

Original Article/Transplantation

Middle hepatic vein reconstruction in adult right lobe living donor liver transplantation improves recipient survival

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ARTICLE INFO

Article history:

Received 18 July 2018

Accepted 25 January 2019

Available online 31 January 2019

Keywords:

Living donor liver transplantation

Right lobe graft

MHV reconstruction

Survival

Complications

ABSTRACT

Background: The efficacy and necessity of middle hepatic vein (MHV) reconstruction in adult-to-adult right lobe living donor liver transplantation (LDLT) remain controversial. The present study aimed to evaluate the survival beneficiary of MHV reconstructions in LDLT.

Methods: We compared the clinical outcomes of liver recipients with MHV reconstruction ($n = 101$) and without MHV reconstruction ($n = 43$) who underwent LDLT using right lobe grafts at our institution from January 2006 to May 2017.

Results: The overall survival (OS) rate of recipients with MHV reconstruction was significantly higher than that of those without MHV reconstruction in liver transplantation ($P = 0.022$; 5-yr OS: 76.2% vs 58.1%). The survival of two segments (segments 5 and 8) hepatic vein reconstruction was better than that of the only one segment (segment 5 or segment 8) hepatic vein reconstruction ($P = 0.034$; 5-yr OS: 83.6% vs 67.4%). The survival of using two straight vascular reconstructions was better than that using Y-shaped vascular reconstruction in liver transplantation with two segments hepatic vein reconstruction ($P = 0.020$; 5-yr OS: 100% vs 75.0%). The multivariate analysis demonstrated that MHV tributary reconstructions were an independent beneficiary prognostic factor for OS (hazard ratio=0.519, 95% CI: 0.282–0.954, $P = 0.035$). Biliary complications were significantly increased in recipients with MHV reconstruction (28.7% vs 11.6%, $P = 0.027$).

Conclusions: MHV reconstruction ensured excellent outflow drainage and favored recipient outcome. The MHV tributaries (segments 5 and 8) should be reconstructed as much as possible to enlarge the hepatic vein anastomosis and reduce congestion.

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Introduction

Living donor liver transplantation (LDLT) was first reported in 1994 [1], and it is a very important therapeutic modality to overcome organ shortages for patients with end-stage liver disease (ESLD) [2–4]. Currently, LDLT using the right lobe is an established procedure for adult patients to alleviate the problem of small-for-size grafts [5]. Most transplant centers use right lobe grafts without a middle hepatic vein (MHV) trunk (modified right liver graft) to ensure donor safety [5–7]. Hepatic venous outflow of the right anterior sector (segments 5 and 8) primarily drains into the MHV [6–8]. Therefore, LDLT using modified right liver graft

often causes severe congestion of the right anterior sector [4,9]. Congestion within the anterior segment of a right lobe graft causes serious complications, such as early graft dysfunction and sepsis [4,10–12], which results in mortality. Additionally, hepatic vein obstruction can be compensated by the establishment of collateral circulation after ligation of the major hepatic veins [13,14]. However, the reconstruction of MHV tributaries remains controversial.

In our present study, we retrospectively analyzed 144 right lobe LDLT to evaluate the effects of MHV reconstruction on recipient prognosis and postoperative complications.

Methods

Patients

A total of 144 adult patients underwent LDLT using right liver graft in our institution between January 2006 and May 2017. The

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Fig. 1. **A:** The reconstruction of MHV tributaries from segment 5 (V5) were performed with one straight frozen blood vessels (arrowhead). **B:** The reconstruction of MHV tributaries from segment 5 and 8 to inferior vena cava (IVC) with two straight frozen blood vessels (arrowhead). **C:** The Y-shaped frozen blood vessels (arrowhead) were used as an interposition graft between the recipient's IVC, V5 and V8.

Table 1
Demographic characteristics of adult living donor liver transplantation patients ($n = 144$).

Characteristics	Data
Age (yr)	43.5 (14–67)
BMI (kg/m^2)	22.25 \pm 2.96
Sex (male/female)	119/25
GRWR	1.07% \pm 0.22%
MELD score	21 (6–54)
CTP score	10 (5–14)
Primary disease of adult recipients	
Fulminant hepatic failure	4 (2.8%)
Hepatitis B-related cirrhosis	56 (38.9%)
Biliary cirrhosis	8 (5.6%)
Alcoholic cirrhosis	4 (2.8%)
HBV without cirrhosis and tumor	25 (17.4%)
Graft dysfunction without tumor	1 (0.7%)
HCC	44 (30.6%)
Other	2 (1.4%)

MELD: model for end-stage liver disease; CTP: Child-Turcotte-Pugh; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; GRWR: graft/recipient's body weight ratio.

Table 2
Detail of the reconstruction of the middle hepatic vein (MHV) tributaries ($n = 101$).

Reconstruction	Data
Reconstructed veins	
V5	39 (38.6%)
V8	7 (6.9%)
V5 and V8	55 (54.5%)
Vein shape	
Y-shaped	44 (42.6%)
Straight	57 (56.4%)

Table 3
Demographics and clinical data of reconstruction of the middle hepatic vein (MHV) tributaries.

Variables	MHV reconstruction		P value	Number of hepatic segment reconstruction			The shape of the vein reconstruction in two segments		
	With ($n = 101$)	Without ($n = 43$)		Two ($n = 55$)	One ($n = 46$)	P value	Straight ($n = 19$)	Y-shape ($n = 36$)	P value
Age			0.854			0.094			0.069
≥ 44 yr	72 (71.3%)	30 (69.8%)		12 (21.8%)	17 (37.0%)		1 (5.3%)	11 (30.6%)	
< 44 yr	29 (28.7%)	13 (30.2%)		43 (78.2%)	29 (63.0%)		18 (94.7%)	25 (69.4%)	
Sex			0.481			0.869			0.973
Male	82 (81.2%)	37 (86.0%)		45 (81.8%)	37 (80.4%)		15 (78.9%)	30 (83.3%)	
Female	19 (18.8%)	6 (14.0%)		10 (18.2%)	9 (19.6%)		4 (21.1%)	6 (16.7%)	
MELD			0.796			0.150			0.132
≥ 21	54 (53.5%)	24 (55.8%)		33 (60.0%)	21 (45.7%)		14 (73.7%)	19 (52.8%)	
< 21	47 (46.5%)	19 (44.2%)		22 (40.0%)	25 (54.3%)		5 (26.3%)	17 (47.2%)	
CTP			0.212			0.283			0.190
≥ 10	52 (51.5%)	27 (62.8%)		31 (56.4%)	21 (45.7%)		13 (68.4%)	18 (50.0%)	
< 10	49 (48.5%)	16 (37.2%)		24 (43.6%)	25 (54.3%)		6 (31.6%)	18 (50.0%)	
GRWR			0.578			0.548			0.563
$\geq 1.07\%$	45 (44.6%)	17 (39.5%)		26 (47.3%)	19 (41.3%)		10 (52.6%)	16 (44.4%)	
$< 1.07\%$	56 (55.4%)	26 (60.5%)		29 (52.7%)	27 (58.7%)		9 (47.4%)	20 (55.6%)	

MELD: model for end-stage liver disease; CTP: Child-Turcotte-Pugh; GRWR: graft-to-recipient weight ratio.

MHV was not included in all grafts. The mean follow-up period was 3070 days (range 1–3963), and the last date of follow-up was November 17, 2017. This study was approved by the Ethics Committee of our hospital.

Preoperative evaluation of donor liver

The liver volume of patient was estimated by computed tomography (CT). Donors with right hemiliver volume greater than 70% of the whole liver were rejected as prospective donors. The graft-to-recipient weight ratio (GRWR) was $\geq 0.8\%$ for transplantation. The diameters of the MHV tributaries (segments 5 and 8) were evaluated using CT prior to transplantation.

Intraoperative assessment of hepatic venous congestion

The right hepatic artery was clamped to access the congested area after transection of the liver parenchyma and prior to dissection of the portal vein and hepatic artery. Intraoperative Doppler ultrasonography was performed to evaluate the flow in the veno-occlusive area. Venous reconstruction is recommended in our center when the diameter of V5 (drains segment 5) and V8 (drains segment 8) was greater than 5 mm. The congested area was examined using the clamping test or ultrasonography, and the MHV tributaries should be reconstructed when this area was larger than half of the anterior segment surface. Donor right hemihepatectomy without the main trunk of the MHV was performed. The MHV tributaries and the inferior right hepatic vein (RHV) were isolated and preserved when their diameter > 5 mm. The donor right hemiliver was flushed with University of Wisconsin (UW) solution through the right portal vein.

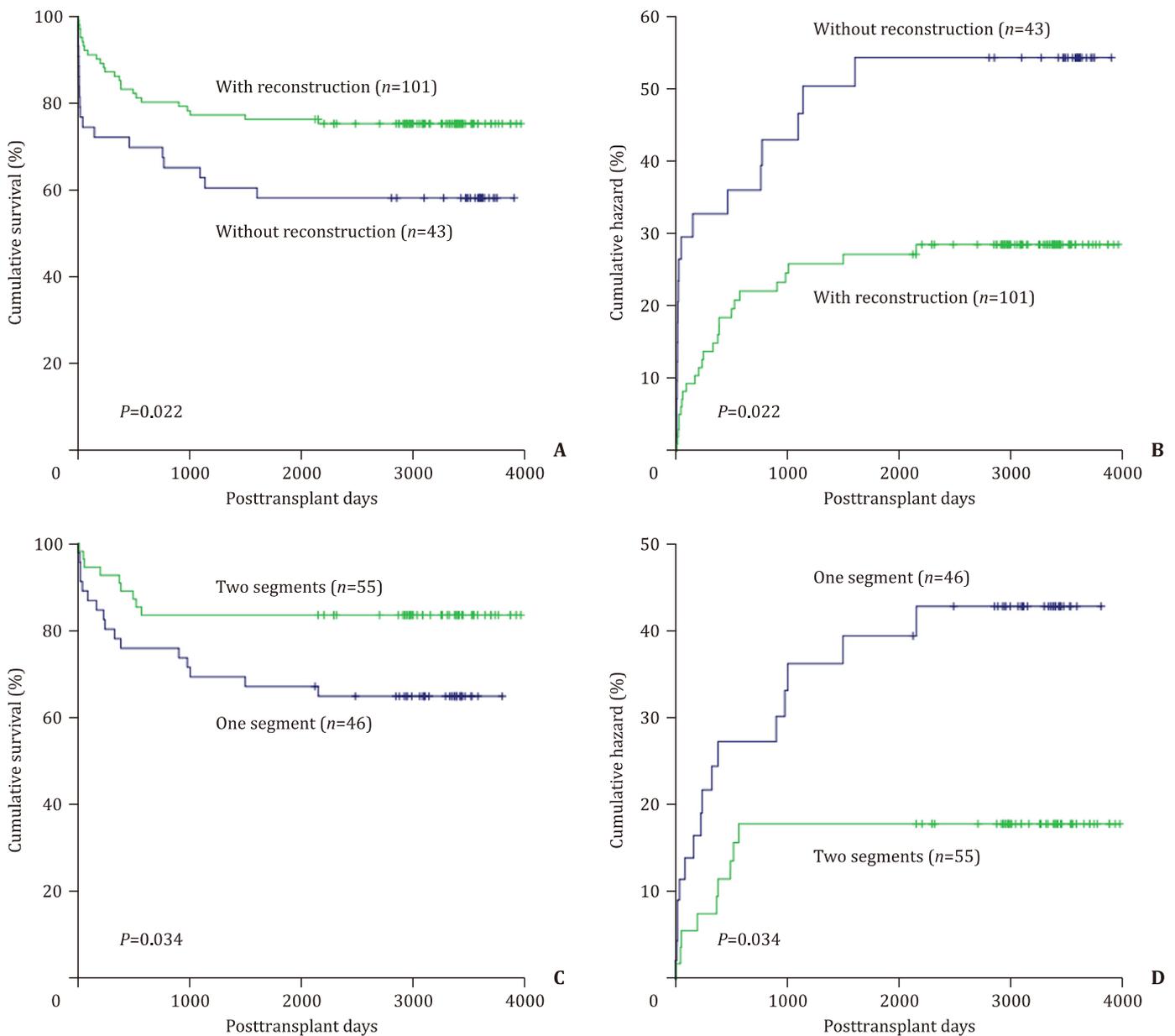


Fig. 2. A and B: Patients with middle hepatic vein reconstruction (green lines) had significantly better survival and lower death risk than those without hepatic vein reconstruction (blue lines); **C and D:** Two segments (segment 5, 8) hepatic vein reconstruction had better survival than the only one segment (segment 5 or segment 8) hepatic vein reconstruction.

main complications of adult LDLT included metabolic complications, bleeding, biliary complications, postoperative infection, rejection, vascular complications and tumor recurrence. Patients with MHV reconstruction had more biliary complications than those without MHV reconstruction (28.7% vs 11.6%, $P=0.027$). The overall survival (OS) rate of candidates with MHV reconstruction was significantly higher than those without MHV reconstruction ($P=0.022$; 5-yr OS: 76.2% vs 58.1%). Furthermore, the overall survival rate of the patients with two segments (segments 5 and 8) hepatic vein reconstruction was higher than that of patients with only one segment (segment 5 or segment 8) hepatic vein reconstruction ($P=0.034$; 5-yr OS: 83.6% vs 67.4%) (Fig. 2). There was no significant difference between the survival of patients using straight vascular bridged and Y-shaped veins ($P=0.142$; 5-yr OS: 82.5% vs 68.2%). However, the survival of patients with two segments hepatic vein reconstruction (segments 5 and 8) using two straight vascular-bridged veins was better than the Y-shaped veins

($P=0.020$; 5-yr OS: 100% vs 75.0%) (Fig. 3). Univariate analyses revealed that HBV, HCC and MHV tributary reconstructions significantly correlated with OS. Multivariate analysis demonstrated that MHV tributary reconstruction was an independent beneficiary prognostic factor of OS (hazard ratio=0.519, 95 CI=0.282–0.954, $P=0.035$) (Table 5).

Discussion

Previously, the left lobe was the major graft used in adult LDLT [16]. However, with the increase in graft-size insufficiency, the small-for-size syndrome becomes one of the common post-transplantation complications, thus the right lobe graft substituted for the left [16]. The necessity of MHV reconstruction in LDLT using a right liver graft remains controversial [17,18]. The MHV tributaries were not reconstructed in previous studies. Lee et al. [19] first reported that several patients without MHV

Table 5
Univariate and multivariate analysis of factors associated with overall survival (n = 60).

Variables	Overall survival			
	Univariate		Multivariate	
	HR (95%CI)	P value	HR (95%CI)	P value
Age (yr, <44/≥44)	1.368 (0.731–2.563)	0.327		
Sex (male/female)	0.869 (0.387–1.953)	0.734		
MELD (<21/≥21)	0.852 (0.468–1.550)	0.600		
CTP scores (<10/≥10)	1.044 (0.573–1.902)	0.887		
GRWR (<1.07%/≥1.07%)	0.732 (0.394–1.359)	0.323		
Liver cirrhosis	0.614 (0.324–1.162)	0.130		
HCC	4.369 (1.056–18.067)	0.039	0.696 (0.375–1.291)	0.250
HBV	0.535 (0.293–0.977)	0.026	3.966 (0.944–16.66)	0.060
MHV reconstruction	0.501 (0.273–0.918)	0.022	0.519 (0.282–0.954)	0.035

Univariate and multivariate analysis: Cox proportional hazards regression model. HR: hazard ratio; MELD: model for end-stage liver disease; CTP: Child-Turcotte-Pugh; GRWR: graft-to-recipient weight ratio.

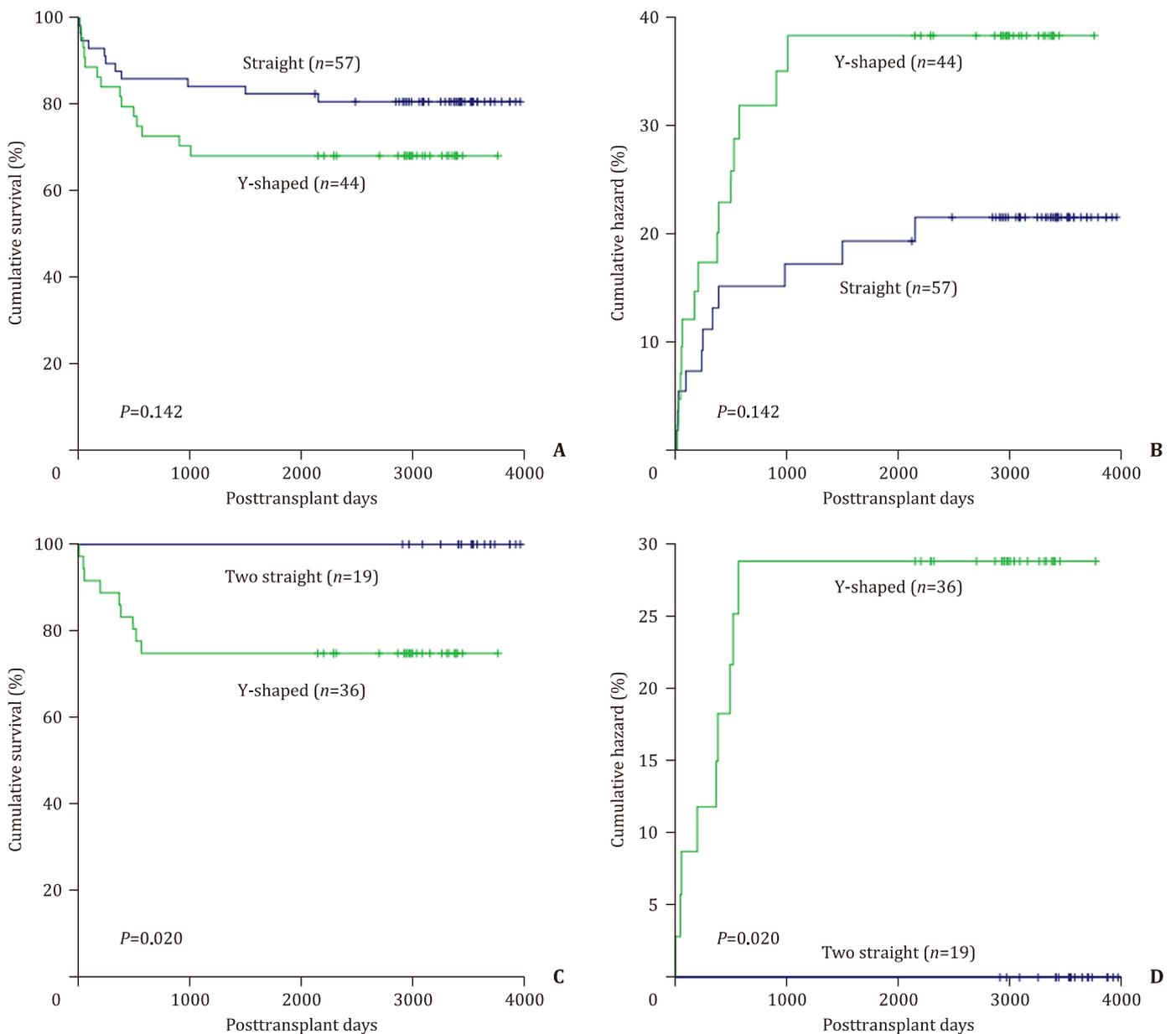


Fig. 3. A and B: The survival between patients using straight vascular bridged and Y-shaped was not statistically different. **C and D:** In the patients with two segments hepatic vein reconstruction (segment 5, 8), the survival of using two straight vascular bridged was better than using Y-shaped (P=0.020).

reconstruction suffered severe congestion of the right anterior sector, which resulted in progressive graft dysfunction and septic complications. Marcos et al. [20] reported that right lobe LDLTs without the MHV had an excellent recipient and graft survival rate (88%). There was no significant difference in the extent of congestion of the anterior segment between the MHV reconstruction and non-MHV reconstruction one month after transplantation [7,21,22]. However, a previous study [23] demonstrated that serious congestion of the right anterior segment in some right lobe grafts may occur after transplantation and may influence graft regeneration and increase graft injury and loss. Kim et al. [9] advocated for the selective reconstruction of MHV tributaries in patients with small-for-size grafts of GRWR <0.8% but not for all grafts. Lee et al. [24] recommended that the reconstruction of MHV drainage from the anterior segment was necessary when the V5 or V8 were larger than 5 mm in diameter during donor hepatectomy.

The present study showed that MHV reconstruction significantly improved the outcomes of adult LDLT patients. Reconstruction of both segment 5 and segment 8 improved recipient survival compared with those with only one segment reconstruction. Some small MHV tributaries (<5 mm in diameter) also required reconstruction. This finding is consistent with Mori et al. [25], Suehiro et al. [26] and Takemura et al. [27]. They revealed that hepatic venoplasty using a patch may enlarge the hepatic vein anastomosis and prevent outflow obstructions after hepatic vein reconstruction. We used Y-shaped or two straight vascular reconstructions of two liver segments during surgery and found that patients with the two straight vascular reconstructions improved survival compared with those with the Y-shaped veins in adult LDLT. This result indicates that the effect of straight veins reconstruction is better than Y-shaped vascular reconstruction on reducing graft congestion. The Y-shaped vein is more liable for thrombus formation and this may explain why straight vascular reconstruction had higher survival than Y-shaped reconstruction.

The survival curve demonstrated that the OS of straight vascular bridged was not significantly different compared with the Y-shaped vein (Fig. 3A). This result may be because that the straight vascular bridged vein was used more often for the reconstruction of one segment (segment 5 or segment 8). The number of segments of hepatic vein reconstruction significantly influenced this result.

Biliary complications were associated significantly with MHV reconstruction. This may be due to the longer time needed for the reconstructive surgery which means relatively longer ischemic time in comparison with non-reconstruction surgery. But the specific mechanism for this phenomenon can be understood hopefully in the nearest future by designing a randomized controlled animal experiment. Other complications were not correlated significantly with MHV reconstruction.

This study has limitations. The number of adult LDLT patients was small; the effect of hepatic vein reconstruction on the survival rate of hepatocellular carcinoma patients in adult LDLT should be studied in more detail.

In conclusion, the present study demonstrated that MHV reconstruction improved the survival of adult LDLT patients. The 5 and 8 segments of the right liver should be reconstructed simultaneously, and two straight vascular-bridged veins were better than Y-shaped veins or one segment vein reconstruction.

Contributors

XX and ZSS proposed the study. GHJ performed the research and wrote the first draft. GHJ, WK, CKC and LZK collected and analyzed the data. All authors contributed to the design and interpretation of the study and to further drafts. ZSS is the guarantor.

Funding

This study was supported by a grant from the National Science and Technology Major Project of China (2017ZX100203205).

Ethical approval

This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhejiang University School of Medicine.

Competing interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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