ORIGINAL ARTICLE

FEASIBILITY OF LEFT LOBE GRAFT IN ADULT LIVING DONOR LIVER TRANSPLANTATION

Khaled Amer,[1] Mohammed Asar,[2]Ahmed S.Elbalouly,[2] Yukihiro Inomatac,[3] Koichi Tanakad[4]

[1]Armed forces College of Medicine, [2]Department of Surgery, Faculty of Medicine, Alazhar University, [3]Department of Pediatric Surgery & Transplantaiton, Kumamoto University, Kumamoto, Japan, [4]Foundation for Kobe International Medical Alliance, Kobe, Japan,

Correspondence to: Khaled Amer, Mohammed Asar Email: dramertx@gmail.com

Abstract

The objective: of this study is to assess the feasibility of LLG as an option in the Adult Living Donor Liver Transplantation. The study aims to consider the anatomical advantages of the Left Lobe Graft, the safer Donor's hepatectmy and to innovate criteria for Left Lobe Graft selection. Data on 34 consecutive LL LDLTs, including two retransplants, were retrospectively compared with those of 34 RL LDLTs, in terms of survival, complications and donor morbidity. The mean GRWR of LL grafts was 0.71% whereas that of RL grafts was 0.88%. The 1-year patient survival rates of LL LDLT were 85.3%,, which were comparable to those of RL LDLT (85.3%). The incidence of small-for-size syndrome was higher in LL LDLT (11.8%) than in RL LDLT (5.9%). The overall donor morbidity rates were comparable between LL (20.5%) and RL (14.7%), whereas postoperative liver function tests and hospital stay were significantly better in LL donors. **Conclusion:** Adult LL LDLT has comparable outcomes to that of RL LDLT. To minimize the risk to the donor, LL-LDLT could be an ideal option in adult-to-adult LDLT.

INTRODUCTION

Living donor liver transplantation (LDLT) was first initiated in children in 1989 in response to a severe organ shortage from pediatric donors.(1) At the start of adult LDLT, left lobe (LL)-LDLT was the only option available because of the potential risk for the donor in right lobe (RL)-LDLT. However, the use of LL grafts for adults was severely limited due to their size limitation. Generally, a LL graft can provide only 30–50% of the required liver volume for an adult recipient, and has been thought to be too small for adult recipients to sustain their metabolic demand.(2) During this process, the graft type has shifted from the left side of the liver to the right side of the liver to overcome the problems encountered with "small-for-size grafts," that is, a <1.0% graft-to- recipient body weight ratio (GRWR). The use of "small-for-size grafts" leads to "small-for size syndrome," including poor bile production, delayed synthetic function, prolonged cholestasis and intractable ascites, with subsequent septic complications and higher mortality.(3)

Graft size plays a role in determining outcomes after liver transplants, but it is not the only factor. The likelihood of small-for size syndrome is influenced not only by the size of the graft but also likely by other factors such as the degree of portal hypertension, MELD score, and spleen size. Perhaps a better term than small-for-size to describe this syndrome is small-for-need.(4) The crucial prerequisite to performing LDLT is a minimal morbidity and mortality risk to the healthy living donor. Unfortunately, sporadic donor deaths associated with RL donations have been reported in the United States(5) and Europe,(6) as well as in Japan.(7) It is

reported that operative mortality for the RL donor is estimated to be as high as 0.5–1%.[8]

MATERIAL AND METHODS

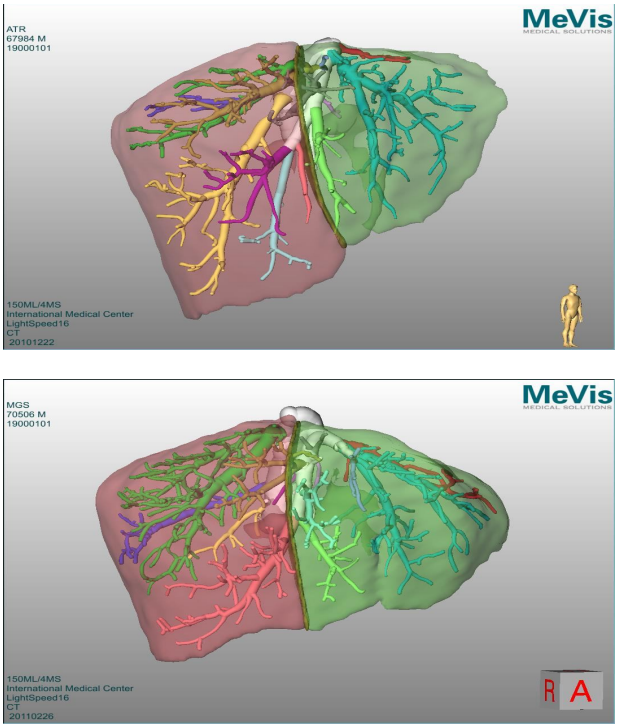
The study was retrospectively done in the period between June 2009 and December 2012, including 68 LDLT cases performed at the International Medical Center (IMC, Cairo) and Kumamoto University Hospital (Kumamoto, Japan). This Comprised 68 adults (aged ≥ 18 years). Of the 68 adults, a total of 34 patients (50%) underwent LDLT using Left Lobe grafts all without the caudate lobe, whereas 34 patients (50%) received Right Lobe grafts all without middle hepatic vein (MHV). The relation of the donors to recipients was Son (n =15), Daughter (n = 8), Brother (n = 8), Wife (n = 5), Sister (n = 4), Husband (n = 4), Mother (n = 2), Cousin (n = 2), Aunt (n = 1) and others (n = 20). The indications for liver transplantation in LLG recipients were HCV cirrhosis (n = 12), HCC (n = 9), Cryptogenic cirrhosis (n = 3), Biliary Atresia (n = 2), Primary Biliary Cirrhosis(PBC) (n = 2), Alcoholic cirrhosis (n = 1), Familial Amyloid Poly neuropathy(FAP) (n = 1), Fulminant Hepatic Failure (FHF) (n = 1) and Retransplantation (2 cases due to chronic rejection with prior indications of Allagile syndrome and Biliary Atresia respectively). While the indications for RLG recipients were HCC (n = 16), HCV cirrhosis (n = 8), HBV cirrhosis (n = 4), AutoImmune Hepatitis (AIH) (n = 1), FHF (n = 1), Primary Sclerosing Cholangitis(PSC) (n = 1), Multiple Developmental Liver Cysts (n = 1), and Retransplantation (2 cases due to chronic rejection with prior indications of FAP and Biliary Atresia respectively). The preoperative characteristics of the donors and the recipients in the 2 groups are described and compared in Table 1.

Table 1. Patient characteristics.

	Left Lobe(n=34)	Right Lobe(n=34)	p-Value
Recipient			
Age (years)	51.1 ± 12.6	51.6 ± 12.1	NS
(Range)	(18-69)	(22-65)	
Sex (M / F)	21 / 13	19 / 15	NS
Body weight (kg)	64.7 ± 13.2	70.1 ± 16.2	NS
Etiology (n)			NS
Cirrhosis	16	12	
HCC	9	16	
Cholestatic	5	1	
FHF	1	1	
Retransplant	2	2	
Others	1	2	
Child-Pugh	8.3 ± 1.8	8.9 ± 2.5	NS
A / B / C	5 / 23 / 6	7 / 11 / 16	
MELD score	14.9 ± 6.6	16.7 ± 6.9	NS
<10 (n)	6	4	
≥ 10, <20	21	23	
≥ 20, < 30	5	5	
≥ 30	2	2	
Graft			
Estimated GW (g)	503.5 ± 100.8	738.6 ± 166.5	<0.0001
Estimated GRWR (%)	0.79 ± 0.11	1.08 ± 0.22	<0.0001
Actual GW (g)	455.4 ± 109.9	619.7 ± 151.6	<0.0001
Actual GRWR (%)	0.71 ± 0.10	0.88 ± 0.22	0.0003
<0.6% (n)	4	0	
≥0.6, <0.8%	25	8	
≥0.8, <1.0%	4	18	
≥1.0%	1	8	
Donor			
Age (years)	33.6 ± 12.1	39.2 ± 14.1	NS
(Range)	(20-66)	(21-63)	
Sex (M / F)	29 / 5	18 / 16	0.0034
Blood type compatibility(n)			NS
Identical	14	16	
Compatible	15	11	
Incompatible	5	7	

Graft Selection Criteri

The volume of the graft had to satisfy a minimum graft-to-recipient weight ratio (GRWR) of 0.7% for recipients with low Model for End-Stage Liver Disease (MELD) scores (<15) and a GRWR of 0.8% for recipients with high MELD scores (>15). RL graft could be selected when the volume of the left lobe plus the caudate lobe (LLI or RLV) was >30%. In this study we were relatively obliged to select LLG in some cases due to the very complicated anatomy of the right hepatic system in the absence of alternative donor even the MELD score of the recipients was >15 but fortunately the LLG volume could satisfy GRWR of 0.7 or more . Figure 5.2,5.3 shows two examples of these cases showing very complicated right hepatic venous system that would cause an outflow reconstruction problem if RLG without MHV was selected and not to mention the risk for the donor if RLG with MHV was selected where LLG could provide a very accepted alternative to RLG (Figs. 1,2).



Figs 1,2. Complicated Right Hepatic venous system.

Operative Procedure (LLG without Caudate lobe).

Donor Hepatecomy

An upper midline incision is made(could be extended to right subcostal region)Fig.3. This is followed by mobilization of the liver. Then cholecystectomy & cholangiograpgy is done for proper identification and confirmation of prior imaging of biliary anatomy, thus identifying left Hepatic Duct(s) and marking of cutting point for later transaction. Hilar Dissection starts afterwards, the left hepatic artery is dissected free from the surrounding tissue. The middle and right hepatic arteries and the left and right main branches of the portal vein are dissected free and encircled with vessel loops. To start Parenchymal Transection at first identification of middle hepatic vein using intraoperative US, then the transaction plane would be 1cm to the right of the vein or without US by shifting 1 or 2 cm to the cantlie's line. In some cases we may depend on demarcation line (fig.4)after identification of it by Pringle's Maneuver. Transection is done with the aid of Cavitron Ultrasonic Aspirator (CUSA), Harmonic Scalpel, Irrigation monopolar or bipolar electrocautery and Coagulation monopolar electrocautery. Graft is then removed to backtable then all stumps are closed (Fig. 6).

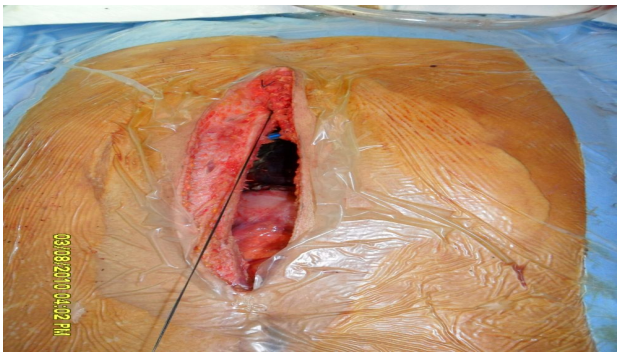


Fig 3. Midline incision.

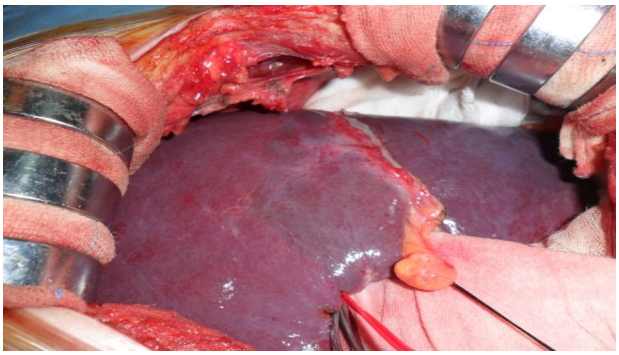


Fig 4. Demarcation line.

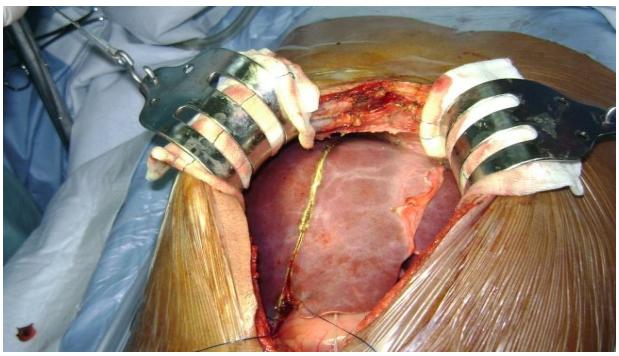


Fig 5. Transiction Line.

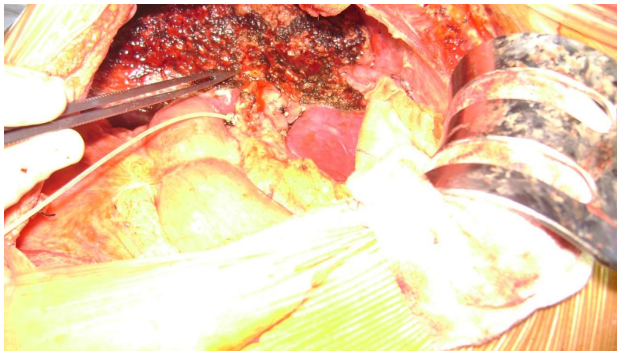


Fig 6. After Graft removal.

Graft Implantation:

The recipient native hepatectomy is performed in a standard fashion. After bleeding is controlled, vascular and biliary stumps are prepared for anastomosis. The common stump of the MHV and LHV is elongated, with removal of the diaphragmatic crus and the inferior phrenic vein(fig.7). In this series, Outflow modulation is done as the RHV stump is clamped horizontally together with the MHV / LHV stump, and its border is cut open to make a large, common hole in line with the graft hepatic vein. This modulation is to minimize Ischemia Reperfusion Injury specially with small grafts as a strategy against development of Small For Size Syndrome (SFSS). Portal vein reconstruction done between Left Portal branch of graft to the main portal trunk of recipient or one of the main branches according to the size. Hepatic Artery reconstruction done between graft artery and either of recipient branches of hepatic artery. None of grafts with more than one artery required 2nd anastmosis based on backflow stream(Fig. 8). Bile duct reconstruction done in duct to duct fashion as a rule unless the case requires Roux- Y Hepatico-Jejunostomy as in Biliary Atresia or in some cases with more than one bile ducts.

Measurement of Portal Pressure:

In case of the presence of portal hypertension specially in HCV patients (in both groups), the continuous portal pressure was monitored by cannulation of the inferior mesenteric vein The readings of the portal pressure were taken at 3 time points: before total hepatectomy, during the anhepatic phase, and after all the vascular anastomosis and prior to closure of the wound. Portal pressure <20mm / Hg was accepted, While >20mm / Hg was considered high considering modulation to lower the pressure. No inflow modulation was done in this series. Temporary portocaval shunt was done in two cases in anhepatic phase to minimize bowel congestion.

Immunosuppressive drugs:

The immunosuppressive regimen consisted of a combination of calcineurin inhibitor (Tacrolimus Prograf or Cyclosporine: Neoral) and steroids with or without mycophenolate mofetil (MMF; CellCept). Currently, the triple regimen including calcineurin inhibitor, steroids and MMF has been the standard protocol for HCV patients. Steroids were basically tapered off by 6 months after LDLT. MMF 1000–2000 mg / day was started from postoperative day 1 and maintained for 3–6 months. For ABO incompatible LDLT, the protocol consisted of a single dose (375 mg / m2) of Rituximab (Rituxan) 2–4 weeks before LDLT. The immunosuppressive dose was adjusted on daily bases guided by trough level.

Definition of small-for-size syndrome:

The definition of SFSS was as reported by Kyushu University group. Briefly, SFSS is defined as having prolonged functional cholestasis (total bilirubin>10 mg / dL at postoperative day 14) and intractable ascites (daily production of ascites of >1 L at postoperative day 14 or >500 mL at postoperative day 28).

Statistical analysis: Continuous variables were compared using a two-tailed, unpaired Student t test for independent samples. All values are expressed as mean ±standard deviation. p-Values ≤ 0.05 were considered significant. All statistical analyses were done using GraphPad software.

Follow Up Period

This study involved follow up of 1 year for Recipients and for 3 months for Donors postoperatively.

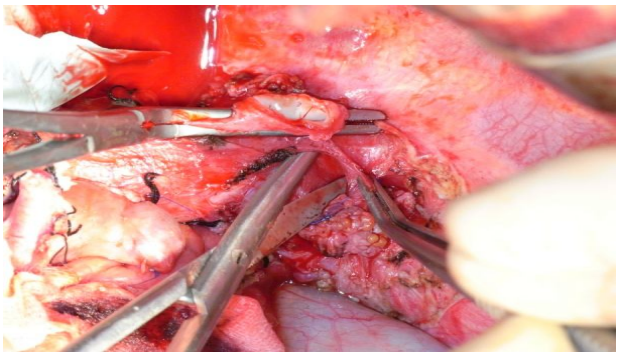


Fig 7. IVC Preparartion.

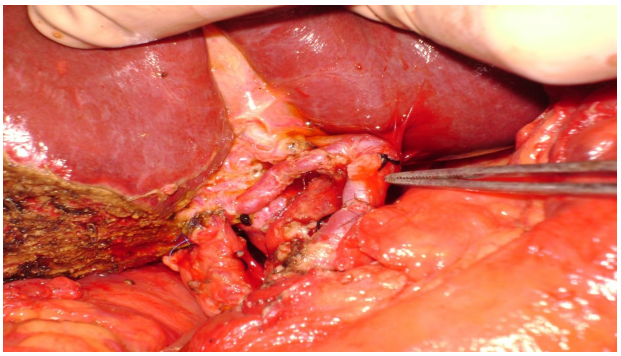


Fig 8. Double Artery Graft (Single Anastmosis).

RESULTS

Patient characteristics

Detailed demographic data for the recipients and donors are presented in Table 1. There were no significant differences in patient age and MELD score between RL and LL groups. The mean Actual Graft Weight of LL grafts was 455 g (range 280–680 g), which was significantly smaller than that of RL grafts (620 g, range 360–1020g, $p < 0.0001$). The mean Actual GRWR was 0.70% (range, 0.50-1.01%) in LL grafts, which was, again, significantly smaller than those of RL grafts (0.88% range 0.65-1.20%, $P<0.0003$). Twelve LL grafts were extremely small, namely, GRWR<0.7%, although the preoperative predicted GRWR was >0.7%.

Donor operative outcomes

Table 2 shows the comparison of operative outcomes between LL and RL donors. The mean operative time was comparable whereas blood loss was significantly less in RL donors (242 mL vs. 375 mL). However, no donors of either group needed blood transfusion. Postoperative liver function tests including peak total bilirubin, peak aspartate aminotransferase and alanine aminotransferase were significantly better in LL donors. Furthermore, lengths of hospital stay were significantly shorter in LL donors (11.9 days vs. 18.2 days), whereas overall morbidity rates were comparable. These data suggest that LL donation is potentially safer than RL donation, although there was no procedure-related mortality in either group. One LL donor developed loss of appetite and depression. Two LL donors and one RL donor developed wound sequelae (Clavian I). Two LL and four RL donors developed bile leakage/biloma where the two LL donors required US guided drainage and Endoscopic Naso-Biliary Drainage tube(ENBD), while the four RL donors required US drainage only (Clavian IIIa). Two LL donors developed bile leakage at closure stump site and required surgical intervention (Clavian IIIb). In terms of procedure-related complications, we have not experienced any Clavien's grade IV and V complications so far.

Table 2. Donors Operative Outcomes.

	Left Lobe(n=34)	Right Lobe	p-Value
Donor			
Operative time (min)	430 ± 91	403 ± 69	NS
Blood loss (mL)	375 ± 336	242 ± 168	0.051
Blood transfusion (%)	0	0	NS
Postoperative LFTs			
Peak T.Bil (mg/dL)	1.8 ± 0.4	3.0 ± 0.7	<0.0001
Peak AST (IU/L)	217 ± 117	308 ± 76	0.0001
Peak ALT (IU/L)	253 ± 156	313 ± 90	0.053
Morbidity (%)	20.5	14.7	NS
Clavien I	8.8	5.9	
Clavien II	0	0	
Clavien IIIa	5.9	8.8	
Clavien IIIb	5.9	0	
Clavien IV	0	0	
Clavien V	0	0	
Hospital stay (days)	11.9 ± 8.0	18.2 ± 7.0	0.001

Overall patient and graft survival rate

The overall 1- year patient survival rates were 85.3% for both LL & RL grafts, i.e. comparable results. Figure 9 shows patient survival in LL grafts according to the GRWR. To investigate the impact of the graft size, the GRWR was classified into four subgroups as follows: (GRWR <0.6%), (GRWR ≥0.6, <0.8%), (GRWR ≥0.8, <1.0%), (GRWR ≥1.0%). There was no significant difference in overall survival rates between these subgroups. Furthermore, 29 (85.3%) out of 34 LL grafts in this series were GRWR <0.8%. The 1-year survival rates of this group of patients were 85.7%, which were comparable to those of patients with LL grafts of GRWR ≥0.8 (80%). Also to be considered that 4 patients of LL graft were <0.6% and all of them survived the 1st year post transplant.

Recipient operative outcomes

Table 3 shows a comparison of operative data between LL and RL recipients. The mean operative time was comparable in both groups. Only one case of each group (3%) required temporary Porto-caval shunt because of small for size graft in LL case and because of intestinal congestion in RL case. No additional measures were done for all for small for size grafts <0.8% (29 LL cases & 8 RL cases). Figure 10 compares the 1-year graft survival rates between LL and RL LDLT according to the MELD scores. In all categories, the LL group revealed comparable results with the RL group. However, in patients with a MELD score ≥20, the LL group (n = 7) tended to show better outcome than RL group (n = 7) 100% & 57.1% Subsequently. Three cases of RL group with MELD score ≥20

because of Sepsis (n=2), and Chronic rejection(n=1), this explains that the relatively better LL results is this subgroup is not related to the high MELD score.

The overall complications were comparable in both groups (35.3% in LL group vs. 38.2% in RL group). Complications of LL group included SFSS (n = 4), Bile Leak"Relaparotomy" (n = 1), HCC Recurrence (n = 1), Prolonged Ascites (n = 2), Prolonged Cholestasis (n = 1), Infection (n = 1), Acute Tubular Necrosis (n = 1), and Diaphragmatic Hernia (n = 1). While RL complications included SFSS (n = 2), Massive Intra-abdominal Bleeding "Relaparotomy" (n = 1), Hepatic Artery Thrombosis (n=1), Acute Cellular Rejection (n = 2), Bile Leak (n=1), Prolonged Ascites (n=2), Infection (n=4).

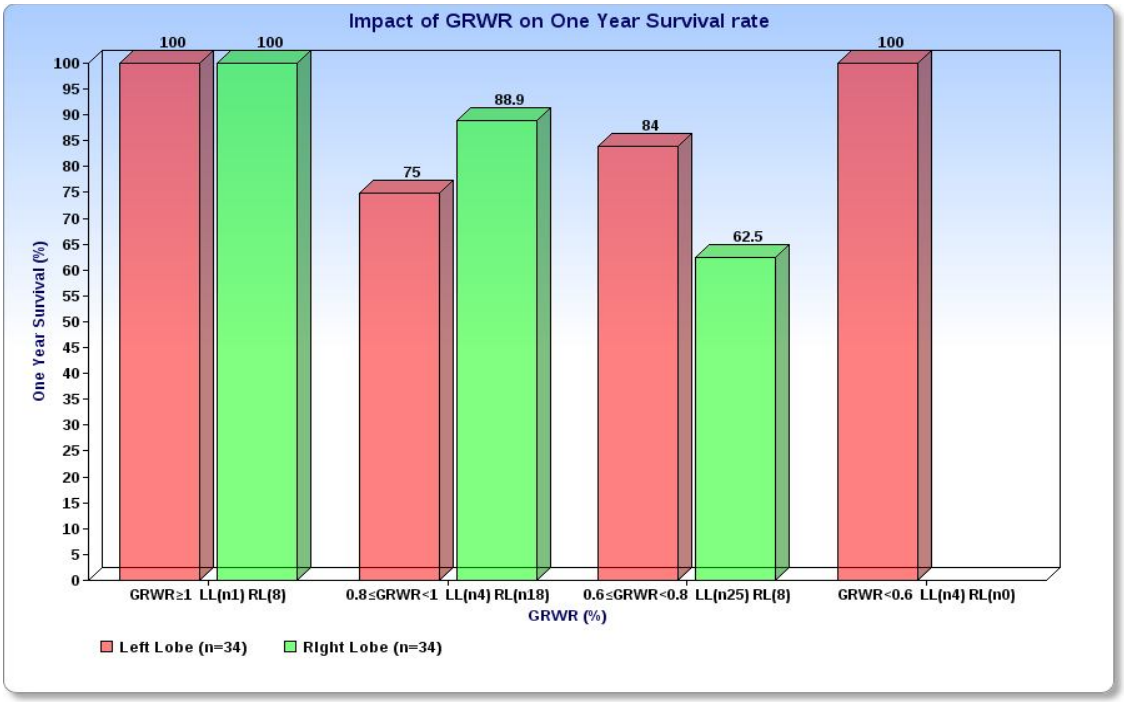


Fig 9. The impact of GRWR on One year survival rates.

Table 3. Recipients Operative Outcomes.

	Left Lobe(n=34)	Right Lobe	p-Valu
Recepient			
Cold Ischemia Time	92.4 ± 81	135.7 ± 77.3	0.0376
Warm Ischemia Time	47.4 ± 7	50.5 ± 8	NS
Operative Time (min)	777.8 ± 202	811.2 ± 110	NS
Temporary PC Shunt (%)	3.0	3.0	NS
Complications (%)			
Over All	35.3	38.2	NS
SFSS	11.8	5.9	NS
HAT	0	3.0	NS
ACR	0	5.9	NS
Bile leak	3.0	3.0	NS
Prolonged Ascites	5.9	5.9	NS
Prolonged Cholestasis	3.0	0	NS
Intra-abdominal Bleeding	0	3.0	NS
Infection	3.0	11.8	NS
HCC Recurrence	3.0	0	NS
Others	5.9	0	NS
Relaparotomy (%)	3.0	3.0	NS
In-hospital mortality (%)	8.8	14.7	NS

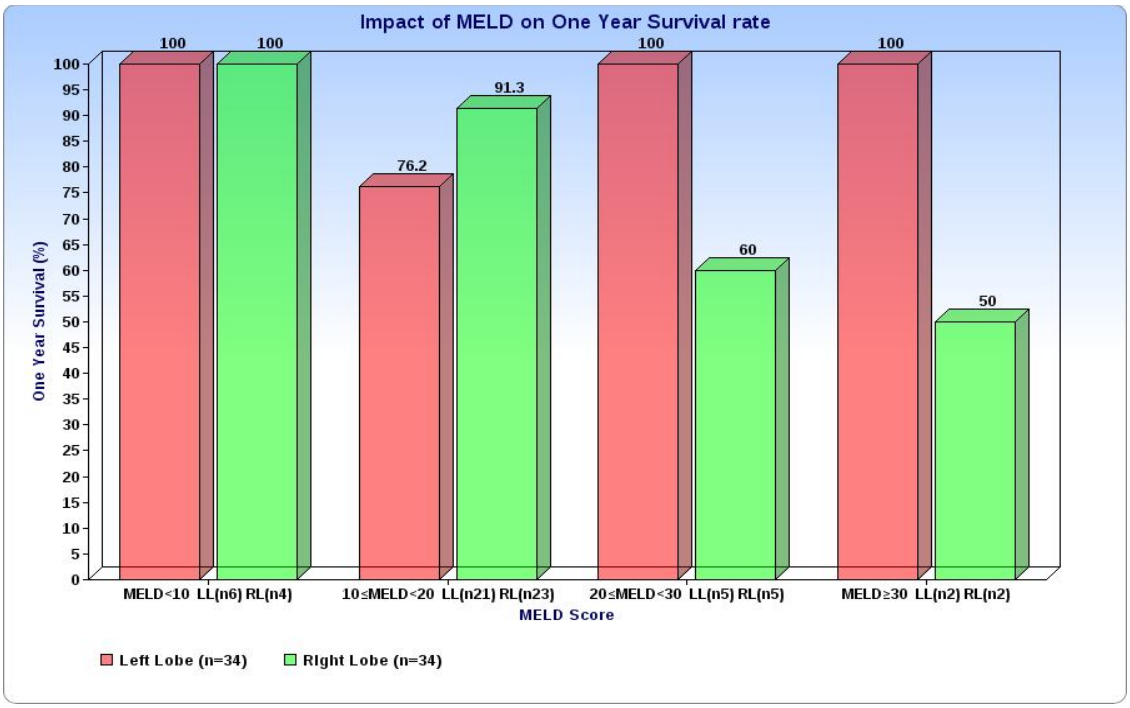


Fig 10. The impact of MELD score on one year survival rates.

Incidence of small-for-size syndrome

The incidence of SFSS was higher in LL LDLT (11.8%) than in RL LDLT (5.9%). Development of SFSS is multifactorial, but parameters to be considered are Graft Quality " donor age", graft size "GRWR", Metabolic Load "MELD" in Relation to Portal Hypertension". Therefore, graft size is not the sole determinant to develop SFSS in this series. Only one case died directly as a sequence of SFSS (LLG case), while the other five cases recovered completely conservatively.

Causes of Graft loss

Within the 1st year posttransplant, in LL group 5 patients died from: Bile Leak/Sepsis (n=1, POD 67), SFSS/Sepsis (n=1, POD 54), Recurrent HCC (n=1, POD 267), Chronic Rejection (n=1, POD 243), Acute Tubular Necrosis (n=1, POD 6). In Hospital Mortality "directly post-transplant" was 2 out of 5. In RL group 5 patients died from: Hepatic Infarction (n=1, POD34), Multiple Hepatic Abscesses (n=1, POD 63), Chronic Rejection (n=1,PoD 297), Sepsis (n=2, POD 55,70). All deaths were In Hospital Mortality.

DISCUSSION

This study clearly showed that the outcomes of LL LDLT were comparable with those of RL LDLT, although SFSS occurred more often in LL LDLT. However, this does not necessarily lead to graft loss. In this series, only one patient lost his graft directly as a result of SFSS.

SFSS is characterized clinically by a combination of prolonged functional cholestasis, intractable ascites and a delayed recovery of both prothrombin time and encephalopathy. The mechanism of SFSS remains unknown but is probably multifactorial. Excessive portal perfusion and pressure to the small graft is suggested to be one of the most important factors.[9]

Therefore, in this series we modulated the outflow of the graft during caval drainage by making one big oval vein opening on recipient side by opening the three hepatic veins together or at least increasing Left & Middle hepatic vein caliber by snipping on IVC thus, minimizing graft congestion and decreasing the perfusion injury specially in the presence of high portal pressure/flow as in high MELD score cirrhotic patients which was very effective. Intraoperatively, it was proved both clinically and radiologically as graft was soft, portal pressure <20 mmHg and venous outflow signal was excellent. This suggests that with proper venous drainage, relatively smaller grafts can tolerate high portal flow/pressure.

Yamada et al., selectively used HPCS for LL grafts with GWRW between 0.6 and 0.8 and showed 100% patient survival.[10] Botha et al. also reported excellent results in patients with small LL grafts (the median GWRW was 0.67%) with HPCS: the 1-year patient and graft survival were 87% and 81%, respectively.[11] They all concluded that a small LL graft with modulation of

portal flow by HPCS may prevent SFSS while at the same time providing adequate liver volume. Furthermore, the Kyoto group showed that portal venous pressure <15 mmHg was the major factor for a better outcome.[12]

The current approach in managing the problem of SFSS of Kyushu group is to perform splenectomy aggressively In terms of the usefulness of splenectomy for low GRWR (<0.8) patients, the 1-year graft survival rates in patients with splenectomy were 93.4%, which was significantly better than those without splenectomy (79.2%). Therefore, they believe concomitant splenectomy is very useful especially for patients with a small graft to control the portal flow and platelet count, thereby improving the overall results.[9]

Focusing on the ''flow'' rather than in the ''size'' may improve our understanding of the pathophysiology of the ''small-for-size'' syndrome and ''post-hepatectomy liver failure'' and it would have important implications for the clinical management of patients at risk. First, hepatic hemodynamic parameters would have to be measured in hepatic surgeries. Second, these parameters (in addition to liver mass) would be the principal basis for deciding the ''safe'' threshold of viable liver parenchyma. Third, the hepatic hemodynamic parameters are amenable to manipulation and, consequently, the ''safe'' threshold may also be manipulated. Shifting the paradigm from ''small-for-size'' to ''small-for-flow'' syndrome would thus represent a major step for optimizing the use of donor livers, for expanding the indications of hepatic surgery, and for increasing the safety of these procedures.[13]

By analysis of the 6 cases that developed SFSS in this study, The GRWR was significantly smaller in LL patients (<0.8%) than RL patients (>0.8%) this should drive us to think about the functional volume rather than the actual volume, also the donor age was relatively old in both groups denoting bad compliance or quality of the graft. The only case that died from SFSS was a LLG case and the recipient was quite old 69 years, while all cases recovered even with grafts <0.6%, so, SFSS is multifactorial.

Regarding graft size, this series suggests that small for size grafts " <0.8% GRWR" function very well with rapid recovery even with extremely small grafts "<0.6% GRWR" patient can survive with smooth postoperative coarse. 37 patient received small for size grafts "29 LLG & 8 RLG" with survival rate of 81%. These results suggest that graft size is not the only determinant of successful LDLT and also that smaller grafts could be used safely if carefully selected. Actually LLG provides an ideal option for many cases thought to be inconvenient previously with great attention paid to size only.

Regarding donor safety, LL donation is safer than RL donation if we consider shorter operative time, better liver functions postoperatively, rapid recovery, less hospital stay and not to mention the quite larger remnant liver volume. With the innovation of "Midline Incision", both cosmetic and pain wise has improved which give more advantages for LL donation.

Based on understanding the results of this study and recent studies concerned with improving the outcomes of SFSG, an algorithm could be proposed for proper graft selection without controlling the portal pressure by dividing the patients into Cirrhotic group and Non-Cirrhotic group, in Cirrhotic group the portal hypertension is usually prominent even the MELD score is not relatively high. In this case we select LLG if MELD score is ≤ 15 and estimated GRWR is 0.7% or more. While in Non-Cirrhotic group portal hypertension is not so prominent so we select LLG with any MELD score and estimated GRWR is 0.7% or more (Fig. 11).

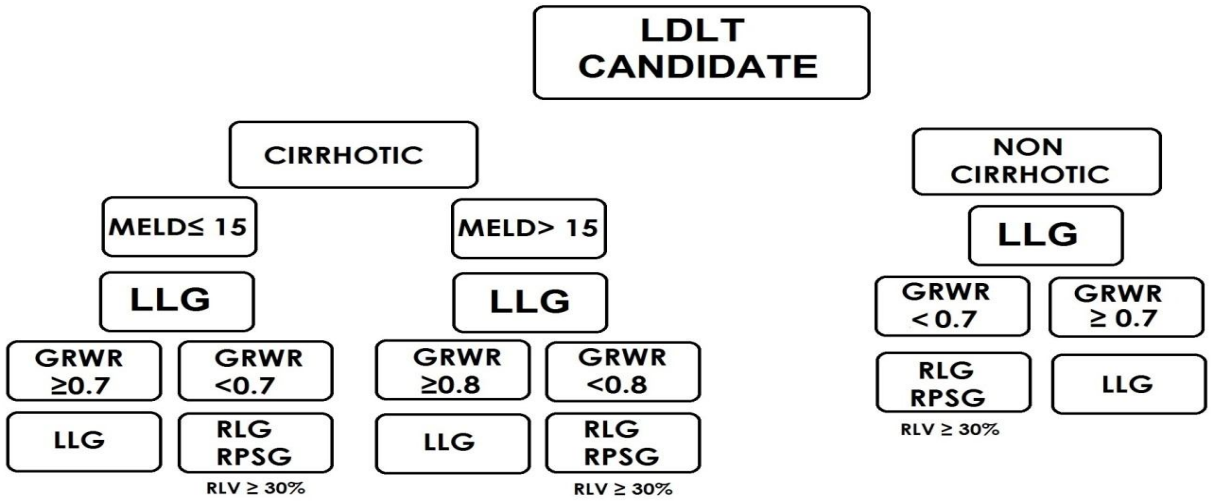


Fig 11. Innovated Graft Selection Algorithm RLV (Remnant Liver Volume), RPSG (Right Posterior Segment Graft).

In conclusion, with proper recipient & donor selection and refinement of surgical procedures, postoperative management LLG can provide a good option for LDLT with minimal burden for donors with very good overall results that could be compared to RLG with many advantages on LLG side regarding anatomical and technical points of view.

Abbreviations: GRWR, graft-to-recipient weight ratio; MELD, Model of Endstage Liver Disease HPCS, hemiportocaval shunt; LDLT, living donor liver transplantation; LL, left lobe; MHV, middle hepatic vein; PCS, portocaval shunt; RL, right lobe; RPS, right posterior segment; SFSS, small-for-size syndrome.

REFERENCES

1. Raia S, Nery JR, Mies S. Liver transplantation from live donors. Lancet. 1989;21:497.

2. Emond JC, Renz JF, Ferrel LD et al. Functional analysis of grafts from living donors. Ann Surg. 1996;224:544–54.

3. Kiuchi T, Kasahara M, Uryuhara K, et al. Impact of graft size mismatching on graft prognosis in liver transplantation from living donors. Transplantation 1999; 67: 321–327.

4. Mark J. Hill, Michael Hughes, Tun Jie, et al. Graft Weight/Recipient Weight Ratio: How Well Does It Predict Outcome After Partial Liver Transplants?. Liver Transpl. 2009;15:1056-62.

5. Miller C, Florman S, Kim-Schluger L, et al. Fulminant and fatal gas gangrene of the stomach in a healthy live liver donor. Liver Transpl. 2004;10:1315–19.

6. Broering DC, Wilms C, Bok P, Fischer L, Mueller L, Hillert C, Lenk C, et al. Evolution of donor morbidity in living related liver transplantation: a single-center analysis of 165 cases. Ann Surg. 2004;240:1013–26.

7. Akabayashi A, Slingsby BT, Fujita M. The first donor death after living-related liver transplantation in Japan. Transplantation. 2004;77:634.

8. Brown RS Jr, Russo MW, Lai M, Shiffman ML, Richardson MC, Everhart JE, Hoofnagle JH. A survey of liver transplantation from living adult donors in the United States. N Engl J Med. 2003;348:818-25.

9. Soejima Y, Shirabe K, Taketomi A, Yoshizumi T, Uchiyama H, Ikegami T, Ninomiya M, Harada N, Ijichi H, Maehara Y.Left lobe living donor liver transplantation in adults. Am J Transplant. 2012;12:1877-85.

10. Yamada T, Tanakab K, Uryuhara K, Ito K, Takada Y, Uemoto S. Selective Hemi-Portocaval Shunt Based on Portal Vein Pressure for Small-for-Size Graft in Adult Living Donor Liver Transplantation American Journal of Transplantation. 2008;8:847–53.

11. Botha JF, Langnas AN, Campos D, et al. Left lobe adult-to-adult living donor liver transplantation: Small grafts and hemiportocaval shunts in the prevention of small-for-size syndrome. Liver Transpl. 2010;16:649–57.

12. Ogura Y, Hori T, El Moghazy WM, et al. Portal pressure <15mm Hg is a key for successful adult living donor liver transplantation utilizing smaller grafts than before. Liver Transpl. 2010;16:718– 28.

13. Asencio JM, Vaquero J, Olmedilla L, García Sabrido JL. "Small-for flow" syndrome: shifting the "size" paradigm: Medical Hypotheses. 2013;80:573–57.