations. However, CT volumetry is currently the standard and most accurate method for measuring volumes in LDLT. Another confounding factor is the pattern of segment IVb venous drainage. In Group 1 donors, segment IVb venous drainage was routinely preserved when procuring the MHV but this was not done in donors with larger remnant liver volume. This can affect the remnant liver function as well as the liver regeneration rate in these 2 groups of donors.

When faced with a recipient who requires a liver transplantation and having only 1 suitable donor who may not have enough residual liver volume, the transplant surgeon has the following options. The first is to deny the patient LDLT and place him on the waiting list for deceased donor liver transplantation. The second option is to use the right posterior segment or left lobe with caudate lobe (ELLC) to increase graft mass to meet the demands of an adult. The third option is to use the left lobe of these donors with auxiliary partial liver transplantation. In rare instances where there are several donors who have marginal remnant liver volume, dual grafts can be used.

In Asia, where deceased donor liver donation is not as common as in Europe and North America, the wait for a liver could be long. This problem has been discussed in other studies.[26]

Leelaudomlipi et al,[27] in a volumetric analysis of liver segment in living donors, found that 25% them had right lobe volume of more than 70%, but 72% had a large right posterior segment compared with the left lobe with the caudate. Sugawara et al[28] analyzed 6 LDLT with right posterior segment and found them to be associated with stretched hepatic vein anastomosis leading to outflow problems, bile leakage from the cut edge of the liver, and a higher blood loss. The caudate lobe accounts for about 2% to 3% of the whole liver and its procurement with the left lobe increases the liver mass of the extended left lobe graft by 9%.[29] In one series, the authors found that the concomitant resection of the caudate lobe produced additional gain in graft mass in greater than 80% of livers but a small proportion of grafts do not benefit from the addition of the caudate lobe.[30] The other possibility is to use the small left lobe of these donors as an auxiliary partial orthotopic liver transplantation. This is of limited use, however, and it cannot be used if the native liver has a transmissible disease such hepatitis B or C, if the native liver has lost its function or if the native liver has a risk of turning carcinogenic, for example in patients with primary sclerosing cholangitis.[19] Kasahara et al[31] in a review of their experience with auxiliary partial orthotopic LDLT found that these patients had higher biliary complications and the need for re-transplantation was greater. The use of dual donors has also been popularized by some. Lee et al[32] have reported that this is indeed a reasonable option. The use of dual grafts can be considered if the recipient has several donors who have small remnant liver volume after right lobe graft donation. However, dual grafts are complex and another healthy donor is put at a small, but real, surgical risk. Moreover, the instances of recipients who have several donors but

all having small remnant liver volume after right lobe graft donation are rare.

In our center, we routinely ensure a minimum of 30% remnant liver volume in our right lobe donors. We will still keep to this guiding principle when selecting donors. When faced with the situation of a single suitable donor with marginal remnant liver volume for a recipient, however, we do not dismiss the donor without further re-evaluation and a lengthy discussion between the transplant team and the family. After considering the pros and cons, the use of the donor may be considered. If another solution arises, we will certainly take that option. Thus, in conclusion, if need be, the use of donors with less than 30% remnant liver volume can be judiciously considered but should be used as a last resort.

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