Research Article

Venous Outflow Complication after Living Donor Liver Transplantation Using Right-Liver Graft without Middle Hepatic Vein

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Received: 18 Apl 2019

Accepted: 18 May 2019

Published: 25 May 2019

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1. Abstract

Hepatic venous outflow complications are major obstacles to success of living donor liver transplantation (LDLT), especially using a right-liver graft without the middle hepatic vein (MHV). The aim of this study wasto clarify hepatic venous outflow complication, the risk factors for hepatic venous stenosis and the role of endovascular intervention in its management in LDLT using a right-liver graft without the MHV. In 504 LDLT, 232 patients underwent LDLT using a right-liver graft without the MHV and reconstruction of MHV tributaries. Hospital mortality was 2.2%. In 51 of 232 patients, 56 stenosis; 8 in the right hepatic vein (3.4%), 43 in reconstructed MHV tributaries (18.5%) and 5 in the right inferior hepatic vein (2.2%) were detected during 14 days after LDLT. Nineteen patients (8.2%) with severe hepatic venous congestion had an immediate endovascular stent-placement resulting in a significant improvement of liver function tests in 17 patients. Univariate analysis showed material for interposed vein graft was the only significant predictor affecting early stenosis of reconstructed MHV tributaries. Late stenosis in interposed vein graft occurred in 30 patients (12.9%) without requiring treatment. The patency rates of reconstructed MHV tributaries at 14, 90 and 180 days were 81.4%, 75.6% and 72.2%, respectively.In conclusion,reconstruction of MHV tributaries in LDLT can be performed with satisfactory patency rates and the hepatic congestion can be effectively treated by endovascular stent-placement, contributing to low hospital mortality.

2. Introduction

Living donor liver transplantation (LDLT) using right-liver has been accepted as a means to overcome the graft shortage in adult patients waiting for liver transplantation, because a right-liver graft provides adequate graft size and avoids small-for-size syndrome [1-6]. However, right-liver LDLT is technically more demanding than left-liver LDLT in view of venous outflow reconstruction. In particular, this procedure requires reconstruction of separate hepatic veins such as the right hepatic vein (RHV), the middle hepatic vein (MHV) and the right inferior hepatic veins (RIHV), resulting in higher incidence of mechanical or functional stenosis of one or all of the hepatic veins as compared to whole-liver transplantation [7-9].

We and others have previously reported that a right-liver graft has a potential risk of severe congestion in the right anterior sector when transplanted without the MHV [8-12]. Although the best solution is under debate, two basic approaches in surgical techniques for maximizing venous outflow have been advocated to date; some centers have performed a right-liver graft including the MHV,[2] while others advocated selective reconstruction of larger segment V and VIII venous tributaries (V5, V8) when using a right liver without the MHV [13-15]. Although inclusion of the MHV facilitates adequate and uniform venous drainage of the right-liver graft, it may jeopardize the donor because of congestion of segment IV in the donor remnant liver [16, 17].

In our center, a right-liver graft without the MHV and with routine reconstruction of V5 and V8 using interposed vein grafts is currently a standard method of right-liver LDLT[13-18]. However, a controversy exists that reconstructing MHV tributaries with interposed vein grafts do not always provide sufficient venous drainage in the anterior sector[19, 20]. Furthermore, the early complications and the long-term patency of the vein grafts remain to be clarified.

The aim of this study was to clarify the venous outflow complications and the risk factors for the hepatic venous stenosis in right-liver LDLT without the MHV, whose tributaries are routinely reconstructed with interposed vein grafts. We also assessed the efficacy of endovascular stent placement in the management of venous outflow complications.

3. Methods

3.1. Patients

The adult LDLT program started at Asan Medical Center in 1997, and the current surgical procedure of right-liver LDLT without the MHV was established in early 1999. Thus the 3 years from January 2002 to December 2004 were chosen as a study period to avoid potential bias relating to any major alterations in surgical procedure, and to provide a sufficiently long follow-up period. During the study period, 504 LDLTs were performed using 367 single-grafts (257 right liver, 109 left liver or left lateral segment and 2 posterior sector) and 137 dual-grafts.[21] Among 257 patients with a single right-liver graft, 232 consecutive patients (90.3%) who underwent reconstruction of MHV tributaries were analyzed in this study. The characteristics of these recipients are summarized in **Table 1**.

3.2. Donor evaluation

Potential donors for right-liver LDLT were evaluated according to the institutional protocol as described previously[22]. The minimal graft volume for an adult recipient was set at greater than 0.8% of an estimated graft-to-recipient weight ratio (GRWR). The potential indication for right-liver graft with the MHV was a GRWR of less than 0.8% with right-liver graft and congestion-free remnant left liver volume of more than 30% of the whole liver volume in donor.[22] According to the criteria with the aid of a dual-graft technique, we performed only 3 cases with right-liver LDLT with the MHV in the study period, and these were excluded from the analysis in this study.

Table 1. The standard venous outflow reconstruction of a right-liver graft without the middle hepatic vein (MHV): the cadaveric iliac vein graft is anastomosed to the veins of segment V (V5) and VIII (V8) and joins the stump of common trunk of the MHV and the left hepatic vein (LHV).

Characteristics	n	Mean ± SD or Percent
Recipient Demographics		
Age (yr)		49.0 ± 6.4
Gender		
Female	49	21.1%
Male	183	78.9%
Body weight (kg)		66.9 ± 10.1
Diagnosis (multiple diagnosis possible)		
Hepatitis B virus cirrhosis	196	84.5%
Hepatocellular carcinoma	55	23.7%
Fulminant liver failure	11	4.7%
Hepatitis C virus cirrhosis	10	4.3%
Alcoholic cirrhosis	9	3.9%
Primary biliary cirrhosis	2	0.9%
Secondary biliary cirrhosis	2	0.9%
Primary sclerosing cholangitis	2	0.9%
Wilson's disease	2	0.9%
Cryptogenic cirrhosis	2	0.9%
Other	4	1.7%
Child's class		
A	25	10.8%
B	63	27.2%
C	144	62.0%
MELD score		
-10	30	12.9%
11-20	94	40.5%
21-30	58	25.0%
31-40	37	15.9%
40-	13	5.6%
Donor Demographics		
Age (yr)		28.5 ± 9.4
Gender		
Female	78	33.6%
Male	154	66.4%
Body weight (kg)		64.6 ± 9.5
Operative Profile		
Cold ischemic time (min)		43 ± 10
Warm ischemic time (min)		38 ± 11
Total ischemic time (min)		85 ± 7
Graft weight (g)		666.1 ± 105.0
Graft-recipient weight ratio (%)		1.01 ± 0.17
Operating time (min)		688 ± 196

3.3. Donor operation

Donor right hepatectomy was performed by a standardized procedure as described previously [22]. In brief, before parenchymal transection, the right liver was mobilized and the sizable RIHV (> 5mm) was preserved with a caval cuff for reconstruction. Parenchymal transection was performed to the right of the MHV using an ultrasonic dissector to expose the MHV without inflow occlusion. During parenchymal division, all major (> 5 mm in diameter) MHV tributaries were preserved and temporarily occluded by Bulldog vascular clump or tied with heavy silk over a short rubber band for future reconstruction. When the recipient team was ready for the liver graft, the right-

Citation: Ogata S, Song GW, Ahn CS, Moon DB, Hwang S, Ha TY,Ku Y and Lee SG, Venous Outflow Complication after Living Donor Liver Transplantation Using Right-Liver Graft without Middle Hepatic Vein. Japanese Journal of Gastroenterology and Hepatology. 2019; 1(3):1-7.

liver graft was procured.

3.4. Back-table operation

We reconstructed all of MHV tributaries and the RIHV greater than 5 mm in diameter. Interposed vein grafts were used to bridge the distance between the recipient's MHV and left hepatic vein (LHV) stump and the venous ends (V5 and V8) at the cut surface of the liver graft.[13,18] The recipient's left portal vein, saphenous vein greater than 5 mm in diameter, dilated Para umbilical vein, or cryopreserved iliac vein or artery was used as a source of interposed vein grafts.[23] When multiple RIHV orifices were present, venoplasty using recipient's saphenous veins, portal vein or hepatic vein were performed to construct a single orifice [24].

3.5. Recipient operation

A total hepatectomy was performed while preserving the inferior vena cava IVC). During anhepatic phase, portal blood was diverted through passive veno-veno bypass (Anthron tube, Toray Industries, Tokyo, Japan) in the absence of collaterality. The RHV orifice was enlarged with an anterior wall incision of the IVC and rectangular patch of the saphenous vein to obtain sufficient venous outflow.[18] Anastomosis of the RHV was performed in an end-to-side fashion with continuous suture. The RIHV was anastomosed to the side wall of the IVC. Portal vein anastomosis was performed with a continuous suture. After reperfusion, the interposed vein graft was anastomosed to the recipient's MHV and LHV stumps or directly to the IVC with a continuous suture (**Figure 1**). Arterial and biliary reconstructions were carried out as described elsewhere in our previous report [13].

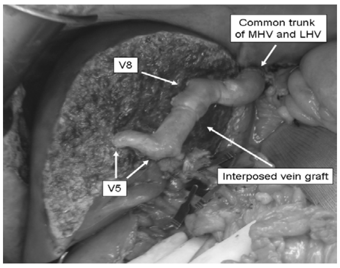

Figure 1: The standard venous outflow reconstruction of a right-liver graft without the middle hepatic vein (MHV): the cadaveric iliac vein graft is anastomosed to the veins of segment V (V5) and VIII (V8) and joins the stump of common trunk of the MHV and the left hepatic vein (LHV).

3.6. Follow-up and management of venous outflow complications

Doppler ultrasonography (Doppler US) and 2-phase CT studies were used for patency follow-up of venous outflow as previously described [25,26]. Venous stenosis was suspected when Doppler US showed a persistent monophasic wave pattern or slow Doppler flow less than 10 cm/second. In either situation, we routinely performed a 2-phase CT study and hepatic venous outflow complications were confirmed when the interposed vein grafts were not opacified and low-attenuation areas were demonstrated in the liver graft. A low-attenuation lesion was defined as an area of less than 1.00 relative Hounsfield units on both noncontrast phase and hepatic arterial phase of the 2-phase CT studies[25]. When serum aspartate aminotranseferase level of more than 500 IU/L were encountered during the first 24 hours after LDLT or routine ultrasonography detected abnormal findings as described above, we immediately carried out a CT study.

Venous outflow stenosis of the RHV, V5, V8 or RIHV was treated using a percutaneous transjugular approach of balloon dilatation and metallic stent placement when their congestion volume was estimated as more than 30% of the graft volume and their GRWR was less than 1.0 [27, 28]. No additional anticoagulant therapy was administrated to the patients with metallic stent. During the first month after LDLT, a CT study was performed weekly. Thereafter, it was performed twice a month and the follow-up interval was widened to 1 or 2 times per year. Of special note, every CT section and 3-dimensional reconstruction image were studied to evaluate the enhancement states and running courses of interposed vessel graft. Vessel size discrepancy or stenosis at the liver cut surface, amount and nature of parenchymal perfusion defect, and their respective interval changes were also precisely determined.

3.7. Statistical Analysis

Statistical analysis was performed using Medcalc® version 7.3 (Frank Schoonjans, Broekstraat, Belgium) software. Fisher's exact test or chi-square test was used for qualitative variables. Wilcoxon's test was used for quantitative variables. Survival curves were estimated by the Kaplan-Meier method and compared with log-rank test. $P < 0.05$ was considered significant.

4. Results

Among 232 patients who underwent LDLT with reconstruction of MHV tributaries, 183 were men and 49 were women, with a median age of 49 years (range, 22-67 years). Details of recipient characteristics are presented in Table 1. Reconstruction of the MHV including V5 only (n=24), V8 only (n=44) or both (n=164) were performed in all 232 patients with autogenous vein (n=168) or cryopreserved iliac vein or artery (n=64) from deceased donors. Median number of reconstructed MHV tributaries was 2 (range: 1-6). Median maximum diameter of MHV tributaries was 7 mm (range: 5-15 mm) (**Table 2**). The RIHV were reconstructed with direct anastomosis to the IVC in 133 patients (57.3%). Venoplasty of the RIHV was performed to unify multiple orifices on the back table in 19 patients (8.2%). Median cold and warm ischemic times were 43 (range, 35-55) and 38 minutes (range, 25-49), respectively, and total ischemic time was 86 minutes (range, 79-89). No abdominal bleeding from the venous anastomosis requiring re-operation for hemostasis was encountered postoperatively. Five recipients (2.2%) died within the same hospital admission for liver transplantation.

Table 2. Univariate Analysis of Potential Predictor for Stenosis of the Reconstructed MHV Tributaries within 14 Days after right-liver LDLT.

Variables	N	Stenosis (%)	P
Recipient age (years)			
< 50	127	28 (22.0)	0.852
≥ 50	105	15 (14.3)	
Donor age (years)			
< 40	196	36 (18.4)	0.819
≥ 40	36	7 (19.4)	
GRWR (%)			
< 0.8	26	4 (15.6)	0.789
≥ 0.8	206	39 (18.9)	
Child's class			
A	25	5 (20.0)	0.794
B or C	207	38 (18.4)	
MELD score			
< 30	173	37 (21.4)	0.158
≥ 30	50	6 (12.0)	
No. of MHV tributaries			
1	55	11 (20.0)	0.754
2	132	26 (19.7)	
3	37	5 (13.5)	
≥ 4	8	1 (12.5)	
Maximum diameter of MHV tributaries (mm)			
5	78	18 (23.1)	0.149
9-Jun	90	18 (20.0)	0.062*
≥ 10	65	7 (10.8)	
Materials for interposed vein graft			
Autogenous veins	168	38 (22.6)	0.008†
Saphenous vein only	110	28 (25.5)	0.026
Portal vein and Saphenous vein	48	7 (14.6)	
Umbilical vein and Saphenous vein	10	3 (30.0)	
Cryopreserved vessels	64	5 (7.8)	
Cryopreserved iliac vein	47	4 (8.5)	
Cryopreserved iliac artery	17	1 (5.9)	

*5-9 vs. ≥ 10 mm in diameter. †autogenous veins vs. cryopreserved vessels. LDLT: living donor liver transplantation, GRWR: graft-recipient-weight ratio, MHV: middle hepatic vein

Early and late stenoses of hepatic vein including the RHV or MHV tributaries or the RIHV were identified by the follow-up Doppler US and confirmed by CT scan in 84 patients (36.2%). In 51 of 232 patients, 56 stenoses, comprising 8 in RHV (3.4%), 43 in MHV tributaries (18.5%) and 5 in RIHV (2.2%) were detected in 51 patients (22.0%) during 14 days after LDLT. Among them, 16 patients with GRWR of less than 1.0 or congestion volume of more than 30% of graft volume immediately underwent endovascular stent placement for the treatment of RHV (n=6), interposed vein graft (n= 11) or RIHV (n=1) stenosis [28,29]. The remaining 32 patients did not undergo immediate hepatic venogram or stent placement because GRWR was more than 1.0 and congestion volume was estimated as less than 30% of graft volume. Among these, 29 patients recovered, while 3 patients eventually underwent stent placements for the treatment of interposed vein graft stenosis due to a subsequent increase of congestion volume. As a result, 75% (6/8) of patients with RHV-stenosis and 33% (14/43) of patients with stenosis in the reconstructed MHV required enlargement of the vein with endovascular stent. Improvement in liver function test results and reduction or disappearance of hepatic low-attenuation areas on follow-up 2-phase CT studies performed within 1 week following stent placements were observed in 17 of 19 patients (89.5%).

In univariate analysis out of 8 variables, only one, material for interposed vein graft, proved to be a significant predictor for stenoses of the reconstructed MHV tributaries during 14 days after LDLT (Table 2). Reconstruction with cryopreserved vessels had a significantly lower incidence of venous stenosis compared with that in autogenous vein grafts (5/64: 7.8% vs. 38/168: 22.6%, P = 0.008). Among autogenous vein grafts, the portal vein showed a trend of better patency rate. Clinical factors such as recipient and donor age, GRWR and model for end-stage liver disease (MELD) score did not affect early venous stenosis.

Late venous outflow complications occurred in 37 patients. RHV stenosis was detected by follow-up 2-phase CT studies in 5 patients. Two patients presented ascites, followed by rising liver function tests. Stent placement was performed at postoperative days 35 and 42. The remaining 3 patients showed complete venous perfusion with a significant increase of diameter in reconstructed MHV or RIHV without any symptoms. Late stenosis of the reconstructed MHV tributaries with interposed vein graft was identified by follow-up 2-phase CT studies without symptom in 30 patients. The patency rates at 14, 90 and 180 days in the interposed vein graft for reconstruction of MHV tributaries were 81.4%, 75.6% and 72.2%, respectively. Although reconstruction of MHV tributaries with cryopreserved vessels demonstrated 92.2% of patency rate within 14 postoperative days, the patency rate was 60.3 % at 1 year, which was profoundly lower than that for autogenous vein grafts (71.7%).

5. Discussion

Right-liver LDLT is an established treatment option for adult patients with end-stage liver disease.[1-6] However, the management of hepatic venous outflow has not yet reached to a consensus. In order to have a maximal functional liver volume without venous congestion, especially to the anterior sector, many transplant centers have recently advocated various approaches such as routine inclusion of the MHV in the graft[2],selective reconstruction of MHV tributaries depending on the results of hepatic artery or hepatic vein occlusion-test[5,14,15]or donor-recipient weight ratio[1]. We have reported the initial experience of five LDLTs conducted without drainage of the right anterior sector in 2001[8].Two of the five recipients showed severe graft congestion and one of them died 20 days after LDLT. Based on these observations, a decision was made to perform routine reconstruction of V5 and V8 with interposed vein grafts irrespective of the intraoperative occlusion-test results to avoid congestion in the right-liver graft without the MHV[13]. This is the largest single-center study focusing on venous outflow complications after LDLT using a right-liver graft without the MHV.

In the present study the interposed vein grafts for reconstruction of MHV tributaries was patent and prevented hepatic congestion in the anterior sector in 81% of the recipients during the first 14 days after LDLT, while severe hepatic congestion was observed in 5.6% of patients. Ito et al reported that the graft congestion was similar between the grafts with and without reconstruction of MHV tributaries using interposed vein grafts after LDLT as measured by the MRI scoring system[20]. The discrepancy could be explained by following reasons. First, only autogenous vein grafts with insufficient diameter or length were used in their study. Second, they evaluated hepatic venous congestion one month after LDLT when venous collaterals to RHV had been most likely developed. Most important, the present study has reconfirmed our previous findings that endovascular stenting resulted in a significant improvement of graft function as assessed by biochemical data and 2-phase CT scan[27,28].These findings strongly indicate the need of reconstruction of MHV tributaries in right-liver LDLT without the MHV.

Our data demonstrated that 14 of 43 patients (33%) with early stenosis of interposed vein graft had life-threatening hepatic dysfunction caused by severe hepatic congestion in the anterior sector. All of the 14 patients received stent-placement in the interposed vein graft and 12 of them recovered[27,28]. They could not be rescued if reconstruction of MHV tributaries had not been performed. The remaining 29 patients, in spite of stenosis of the vein graft, had mild graft congestion and recovered without interventional therapy. Most of these patients prolonged an impairment of liver function, while some recovered uneventfully (data not shown). These results suggest that reconstruction of the MHV was unnecessary in some of these patients. However, it is difficult to predict post-transplant liver function pre or intra-operatively, even if congested volume in the right-liver graft can be estimated[4,14,15,19]. Although it is generally agreed that a Child-Pugh A patients can tolerate a right-liver graft without the MHV well[29], most of the patients in this series had a Child-Pugh B or C. Moreover, it took less than one hour to reconstruct MHV tributaries with interposed vein graft on the back table and the procedure had no harmful effect postoperatively. These findings altogether support our current policy to reconstruct MHV tributaries when technically feasible. Further studies are needed to clarify the exact cutoff value of congestion free graft volume, portal vein pressure and MELD score to determine the need of MHV reconstruction preoperatively.

Univariate analysis demonstrated that autogenous vein graft was the only significant factor contributing to the venous stenosis. It is reasonably assumed that cryopreserved iliac veins or arteries better suit to the reconstruction of MHV tributaries, because they have a greater diameter, enough length for anastomosis to the MHV stump and fewer tributaries requiring suture as compared to autogenous vein graft.[23] However, in the long run, the rate of stenosis in cryopreserved vessels was higher than in autogenous veins 12 months after LDLT. This finding was comparable to previous finding by others using cryopreserved vein grafts for the reconstruction of the portal vein[30,31]. It should also be noted that late stenosis in reconstructed MHV tributaries resulted in neither hepatic congestion nor dysfunction in this study. It is most likely that intrahepatic collaterals to the RHV or the RIHV gradually develop. Thus, we recommend cryopreserved iliac vessels as an appropriate material for reconstruction of MHV tributaries at present.

It has been reported that hepatic venous outflow obstruction ranged from 2 to 16% in adult LDLT[7,26]. The higher rates of venous outflow obstruction in LDLT compared to whole liver transplantation may be attributed to anatomical or technical factors such as a smaller orifice of hepatic vein in the graft, and kinking of graft venous anastomosis due to instability of partial liver[32] or alteration in position during graft regeneration[33]. The high rate (5.6%) of RHV-stenosis in our study contrasts to those of previous studies. There are several possible answers for this. First, our study included both early and late venous complications. Second, there was a frequent lack of diagnosis, in particular, early venous complications in other studies, because clinical manifestations of outflow venous complications such as ascites or abnormal liver function tests are common and nonspecific after LDLT. Third, mild or temporary stenosis within a week after LDLT was counted by a routine CT study in the present series. The majority of these patients with early stenosis in RHV underwent stent placement had a successful recovery.[27]These results indicated that early detection of venous outflow impairment and a prompt stenting are important factors contributing to a low hospital mortality rate. Indeed, we did not reoperate any of patients for early and late venous outflow obstruction in this series.

In conclusion, LDLT with routine reconstruction of MHV tributaries and the RIHV could be performed with satisfactory patency rate of these veins. Although severe hepatic congestion was caused by the venous stenosis during early postoperative period, endovascular stenting were effective in the majority of these patients contributing to a low hospital mortality rate. Therefore, we strongly recommend routine reconstruction of MHV tributaries and the RIHV, to avoid congestion and to improve function in the right-liver graft.

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