

Clinical study on safety of adult-to-adult living donor liver transplantation in both donors and recipients

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Abstract

AIM: To investigate the safety of adult-to-adult living donor liver transplantation (A-A LDLT) in both donors and recipients.

METHODS: From January 2002 to July 2006, 50 cases of A-A LDLT were performed at West China Hospital, Sichuan University, consisting of 47 cases using right lobe graft without middle hepatic vein (MHV), and 3 cases using dual grafts (one case using two left lobe, 2 using one right lobe and one left lobe). The most common diagnoses were hepatitis B liver cirrhosis, 30 (60%) cases; and hepatocellular carcinoma, 15 (30%) cases in adult recipients. Among them, 10 cases had the model of end-stage liver disease (MELD) with a score of more than 25. Donor screening consisted of reconstruction of the hepatic blood vessels and biliary system with 3-dimension computed tomography and volumetry of whole liver and right liver volume. Various improved surgical techniques were adopted in the procedures for both donors and recipients.

RESULTS: Forty-nine right lobes and 3 left lobes (2 left lobe grafts for 1 recipient, 1 left lobe graft for 1 recipient who had received right lobe graft donated by relative living donor) were obtained from 52 living donors. The 49 right lobe grafts, without MHV, weighed 400 g-850 g (media 550 g), and the ratio of graft volume to recipient standard liver volume (GV/SLV) ranged from 31.74% to 71.68% (mean 45.35%). All donors' remnant liver volume was over 35% of the whole liver volume. There was no donor mortality. With a follow-up of 2-52 mo (media 9 mo), among 50 adult recipients, complications occurred in 13 (26%) cases and 4 (8%) died postoperatively within 3 mo. Their 1-year actual

survival rate was 92%.

CONCLUSION: When preoperative CT volumetry shows volume of remnant liver is more than 35%, the ratio of right lobe graft to recipients standard liver volume exceeding 40%, A-A LDLT using right lobe graft without MHV should be a very safe procedure for both donors and recipients, otherwise dual grafts liver transplantation should be considered.

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Key words: Adult-to-adult living donor liver transplantation; Middle hepatic vein; Dual grafts; Right lobe graft; Standard liver volume; Grafts; Weight; Complication

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INTRODUCTION

With the shortage of donation of livers worldwide, the first pediatric living donor liver transplantation (LDLT) was performed by Raia in Brazil in 1989^[1]. Yamaoka reported the first case of adult to adult LDLT (A-A LDLT) in 1993^[2]. Fan reported for the first time a case of A-A LDLT using extended right lobe graft in 1997^[3]. Since then, its application has successfully expanded from pediatric to adult patients. But A-A LDLT has not become effective for patients with end-stage liver disease until 2000. The risk of donors has obviously increased with A-A LDLT. Although liver transplantation was performed for donors because of remnant liver failure^[4,5], the mortality of donors was about 0.2%-0.3%^[6]. If recipient's body weight is much higher than donor's, the graft can not meet the needs of metabolism, thus resulting in small-for-size syndrome^[7], or even the death of recipient. So it is a serious problem at present to make both donors and recipients safe, and for recipients to receive an adequate volume of graft for metabolism.

Since July 2001 we have performed the first case of pediatric LDLT in our hospital. A-A LDLT was performed

in January 2002^[8,9]. Till July 2006, 62 cases of LDLT have been performed, including 50 cases of A-A LDLT. This article aims to discuss about our experience how to make both donors and recipients safe in A-A LDLT and the indications for dual grafts liver transplantation.

MATERIALS AND METHODS

Materials of recipients

From January 2002 to July 2006, 50 cases of right lobe graft A-A LDLT were performed in our hospital, including 47 right lobe graft without middle hepatic vein (MHV) liver transplantation and 3 dual graft liver transplantation (dual relative donated left lobe grafts 1, relative right lobe graft and relative left lobe graft 1, relative right lobe graft and cadaveric left lobe graft 1^[10]). Among the 50 recipients there were 43 men, and 7 women, aged 18-63 years (mean age of 39 years). Primary diseases of recipients included liver cirrhosis after hepatitis B, 30 cases (12 of them had acute liver failure); diffuse ischemic intrahepatic biliary stenosis (DI IBS), 2; Budd-Chiari syndrome with liver cirrhosis^[11], 1; postoperative liver failure after three right lobe hepatectomy caused by hepatic trauma, 1; hepatocellular carcinoma, 15; and cholangiocarcinoma, 1. There were 15 (30%) cases at risk among the 50 cases, including 7 cases of acute severe hepatitis, 5 fulminant liver failure, 2 DI IBS with liver failure, and 1 liver failure after hepatectomy. All these patients underwent A-A LDLT at emergency. According to Child-Pugh classification, there were 18 cases of grade A, 7 of grade B, and 25 of grade C. By United Network for Organ Sharing classification, there were 10 cases of stage I, 10 of stage II a, 12 of stage II b, and 18 of stage III. The model of end-stage liver disease scores were: ≤ 18 , 35 cases; 19-24, 5 cases; 25-30, 1 case; and > 30 , 9 cases. Among 16 malignant cases, no one exceeded 18 scores.

Materials of donors

There were 52 cases, including 16 men and 36 women, with an age range of 9-65 years (mean age 38 years). The relationship between recipients and donors included father 3, mother 8, brother 14, sister 3, spouse 7 (grafts were all donated by wives in this group), children 3, and others 5.

The donors and recipients were blood group identical in 39 cases and compatible in 13 cases. All donors in this group voluntarily donated part of their liver. The ethical aspect of this study was approved by the Ethical Committee of our hospital.

Preoperative evaluation for donors

Physical examination and retrospective analysis of donors' medical records were performed before their operations. The donors and recipients must be blood group identical or compatible. Hepatitis, syphilis, HIV, or Epstein-Barr virus, cytomegalovirus, tuberculosis infection constituted an ineligibility for potential donor. Hepatic blood vessels and biliary system were reconstructed before operation, and the volume of the total liver and right hemiliver were evaluated and calculated with 3-dimension computed tomography (3-D CT). As a potential donor, the right lobe

graft volume should not exceed 65% of the total liver, while if the ratio of right lobe graft volume to recipients' standard liver volume is less than 40%, the recipients should undergo dual graft liver transplantation.

To minimize the risk and complications of donors, we have adopted the following managements: (1) to abandon preoperative endoscopic retrograde cholangiopancreatography (ERCP), instead of cholangiography intraoperatively; (2) to study the tracks and variations of hepatic artery with 3-D CT before operation; (3) to abandon routine hepatic puncture for biopsy before operation unless patients were supposed to have fatty liver^[12].

Operative approaches in donors

Using right Mercedes (Chevron with vertical extension) incision from xiphoid process to midaxillary line, we unfolded abdominal cavity with suspended abdominal puller. All donated livers were right lobe grafts without MHV. We identified hepatic incision line (the line from the gallbladder fossa below the inferior vena cava) with intraoperative ultrasonography to confirm the tracks of MHV, aided by observing the color change of right and left lobes when right hepatic artery and right tributaries of portal vein (PV) were clamped. Without clamping hepatic blood vessel, we resected liver with cavitron ultrasonic surgical dissector, using temporarily bipolar electric coagulation hemostasis to deal with the section plane. According to the caliber of conduits, we selected different methods of hemostasis such as titanium clamp or ligation. The crassitude tributaries of MHV could be temporarily clamped for anastomosis via interpositioning a vein graft when grafts were planted. Operation should be performed meticulously when dissociating around hepatic hilar. One should carefully analyze the cholangiographic film intraoperatively in order to know whether there are branches or variations in the right hepatic duct, snip connective tissue and bile duct of hilar plate, meanwhile carefully distinguish minute orifices of hepatic ducts, making markers with thin sutures for anastomosis when planting grafts.

We dissected liver tissue till making total right lobe graft dissociated with heparinizing the whole donor body, in turn clamped and cut off the right hepatic artery, right tributary of PV and right hepatic vein, placed the graft into the container filled with 4°C University of Wisconsin (UW) solution, then removed it to back table for perfusion.

We continuously stitched the orifices of the right tributary of PV with 5-0 sutures, while the orifices of right hepatic duct were stitched at intervals with 6-0 sutures, without interfering with the blood flow in the trunk and left tributary of PV, and the bile flow direction in common hepatic duct.

Bench

We perfused the grafts from PV with 2 liters of 4°C UW solution, rinsed biliary tracts, repaired orifices of hepatic vein, and kept it as large as possible so as to provide sufficient venous outflow. On back table, we anastomosed recipients' great saphenous vein or cadaveric iliac blood vessels to crassitude tributaries of MHV. We measured and

recorded the hepatic vasculatures and the orificia caliber of bile duct and weight of grafts, then calculated the ratio of grafts to recipients' weight (GRWR)^[13] and the ratio of grafts volume to recipients' standard liver volume (GV/SLV)^[14].

Operative techniques in recipients

Operation was performed following the routine procedures of our hospital^[9,15]. When resecting recipients' liver, we attentively reserved posterohepatic inferior vena cava's (IVC) integrity, dissociated right hepatic vein cling to IVC, reserved the orificia of right hepatic vein (RHV), along with the end axis enlarged IVC downward, making it suitable for donor's RHV and anastomosis^[12]. It was necessary to make ellipsed incision on suitable parts of IVC when the orificia of crassitude tributaries of right hepatic inferior vein or MHV were jointed with IVC by interpositioning the great saphenous vein or cryopreserved cadaveric blood vessels. We adopted end-to-end anastomosis of grafts' right tributaries of PV to recipient's PV trunk, maintained a suitable length for PV trunk after anastomosis, then opened blood flow in hepatic vein and PV, recovered blood perfusion of grafts and ended nonhepatic phase period. With loupe, we finished hepatic artery anastomosis and adopted end-to-end anastomosis of right hepatic duct to common hepatic duct, or Roux-en-Y choledochojejunostomy. If right hepatic duct had many tributaries and their caliber ≤ 2 mm, biliary tracts should be reconstructed under microscope^[16].

Splenectomy should be performed at the same time if donors suffered from splenomegaly and hypersplenism (blood platelet $\leq 30 \times 10^9/L$). If PV pressure was > 25 cmH₂O, splenic artery ligation should be performed for recipients in order to alleviate PV pressure^[17].

RESULTS

Preoperative CT evaluation of hepatic volume

We have evaluated the volume of remnant liver with CT. According to the volume of the total liver and right lobe grafts with MHV and right lobe grafts without MHV, we calculated the volume of remnant liver with and without MHV after resection. The evaluation results of 50 donors showed that the volume of remnant liver with MHV $< 30\%$ in 10 cases, $30\%-35\%$ in 24 cases, $> 35\%$ in 16 cases, while the volume of remnant liver without MHV $< 30\%$ in 0 case, $30\%-35\%$ in 5 cases, and $> 35\%$ in 45 cases. According to the Fan criteria^[13], the volume of remnant liver should exceed 30% . In this study, there were 10 cases with a volume of remnant liver with MHV of less than 30% , which would be ineligible for potential donor, thus reducing the donor pool. According to Lee criteria^[14], the volume of remnant liver should exceed 35% , resulting in just 16 cases of donors. The volume of remnant liver without MHV ranged from 30% to 35% in 5 cases. Considering the safety of 3 among 5 cases whose volume of remnant liver was less than 35% ; we adopted dual grafts liver transplantation.

Clinical results in donors

Among 52 donors, we resected right lobe grafts in 49

cases and left lobe grafts in 3 cases (2 left lobe grafts for 1 recipient, 1 left lobe graft for 1 recipient who had received right lobe graft donated by a relative living donor). Grafts of 49 cases were all without MHV, and the weight ranged from 400 g to 850 g (mean weight 550 g). The ratio of right lobe graft to recipient's standard liver volume was $31.74\%-71.68\%$ (mean 45.35%). The ratio of graft to recipient's body weight was $0.72\%-1.31\%$ (mean 0.91%). Intraoperative total blood loss volume of donors ranged from 250 mL to 735 mL (mean 345 mL), and these blood was all retransfused with autologous blood recovery system. Only 4 cases in this group received allogeneic RBC transfusion of 200 mL to make up the intraoperative blood loss. Operation time varied from 380 min to 620 min (mean 425 min).

Donors had the following complications: transient chyle leakage, recovered after symptomatic treatment; portal venous thrombosis, received second thrombectomy, mending leakage with a patch of great saphenous vein; subphrenic effusion, cured by surgical drainage; and pleural effusion, recovered after repeated thoracic cavity puncture. There was no donor death, and the hospitalized time ranged from 7 to 30 d (mean 11 d). All donors are well and have returned to their daily life and work.

Clinical results in recipients

GRWR was $0.72\%-1.17\%$. There were 12 cases $> 1.0\%$, 31 cases $0.8\%-1.0\%$, and 7 cases $< 0.8\%$. Mean intraoperative blood loss volume was 980 mL. We used autologous blood recovery system for patients with benign diseases. No allogeneic blood transfusion (44%) was made in 22 cases, and the mean operation time was 542 min (range 365-1400 min). Five cases with fulminant liver failure received venous bypass during operation, while the other 45 cases did not.

Among the 50 cases, except for right hepatic vein, we additionally anastomosed right inferior hepatic vein to IVC in 19 cases, and interposed vein grafts on V segmental tributaries (V5) of MHV in 20 cases, and on VIII segmental tributaries (V8) in 13 cases (single tributary in 9 cases and double tributary in 12 cases).

We found PV variations in 9 cases, and right anterior and posterior sectoral PV and left PV all directly arise from the PV trunk. So there were two PV orificas on the section plane of right hemiliver, we connected orificas of right anterior and posterior sectoral PV to form a big one, then anastomosed it to recipients' PV trunk in 7 cases, and anastomosed two orificas to both right and left PV in 2 cases.

We adopted end-to-end anastomosis of right hepatic duct to recipients' common bile duct in 34 cases of bile duct anastomosis. Three cases received T tube drainage, while 31 cases did not. Among 16 cases who underwent choledochojejunostomy, 3 cases had 3 hepatic duct orificas, 11 cases had 2, and 2 cases had 1. Thirty-three orificas were routinely anastomosed with magnifying glasses. There were 11 orificas in 5 cases with calibers less than 2 mm, for which operative microscope was used for the anastomosis.

All cases in this study were followed up for 2-52 mo (mean 9 mo). Four (8%) patients died at 21 d, 27 d, 31 d, and 42 d after operation respectively. The causes

included: small-for-size syndrome 1, multiple organs failure caused by pulmonary infection 2, and renal failure 1. Complications occurred in 13 (26%) cases which included hepatic artery embolization (2), biliary leakage (2), subphrenic abscess (1), anastomotic bleeding in Roux-Y jejunostomy (1), hepatic venous stenosis (1), small-for-size syndrome (1), pulmonary infection (3), and renal failure (2). The one-year survival rate was 92%.

DISCUSSION

Making donors safe

Based on familial relationship or friendship, a healthy adult voluntarily donates part of liver, who hopes this will be safe for both donors and recipients. For a surgeon, there is great pressure to ensure operations successful for both donors and recipients. The rationality of LDLT has not been acknowledged worldwide until the first pediatric case was performed in 1989^[1].

Pediatric LDLT is that an adult donates small part of liver for a child patient. Donor's safety can be ensured and risk is low. In 1993 Yamaoka *et al*^[2] and in 1997 Fan *et al*^[3] respectively successfully performed A-A LDLT using right hemiliver. Compared with pediatric LDLT, the risk of A-A LDLT obviously increased when resecting the right hemiliver. So this operation has not been extensively performed in Europe and America, especially as one donor died of gas gangrene of the stomach in America in 2002^[18], enthusiasm for A-A LDLT was lessened with one disaster after another. Data in 2006 indicated that there were more than 2000 LDLT cases in America, 1000 in Europe, 2000 in Asia, respectively. The number of donor deaths have reached 14 all over the world with a mortality of about 0.2%-0.3%. So donor's safety has been widely and closely noticed^[19].

If we resect too much of a donor's liver, the volume of remnant liver will become too small to meet the needs of the donor's metabolism, leading to dysfunction of liver after operation, liver failure, or even death. On the other hand, if we resect too small part of donor liver, the graft also cannot meet the needs of a donor's metabolism. It is still a challenging subject attempting to tackle this contradiction. At present, it is well acknowledged that the volume of total liver and right hemiliver can be calculated with 3-D CT. Fan thought that it was effective to ensure the safety of donors provided the volume of evaluated remnant liver exceeded 30% of the total liver^[13]. So he advocated that we should resect the right lobe graft with MHV, while Huang recently thought the volume of evaluated remnant liver exceeded 35% of total liver^[4], and suggested that we should resect right lobe graft without MHV.

In this paper we consecutively calculated the volume of donor's liver in 50 A-A LDLT cases. The results show that if we resect the right lobe graft with MHV, the volume of remnant liver was < 30% in 10 cases, 30%-35% in 24 cases, and > 35% in 16 cases. According to the Fan's criteria, 10 cases could not be the candidates for donor, thus dramatically lowering the score of donor liver. Otherwise if we resect right hemiliver without MHV, none case had remnant liver volume < 30%, 5 cases 30%-35%, and the others > 35%. According to Fan's criteria, all donors in

this study can be candidates for donors, donor pool can be enlarged, while donor safety should be addressed with the increased risk. Alternatively, according to Huang's criteria, 5 cases in this group would be ineligible for donors, donor safety could be enhanced while the donor pool was being reduced.

Both to maximize to make donors safe and to prevent reduction of donor pool, we resected 47 right lobe grafts without MHV among 52 cases, the other 3 cases received dual grafts liver transplantation. In this way, we have not only ensured donor safety, but achieved satisfactory results.

Making recipients safe

Being different from total liver transplantation, the recipients only received parts of donor's liver in A-A LDLT. It is still controversial discerning the optimal volume of graft for metabolism. At present, there are two standards worldwide: one is GRWR and the other is GV/SLV. It is generally thought that the former should be more than 0.8%^[13], and the latter should be more than 40%^[14]. In 49 cases of this group, GV/SLV ranged from 31.74% to 71.66% (mean 45.35%), and GRWR from 0.72% to 1.31% (mean 0.91%). Among these cases, GRWR was < 0.8% in 7 cases, and GV/SLV was < 40% in 6 cases, but GV/SLV all exceeded 40% in 3 cases according preoperative CT evaluation, and the other 3 cases whose GV/SLV < 40% underwent dual grafts LDLT. After resection during operation, GV/SLV < 40% was found in 6 cases. This result showed that there are differences between CT evaluation and grafts real weight. Yet clinical study in this group proved that a little error did not influence clinical prognosis. So preoperative CT evaluation has instructive significance for clinical practice.

One case in this group did not receive reconstruction for crassitude tributaries of MHV at its inception in our hospital, causing right anterior lobe of right hemiliver congestion and swelling, and liver dysfunction, small-for-size syndrome and death finally^[12]. GV/SLV in this case was 52.98%, which was not definitely related to graft size.

Occurrence of small-for-size syndrome was related to not only small size of grafts, circumfluence of hepatic vein or other factors, but also high pressure in PV, or hyperperfusion of PV which lead to injury of epithelioid cell in hepatic sinus of grafts^[20]. Ito *et al*^[17] proved that portal hypertension, ligating splenic artery could make PV pressure decrease by 5-10 cmH₂O, obtaining more satisfying clinical results. Therefore, 5 cases in this group with splenoparectasis and blood platelet < 30 × 10⁹/L were routinely underwent splnectomy, other 6 cases with PV pressure > 25 cmH₂O underwent ligation of splenic artery, the results were satisfactory.

About dual grafts

It was effective to use dual grafts to solve the problem of too small size of graft and make donors safe. This approach was first reported by Lee *et al*^[21]. It requires 3 operation groups performing 3 operations simultaneously, and the cost is high; while if we adopt double left lobe grafts for liver transplantation, we have to turn over 180° and place ectopically at the location of right one. Therefore, surgical techniques became demanding,

increasing the risk of complications. Therefore it is not a popular procedure worldwide^[19]. We adopted one smaller right lobe graft and one left lobe graft, and placed them at primary locations, which have overcome the shortcomings of difficulties for operation^[10]. Additionally, it was quite strict controlling the indications of right lobe graft LDLT in South Korea that almost 31% A-A LDLT cases underwent dual graft liver transplantation^[4]. Only 3 of 50 cases received dual grafts liver transplantation in this study, while other 47 cases underwent right lobe graft LDLT. These protocols can not only make both donors and recipients safe, but also obviously reduce medical cost and consumption of medical materials. The clinical results were satisfactory.

In our experience, right lobe grafts without MHV is adopted, volume of remnant liver is more than 35%, preoperative evaluation with CT and the ratio of right lobe graft to recipients standard liver volume exceeding 40%, are all effective indices to make both donors and recipients safe in right hemiliver LDLT, otherwise we should expect to adopt dual grafts liver transplantation.

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