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Adult Living Donor Liver Transplantation for Patients With Portal Vein Thrombosis: A Single-center Experience

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Background. Living donor liver transplantation (LDLT) for patients with portal vein thrombosis (PVT) is associated with several technical challenges for its complicated procedures and poor outcomes. Some institutions still consider preexisting PVT as a relatively contraindication for LDLT. **Methods.** Between April 2010 and May 2016, 129 adults underwent LDLT at our institution, and 28 (21.7%) of whom had preexisting PVT. Portal vein thrombosis was diagnosed using preoperative imaging techniques and intraoperative findings. The characteristics and outcomes of the cases were retrospectively evaluated. **Results.** The type of PVT included Yerdel grade 1 in 21 (75.0%) cases, grade 2 in 3 (10.7%) cases, and grade 3 in 4 (14.3%) cases. There were no cases of Yerdel grade 4 PVT. After removing thrombus inside the vessel, we performed simple portal vein anastomosis in 25 (89.3%) cases, patch technique with vascular graft in 1 case (3.6%), and an interposition technique with vascular graft in 2 cases (7.1%). Compared with the non-PVT group, cold ischemic time was longer ($P = 0.012$) and the rate of postoperative PVT was higher ($P = 0.001$) in PVT group. In the comparison between the recipient without and with postoperative PVT, the existence of preoperative PVT was the independent risk factor in the multivariate analysis (hazard ratio, 7.511; 95% confidence interval 1.382-40.820; $P = 0.020$). **Conclusions.** Although it had a technically complicated operation, LDLT could be safely performed in the patients with PVT in our institution.

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Portal vein thrombosis (PVT) is one of the major complications of liver cirrhosis.[1] Preexisting PVT had been previously considered as an absolute contraindication for liver transplantation (LT) due to the difficulty in establishing sufficient portal blood flow to the graft liver after portal vein (PV) anastomosis.[2,3] Yerdel et al[4] reported higher rates of postoperative complications and in-hospital mortality of PVT cases undergoing deceased donor liver transplantation. Kadry et al[5] also reported that 61.7% of transplant institutions consider preexisting PVT in potential recipients as an absolute or relative contraindication for living donor liver transplantation (LDLT). Liver allografts require adequate portal flow to survive and declining of portal patency due to PVT is the major factor to hindering it. Although recent advances in surgical techniques and patient care have made it possible to perform LT even in PVT cases, the presence of PVT in the recipient before operation is frequently considered as a controversial issue for LDLT candidates. In LDLT settings, it is more difficult to obtain appropriate vein grafts than in deceased donor liver transplantation, and it is one of the factors that would be a prevention for PV reconstruction in PVT cases. Preoperative detailed information of PVT and well-planned surgical strategy might be helpful toward overcoming these problems. Here, we introduce our current outcomes of adult LDLT for PVT patients.

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MATERIALS AND METHODS

Patients

From April 2010 to May 2016, LDLTs were performed in 129 adults (≥18 years old) at Kumamoto University Hospital. The patients with preexisting PVT were classified as the PVT group (n = 28) and compared with the non-PVT group (n = 101). Portal vein thrombosis was diagnosed using preoperative imaging techniques and intraoperative findings. As the preoperative imaging tools, dynamic multidetector computed tomography (MD-CT) scan was extensively used in evaluating PVT, and magnetic resonance imaging was also performed in patients with renal dysfunction or a contraindication to the contrast medium used in MD-CT. Portal vein thrombosis was classified into 4 grades according to the Yerdel's grading system[4]: grade 1: PV is minimally or partially thrombosed, less than 50% of the vessel lumen; grade 2: more than 50% occlusion of the PV, including total occlusion; grade 3: complete thrombosis of both the PV and the proximal superior mesenteric vein (SMV); and grade 4: complete thrombosis of the PV as well as the proximal or distal SMV. All the PVT cases were in indication for LDLT unless we could not recognize recipient PV with an adequate thickness. There was only 1 case that we decided as the contraindication for LDLT because of the massive PVT which was filled from distal region of SMV to PV trunk and completely occluded the vessel lumen.

Surgical Procedures

We initially attempted a simple thrombectomy or eversion thromboendovenectomy for all PVT cases after removal of the native liver (Figure 1A). When we confirmed sufficient front flow after the removal of PVT, a simple anastomosis between the recipient PV and graft PV was performed. If the thickness or length of the recipient PV was not sufficient after thrombectomy, the PV wall was enlarged with a venous patch graft or extended by interposition with a vein graft. As the patch graft, a donor ovarian vein or PV harvested from the removed native liver was formed rectangular and placed on the recipient's anterior wall of original PV which was cut longitudinally (Figure 1B-D). The external iliac vein was used to interpose between the recipient's PV and graft PV (Figure 1E, F). Routine anticoagulation therapy was not performed to prevent postoperative bleeding in an early period after surgery. The definition of routine anticoagulation therapy in our institution was the immediate administration of heparin followed by oral intake of warfarin after LDLT. In all cases, daily ultrasound examination was performed to check the blood flow of the graft liver after LDLT. In PVT group, dynamic MD-CT was routinely performed in a month after surgery to detect recurrence of PVT. When we find recurrence of PVT, continuous venous administration of heparin is started, aiming the value of APTT as twice the control. After we can confirm the stable oral intake, heparin administration would be replaced to oral intake of warfarin, aiming 1.5 to 2.0 value of PT-INR.

Statistical Analysis

Starting time for all survival analyses was the date of the LDLT, and death from any cause was treated as a failure in survival analyses. The survival curve for each group was estimated using the Kaplan-Meier method and compared by the

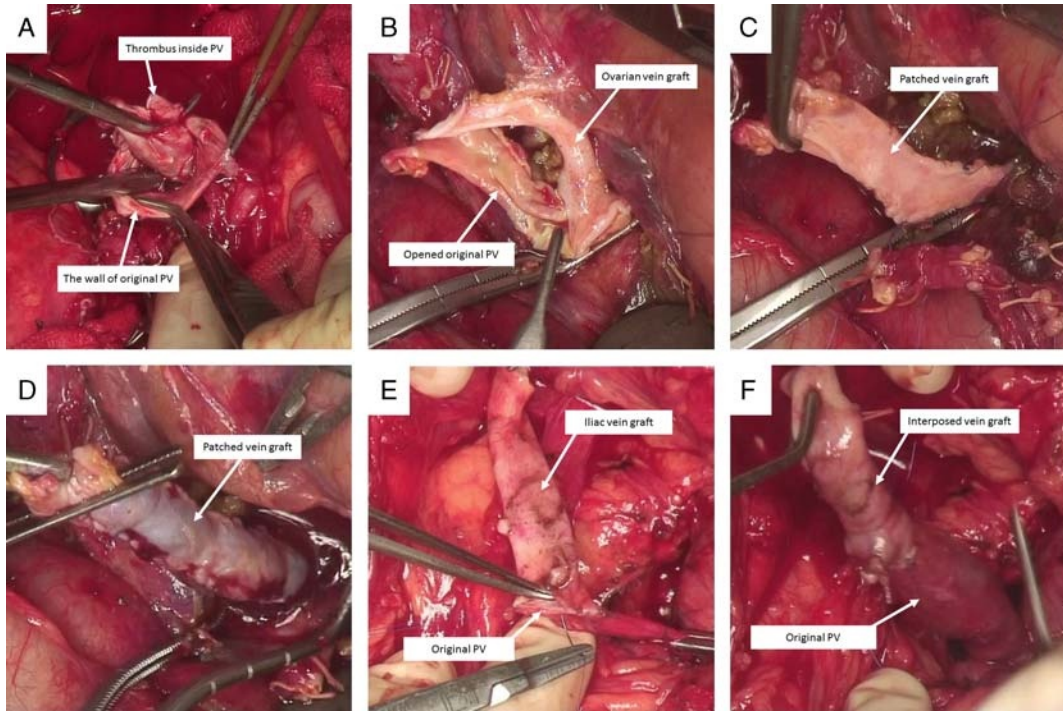

FIGURE 1. Findings in portal reconstruction of recipients with PVT. We initially attempted a simple thrombectomy after removal of the native liver (A). As the patch graft, a donor ovarian vein or PV harvested from the removed native liver was formed rectangular and placed on the recipient's anterior wall of original PV which was cut longitudinally (B and C). After the patch graft reconstruction, it could be confirmed to be thick enough by filling the PV with blood flow (D). The external iliac vein was used to interpose between the recipient's PV and graft PV (E). After the interposition reconstruction, it could be confirmed to be long and thick enough by filling the PV with blood flow (F).

TABLE 1.

Preoperative variables of the recipients

	Non-PVT group (n = 101)	PVT group (n = 28)	*P*
Recipient age	52.2 ± 13.00	52.4 ± 10.84	0.558
Gender (M/F)	41/60	18/10	0.022
BMI (kg/m^2)	24.1 ± 4.64	24.0 ± 4.31	0.970
Primary disease			
FAP	6 (5.9%)	1 (3.6%)	1.000
HBV-LC	7 (6.9%)	2 (7.1%)	0.252
HCV-LC	30 (29.7%)	7 (25.0%)	0.804
FHF	8 (7.9%)	0 (0.0%)	0.200
Alch-LC	11 (10.9%)	1 (3.6%)	0.733
nBnC-LC	16 (15.8%)	2 (7.1%)	0.763
PBC	7 (6.9%)	2 (7.1%)	1.000
PSC	2 (2.0%)	1 (3.6%)	0.523
AIH	1 (1.0%)	1 (3.6%)	0.388
IPH	0 (0.0%)	1 (3.6%)	0.217
BA	3 (3.0%)	1 (3.6%)	1.000
Graft failure	8 (7.9%)	3 (10.7%)	0.703
Poly cystic liver	1 (1.0%)	0 (0.0%)	1.000
Others	1 (1.0%)	0 (0.0%)	1.000
ICU before operation	1 (1.0%)	0 (0.0%)	1.000
MELD score	18.9 ± 7.92	16.8 ± 5.19	0.426
Child-Pugh score	10.2 ± 1.80	10.1 ± 1.96	0.528

AIH, autoimmune hepatitis; Alch-LC, alcoholic cirrhosis; BA, biliary atresia; BMI, body mass index; ICU, intensive care unit; FAP, familial amiloidotic polyneuropathy; FHF, fulminant hepatic failure; HBV-LC, hepatitis B cirrhosis; HCV-LC: hepatitis C cirrhosis; IPH, idiopathic pulmonary hemosiderosis; nBnC-LC: non-B non-C cirrhosis; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis.

log-rank test for nonparametric data. Quantitative data were expressed as the mean ± standard deviation, and qualitative data were expressed as the frequency and rate. All data were analyzed using the Mann-Whitney *U* test, the χ^2 test, log-rank test, and logistic regression analysis. The differences at *P* less than 0.05 were considered to be significant. All statistical analyses were carried out with the SPSS 22 statistical software program (IBM, Japan).

RESULTS

Preoperative Variables of the Recipient

Preoperative variables of the non-PVT and the PVT group are shown in Table 1. In the PVT group, mean recipient age was 52.4 years. Of the 28 patients, 18 were men and 10 were women. The mean body mass index was 24.0 kg/m^2, and none of the patients had been in the intensive care unit before the operation in the PVT group. The mean model for end-stage liver disease (MELD) scores, and Child-Pugh scores of the PVT group were 16.8 and 10.1, respectively. The main disease of the patients was liver cirrhosis from hepatitis C in both groups.

Operative Variables of the Recipient

Operative variables of the non-PVT and the PVT group are shown in Table 2. In the PVT group, donor age was 41.6 years, and 5 cases (17.9%) underwent ABO incompatible transplantation. Graft types included 17 (60.7%) right lobe grafts, 7 (25.0%) left lobe grafts, 1 (3.6%) posterior segment graft, and 3 (10.7%) whole liver grafts (domino transplantation), and the mean graft-to-recipient weight ratio was 0.91% in the PVT group. The mean operative time and blood loss volume of the PVT group were 864.4 minutes and 172.3 mL/kg, respectively. The mean cold ischemic time and warm ischemic time were 172.3 and 50.4 minutes, respectively in the PVT group, with cold ischemic time being significantly longer than in the non-PVT group (*P* = 0.012). The mean hospital stay duration was 59.3 days in the PVT group.

Postoperative Complications of the Recipients

Postoperative complications of the both groups are shown in Table 3. The most frequent complication was CMV infection in non-PVT group (24.8%), and biliary anastomotic stricture in PVT group (28.6%). The rate of postoperative PVT was significantly higher in the PVT group than non-PVT group (25.0% vs 3.0%, *P* = 0.001).

TABLE 2.

Operative variables of the recipients

	Non-PVT group (n = 101)	PVT group (n = 28)	*P*
Donor age	41.5 ± 14.28	41.6 ± 13.07	0.986
ABO compatibility			
identical	60 (59.4%)	15 (53.6%)	0.580
compatible	22 (21.8%)	8 (28.6%)	0.452
incompatible	19 (18.8%)	5 (17.9%)	0.909
Liver graft			
Right lobe	52 (51.5%)	17 (60.7%)	0.386
Left lobe	41 (40.6%)	7 (25.0%)	0.131
Posterior segment	5 (5.0%)	1 (3.6%)	1.000
Whole liver (domino)	3 (3.0%)	3 (10.7%)	0.116
GRWR(%)	0.85 ± 0.21	0.91 ± 0.26	0.217
Operative time (min)	818.8 ± 207.39	864.4 ± 188.78	0.213
Cold ischemic time (min)	129.3 ± 91.85	172.3 ± 99.65	0.012
Warm ischemic time (min)	46.9 ± 8.69	50.4 ± 10.22	0.059
Blood loss per body weight (ml/kg)	166.7 ± 182.15	177.6 ± 150.80	0.239
Duration of hospital stay (day)	74.0 ± 54.78	59.3 ± 20.13	0.943

GRWR, graft-to-recipient weight ratio.

TABLE 3.

Postoperative complications of the recipients

	Non-PVT group (n = 101)	PVT group (n = 28)	*P*
BAS	14 (13.9%)	8 (28.6%)	0.088
Bile leakage	12 (11.9%)	3 (10.7%)	1.000
Cholangitis	8 (7.9%)	2 (7.1%)	1.000
HAT	4 (4.0%)	2 (7.1%)	0.610
HV stenosis	5 (5.0%)	2 (7.1%)	0.645
PV stenosis	3 (3.0%)	0 (0.0%)	1.000
Postoperative PVT	3 (3.0%)	7 (25.0%)	0.001
DVT	3 (3.0%)	3 (10.7%)	0.116
Rejection	19 (18.8%)	2 (7.1%)	0.245
Bacterial infection	21 (20.8%)	4 (14.3%)	0.441
Fungal infection	7 (6.9%)	0 (0.0%)	0.345
CMV infection	25 (24.8%)	7 (25.0%)	0.111
AKI	5 (5.0%)	1 (3.6%)	1.000
Hemorrhage	9 (8.9%)	2 (7.1%)	1.000
Relaparotomy	13 (12.9%)	1 (3.6%)	0.300
Others	14 (13.9%)	2 (7.1%)	0.520

BAS, biliary anastomotic stricture; HAT, hepatic artery thrombosis; DVT, deep vein thrombosis; CMV, cytomegalovirus; AKI, acute kidney injury.

Comparison Between the Recipients With and Without Postoperative PVT

Comparison between the recipients with and without postoperative PVT is shown in Table 4. The multivariate analysis of 5 items (existence of preoperative PVT, male, right lobe graft, lower MELD and Child-Pugh score, and longer operative time) that showed significant differences in univariate analysis revealed the preoperative PVT was the independent risk factor in the multivariate analysis (hazard ratio, 7.511; 95% confidence interval, 1.382-40.820; $P = 0.020$).

Grade of PVT and Procedure in the PVT Group

Portal vein thrombosis grades according to Yerdel's classification were: 21 cases (21.7%) of grade 1, 3 cases (10.7%) of grade 2, and 4 cases (14.3%) of grade 3. There were no grade 4 PVT cases. Portal vein reconstructions were conducted with: thrombus removal and normal anastomosis in 25 cases (89.3%), patch graft with vein graft in 1 case (3.6%), and interposition with vein graft in 2 cases (7.1%) (Table 5).

Patient and Graft Survival After LDLT in the Non-PVT and PVT Groups

The overall 1-, 3-, and 5-year patient survival rates were 96.4%, 96.4%, and 96.4% in the PVT group, and 85.1%, 82.2%, 82.2% in the non-PVT group. Patient survival did not differ significantly between the 2 groups (Figure 2A). The overall 1-, 3-, and 5-year graft survival rates were 97.0%, 97.0%, 96.0% in the non-PVT group. No cases in the PVT group required retransplantation for graft failure in 5 years after surgery. Four patients in the non-PVT group undertook retransplantation because of the graft failure but graft survival did not differ significantly between the 2 groups (Figure 2B).

TABLE 5.

Grade of PVT and procedure in the PVT group

		Procedure		
PVT grade	n	Thrombus removal	Patch graft	Interposition
Yerdel 1	21 (21.7%)	19 (76.0%)	1 (100.0%)	1 (50.0%)
Yerdel 2	3 (10.7%)	3 (12.0%)	0 (0.0%)	1 (50.0%)
Yerdel 3	4 (14.3)	3 (12.0%)	0 (0.0%)	0 (0.0%)
Yerdel 4	0 (0.0%)	—	—	—
Total	28 (100%)	25 (89.3%)	1 (3.6%)	2 (7.1%)

DISCUSSION

Some groups have reported favorable outcomes for LT in patients with PVT and have introduced effective strategies for their management, especially to ensure sufficient PV flow to the graft liver, such as the techniques of thrombectomy, jumping grafts, renoportal anastomosis, portocaval hemitransposition, and PV arterialization.[6-10] Based on these results and the development of the managements for patient, PVT may no longer be a contraindication for liver transplantation. In the LDLT settings, there are additional challenges in acquiring appropriate vein grafts, obtaining adequate portal flow, and releasing portal hypertension. Even in this situation, only a few transplantation surgeons have reported a systematic strategy and LDLT outcomes for patients with PVT.[1,6,11,12] The Kyoto group attempted to expand the indications for LDLT in patients with PVT, followed by individual reconstruction of PVs according to the extent of the thrombosis, hemodynamic modifications, and diligent postsurgical follow-up.[6] In our study, there were not significant differences in patient and graft survival between the 2 groups. These good outcomes might be owing to the correct decision of LDLT indication that was comprehensively judged from the general condition and the grade of PVT. However, we should also understand the inherent selection bias with the PVT group being a sufficient risk to undergo liver transplantation because this is a nonrandomized trial.

TABLE 4.

Comparison between the recipients with and without postoperative PVT

	Univariate analysis			Multivariate analysis		
	Without postoperative PVT (n = 119)	With postoperative PVT (n = 10)	*P*	HR	95% CI	*P* (multivariate logistic regression)
Preoperative PVT	21 (17.6%)	7 (70.0%)	0.001	7.511	1.382-40.820	0.020
Sex (M/F)	50/69	9/1	0.005	3.948	0.264-58.926	0.319
Right lobe graft	60 (50.4%)	9 (90.0%)	0.020	7.681	0.438-134.604	0.163
MELD score	18.9 ± 7.51	12.7 ± 3.37	0.002	0.753	0.574-0.988	0.041
Child-Pugh score	10.2 ± 1.82	9.2 ± 1.72	0.033	1.109	0.680-1.811	0.679
Operative time (min)	820.3 ± 207.92	929.1 ± 115.70	0.013	1.003	1.000-1.007	0.053

HR, hazard ratio; CI, confidence interval.

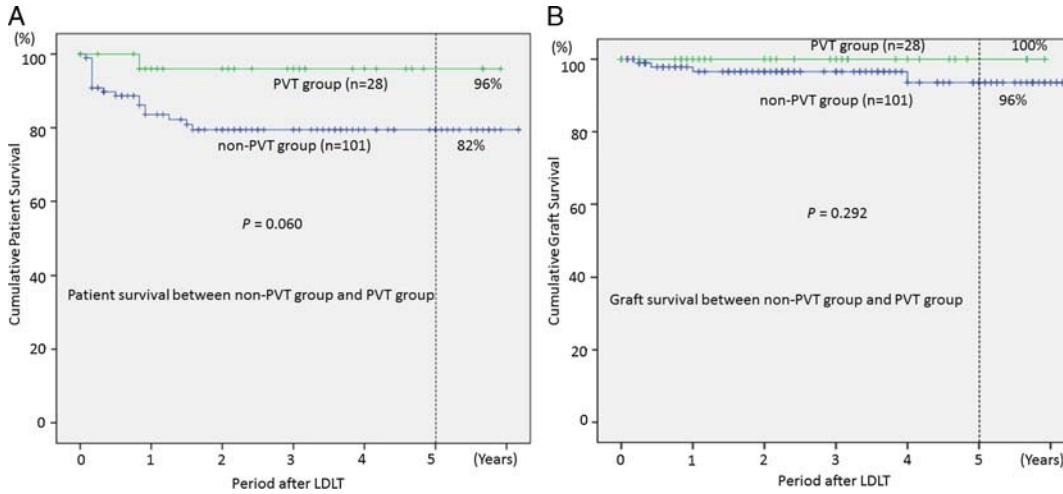

FIGURE 2. Kaplan-Meier survival curve showing differences between the non-PVT group and the PVT group (A). Overall 1-, 3-, and 5-year patient survival rates were 96.4%, 96.4%, and 96.4% in the PVT group, and 85.1%, 82.2%, 82.2% in the non-PVT group. Patient survival did not differ significantly between the 2 groups ($P = 0.060$). Kaplan-Meier graft survival curve showing differences between the non-PVT group and the PVT group (B). Overall 1-, 3-, and 5-year graft survival rates were 100.0%, 100.0%, and 100.0% in the PVT group, and 97.0%, 97.0%, 96.0% in the non-PVT group. Graft survival did not differ significantly between the 2 groups ($P = 0.292$).

Precise PVT evaluations by imaging before LT were necessary to design strategies for successful PV reconstruction. Dynamic MD-CT was most useful for diagnosing PVT and its range of spread. Patients with renal dysfunction or contraindications to the contrast medium should underwent magnetic resonance imaging to evaluate PVT. Mural thin PVTs that were not detected by imaging were sometimes found in PV stumps during the operation. Moon et al[13] reported the efficacy of intraoperative cine-portograms to evaluate remnant PVT and portosystemic collaterals after thrombectomy. The ligation of portosystemic collaterals is also an important procedure to increase the PV flow. In our cases, although most PVTs could be detected by these imaging tools before the operation and removed in surgery, we found certain rates of PVT recurrence in the early period after LDLT. Recurrent thrombus could be successfully treated with anticoagulation therapy alone in all cases. Further strategies for complete PVT removal should be considered because we could not confirm whether the PVT after LDLT was a remnant or de novo thrombus. However, it might have been one of the cause of PVT recurrence that the intraluminal wall of recipient's PV was not smooth even after the total removal of PVT, and it is necessary to consider how to evaluate these properties of endothelium.

Grade 1 or 2 PVT limited to the PV trunk, which either completely or incompletely obstructed the PV, was usually removed as previously reported.[6] Use of the original PV during reconstruction should be attempted as a first choice, unless remnant thrombosis, PV stenosis, or insufficient front blood flow is present. Fortunately, we could confirm sufficient front flow after thrombectomy in almost all cases, but detected PV stenosis in 1 case and shortness of the recipient PV in 2 cases, which required patch graft or interposition technique. Because it is one of the most important procedures to make a large PV anastomosis in obtaining the sufficient PV flow, these kinds of PV plastic techniques are essential for transplant surgeon when they perform LDLT in PVT cases.

Despite of the sufficient thrombus removal, preoperative PVT cases proved to be the risk factor for postoperative PVT onset in our study, so intensive follow-up and timely treatment of complications are necessary when the PV is plastically reconstructed in PVT cases. We performed Doppler ultrasonography twice a day for 1 week after LT and dynamic MD-CT was performed within a month after LDLT in all PVT cases. The late diagnosis of rethrombosis might result in PV stenosis and require treatment with balloon dilatations followed by stent placement. Although these treatments for posttransplant complications are necessary to save both liver grafts and patient lives, early diagnosis would help us to avoid these invasive treatments after transplantation. All of our rethrombosis cases were immediately diagnosed and could be successfully treated with anticoagulation therapy alone.

In conclusion, LDLTs for the recipient with preexisting PVT were safely performed in our institution. It looks like that PVT is no longer an absolute contraindication for LDLT, but transplant surgeons must design precise technical and surgical strategies based on the extent of the PVT to acquire sufficient portal flow to the liver graft. To avoid graft failure from the PV complications after LDLT in PVT cases, intensive follow-up and timely treatment especially for rethrombosis is necessary.

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