TABLE 2. Comparison between VCF group and non-VCF group

	VCF group (n=5)	Non-VCF group (n=8)	*P*
Preoperative factor			
Congestion rate,[a] mean (SD), %	35.9 (7.5)	30.4 (1.8)	NS
Serum AST level, mean (SD), IU/dL	21 (4)	19 (13)	NS
Serum ALT level, mean (SD), IU/dL	25 (6)	19 (20)	NS
Serum T-Bil level, mean (SD), mg/dL	0.8 (0.4)	0.8 (0.3)	NS
Serum PT level, mean (SD), %	94 (6)	93 (9)	NS
RL volume/BSA, mean (SD), cm^3/m^2	412 (28)	492 (22)	<0.01
Anterior sector volume/BSA, mean (SD), cm^3/m^2	250 (25)	266 (45)	NS
Posterior sector volume/BSA, mean (SD), cm^3/m^2	140 (31)	190 (37)	<0.01
Postoperative factor			
Regeneration rate,[b] mean (SD), %	80.1 (3.3)	82.6 (6.4)	NS
Complications greater than Clavien grade 1, n (%)	1 (20.0)	2 (25.0)	NS
Peak serum AST level, mean (SD), IU/dL	480 (156)	400 (110)	NS
Peak serum ALT level, mean (SD), IU/dL	680 (348)	523 (196)	NS
Peak serum T-Bil level, mean (SD), mg/dL	1.6 (0.4)	2.0 (1.0)	NS
Bottom serum PT level, mean (SD), %	67 (2)	70 (10)	NS

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BSA, body surface area; HVC, hepatic venous congestion; NS, not significant; POD, postoperative day; PT, prothrombin time; RL, right lobe; T-Bil, total bilirubin; VCF, venous collateral formation.

[a] Congestion rate (%) was calculated as HVC volume divided by RL volume.

[b] Regeneration rate (%)was calculated as postoperative RL volume on POD 35 divided by preoperative whole liver volume.

collateral development there would be, and how much influence the HVC would have on liver regeneration and VCF in the later postoperative phase.

Scatton et al. (*6*) reported that in the LL donor remnant without an MHV, the regeneration rate of segment VI was lower and the regeneration rate of segments II and III were higher in the global congestion group at 1 month after hepatectomy. Similarly, in this series, the ratio of the anterior sector volume to the RL volume calculated on POD 35 was significantly lower than that calculated preoperatively, whereas this ratio for the posterior sector on POD 35 was significantly higher than preoperatively. However, the anterior sector did not atrophy and became enlarged regardless of the degree of HVC. In the present study, among the 13 cases, obvious VCF between the MHV tributaries, the RHV, and the IRHV was found in 5 (38.5%) cases on POD 35. In contrast to what we had expected, the preoperative congestion rate was not significantly different between the VCF group and the non-VCF group. The fact that the congestion rate decreased from 32.5% to 1.6% on POD 35, and that there was no correlation between the preoperative congestion rate and the liver regeneration rate, might suggest that tiny intrahepatic anastomoses could develop in all cases, even though they could not be visualized using 3D-CT. Preoperative RL volume per square meter of BSA in the VCF group was significantly lower than that in the non-VCF group. Furthermore, the volume per square meter of BSA of the anterior sector was not significantly different between the groups, and that of the posterior sector was significantly lower in the VCF group. From these facts, it is reasonable to assume the following: (1) the smaller the RL donor remnant is, the more overloaded it will become owing to PV inflow; (2) the posterior sector will be more affected by PV inflow, because the anterior branch may be acting as a drainage vein owing to an acute hepatic outflow obstruction; (3) the greater the PV inflow overload is, the more VCF there will be; (4) in the case of obvious VCF, overload may be caused not only by outflow block but also by extra inflow.

In conclusion, in LL LDLT, although the HVC caused by ligation of the MHV tributaries is unavoidable in the RL donor remnant, the HVC had improved dramatically by POD 35 regardless of the development of obvious VCF. There was no correlation between the preoperative congestion rate and the liver regeneration rate. Therefore, the reconstruction of the MHV tributaries in the RL donor remnant may not be necessary in LL LDLT.

MATERIALS AND METHODS

Patients

From May to November 2009 at Kyushu University Hospital, 13 patients underwent LL LDLT. A total of 13 donors were thus the subject of this study. The donors included 11 men and two women. Their median age was 34 years (range, 21–53) and their median body mass index was 22.3 kg/cm^2 (range, 17.8–25.9). Median values estimated using preoperative 3D-CT for total liver volume, extended left and caudate lobe volume, and RL volume were 1189 cm^3 (range, 1029–1491), 409 cm^3 (range, 322–492), and 792 cm^3 (range, 593–1070), respectively. For all donors, 3D-CT was performed preoperatively and on POD 35.

Three-Dimensional Reconstruction and Volumetry

The procedures used have been described elsewhere (*7, 22, 23*). Briefly, multidetector helical CT (MDCT) images were obtained using 2-mm-thick slices represented on CT machines. Enhancement was achieved using an intravenous bolus injection of nonionic contrast medium (Iopamion, Schering, Erlangen, Germany) at a speed of 5 mL/sec. Two types of 3D-CT software were used to achieve 3D reconstruction of the liver, HVC area, and portal and hepatic venous branches from the MDCT data. One type of 3D-CT software was ZIO M900 (Zio Software Inc, Tokyo, Japan), with which it was possible to freely fix the cutoff line. The other was liver segmentation software (Hitachi Medico, Tokyo, Japan), which was used to calculate

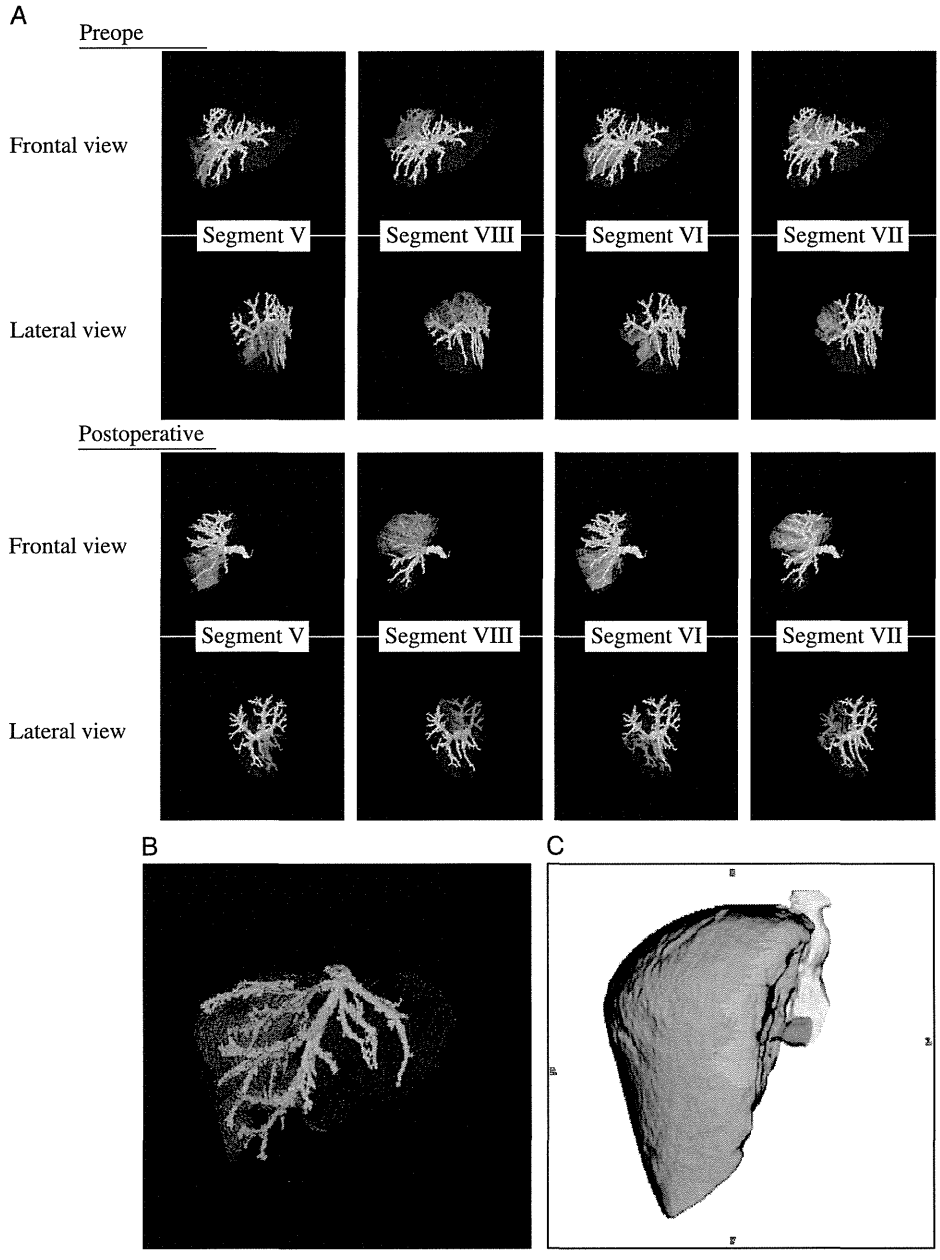

FIGURE 4. 3D-CT images of preoperative and postoperative segmental liver volumes and HVC. A, Preoperative and postoperative segmental liver volumes were calculated using liver segmentation software. Each segmental liver volume was calculated automatically from each PV branch territory and is described in frontal and lateral views. PV and each segmental PV branch are colored green and pink, respectively. The segmental liver volumes are colored light orange. B, Preoperative HVC volume of the MHV tributaries was automatically calculated from each hepatic venous branch using liver segmentation software. HV and the MHV tributaries are colored aqua blue and pink, respectively. Preoperative HVC volume is colored light orange. C, Postoperative HVC volume of the actual congestion area on POD 35 was rendered by two-phase CT using ZIO M900. It was calculated using the difference in attenuation between the congestion area and the noncongestion area. IVC and PV are colored aqua blue and dark blue, respectively. Postoperative HVC volume is colored purple. 3D-CT, three-dimensional computed tomography; HVC, hepatic venous congestion; IVC, inferior vena cava; MHV, middle hepatic vein; POD, postoperative day; PV, portal vein.

the liver volume and the volume of each vessel's (both portal and hepatic venous branches) territories from their diameter and length.

Total and Segmental Liver Volumes, the Ratio to the Right Lobe, and the Liver Regeneration Rate

Total and segmental liver volumes were calculated using liver segmentation software. The volume of the RL was calculated from the right PV territory, and the segmental liver volume of each PV branch was calculated automatically (Fig. 4A). Each volume ratio was calculated as follows: volume of a given segment divided by RL volume (%). The liver regeneration rate was calculated as follows: postoperative RL volume on POD 35 divided by preoperative whole liver volume (%).

Hepatic Venous Congestion Volume and the Congestion Rate

The preoperative HVC volume of the MHV tributaries was automatically calculated from each hepatic venous branch using the liver segmentation software (Fig. 4B). The 3D image reconstructed using this software could reflect the actual congestion volume. The postoperative HVC volume of the actual congestion area on POD 35 was rendered by two-phase CT using ZIO M900 software (Fig. 4C). The CT findings showed that the congestion area had become hyperattenuated because of poor drainage of the contrast medium (*24*). The postoperative HVC volume on POD 35 was calculated using the difference in attenuation between the congestion area and the noncongestion area. The detailed procedures have been described elsewhere (*7*). The congestion rate was calculated as follows: HVC volume divided by RL volume (%). The 13 LL LDLT donors were divided into two groups depending on the degree of congestion rate as previously described (*7*); the congestion rate of the moderate HVC group ranged from 10% to 30%, and that of the severe HVC group was greater than 30%.

Venous Collateral Formation Visualization

Postoperative VCF visualization on POD 35 was obtained from the MDCT data using ZIO M900 software. Detection of the connection between the MHV tributaries, the RHV, and the IRHV using the 3D-CT software was defined as "obvious VCF." Therefore, cases in which the MHV tributaries were patent, and in which the collateral connection could not be found, were not recognized as VCF. The 13 LL LDLT donors were divided into two groups: the VCF group and the non-VCF group.

Evaluation of Postoperative Clinical Parameters

Postoperative liver function tests such as serum aspartate aminotransferase, alanine aminotransferase, total bilirubin, and prothrombin time were measured on PODs 1, 2, 3, 5, and 7. Complications were classified according to Clavien's classification (*25*).

Graft Selection

The criteria for graft selection have been described elsewhere (*7, 8*). Briefly, an LL graft was initially considered as a graft with respect to donor safety. An RL graft was selected when an LL graft was insufficient for the recipient and the remnant liver volume of the donor was greater than 35%.

Surgical Procedure

The surgical procedures for donors have been described elsewhere (*4, 5, 8*). Briefly, donor hepatectomy was performed with intermittent inflow occlusion under the hanging maneuver. In LL grafts, the MHV was procured with the liver graft. Therefore, the MHV tributaries were ligated under hepatectomy. None of the MHV tributaries were reconstructed on the donor side.

Statistical Analysis

Statistical analysis was performed using Student *t* test and chi-square test. The data were considered significant when the *P* value was less than 0.05. All analyses were performed with the use of StatView software (Version 5.0, Abacus Concepts, Berkeley, CA).

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Strategies for Successful Left-Lobe Living Donor Liver Transplantation in 250 Consecutive Adult Cases in a Single Center

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BACKGROUND: Living donor liver transplantation (LDLT) using left-lobe grafts was not generally recognized as feasible due to the problem of graft size.

STUDY DESIGN: We retrospectively evaluated strategies for successful left-lobe LDLT in 250 consecutive cases stratified into 2 eras: Era 1 (n = 121), in which surgical procedures were continually refined, and Era 2 (n = 129), in which established procedures were used.

RESULTS: Graft volume (GV) did not affect the incidence of graft function or survival. Era 2 patients had decreased portal vein (PV) pressure at closure (16.0 ± 3.5 mmHg vs 19.1 ± 4.6 mmHg, $p < 0.01$), increased PV flow/GV (301 ± 125 mL/min/100g vs 391 ± 142 mL/min/100g, $p < 0.01$), and improved graft survival rate (1-year: 90.6% vs 81.8%. $p < 0.01$) despite the smaller GV/standard volume (SLV) ratio (36.2% ± 5.2% vs 41.2% ± 8.8%, $p < 0.01$) compared with Era 1. Patients in Era 2 had lower PV pressure and greater PV flow ($y = 598\text{-}5.7x$, $p = 0.02$) at any GV/SLV compared with cases in Era 1 ($y = 480\text{-}4.3x$, $p < 0.01$), representing greater graft compliance. Univariate analysis for graft survival showed that Era 1, Model for End-Stage Liver Disease (MELD) score ≥20, inpatient status, closing portal venous pressure ≥20 mmHg, no splenectomy, and operative blood loss ≥10L were the risk factors for graft loss, and multivariate analysis showed that Era 1 was the only significant factor ($p < 0.01$). During Era 2, development of primary graft dysfunction was associated with inpatient recipient status ($p = 0.02$) and donor age ≥45 years ($p < 0.01$).

CONCLUSIONS: The outcomes of left-lobe LDLT were improved by accumulated experience and technical developments. (J Am Coll Surg 2013;216:353–362. © 2013 by the American College of Surgeons)

Although living donor liver transplantation (LDLT) is becoming an established procedure for treating patients with end-stage liver disease, particularly in countries where deceased donors are rarely available, a critical issue in considering LDLT is that donor safety is not guaranteed.[1-3] When LDLT was first introduced for adults, left-lobe LDLT was the only option because of the risk of remnant liver failure in the donor after right-lobe donation.[4] However, because of the smaller graft volume (GV) and its possible association with inferior outcomes after left-lobe LDLT, right-lobe LDLT is performed worldwide, but the concept of left-lobe LDLT has been largely ignored except in Japan.[5,6] Nevertheless, the increased risk of morbidity and mortality of healthy donors after right-lobe donation should be taken seriously.[3]

Surgical and nonsurgical refinements in LDLT over the last decade have substantially improved the outcomes of LDLT. Consequently, the issue of GV might become less important based on accumulated experience and technical refinements. In 2009, the Hong Kong group[6] stated that small GV, defined as GV/standard liver volume (SLV) <40%, has been overcome in the context of right-lobe LDLT and has become less important in terms of graft outcomes. The Kyoto group[7] reduced their lower limit of the graft-to-recipient weight ratio (GRWR) in LDLT to 0.6% in combination with portal pressure control. In such situations, combined with the use of smaller grafts with institutional lower limits, left-lobe grafts could be considered instead of right-lobe grafts and could become the primary mode of LDLT again.

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Abbreviations and Acronyms

GRWR = graft-to-recipient weight ratio
GV = graft volume
GW = graft weight
HA = hepatic artery
LDLT = living donor liver transplantation
MELD = Model for End-Stage Liver Disease
PV = portal vein
SLV = standard liver volume

We have long advocated the feasibility of left-lobe LDLT and have performed 250 consecutive left-lobe LDLTs since 1997. During this time, we made various surgical and nonsurgical modifications and refinements. Therefore, the aim of this study was to evaluate the impact of progressive refinements on graft outcomes of left-lobe LDLT performed at a single center. We also sought to identify the factors associated with dysfunctional left-lobe grafts performed using current methods.

METHODS

Patients

Between May 1997 and May 2012, 250 consecutive left-lobe LDLTs in adults were performed at Kyushu University Hospital, under approval of the Ethics and Indications Committee of Kyushu University. The first adult left-lobe LDLT was in a patient with acute liver failure.[8] The major refinements to the surgical techniques and therapies applied are listed in Table 1, with the time of implementation according to the case numbers of left-lobe LDLT.

Graft selection process

Our institute exclusively used left-lobe grafts before December 2000, and the left-lobe LDLT was indicated if the predicted GV/SLV was ≥30%.[9] Since December 2000, we have used right-lobe grafts for selected patients once its effectiveness and safety had became affirmed worldwide.[10] However, a right-lobe graft, without the middle hepatic vein, could be considered if the predicted GV/SLV was ≥35% and the donor's remnant liver volume was ≥35% of the total liver volume.[2] At Kyushu University Hospital, a left-lobe graft with predicted GV/SLV ≥35% is the primary graft type and if it is not available, a right lobe graft is the secondary graft type. However, graft selection is still carried out on a case-by-case basis, considering anatomic and recipient factors. For example, a right-lobe graft is favored for a recipient with a Model for End-Stage Liver Disease (MELD) score ≥25.

For the first 38 cases, graft volumetry was assessed 2-dimensionally using 3-mm thick CT slices and image-analysis software (NIH image 1.61). In subsequent cases, 3-dimensional reconstruction of the liver was performed with helical CT data using zio-M900 software (Zio Software Inc), followed by virtual hepatic lobectomy and calculation of the predicted GV.[11]

Table 1. Refinements of Surgical Techniques and Therapies for Left-Lobe Living Donor Liver Transplantation

First author	Year	Surgical techniques or therapies	Case no.
Nishizaki[8]	2001	Adult-to-adult cases, predicted GV/SLV ≥30%	1
Ikegami[12]	2001	Left-lobe graft with the caudate lobe	17
Shimada[15]	2004	Splenic artery ligation	37
Hiroshige[11]	2003	Three-dimensional CT-based graft volumetry	39
Suehiro[13]	2005	Graft venoplasty and recipient cavoplasty	50
Soejima[2]	2012	Predicted GV/SLV ≥35%	102
Ikegami[16]	2009	Splenectomy for portal venous pressure control	122

GV, graft volume; SLV, standard liver volume.

Surgical procedures

The surgical procedures in the donors and recipients for left-lobe LDLT are summarized as follows. The first 16 left-lobe grafts included the middle hepatic vein without the caudate lobe. From case 17 on, we used left-lobe grafts with the caudate lobe.[12] Parenchymal transection was performed using the Cavitron Ultrasonic Surgical Aspirator (CUSA Valleylab Inc) and a saline-linked radiofrequency dissecting sealer (Tissuelink Tissuelink Medical Inc) using the hanging maneuver.[3] After donor hepatectomy, the graft was perfused, weighed, and stored in University of Wisconsin solution (Viaspan, DuPont Inc).

From case 50 on, venoplasty was performed on the back table to create a wider outflow orifice.[13] The long intervening venous septum was incised perpendicularly, and the underlying liver parenchyma was removed using the Cavitron Ultrasonic Surgical Aspirator. This incision was then stretched along the axis of the septum, and the vessel edges were approximated using interrupted 6-0 polydioxanone sutures. An incision was also made to the superficial veins to create a wide venous orifice, if possible.

The left-lobe grafts were transplanted into the recipient without veno-venous bypass. Portal vein (PV) pressure was continuously monitored during liver transplantation surgery using a cannula (Medicut LCV-UK catheter 14G, Nippon Sherwood Inc) located in the superior mesenteric vein via a terminal jejunal vein. After the hilar dissection, the native liver was completely mobilized from the vena cava. Once the graft was ready for implantation, the PV was tied off and the right hepatic vein was also divided using stapling devices (Endo-GIA 60-2.5, Covidien). Total hepatectomy

was performed after clamping the middle and left hepatic veins. A large side clamp (Potts Liver Transplant Clamp, GEISTER) was applied to control the vena cava with the middle and left hepatic venous orifices. An incision was made to divide the septum between the middle and the left hepatic veins and create a common orifice. The incision was extended to the anterior wall of the vena cava, and simple cavoplasty was performed to increase the size of the anastomosis.[14] The anastomosis was performed with simple intraluminal mattress sutures using 5-0 continuous polydioxanone sutures with an RB1 needle (Ethicon Inc). Short hepatic veins were not reconstructed in any recipient. Hepatic artery (HA) reconstruction was performed under a microscope. Intraoperative PV and HA flows were measured in the recipients after reperfusion using an ultrasonic transit time flow meter (Transonic System, Transonic Systems Inc). From case 41 on, biliary reconstruction was performed by duct-to-duct biliary anastomosis using interrupted 6-0 polydioxanone sutures.

From case 37 forward, splenic artery ligation was performed in 16 patients with splenomegaly to control PV pressure.[15] From case 122 on, we started to perform aggressive splenectomy to control portal pressure.[16] The introduction of tieless splenectomy using a vessel-sealing system (LigaSure Atlas, Valleylab Inc) and endo-stapling devices (Endo-GIA 60-2.5, Covidien) enabled us to perform bloodless procedures. All of the major shunt vessels ($\geq$10 mm) were ligated to prevent portal flow stealing phenomena. After implantation of the graft and shunt ligation, splenectomy was indicated when the PV pressure was $\geq$20 mmHg. For patients with hepatitis C, splenectomy was universally indicated regardless of the PV pressure, for post-LDLT antiviral treatment.

Groups

As described above, we implemented several technical refinements for left-lobe LDLT at Kyushu University; these refinements were introduced during the first 121 cases. Therefore, the 250 consecutive left-lobe LDLT cases were divided into 2 groups: Era 1 (n = 121, up to case 121) and Era 2 (n = 129, from case 122 on) for the analyses (Table 1).

Immunosuppression

The basic immunosuppression protocol consisted of tacrolimus or cyclosporine with mycophenolate mofetil and steroids. Mycophenolate mofetil was used from case 42 on. The target tacrolimus level was 10 to 14 ng/mL for 1 month after LDLT, and was decreased to 7 to 10 ng/mL over the next few months. The target cyclosporine level was 150 to 250 ng/mL for 1 month after LDLT and was decreased to 100 to 150 ng/mL over the next few months. Mycophenolate mofetil was started at a dose of 2 g daily, and tapered down to 1 g daily over 1 to 3 months and tapered off at 6 months. One gram of methylprednisolone was given after reperfusion, decreased from 200 mg to 20 mg daily over 1 week, then switched to oral prednisolone, which was tapered off at 3 months.

Post-transplant medical care

Perioperative prophylaxis consisted of intravenous cefotaxime (4 g/day) and ampicillin sulbactam (6 g/day) 4 times daily for 3 days after LDLT, and was started 30 minutes before surgery. The central venous catheters that had been placed in the internal jugular vein were usually removed within 5 days after LDLT and replaced with a peripheral catheter. Prolonged ascites drainage over 14 days is commonly seen after left-lobe LDLT. The amount of ascites drained via the indwelling abdominal drains was recorded. The fluid loss due to drainage of the ascites was the corrected using intravenous sodium containing 5% albumin solution to maintain serum albumin level $\geq$3.5 mg/dL.

Primary graft dysfunction

Primary graft dysfunction was defined as graft insufficiency with possible early graft loss, without technical, anatomic, immunologic, or hepatitis-related issues.[17] It was defined as delayed hyperbilirubinemia, with total bilirubin $\geq$20 mg/dL, usually occurring after postoperative day 7 and persisting for 7 or more consecutive days.

Smaller graft size has been the major obstacle in LDLT, and hyperbilirubinemia with or without intractable ascites output after LDLT has been called small-for-size graft syndrome. However, studies have documented that small grafts do not necessarily cause or correspond to such clinical outcomes, which could be attributed to multiple factors including disease severity, portal pressure, graft regeneration, and donor age.[17] Therefore, we applied the term *primary graft dysfunction* to represent a poorly functioning graft after LDLT.

Statistical analysis

All analyses were performed in a retrospective manner. Values are expressed as the mean $\pm$ standard deviation. Variables were analyzed using the chi-square test for categorical values or the Mann-Whitney test for continuous variables. Multivariate analyses for categorical variables were performed using the logistic regression model. Cumulative survival analyses were determined using the Kaplan-Meier method with the log-rank test and Cox proportional hazards multivariate model. Only significant variables were enrolled in multivariate analyses. Linear regression was used to compare the relationship between continuous variables. Values of $p < 0.05$ were considered statistically significant.

Table 2. Patient Demographics

Variables	Era 1 (n = 121)	Era 2 (n = 129)	p Value
Recipient age, y	47.5 ± 15.6	51.4 ± 15.1	0.04
Recipient sex, male, n (%)	52 (42.9)	42 (32.6)	0.09
Body mass index, kg/m^2	21.7 ± 4.7	22.5 ± 3.6	0.13
MELD score	15.7 ± 7.4	16.4 ± 7.3	0.29
Child C, n (%)	42 (38.5)	67 (61.5)	0.02
Diseases, n (%)			
Acute liver failure	29 (24.0)	13 (10.1)	0.01
Cholestatic cirrhosis	34 (28.1)	37 (28.7)	
Postnecrotic cirrhosis	51 (42.1)	75 (58.1)	
Others	7 (5.8)	4 (3.1)	
Major shunt vessels, ≥10 mm, n (%)	25 (20.7)	45 (34.9)	0.01
Donor age, y	35.4 ± 11.2	34.9 ± 10.2	0.77
Donor sex, male	91 (74.6)	41 (46.6)	<0.01
Incompatible blood type donor, n (%)	1 (0.8)	9 (7.0)	0.01
GV, g	452 ± 89	399 ± 62	<0.01
GV/SLV, %	41.2 ± 8.8	36.2 ± 5.2	<0.01
GRWR, %	0.84 ± 0.25	0.71 ± 0.13	<0.01
Cold ischemic time, min	67 ± 68	67 ± 33	0.89
Warm ischemic time, min	37 ± 7	39 ± 13	0.08
HA flow, mL/min	112 ± 71	102 ± 55	0.23
PV flow, L/min	1.33 ± 0.54	1.54 ± 0.56	<0.01
PV flow/GV, mL/min/100g	301± 125	391 ± 142	<0.01
Operation time, min	745 ± 161	741 ± 143	0.84
Operative blood loss, L	6.7 ± 11.5	6.7 ± 21.2	0.96
Splenectomy, n (%)	9 (7.4)	89 (69.0)	<0.01
Duct-to-duct biliary reconstruction, n (%)	50 (41.3)	83 (64.3)	<0.01
Acute cellular rejection, n (%)	28 (23.1)	13 (10.1)	<0.01
Cytomegalovirus infection, n (%)	28 (23.1)	28 (21.7)	0.78
Bile duct stenosis, n (%)	37 (30.0)	13 (10.1)	<0.01
HA thrombosis, n (%), n (%)	3 (2.5)	0 (0.0)	0.07
PV thrombosis	3 (2.5)	3 (2.3)	0.94
Primary graft dysfunction, n (%)	18 (14.9)	9 (7.0)	0.04
1-year graft survival rate, %	81.8	90.6	<0.01

Unless stated otherwise, data are reported as means ± SD.
GRWR, graft-to-recipient weight ratio; GV, graft volume; HA, hepatic artery; MELD, Model for End-Stage Liver Disease; PV, portal vein; SLV, standard liver volume.

RESULTS

Characteristics of the recipients, donors, and grafts

The recipients in Era 1 were younger than those in Era 2 (Era 1 vs Era 2: 47.5 ± 15.6 years vs 51.4 ± 15.1 years, p = 0.04, Table 2). There were no differences in terms of the recipients' sex, body mass index, or Model for End-Stage Liver Disease (MELD) score between the 2 eras. The distribution of recipient disease was significantly different between the 2 eras (p < 0.01): acute liver failure was more common in Era 1 (24.1% vs 10.1%), and postnecrotic cirrhosis was more common in Era 2 (42.1% vs 58.1%, p < 0.01). There were more patients with major shunt vessels ≥10 mm in Era 2 than in Era 1 (20.7% vs 34.9%, p < 0.01).

Graft volume was significantly larger in Era 1 than Era 2 (452 ± 89 g vs 399 ± 62 g, p < 0.01), as was GV/SLV (41.2 ± 8.8 % vs 36.2 ± 5.2 %, p < 0.01) and graft-to-recipient weight ratio (GRWR) (0.84 ± 0.25 % vs 0.71 ± 0.13 %, p < 0.01, Table 2). The GV/SLV was more frequently in the range of 40.0% to 49.9% in Era 1, and 35.0% to 39.9% in Era 2 (Fig. 1A).

In terms of donor characteristics, there was no significant difference in donor age. However, there were more male donors in Era 1 (74.6% vs 46.6%, p < 0.01),

and there were more blood-type incompatible donors in Era 2 (0.8% vs 7.0%, $p < 0.01$).

Regarding surgical factors, there were no significant differences in operation time, blood loss, cold or warm ischemic time, or HA flow between the 2 eras. Portal vein flow (1.33 ± 0.54 L/min vs 1.54 ± 0.56 L/min, $p < 0.01$) and PV flow/GV (301 ± 125 mL/min/100 g vs 391 ± 142 mL/min/100 g, $p < 0.01$) were significantly greater in Era 2 than in Era 1. Splenectomy was predominantly performed in Era 2 (7.4% vs 69.0 %, $p < 0.01$); splenectomy was performed in 9 patients in Era 1 to treat pancytopenia for inducing preemptive interferon treatment for hepatitis C (n = 8) and to reduce the lymphocyte count in blood type incompatible LDLT (n = 1).

Acute cellular rejection (23.1% vs 10.1%, $p < 0.01$), bile duct stenosis (30.0% vs 10.1%, $p < 0.01$) and primary graft dysfunction (14.9% vs 7.0%, $p = 0.04$) occurred in significantly fewer cases in Era 2 than Era 1. No significant differences were observed in terms of cytomegalovirus infection, HA, and PV thrombosis between the eras.

Graft volume/standard liver volume and graft outcomes

The maximum total bilirubin concentrations within 1 month after left-lobe LDLT were also plotted against GV/SLV (Fig. 1B). Grafts with maximum total bilirubin ≥20 mg/dL were evenly distributed with GV/SLV and GRWR. The GV/SLV in the serial left-lobe LDLT cases are plotted in Figure 1C. The in-hospital mortality (n = 29) rates in patients with grafts with GV/SLV ≥35% and <35% were 12.6% and 9.2%, respectively ($p = 0.44$). Therefore, GV did not affect in-hospital mortality. The proportions of grafts with GV/SLV <35% were 23.1% in Era 1 and 37.2% in Era 2 ($p = 0.01$), and the 1-year graft survival rates were 81.8% in Era 1 and 90.6% in Era 2, respectively ($p < 0.01$, Fig. 2).

Portal vein pressure and graft outcomes

In Era 2, the graft in- and outflows had been fully optimized, maximizing the graft venous drainage and decompression of the graft inflow by splenectomy. Portal vein pressures at laparotomy were 23.4 ± 6.1 mmHg and 23.9 ± 5.8 mmHg in Era 1 and Era 2, respectively, and were not significantly different ($p = 0.50$). However, PV pressure at the end of the operation was significantly higher in Era 1 than in Era 2 (19.1 ± 4.6 mmHg vs 16.0 ± 3.5 mmHg, $p < 0.01$, Fig. 3A). The mean volume of the explanted spleen was 423 ± 267 g.

Total bilirubin on day 14 after left-lobe LDLT (8.8 ± 8.7 mg/dL vs 6.2 ± 7.5 mg/dL, $p = 0.02$) and the drained ascites volume (0.87 ± 1.21 L/day vs 0.34 ± 0.66 L/day, $p < 0.01$) were significantly lower in Era 2 than in Era 1.

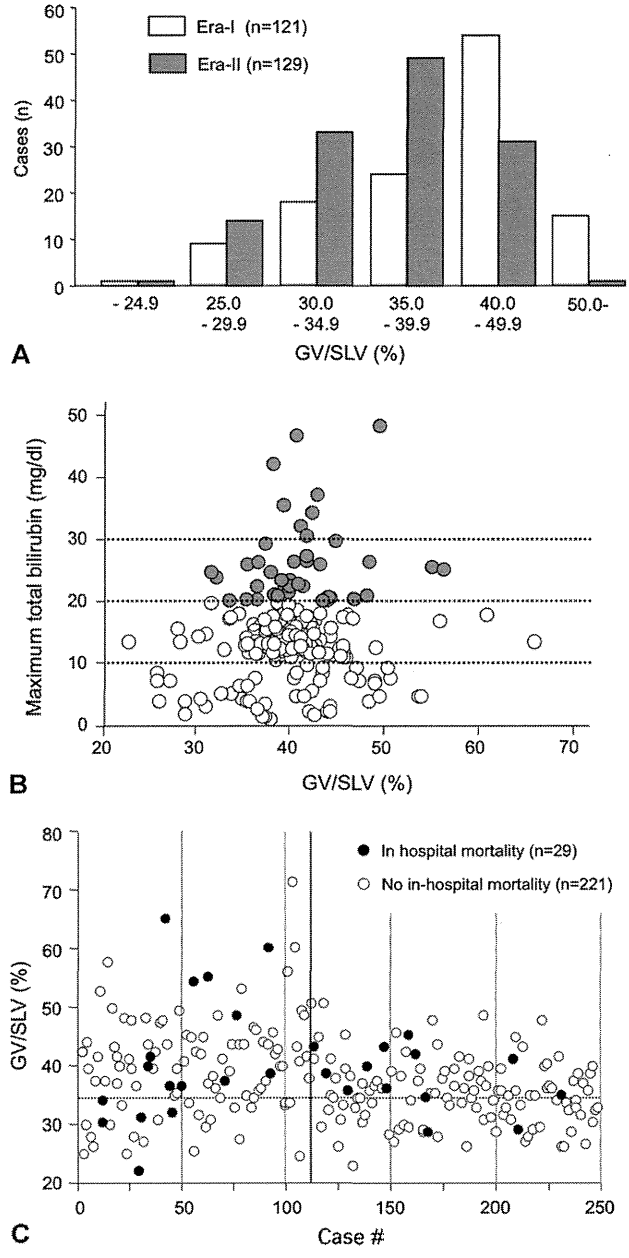

Figure 1. (A) Distribution of actual GV/SLV in Eras 1 (n = 121) and 2 (n = 129). (B) GV/SLV and maximum total bilirubin level within 1 month after transplantation. (C) GV/SLV with or without in-hospital mortality, in individual cases. GV; graft volume, SLV; standard liver volume.

Graft volume/standard liver volume and portal vein flow

Linear regression analysis was performed to evaluate the relationship between GV/SLV and PV flow/GV (Fig. 4).

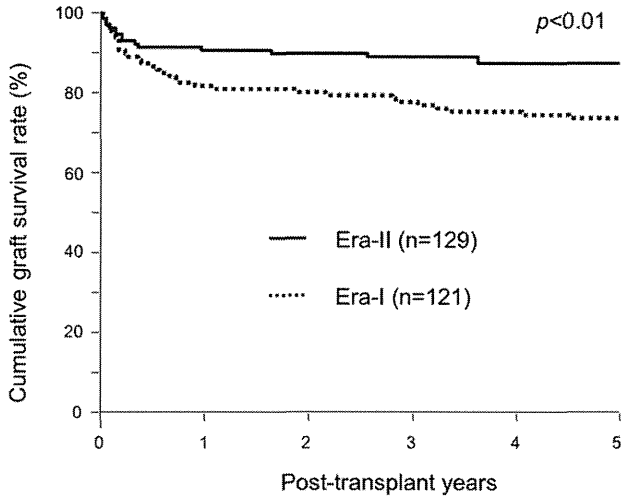

Figure 2. Cumulative graft survival rate in Era 1 (n = 121) and Era 2 (n = 129).

A negative linear correlation was observed between the 2 parameters. Graft PV flow was better in Era 2, characterized by maximum venous outflow and splenectomy (Era 1: y = 480 - 4.3x, r^2 = 0.091, p < 0.01; Era 2, y = 598 - 5.7x, r^2 = 0.043, p = 0.02).

Uni- and multivariate analyses for graft survivals

Univariate analysis for the 5-year graft survivals showed that Era 1 (73.6% vs 87.1%, p = 0.01), MELD score ≥20 (71.9% vs 83.3%, p = 0.02), inpatient status before receiving LDLT (73.6% vs 86.3%, p < 0.01), PV pressure at abdominal closure ≥20 mmHg (85.2% vs 65.3%, p = 0.01), no splenectomy (76.2% vs 86.8%, p = 0.04), and operative blood loss ≥10 L (66.1% vs 82.1%, p = 0.04) were the significant negative factors. Multivariate analysis showed that Era 1 (odds ratio 3.5, 95% CI 1.3 to 10.1, p = 0.01) was the only significant risk factor for graft loss (Table 3).

Causes of hospital mortality included primary graft dysfunction (n = 6), multiorgan failure (n = 6), sepsis (n = 5), intra-abdominal bleeding (n = 4), cerebrovascular accident (n = 2), hepatic artery thrombosis (n = 2), rejection (n = 1), and lymphoma (n = 1).

Risk factors for primary graft dysfunction in the Era 2

Finally, we determined the risk factors for having primary graft dysfunction in left-lobe LDLT, including after the refinement of techniques and treatments (ie, in Era 2). Univariate analysis showed that inpatient status of recipient before LDLT (66.7% vs 29.4%, p = 0.02) and donor age 45 years or more (55.6% vs 15.9%, p < 0.01) were the only risk factors for primary graft dysfunction

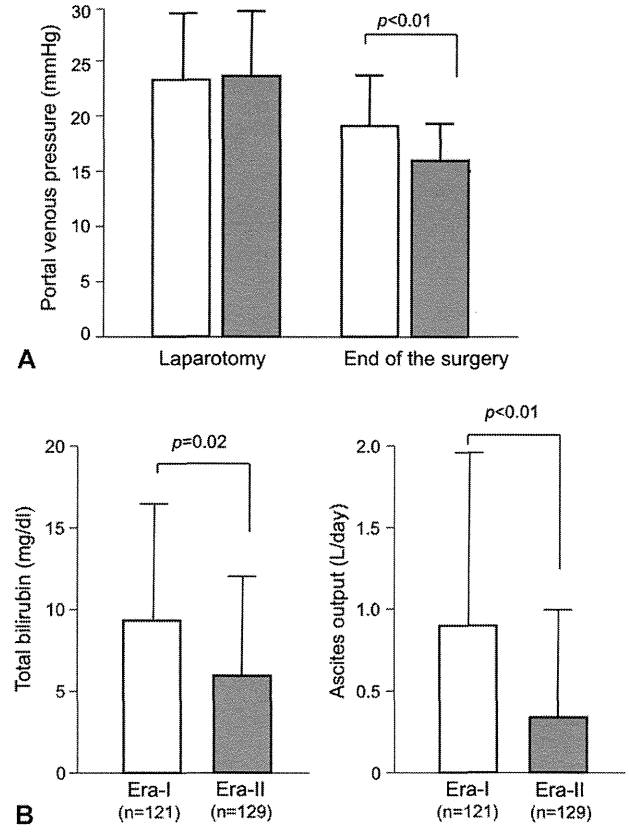

Figure 3. (A) Portal venous pressure at laparotomy and at the end of operation in Era 1 (n = 121) and Era 2 (n = 129). (B) Total bilirubin level and ascites output on postoperative day 14. White bar, Era 1; black bar, Era 2.

(Table 4). Although the number of patients with primary graft dysfunction was small, logistic regression analysis showed that donor age 45 years or greater (yes, odds ratio 5.9, 95% CI 1.4 to 25.2, p = 0.01) and inpatient status of the recipient (yes, odds ratio 4.3, 95% CI 1.1 to 19.2, p = 0.04) were significant risk factors for primary graft dysfunction.

Predicted and actual graft volume in Era 2

The mean predicted and actual GVs were 437 ± 78 g and 400 ± 63 g, respectively, which were significantly different (p < 0.01). The mean predicted and actual GV/SLV ratios were 39.5% ± 6.2% and 36.2% ± 5.2%, respectively, with significant difference (p < 0.01). The mean differences in GV and GV/SLV were 38 ± 55 g and 3.4% ± 5.0%, respectively.

Complications of splenectomy

Complications in splenectomy included pancreas leakage (n = 6, 6.1%), treated percutaneously, and overwhelming

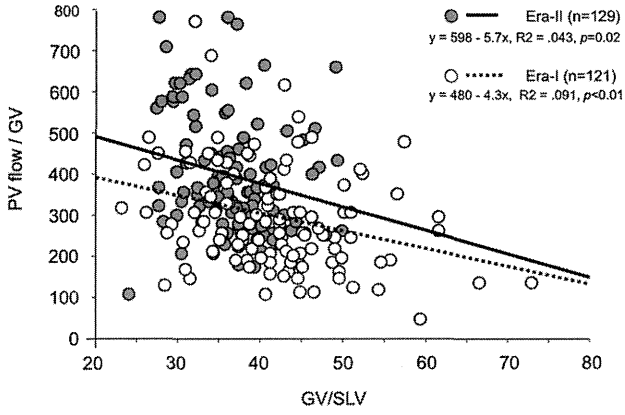

Figure 4. Linear regression analysis for the relationship between GV/SLV and PV flow/GV in Era 1 (n = 121) and Era 2 (n = 129). GV, graft volume; PV, portal vein; SLV, standard liver volume.

postsplenectomy sepsis (n = 3, 3.1%). Two patients had *Streptococcus pneumoniae* sepsis (1 and 2 years after LDLT, respectively) and 1 had *Klebsiella pneumoniae* sepsis 5 years after LDLT. These patients were not vaccinated before LDLT, and they were treated successfully with antibiotics.

DISCUSSION

We have implemented several refinements for left-lobe LDLT, such as wide veno-caval anastomosis and splenectomy to control PV pressure; these have been routinely performed from case 122 on (Era 2). We routinely use left-lobe grafts as the primary graft type in LDLT for patients with predicted GV/SLV ≥35%. By implementing these strategies, graft survival has increased by 10% compared with survival in the preceding era in association with a reduction in the incidence of primary graft dysfunction. Interestingly, implementation of these techniques not only succeeded in reducing PV pressure but also increased the graft PV flow, resulting in increased graft vascular compliance.

We also found that GV did not have a significant negative impact on graft outcomes in our series, although this may be one of the most critical factors for determining graft function. The most reasonable explanation for this result seems to be the multifactorial natures of the factors, which determine graft dysfunction and graft loss. Such factors include recipient status, portal hypertension, operative blood loss, donor age, graft steatosis, and post-transplant complications.[18] Therefore, to account for these factors, each transplant center selects its own lower limit for predicted GV for LDLT. As described earlier, we previously used GV/SLV ≥30% as the borderline threshold for graft selection, and have increased this to 35%. The introduction of right-lobe LDLT in 2000 and the large discrepancy between the predicted and actual GV in some cases were largely responsible for this shift, although lower GV/SLV was not an independent factor for short-term graft survival.[9,19] According to the results of this analysis and our own clinical experience, the threshold GV/SLV could be reduced to 30% again, although it is important to consider the difference in predicted and actual GV/SLV (3.4% ± 5.0%) even in Era 2, as shown in Figure 1C. Taking into account the standard deviation, however, the actual GV/SLV could be <25%, for a predicted GV/SLV of 30%. This relatively small error seems to be caused by minor differences in the virtual and actual hepatectomy plane, expansion of the hepatic parenchyma caused by acute injection of contrast medium on CT scans, and graft dehydration caused by hyperosmotic perfusion solution.[19] Therefore, the lower limit of a predicted GV/SLV of 35% was not associated with a significant negative impact in this study, even though the actual GV/SLV was <30% in some grafts.

Significant technical changes from Era 1 to Era 2 were the graft venoplasty with wide veno-caval anastomosis and splenectomy. Venous drainage is a critical determinant of graft function with right- and left-lobe grafts.[20] Unlike right-lobe grafts, the left lobe is located in an unstable position in the body and graft rotation after regeneration may reduce outflow. Our procedure, in which we create a wider horizontal anastomosis, is a modified form of the Kyoto technique applied in pediatric LDLT, in which an additional caudal incision is made on the vena cava.[13] Although the Tokyo group[21] reconstructs the short hepatic vein from the Spiegel lobe, we do not apply the procedure because of collateral drainage veins from the caudate lobe into the middle hepatic vein.

Excessive portal hypertension is well established as a significant risk factor for graft injury. The most widely performed procedure for portal decompression seems to be creation of a porto-systemic shunt, which Boillot and colleagues[22] first reported as mesocaval shunting in 2002, and followed by hemi-portocaval shunting by Troisi and associates.[23] Troisi and coworkers reported that 1-year graft survival was 75% for hemi-portocaval shunting and 20% without, after LDLT, with GRWR <0.8. In Japan, the Kyoto group[24] performed selective hemi-portocaval shunting for left-lobe LDLT with a GRWR <0.8; graft survival in that study was 100%. However, the same group[25] recently reported that splenectomy is increasingly being performed for portal pressure control. We now avoid creating or keeping shunts, favoring instead blocking major shunt vessels, especially for marginal situations, such as extra-small grafts, older grafts, and severe portal hypertension. We created a hemi-portocaval shunt for an

Table 3. Uni- and Multivariate Analyses for Graft Survival

Variables		n	5-y graft survival rate, %	p Value	
				Univariate	Multivariate
Era 1	Yes	121	73.6		
	No	129	87.1	0.01	0.01
Recipient age ≥60 y	Yes	73	82.9		
	No	177	78.2	0.39	–
MELD score ≥20	Yes	77	71.9		
	No	172	83.3	0.02	0.25
Inpatient status	Yes	139	73.6		
	No	111	86.3	<0.01	0.76
Acute liver failure	Yes	43	76.1		
	No	206	80.6	0.33	–
Hepatitis C	Yes	95	77.9		
	No	153	81.1	0.65	–
Hepatocellular carcinoma	Yes	149	80.1		
	No	101	79.6	0.68	–
Major spontaneous shunts	Yes	70	79.8		
	No	180	80.0	0.91	–
Recipient age ≥45 y	Yes	52	76.2		
	No	198	80.9	0.34	–
GV/SLV <35%	Yes	76	78.8		
	No	174	80.2	0.99	–
GRWR <0.7	Yes	92	78.3		
	No	158	80.7	0.76	–
Blood type incompatible	Yes	10	90.0		
	No	240	79.6	0.59	–
Opening PV pressure ≥25 mmHg	Yes	90	82.8		
	No	105	79.4	0.76	–
Closing PV pressure ≥20 mmHg	Yes	50	69.3		
	No	143	85.2	0.01	0.12
Warm ischemic time ≥60 min	Yes	4	66.7		
	No	246	80.4	0.36	–
Cold ischemic time ≥120 min	Yes	17	70.6		
	No	233	80.9	0.31	–
Splenectomy	Yes	98	86.8		
	No	152	76.2	0.04	0.20
Operative time ≥720 min	Yes	123	78.9		
	No	127	79.6	0.81	–
Blood loss ≥10 L	Yes	26	66.1		
	No	224	82.1	0.04	0.21

GRWR, graft-to-recipient weight ratio; GV, graft volume; HA, hepatic artery; MELD, Model for End-Stage Liver Disease; PV, portal vein; SLV, standard liver volume.

extra-small graft with GV/SLV of 23.7%, which resulted in graft dysfunction caused by portal stealing, followed by relaparotomy, closure of the shunt, and graft recovery.[26] We recently had a patient with decreased portal inflow and stealing into an unrecognized gastroesophageal shunt, resulting in primary graft dysfunction and graft loss, even after surgical division of the shunt vessels.[27] As reported by Hessheimer and coauthors,[28] maintaining appropriate portal inflow into a dynamically regenerating liver to prevent excessive portal flow and portal stealing is technically difficult.

To optimize portal hemodynamics, we ligate the major shunt vessels and perform splenectomy. We try to ligate all of the major shunt vessels, even if the PV pressure increases, and then perform splenectomy. In deceased door liver transplantation, Lüsebrink and associates[29] reported that splenectomy caused increased frequency of severe infectious episodes by 2.5 times. However, in our cases of left-lobe LDLT, the prevalence of septic complications was decreased by splenectomy (9.2% vs 15.1%), although this was not statistically significant. The techniques used in splenectomy for portal hypertensive

Table 4. Risk Factors for Primary Graft Dysfunction after Left-Lobe Living Donor Liver Transplantation in Era 2

Variables	No PGD (n = 120) n	%	PGD (n = 9) n	%	p Value
Recipient age ≥60 y	43	35.8	2	22.2	0.39
MELD score ≥20	29	24.2	4	44.4	0.18
Inpatient status before LDLT	35	29.2	6	66.7	0.02
Acute liver failure	13	10.8	1	11.1	0.99
Hepatitis C	46	38.3	4	44.4	0.76
Major shunt vessels ≥10mm	40	33.3	5	55.6	0.18
Donor age ≥45 y	19	15.8	5	55.6	<0.01
GV/SLV <35%	44	36.7	3	33.3	0.83
GV/SLV <30%	14	11.7	0	0.0	0.28
GRWR <0.7	53	44.1	3	33.3	0.51
GRWR <0.6	18	15.0	1	11.1	0.74
Blood type incompatible donor	9	7.5	0	0.0	0.58
PV pressure at laparotomy ≥25 mmHg	53	44.2	4	44.4	0.99
PV pressure at closure ≥20 mmHg	16	13.3	1	11.1	0.84
PV flow/GV ≥250 mL/min/100g	95	79.2	7	77.8	0.23
Splenectomy	81	67.5	7	77.8	0.54
Warm ischemic time ≥60 min	4	3.3	0	0.0	0.57
Cold ischemic time ≥120 min	6	5.0	0	0.0	0.49
Operative time ≥720 min	51	42.5	5	55.6	0.46
Blood loss ≥10 L	9	7.5	1	11.1	0.70

GRWR, graft-to-recipient weight ratio; GV, graft volume; HA, hepatic artery; LDLT, living donor liver transplantation; MELD, model for end-stage liver disease; PGD, primary graft dysfunction; PV, portal vein; PVP, portal venous pressure; SLV, standard liver volume.

splenomegaly are quite different from those applied in patients without portal hypertension.[16] Tieless procedures using a vessel sealing system and end-stapling devices, as laparoscopic splenectomy, can enable safe splenectomy in LDLT with blood loss of <100 mL.[16] However, care must be taken to give a Pneumococcal vaccination before splenectomy to prevent overwhelming postsplenectomy sepsis. We abandoned splenic artery ligation for PV pressure control because of technical difficulties in isolating the splenic artery buried in the nests of collateral vessels and its inadequate clinical effects, as expected.[15]

The increased compliance of the transplanted left-lobe graft could be attributed not only to the increased graft outflow by venoplasty/cavoplasty but also to the hepatic vasodilatation by splenectomy. Regarding the impact of splenectomy in a portal hypertensive situation, recent reports showed that splenectomy effectively decreased hepatic vascular tonus and increased vascular compliance by blocking the endothelin-1 pathway. In a rodent biliary cirrhosis model, Uehara and colleagues[30] showed that endothelin-1 positive cells were abundantly present in an enlarged spleen for controlling portal inflow, and removing such a large spleen improved hepatic microcirculation by decreasing the portal endothelin-1 level. In a small hepatic graft transplantation model in rodents, Kuriyama and associates[31] showed that splenectomy decreased plasma endothelin-1 level and increased hepatic expression of heat-shock protein, resulting in hepatic vasodilatation. Therefore, in the patients in Era 2 with smaller grafts and splenectomy, both vigorous inflow and abundant endothelin-1 from an enlarged spleen were corrected by splenectomy, resulting in increased graft vascular compliance with increased portal flow and decreased portal pressure.

In Era 2, donor age ≥45 years and inpatient recipient status are still the independent risk factors for primary graft dysfunction. In right-lobe LDLT, Moon and colleagues[32] reported that donor age ≥44 years was associated with significantly worse graft survival for patients with GRWR <0.8. Shah and associates[5] reported that grafts ≥44 years had even graft survivals and graft failure rates with the use of larger grafts, with mean GRWR of 1.3. Advanced liver failure with deterioration in the recipient's general condition, including high MELD, advanced Child class, and inpatient status are all difficult challenges in liver transplantation, even in whole liver transplantation.[33] Although Yi and coworkers[34] reported that small grafts with GRWR <0.8 could be used for patients with a high MELD score, and particularly, patients with hepatitis B infection, the 1-year graft survival rate was 13.6% lower than in patients with low MELD scores. In our series of patients, donor age ≥45 years and recipient inpatient status were still risk factors for primary graft dysfunction in Era 2. Additional studies are needed to address these issues.

CONCLUSIONS

In conclusion, the outcomes of left-lobe LDLT were significantly improved by accumulated experience and technical developments including wide veno-caval anastomosis and splenectomy.

Author Contributions

Study conception and design: Ikegami, Shirabe, Yoshizumi
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Drafting of manuscript: Ikegami, Shirabe
Critical revision: Maehara

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ORIGINAL ARTICLE

One-step reconstruction of the right inferior hepatic veins using auto-venous grafts in living donor liver transplantation

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Abstract
Purposes Reconstruction of the right inferior hepatic vein (RIHV) presents a major technical challenge in living donor liver transplantation (LDLT) using right lobe grafts.
Methods We studied 47 right lobe LDLT grafts with RIHV revascularization, comparing one-step reconstruction, performed post-May 2007 ($n = 16$), with direct anastomosis, performed pre-May 2007 ($n = 31$).
Results In the one-step reconstruction technique, the internal jugular vein ($n = 6$), explanted portal vein ($n = 5$), inferior vena cava ($n = 3$), and shunt vessels ($n = 2$) were used as venous patch grafts for unifying the right hepatic vein, RIHVs, and middle hepatic vein tributaries. By 6 months after LDLT, there was no case of occlusion of the reconstructed RIHVs in the one-step reconstruction group, but a cumulative occlusion rate of 18.2 % in the direct anastomosis group. One-step reconstruction required a longer cold ischemic time (182 ± 40 vs. 115 ± 63, $p < 0.001$) and these patients had higher alanine transaminase values (142 ± 79 vs. 96 ± 46 IU/L, $p = 0.024$) on postoperative day POD 7. However, the 6-month short-term graft survival rates were 100 % with one-step reconstruction and 83.9 % with direct anastomosis, respectively.
Conclusion One-step reconstruction of the RIHVs using auto-venous grafts is an easy and feasible technique promoting successful right lobe LDLT.

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Keywords Living donor liver transplantation · Short hepatic vein · Right inferior hepatic vein · Right lobe · Venous reconstruction

Abbreviations

ALT	Alanine transaminase
AST	Aspartate aminotransferase
EPV	Explanted portal vein
GV	Graft volume
IJV	Internal jugular vein
IVC	Inferior vena cava
LDLT	Living donor liver transplantation
MELD	Model for end-stage liver disease
MHV	Middle hepatic vein
POD	Postoperative day
PT-INR	Prothrombin time international normalized ratio
RHV	Right hepatic vein
RIHV	Right inferior hepatic vein
SLV	Standard liver volume
V5	Segment 5 vein
V8	Segment 8 vein

Introduction

One of the major technical concerns in right lobe living donor liver transplantation (LDLT) is the complexity of the vessels, which need to be revascularized [1, 2]. Specifically, the venous systems in procured right lobe grafts may include several vessels such as the middle hepatic vein (MHV) tributaries and the right inferior hepatic veins (RIHVs). Revascularization of these outflow vessels is imperative for a fully functional right lobe graft, which affords vigorous portal inflows in a LDLT recipient with end-stage liver disease [3–5].

There are two options for reconstructing the MHV tributaries: one technique uses an extended right lobe graft, including the MHV trunk [5]; and the other uses interposition grafts [6]. We described previously how we used the explanted portal vein (EPV) for this purpose [7], but techniques for reconstructing the RIHV are not as well documented. Since 2007, we have been practicing the one-step reconstruction technique exclusively, unifying all the RIHVs with the interposed MHV tributaries and right hepatic vein (RHV) using auto-venous grafts [8]. In this technique, RIHVs are never connected to the inferior vena cava (IVC) separately, but are unified with other outflow vessels and connected with the IVC at the same time. Our technique differs from the conventional one, anastomosing graft RIHVs directly with the IVC.

This article reviews the outcomes of reconstructed RIHVs using the one-step reconstruction technique with an auto-venous graft in right lobe LDLT.

Materials and methods

Patients

Between July 1998 and October 2011, 125 LDLTs using right lobe grafts were performed at Kyushu University Hospital. Among these 125 recipients, 47 (37.6 %) required reconstruction of the RIHVs, whereas 78 (62.4 %) did not. Before May 2007, the RIHVs in the grafts were directly anastomosed ($n = 31$) to the IVC in situ; however, after May 2007, the RIHVs were connected to other outflow veins, including the RHV and the interposed graft from the MHV tributaries, using a patch-shaped venous graft ($n = 16$). All the LDLTs were performed after obtaining full informed patient consent and approval by the Liver Transplantation Committee of Kyushu University.

Graft selection

Grafts were selected as previously described [9]. Left lobe grafts were considered as the primary graft type if the desired GV/SLV was >35 %, whereas right lobe grafts were considered if the simulated GV/SLV of the left lobe graft was <35 % and the donor's remnant liver volume was >35 %. Before May 2007, the RIHVs or MHV tributaries were reconstructed if the estimated corresponding congested volume was >25 % or the deducted congested volume from the GV was <40 %. After May 2007, the indication for reconstruction of the RIHVs and MHV tributaries became more simplified: those with a congested volume >10 % of the GV or a size >5 mm were considered for reconstruction.

Donor surgery

In order to prevent biliary complications, donor hilar dissection was performed only at the corresponding first Glissonean branch [10] and donor parenchymal transection was performed using the Cavitron Ultrasonic Surgical Aspirator (CUSA™, Valleylab Inc., Boulder, CO). The significant RIHV and MHV tributaries were double-clamped with large clips and divided. After donor hepatectomy, the graft was perfused, weighed, and stored in University of Wisconsin solution (Viaspan™, DuPont Inc., Wilmington, DE).

Bench surgery and recipient surgery

In order to procure the IJV, a collar or oblique incision was made in the neck and the sternocleidomastoid muscle was retracted laterally. The overlying omohyoid muscle was divided to expose the IJV, which was isolated with vessel tape and dissected from the surrounding tissue, down to the level of its junction with the subclavian vein. To avoid injuring the branches of the facial nerve, cranical dissection was never performed above the level of the angle of the mandible. The procured IJV, usually 7–9 cm in length, was placed in heparinized saline for the bench surgery.

The hilar portal vein was procured from the explanted liver, as previously described [8]. If available, a shunt vessel of appropriate length and caliber was also procured. This type of suitable shunt vessel is usually available in patients with portal vein thrombosis [11], providing two auto-vein grafts for the bench surgery. We recently began reserving the IJV graft for interposing the MHV tributaries and other venous grafts for the patch graft to unify the orifices of the outflow veins. Next, the MHV tributary was anastomosed to the interposition graft using continuous 7-0 Prolene™ sutures (Ethicon Inc, Somerville, NJ), taking care to prevent stenosis. The venous orifices, including the RHV, RIHVs, and the interposed venous graft for the MHV tributaries, were connected together using continuous 6-0 Prolene™ sutures. To make the in situ anastomosis easier, a cuff might be attached around the RHV.

Recipient surgery

A right lobe graft with a large, unified venous orifice was implanted into the recipient, after dividing the bridge between the hepatic veins by creating a longitudinal incision in the anterior wall of the IVC [8]. The venous anastomoses were all performed using 5-0 continuous PDS-II™ sutures (Ethicone Inc, Somerville, NJ). After reconstruction of the portal vein with continuous 6-0 PDS-II™ sutures, the liver graft was reperfused. Arterial reconstruction was then performed under microscopy with interrupted 8-0 Prolene™ sutures.

Evaluation of the patency of the grafts

Follow-up computed tomography (CT) scans with intravenous contrast were taken 1 week, 1 month, 3 months, 6 months, and yearly after the LDLT. CT scans after abnormal liver function test results were also performed as necessary. Non-visualized RIHVs or parenchyma that was poorly enhanced by intravenous contrast were judged to be occlusions.

Statistical analysis

Values are expressed as mean ± SD. Variables were analyzed using the χ^2 tests for categorical values or the Mann–Whitney's test for continuous variables. Cumulative survival analyses were calculated using the Kaplan–Meier method. A P value < 0.05 was considered significant.

Results

Donor and recipient data

Forty-seven patients underwent reconstruction of the RIHVs during right lobe LDLT. All of the right lobe grafts were modified right lobe grafts that did not include the main middle hepatic vein (Table 1). The donors comprised 20 men and 27 women, with a mean age of 37.9 ± 10.8 years. The mean operation time was 448 ± 53 min and the mean blood loss was 421 ± 194 ml. The mean graft volume was 571 ± 60 ml and the mean graft volume (GV)/standard liver volume (SLV) was 46.9 ± 4.9 %. The grafts with one-step reconstruction of the RIHVs ($n = 16$) had less GV/SLV than those ($n = 31$) with direct anastomosis (43.6 ± 3.8 vs. 48.7 ± 6.9, $p = 0.010$).

The recipients comprised 28 men and 19 women, with a mean age of 49.6 ± 8.4 years. The causes of liver disease were acute liver failure ($n = 2$), cholestatic liver diseases ($n = 9$), post-necrotic liver cirrhosis ($n = 35$), and others ($n = 1$). Twenty of these patients had hepatocellular carcinoma. The mean model for the end-stage liver disease score was 17.2 ± 4.2. The mean operative time was 939 ± 149 min, the mean blood loss during surgery was 6.7 ± 4.0 L, and the mean cold and warm ischemic times were 136 ± 51 and 51 ± 8 min, respectively. The grafts with one-step reconstruction of the RIHVs ($n = 16$) were subjected to longer cold ischemic time than those ($n = 31$) with direct anastomosis (182 ± 40 vs. 115 ± 63, $p < 0.001$).

Table 1 Patient characteristics

	One-step reconstruction ($n = 16$)	Direct anastomosis ($n = 31$)	p value
Donor			
Age (year)	37.6 ± 12.6	38.1 ± 11.7	0.892
Gender, male	6 (37.5)	14 (45.2)	0.614
Operative time (min)	448 ± 93	449 ± 49	0.923
Blood loss (ml)	363 ± 163	452 ± 386	0.385
Graft			
GV (g)	542 ± 54	586 ± 83	0.063
GV/SLV (%)	43.6 ± 3.8	48.7 ± 6.9	0.010
RIHV			
Size (mm)	12.7 ± 3.2	12.3 ± 4.9	0.781
Number >2	4 (25.0)	8 (26.7)	0.943
Recipient			
Age (year)	48.4 ± 12.6	50.2 ± 11.2	0.615
Gender, male	11 (68.7)	17 (54.8)	0.357
MELD score	18.2 ± 5.6	16.8 ± 5.7	0.456
Acute liver failure	1 (6.3)	1 (3.3)	0.916
Recipient surgery			
Operative time (min)	902 ± 171	997 ± 211	0.105
Blood loss (L)	4.7 ± 2.9	7.7 ± 4.6	0.035
Cold ischemic time (min)	182 ± 40	115 ± 63	<0.001
Warm ischemic time (min)	50 ± 13	52 ± 7	0.304

GV graft volume, *MELD* model for end-stage liver disease, *RIHV* right inferior hepatic vein, *SLV* standard liver volume

Venous grafts used for the one-step reconstruction technique

The venous grafts used for one-step reconstruction of the RIHVs and the MHV tributaries are summarized in Table 2. The auto-venous patch grafts for RIHVs included the EPV ($n = 4$), internal jugular vein (IJV, $n = 6$), shunt vessels ($n = 2$), IVC ($n = 3$) and saphenous vein ($n = 1$). The shunt vessels available for this purpose included the umbilical vein ($n = 1$) and ovarian vein ($n = 1$).

Figure 1 illustrates a one-step reconstruction of the RIHVs and MHV tributaries of a right lobe LDLT graft. Preoperative three-dimensional venous images obtained by thin-slice computed tomography (CT) showed that the graft had two RIHVs and two MHV tributaries. The dilated ovarian vein was procured and used for interposing the MHV tributaries and the IJV was opened and used for a patch graft to unify the venous orifices. The patency of the RIHVs and the MHV tributaries was confirmed on an enhanced CT scan performed 5 months after LDLT.

The IVC was used as an auto-venous patch graft in three patients. In two patients, the anterior wall of the recipient's hepatic IVC was procured under clamping of the supra- and infra-hepatic IVC and on veno-venous bypass. The

Table 2 The vascular grafts used for one-step reconstruction of the right inferior hepatic veins with or without middle hepatic vein tributaries

Patch graft for RIHV	Interposition graft for MHV tributaries	*N*	Comments
EPV	IJV	3	
	EPV	1	
IJV	IJV	2	
	EPV	3	
	Shunt vessels	1	Ovarian vein ($n = 1$)
Shunt vessels	EPV	2	Umbilical vein ($n = 1$)
			Ovarian vein ($n = 1$)
IVC	EPV	3	Anterior IVC wall ($n = 1$)
			Full IVC ($n = 2$)
Others	EPV	1	Saphenous vein

EPV explanted portal vein, *IJV* internal jugular vein, *IVC* inferior vena cava, *MHV* middle hepatic vein, *RIHV* right inferior hepatic vein

procured auto-IVC was sutured with the venous orifices of the liver graft on the back-table and the graft with completed venoplasty was implanted in situ. In one patient, the total hepatic IVC was procured from the recipient and sutured with the veins of the right lobe graft, followed by implantation.

Liver function tests after LDLT

The changes in liver function test results, including aspartate aminotransferase (AST), alanine transaminase (ALT), prothrombin time international normalized ratio (PT-INR) and total bilirubin, were compared between the 16 patients who underwent one-step reconstruction and the 31 patients who underwent direct anastomosis (Fig. 2). The AST, PT-INR, and total bilirubin values did not differ significantly at any time; however, the ALT values were increased significantly in the patients with one-step venous reconstruction (142 ± 79 vs. 96 ± 46 IU/L, $p = 0.024$) on postoperative day (POD) 7.

Patency of the reconstructed RIHVs

Follow-up CT scans showed no obstructed RIHVs in the one-step reconstruction group, but five in the direct anastomosis group. The mean time from LDLT to the occlusion was 21 ± 12 days (7, 9, 19, 22, 50 days). Daily ultrasound detected an occluded RIHV in three (60 %) of five patients. Because four patients with occlusions presented minor clinical signs including increased ascites, neither stenting nor revision was performed. Only one patient died, of drastic circulatory collapse 12 h after detection of the occluded RIHV, so active treatment could not be performed. The 6-month occlusion rate of RIHVs in the one-step reconstruction group and the direct anastomosis group was 0 versus 18.2 %, respectively (Fig. 3).

Graft survival

The 3- and 6-month graft survival rates for grafts with one-step reconstruction and those with direct reconstruction were 100 and 100 % vs. 87.1 and 83.9 %, respectively. Among the five patients with grafts associated with early mortality in the direct anastomosis group ($n = 31$), only one died with graft dysfunction caused by an obstructed RIHV. Other causes of mortality included occluded MHV tributaries ($n = 1$) and graft dysfunction due to a small graft size ($n = 1$), and sepsis ($n = 2$). These patients all had patent RIHVs.

Discussion

The optimal technique for creating hepatic venous outflow in right lobe LDLT remains elusive. Right lobe grafts, especially modified right lobes without the main MHV, frequently have multiple venous orifices to be reconstructed, including the main RHV, MHV tributaries, and the RIHVs [2–4]. Although several reports focus on the technical refinements devised to resolve the issues of the MHV tributaries, little attention has been paid to the reconstruction of the RIHVs; thus, direct anastomosis of the RIHV to the IVC has remained the standard procedure. However, direct anastomosis is difficult because the in situ anastomosis of the small RIHV is usually performed in a deep, narrow and often bloody surgical field [7]. Moreover, it requires adjustments to the exact length, size, and orientation of the vessels, considering the changes resulting from graft regeneration.

Since 2007, we have used a one-step reconstruction technique for such cases [8]. This technique involves joining all of the venous orifices together in and around a large square venous patch graft. The most useful feature of this one-step technique is the ease of the in situ veno-venous anastomosis, with no kinking or malalignment of the RIHVs [8]. The complex quilting creates a wide unified venous orifice that needs to be completed during the cold phase. In the present series, although the cold ischemic time was longer and the ALT was higher in the patients who received grafts with the one-step reconstruction technique than in those who underwent the direct anastomosis, there was no significant difference in short-term graft outcomes. The one-step reconstruction technique resulted in a 100 % patency rate of the revascularized

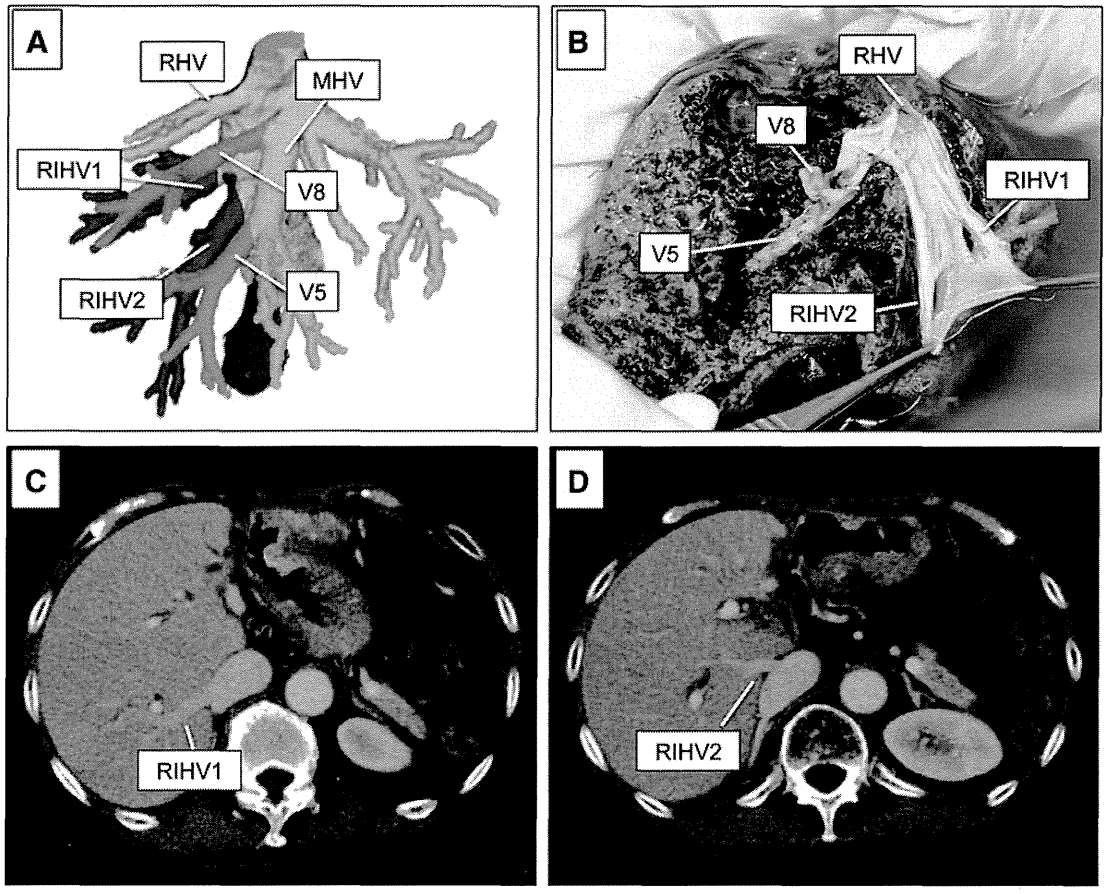

Fig. 1 Preoperative three-dimensional venous images showed two right inferior hepatic veins (*RIHVs*) and two middle hepatic vein (*MHV*) tributaries in the graft (**a**). The dilated ovarian vein was used for interposing the segment 5 vein (*V5*) and the segment 8 vein (*V8*), and the internal jugular vein (IJV) was used for a patch graft to unify the venous orifices (**b**). The patency of the RIHVs was confirmed by computed tomography (**c**, **d**). *PT-INR* prothrombin time international normalized ratio, *RHV* right hepatic vein

RIHVs and a 100 % short-term graft survival rate, which could be attributed to the ease of the one-step technique for creating a fine and wide venous anastomosis in a large surgical field.

Several other techniques for RIHV reconstruction without direct anastomosis have been reported. Sugawara et al. [6] proposed double IVC techniques, in which the venous orifices of a right lobe graft are anastomosed in a cryopreserved IVC procured from a deceased donor and then the newly created pouch-shaped cava is anastomosed side-to-side to the recipient's native IVC. Although in situ anastomosis is easy in the double IVC technique, the regenerating graft might compress the reservoir-like pouch, causing outflow insufficiency under the long slit-shaped anastomosis. Moreover, there seems to be no evidence of forming a reservoir. Yaprak et al. [12] recently described using a cryopreserved aortic patch for a similar purpose. The non-tubular shape of the aortic patch with its durable properties would be more appropriate; however, the availability of aortic grafts without atherosclerosis might be limited. Furthermore, we cannot exclude the possible transmission of uncommon pathogens when these cryopreserved vascular grafts are used [13]. Hwang et al. [14] recently reported how the funnel-shaped procurement of RIHVs with its accurate anastomosis to the recipient's IVC, under extensive IVC dissection, was the key for directly reconstructing the RIHVs, resulting in a RIHV stenosis rate as low as 2.9 %. Although the stenosis rate in their series is low, the difficulties of in situ anastomosis of the RIHVs in a restricted surgical field make us reluctant to use their techniques. We used EPV and shunt vessels as auto-venous grafts. Shunt vessels that can be used as venous grafts are usually limited to a large paraumbilical vein or large meso-systemic shunts including a dilated ovarian vein or a dilated inferior mesenteric vein [15, 16]. These veins have the properties of a straight shape and a large diameter without branches. Other shunt vessels, including the splenorenal shunt, gastrorenal shunt and gastroparaesophageal shunt are not suitable for venous grafts. EPV usually offers a larger caliber with a thick wall

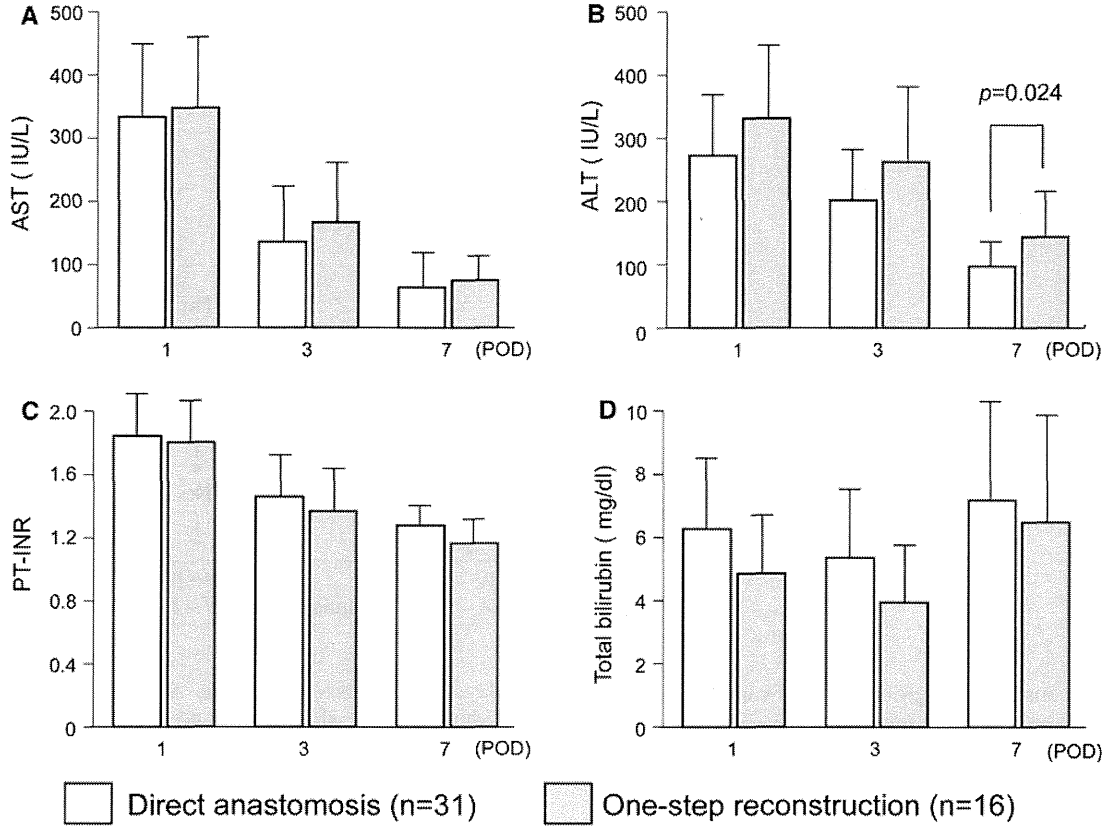

Fig. 2 Chronological changes in the liver function tests in the direct anastomosis group ($n = 31$) versus the one-step reconstruction group ($n = 16$). *ALT* alanine transaminase, *AST* aspartate aminotransferase, *POD* postoperative day, *PT-INR* prothrombin time international normalized ratio

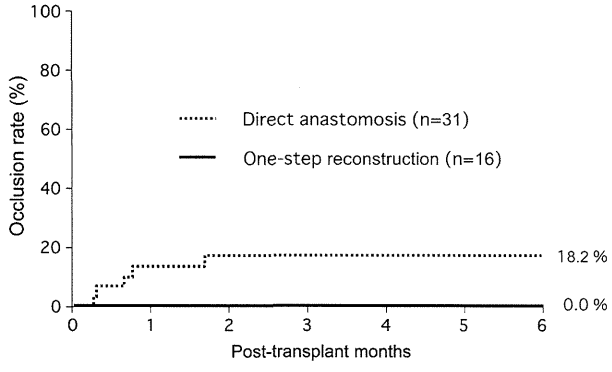

Fig. 3 Patency rate of the reconstructed right inferior hepatic veins (RIHVs) after direct anastomosis ($n = 31$) versus one-step reconstruction ($n = 16$)

and considerable length, making it a venous graft that is easy to handle [7]. However, it is not available in patients with portal vein thrombosis or hilar hepatocellular carcinomas. Recently, we used the IJV exclusively as a venous graft. The IJV has a large caliber of approximately 1 cm and sufficient length of up to 7–9 cm. In the field of liver transplantation, the IJV was first used as a jump portal venous graft in pediatric patients with extrahepatic portal venous obstruction [17]. Because the IJV usually has a healthy venous wall, it is suitable for fine anastomosis. The only technical concern is not to dissect into the cranial side over the mandible, to avoid facial nerve damage [18]. Therefore, we now prefer to use the IJV for reconstructing fine MHV tributaries. The current institutional guidelines for the selection of auto-venous grafts are summarized in Fig. 4. The most common combination is the IJV and EPV. If the EPV is not available, usable shunt vessels are sought and if neither the EPV nor shunt vessels are available, auto-IVC is used for reconstructing RIHVs.

One of the main limitations of this study is that the learning curve is unaccounted for. Knowledge gained not only in surgical techniques but also in post-transplant care could explain the better outcomes in the one-step reconstruction group. In fact, operative blood loss and acute rejection (data not shown) were significantly reduced in the one-step reconstruction group. The other limitation of this study is that no stenting was performed for the occluded vessels, although no occlusion was observed in the

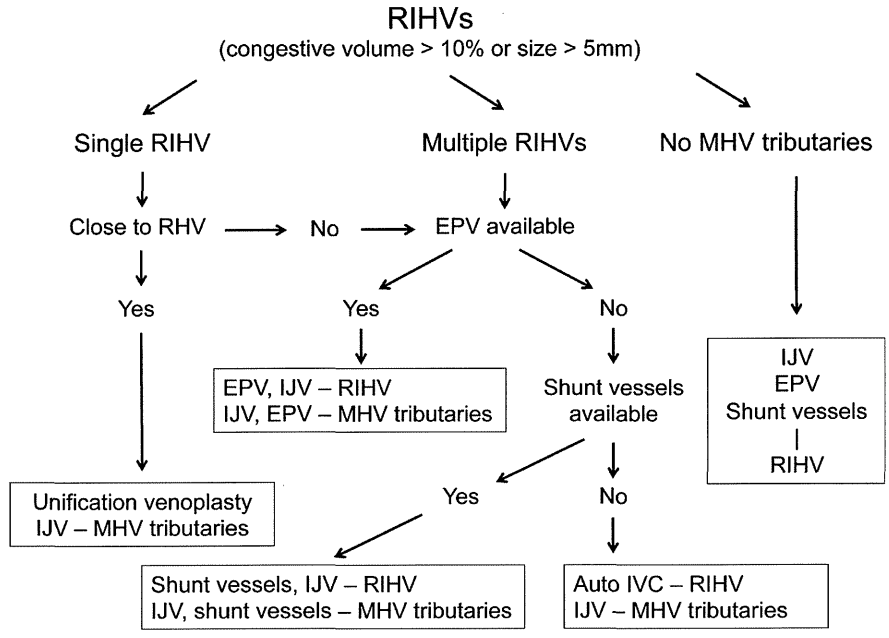

Fig. 4 Current institutional guidelines for reconstructing right inferior hepatic veins (*RIHVs*). *IVC* inferior vena cava, *IJV* internal jugular vein, *MHV* middle hepatic vein, *RHV* right hepatic vein

one-step reconstruction group. As Hwang et al. [14] reported aggressive stenting for reconstructed RIHVs should be performed by an experienced radiologist to optimize graft outflow.

In conclusion, we consider that one-step reconstruction of the accessory hepatic veins, including the RIHVs, using auto-venous grafts, including IJV, EPV or major shunt vessels, is feasible and effective in right lobe LDLT.

Conflict of interest No source of support was received for this work. No financial or other conflict of interest exists with the authors (Ikegami et al.).

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