Clinical Transplantation

Risk factors for intraoperative portal vein thrombosis in pediatric living donor liver transplantation

Abstract: Pathologic changes of the recipient native portal venous system may cause thrombosis of the portal vein, especially in pediatric living donor liver transplantation (LDLT). This study assessed the utility of Doppler ultrasound (US) for the detection of intraoperative portal vein occlusion and identification of predisposing risk factors in the recipients. Seventy-three pediatric recipients who underwent LDLT at Chang Gung Memorial Hospital, Taiwan, from 1994 to 2002 were included. Preoperative and intraoperative Doppler US evaluation of the portal vein was performed. Age, body weight, native liver disease, type of graft, graft recipient weight ratio (GRWR), type of portal anastomosis, portal velocity, portal venous size and presence of portosystemic shunt were analyzed for statistical significance of predisposing risk factors. Eight episodes of intraoperative portal vein thrombosis, with typical findings of absent Doppler flow in portal vein and prominent hepatic artery with a resistant index lower than 0.5 ($p < 0.001$), were detected during transplantation, which was then corrected by thrombectomy and re-anastomosis. Children age ≤ 1 yr ($p = 0.025$), weight ≤ 10 kg ($p = 0.024$), low portal flow ≤ 7 cm/s ($p = 0.021$), portal venous size ≤ 4 mm ($p = 0.001$), and GRWR > 3 ($p < 0.017$) were all risk factors for intraoperative portal vein thrombosis. Doppler US is essential in the preoperative evaluation, early detection and monitoring of outcome of the portal vein in liver transplant.

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Liver transplantation has become an important treatment option in the management of end-stage liver disease (1). The combination of recent improvements in operative technique, immuno-suppression therapy, and organ utilization has contributed to better post-transplant outcomes (2). However, vascular complications are still significant causes of graft failure in liver transplantation, especially in pediatric cases. The incidence of portal vein thrombosis is not uncommon in pediatric transplant recipients ranging from 4 to 16% (3, 4). Children with pathological portal veins, most commonly seen in biliary atresia, remain a challenge to the surgeon although various technical skills has been employed for portal vein reconstruction to attain optimal flow (5, 6). Graft loss of up to 70% has been reported (7). In our experience, portal vein thrombosis occur early right after portal vein anastomosis during transplantation. The goal of this study was to identify characteristic Doppler pattern and the risk factors of perioperative portal vein thrombosis in children undergoing living donor liver transplantation (LDLT).

Methods and materials

Seventy-three pediatric patients underwent living LDLT in our center from 1994 to 2002, among whom one re-transplanted patient was excluded.

All grafts were harvested from healthy adult living donors who expressed a fully informed voluntary offer. The donors were 76 parents (19 fathers and 47 mothers), four grandparents (three grandmothers and one grandfather), and one aunt. The required volume for liver resection of the donors, which was 1–3% of the recipient's body weight, was calculated on preoperative computed tomography. Range of resection for donation was selected from among left lateral segment, extended lateral segment with a part of the medial segment, left lobe with middle hepatic vein.

Preoperative study of the vascular system were Doppler ultrasound (US) for portal vein to record flow direction, caliber size and velocity, and angiography, magnetic resonance venography or computer tomography angiography to document the presence of collateral circulation and portosystemic shunt.

Intraoperative Doppler US studies of the hepatic veins, portal vein and hepatic artery was performed sequentially after reperfusion of the portal vein and hepatic artery and immediately after abdominal closure. Re-examination was also performed after re-reconstructive management during operation. An Acuson 128 scanner (Acuson, Mountain View, CA, USA) with 7.0 or 4.0 MHz scanner in the imaging and Doppler mode was used in all recipients to measure the angle with corrected flow velocity and the cross-sectional area of the horizontal portion of the left portal vein. Operations for the donors and recipients were performed according to the principles we reported earlier (8). Two methods of portal vein reconstruction, branch patch and vein graft interposition were employed.

Analysis of risk factors for intraoperative portal vein thrombosis

Patients with and without intraoperative portal vein thrombosis were compared using the nine1 clinico-pathological variables related to potential risk of occlusion, including six host-related factors: age, body weight, native liver disease, type of the graft, GRWR and type of portal anastomosis. Anatomical factors documented on imaging studies included for analysis were flow rate and caliber of the pre-transplant native portal vein, and presence of portosystemic shunt (> 5 mm).

Results

There were 36 males and 37 females patients with age of 2.98 ± 3.08 yr (mean ± SD range, 0.5–17)

and body weight of 12.44 ± 7.88 kg (mean ± SD range, 1–63). Pre-transplant diseases included biliary atresia (60 cases), glycogen storage disease (five cases), Wilson's disease (one case), Alagille syndrome (one case) and neonatal hepatitis (six cases). The 1-yr actuarial survival rate after LDLT of the 73 cases was 97.26%.

Condition of the native portal vein at preoperative survey

Portal vein blood flow was hepatopedal in 62 cases and hepatofugal in eight cases. Absent portal flow was noted in three cases. The caliber of the portal vein was 5.49 ± 2.12 mm (mean ± SD range, 0–16), and the velocity of the portal flow was 7.64 ± 6.38 cm/s (mean ± SD range, −12–19). Twenty-nine cases had prominent portal-systemic shunt (> 5 mm).

Type of grafts and operation

The grafts transplanted included 40 left lateral segments, 27 extended left lateral segments, four left lobe with middle hepatic vein and two right liver lobes. The GRWR was 2.64 ± 0.93 (mean ± SD range, 1.27–5.12) for maintenance of adequate graft weight. Seventy-two cases had patch anastomosis for portal vein reconstruction, and one patient had ovarian vein graft due to total occlusion of the native portal vein before surgery.

Complications after portal vein reconstruction

The portal vein velocity was 24.46 ± 9.68 with range of 12–51 cm/s in non-complicated cases. Portal vein occlusion was noted in eight cases right after re-perfusion. Absent portal blood flow (velocity = 0), readily detectable strong pulsative hepatic artery, and increased velocity at the end diastolic phase were observed in all cases on intraoperative Doppler US. Marked decrease of resistance index below 0.5 (0.46 ± 0.02 with range of 0.45–0.49) was noted in all eight cases with portal vein thrombosis. All these values subjected to statistical evaluation showed significant differences between the group with intraoperative portal vein thrombosis (0.46 ± 0.02 with range of 0.45–0.49) and the uncomplicated group (0.78 ± 0.09 with range of 0.60–0.92) (p < 0.001).

All eight cases with intraoperative portal vein thrombosis had blood clot at both side of the anastomosis on subsequent re-operation for thrombectomy and reanastomosis of the portal vein. Closure of splenorenal shunt (n = 2) and prominent coronary vein (n = 4) was also per-

formed in six cases. No recurrent portal vein thrombosis was noted after liver transplantation among these eight cases.

One case had late portal vein occlusion at 6 months after transplantation due to intestinal perforation with repeated peritonitis. No other related risk factor was found in this patient. Among the eight cases with pre-transplant hepatofugal flow, intraoperative portal vein thrombosis was found in two patients. Among the three cases with preoperative absent portal flow, interposition graft with the ovarian vein was used in one patient, while patent portal vein was noted in the explanted native liver of the other two patients.

The size and velocity of the native portal vein, the clinical characteristics of the recipient's age, body weight, type of graft, native liver disease, and the graft weight and anastomotic method used, were subjected to statistical analysis to evaluate the risk factors for intraoperative portal vein occlusion. Age equal or younger than 1 yr (p = 0.025), body weight ≤10 kg (p = 0.024), portal flow ≤7 cm/s (p = 0.021), portal vein caliber ≤4 mm (p = 0.001), and graft recipient weight ratio (GRWR) > 3 (p < 0.017) were found to be associated with higher risk for intraoperative portal vein occlusion (Tables 1 and 2).

Discussion

Technically satisfactory vascular anastomosis to allow adequate blood supply to the graft is essential for successful liver transplantation and long-term graft survival. Direct visualization of congestive liver with decreased blood pressure or palpation of a pulsatile vessel is suggestive of intraoperative hepatic vein or hepatic artery occlusion, respectively, but intraoperative portal vein thrombosis is clinically silent (9, 10). Our study demonstrate the critical role of intraoperative Doppler US in early detection of intraoperative portal vein thrombosis that allow early intervention to avoid prolonged warm ischemia time leading to suboptimal liver graft or even primary non-functioning graft.

Advance surgical techniques such as direct venous graft, jump graft, or even hemiportcaval anastomosis has been developed to manage occlusive portal vein anomalies but high morbidity and mortality rate is still noted due to the complexities of the procedures (11, 12). Thus attempts to identify risk factors for intraoperative portal vein thrombosis is imperative to provide better preoperative planning or intraoperative management to secure optimal graft survival.

Table 1. Host-factors related to intraoperative portal vein occlusion

	No. of cases	Mean ± SD	Intraoperative portal vein thrombosis (n)	No intraoperative portal vein thrombosis (n)	p-values Fisher's exact test
Age (yr)					
≤ 1	19	0.79 ± 0.18	5	14	0.025
>1	54	3.7 ± 3.09	3	51	
Body weight (kg)					
≤ 10	35	7.95 ± 1.42	7	28	0.024
>10	38	16.57 ± 9.16	1	371	
Native liver disease					NS
Biliary atresia	60		6	54	
Glycogen storage disease	5		0	5	
Wilson disease	1		0	1	
Alagille syndrome	1		0	1	
Neonatal hepatitis	6		2	4	
Type of graft					NS
LLS	40		7	33	
ELLS	27		1	28	
LL	4		0	4	
RL	2		0	4	
GRWR					
≤ 3	48	2.07 ± .49	2	496	
>3	25	3.72 ± 0.55	6	19	0.017
Type of anastomosis					NS
Branch patch	72		8	64	
Venous graft	1		0	1	

LLS, left lateral segment; ELLS, extended left lateral segment; LL, left lobe; RL, right lobe; GRWR, graft recipient weight ratio.

Table 2. Anatomical factors related to intraoperative portal vein thrombosis

	No. of cases	Mean ± SD	Intraoperative portal vein thrombosis (n)	No intraoperative portal vein thrombosis (n)	p-Values (Fisher's exact test)
Velocity of portal vein (cm/s)					
≤ 7	21	1.03 ± 6.27	6	20	0.021
>7	52	11.34 ± 2.13	2	45	
Size of portal vein (mm)					
≤ 4	16	3.35 ± 0.13	6	10	0.001
>4	57	6.09 ± 0.19	2	55	
Portosystemic shunt (mm)					NS
Shunt > 5	29		5	24	
No shunt	43		3	40	

Well-documented risk factors for portal vein thrombosis included small, hypoplastic or sclerotic portal veins, usually associated with extremely young age or low recipient body weight, commonly seen in biliary atresia with other coexisting vascular anomalies (13, 14). The significant predictive factors in our series including age younger than 1 yr, body weight lower than 10 kg, portal vein caliber smaller than 4 mm, were comparable with these documented risk factors.

Low portal flow, implying reduced flow volume due to collaterals and shunting vessels as severity of liver cirrhosis progress, would promote portal vein thrombosis (15). We proposed that portal venous velocity below 7 cm/s at pre-transplant evaluation to be predictive of intraoperative portal vein thrombosis as evident in our series.

Small-for-size graft (< 1% of recipient body weight) has been documented to have lower graft survival rate, as shown in rat model of irreversible endothelial injury during the transient changes after reperfusion (16, 17). Creation of portosystemic shunt for portal flow diversion would avoid venous congestion and over-perfusion (18). However, in our series, due to low probability of the availability of other suitable donors, relatively big and heavy grafts had been used. The exerted mass effects on the vascular structure may have increased the risk of vascular complication such as intraoperative portal venous thrombosis.

There was no statistically significant difference between the surgical techniques used for portal vein anastomosis in our series. The eight cases with intraoperative portal vein thrombosis had sustainable adequate portal flow after transplant without recurrent portal vein thrombosis using the same re-anastomosis method of branch patch anastomosis.

The presence of portosystemic shunt was not associated with intraoperative portal vein thrombosis in our series. However, early closure of the shunts would result in increased portal vein flow that might influence the transient hemodynamic changes of the portal venous system at the reperfusion period. In addition to the surgical closure of the shunt, repositioning of the liver graft in a proper site, and eliminating factors that increase resistance of the graft or portal vein such as hepatic venous outflow obstruction, kinking or stretching of the portal vein allowed adequate blood flow to the graft. Doppler US provided accurate guidance when monitoring portal flow and inflow to the graft during these manipulations.

Our study showed that Doppler US for pre-operation evaluation, intraoperative monitoring of the portal flow for early detection of portal vein thrombosis, follow-up evaluation after re-anastomosis was indispensable. We have also established significant predictive factors based on the large group of liver allograft recipients studied. We advocated the identification of high-risk group at pre-transplantation evaluation so that interpositional vein grafts could be considered for patients with the pathological portal vein. Doppler US-guided proper positioning of the portal vein, which takes only a few minutes during the process of artery anastomosis should become a regular practice in high-risk cases.

It is concluded that preoperative identification of high-risk patients for intraoperative portal vein thrombosis would decrease the need for intraoperative re-anastomosis and further maintain long-term graft survival.

Acknowledgements

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