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ORIGINAL ARTICLE

Indirect Doppler ultrasound abnormalities of significant portal vein stenosis after liver transplantation

Jieun Byun[1] · Kyoung Won Kim[1] · Sang Hyun Choi[1] · Sunyoung Lee[1] · Jeongjin Lee[2] · Gi Won Song[3] · Sung Gyu Lee[3]

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Abstract

Purpose To determine indirect Doppler ultrasound (DUS) abnormalities associated with significant portal vein (PV) stenosis (PVS) in recipients of liver transplantation (LT).

Methods This retrospective study was approved by our institutional review board. Between February 2006 and May 2017, 41 LT recipients were diagnosed with significant PVS, defined as having more than 50% narrowing of PV diameter for any reason, including thrombosis or flow disturbance associated with prominent collateral vessels on portal venography. We reviewed the DUS findings of hepatic arteries (HAs) as well as PVs of them, before and after treatment of PVS, and in comparison, with a one-to-one case-matched control. Inter-group comparison of frequency in DUS abnormalities was performed using Chi square (χ^2) with Fisher's exact test and McNemar's test. Diagnostic values of each abnormal DUS finding and combinations were also evaluated.

Results DUS of significant PVS showed "no demonstrable color flow," either at recipient PVs or anastomoses (26.7%), and showed turbulence (66.7%) and hepatofugal portal flow (HFPF; 20.0%) at the graft PVs. HFPF was more frequently observed in those with "no demonstrable color flow" at recipient PVs or anastomoses ($p = 0.006$). DUS of graft HAs revealed tardus–parvus waveforms (20.9%) and prolonged systolic acceleration times (16.3%), more commonly in the "no demonstrable color flow" group ($p = 0.012$). These indirect DUS abnormalities disappeared and resolved on follow-up DUS after treatment. In the control group, such Doppler abnormalities were less frequently shown than in the PVS group ($p \leq 0.01$, respectively). When one of the portal-blood flow velocity (PFV)-related index abnormalities (such as increased time average velocity [TAV] at anastomosis and TAV ratio between recipient PV and anastomosis) or "no demonstrable color flow" were shown in DUS as well as one of the indirect DUS abnormalities, sensitivity, and specificity was 71.11 and 97.78%, respectively.

Conclusion In addition to PFV-related abnormalities, DUS occasionally shows "no demonstrable color flow" either at recipient PVs or anastomoses, and indirect Doppler abnormalities such as turbulence, HFPF at graft PVs, and abnormal waveforms at graft HAs in LT recipients with significant PVS. The combination of PFV-related abnormalities and indirect DUS abnormalities would be helpful for diagnosis of PVS.

Keywords Portal vein stenosis · Doppler ultrasonography · Liver transplantation

Introduction

Liver transplantation (LT) is generally accepted as an effective curative treatment for patients with end-stage hepatic disease, with better post-transplantation outcomes associated with improvements in surgical techniques and organ utilization [1, 2].

Despite advances, however, vascular complications remain a major cause of graft dysfunction–morbidity and failure, and mortality, following LT [2, 3]. Although extensive research has been conducted on the radiologic diagnosis of significant hepatic artery (HA) obstruction, which is

✉ Kyoung Won Kim
kimkw@amc.seoul.kr

[1] Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, 88 Olympic-Ro 43-Gil, Songpa-Gu, Seoul 05505, South Korea

[2] School of Computer Science and Engineering, Soongsil University, Seoul, South Korea

[3] Division of Liver Transplantation and Hepatobiliary Surgery, Departments of Surgery, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea

known to be the most common and threatening complication leading to graft loss, relatively little attention has been given to portal vein (PV) complications, probably due to the rarity of unexpected complications in large PVs. However, PV stenosis (PVS) may also have critical consequences, such as graft dysfunction, reoccurrence of clinically substantial portal hypertension, and impaired liver regeneration after LT [4–7].

Confirmation of PVS is achieved by identifying and quantifying stenosis, as well as the pressure gradient across the stenosis site on invasive portal venography [8]. However, it cannot be used as a screening test due to its invasiveness, high cost, radiation exposure, and use of nephrotoxic agents. Doppler ultrasound (DUS) is an established initial method for screening hepatic vascular complications after LT. It provides both anatomical data on anastomosed hepatic vessels and information on hemodynamic alterations that occur due to vascular complications [3, 9, 10]. It has been suggested that portal-blood flow velocities (PFVs) of more than 125 cm/s and three- or fourfold velocity gradients through stenotic areas are reliable DUS abnormalities suggestive of PVS [6, 11, 12]. In clinical practice, however, particularly after living donor LT (LDLT), PFVs vary depending on the degree of preoperative portal hypertension, and donor-recipient PV size match, and DUS may frequently show such abnormalities of PFV-related indices even in patients without significant PVS, as well [13]. Therefore, indirect DUS abnormalities associated with significant PVS would also be helpful to enhance the diagnostic confidence and reliability.

The purpose of our study was to determine indirect DUS abnormalities associated with significant PVS by comparing DUS before and after treatment for significant PVS in recipients of LT.

Materials and methods

The study was approved by our institutional review board, which waived the requirement for informed consent due to the retrospective nature of the analyses.

Subjects

Between February 2006 and May 2017, 4187 LTs were performed in adults (aged 18 years or older) at a single institution. Among these patients, we found 49 recipients (1.2%) diagnosed with significant PVS, including 11 recipients with thrombotic PVS on portal venography who subsequently underwent endovascular or surgical intervention. We excluded two patients with other co-existing complications of acute cellular rejection ($n=1$) or other hepatic vascular complications ($n=1$). Among the remaining 47 patients, 41 who underwent DUS < 1 week before diagnosis were included in our study (mean ± standard deviation [SD], 44.7 ± 11.3 years; range, 17.9–66.6 years), including 27 men (47.1 ± 9.2, 26.4–66.7 years) and 14 women (39.4 ± 13.9, 17.9–62.5 years).

Of the 41 recipients, 11 underwent orthotopic whole LT from deceased donors, two received split LT from deceased donors, and the remaining 28 underwent LDLT using right ($n=22$) and dual ($n=6$) lobe grafts; four of the six recipients who received LDLT using dual grafts had bilateral PVS on portal venography. Thus, a total of 45 grafts were enrolled as the PVS group in this study.

For comparison with the PVS group, a control group of LT recipients without PVS was selected from the database of our institution by a one-to-one case-matched methodology according to the following matching criteria: age, sex, type of liver graft, and postoperative days of DUS after LT. A flow chart of recruitment for both the PVS and control groups is provided in Fig. 1, and clinical characteristics are given in Table 1.

Portal venography

Portal venography was performed due to concerning findings from routine follow-up DUS and computed tomography (CT), or clinical concerns of portal hypertension, such as elevated liver enzymes or ascites.

The median time from LT to diagnosis of significant PVS was 70 days (interquartile range [IQR], 13.8–285.8; 95% confidence interval [CI], 17.9–237.3).

Portal venography was performed by an experienced interventional radiologist using one of the three methods: (1) trans-hepatic approach, (2) trans-splenic approach, or (3) intraoperative approach. Intrahepatic PV branch, splenic branch, or inferior mesenteric vein was punctured with a 21-gauge Chiba needle (Cook, Bloomington, IN, USA) or a 18-gauge angiocatheter (Becton Dickinson Korea, Seoul, Korea), which was exchanged for a 5-F cobra catheter or 7-F sheath (cook) over a 0.035-inch angled hydrophilic guide wire (Terumo, Tokyo, Japan). Portal venography was then obtained with an iodinated contrast medium (240 mgI/ml). PVS on portal venography was defined as more than 50% narrowing of blood vessel diameter for any reason, including thrombosis or flow disturbance associated with prominent collateral vessels.

Doppler ultrasound at time of portal vein stenosis

The mean ± SD (range) time interval between DUS and diagnosis of significant PVS was 2 ± 2 (0–7) days.

DUS examinations were carried out by board-certified radiologists using one of the three units: Sequoia 512 (Siemens Acuson, Mountain View, CA), Aplio 500 (Toshiba

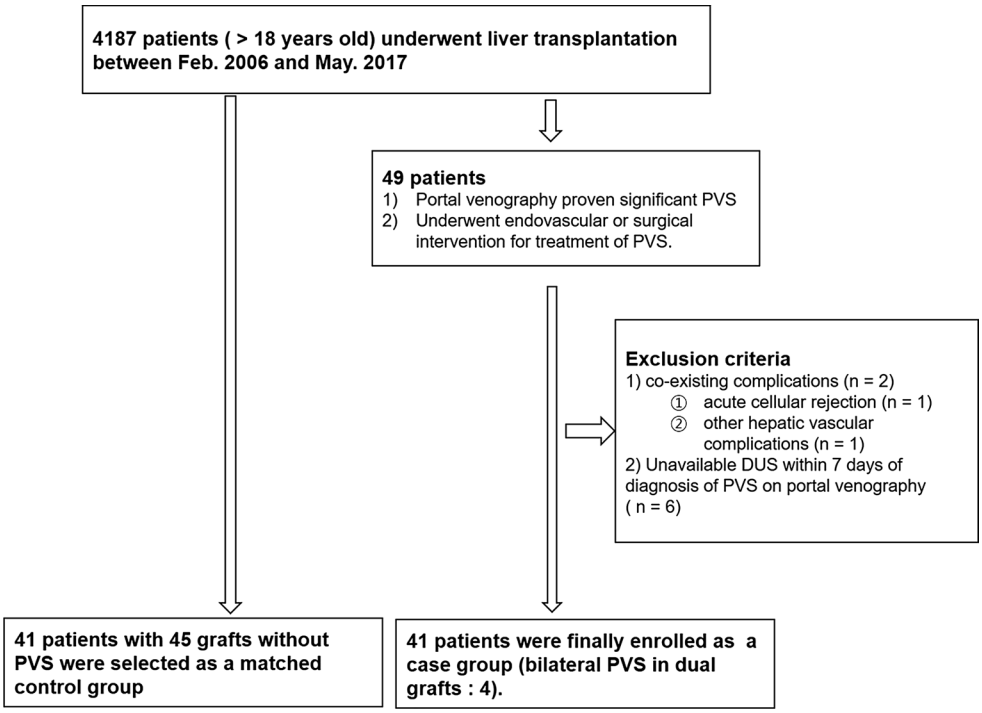

Fig. 1 Flow diagram of patient inclusion process

Medical System, Otawara, Japan), or Aixplorer (Supersonic Imagine, Aix-en-Provence, France).

For DUS examination, LT recipients were placed in the supine position with head elevated and the right arm abducted. Most examinations were performed using right oblique intercostal scanning, except for evaluating left graft of dual grafts or left lobe of whole liver with the following three steps: (1) gray-scale ultrasound; (2) color DUS examination; and (3) spectral DUS examination. The color-encoded area was expanded to cover the area from the anterior liver surface to the inferior vena cava. The spectral waveform was obtained from a small sample volume (1.5 ~ 3.0 mm) that was placed in the center of the target vessel with adjusting velocity scale and angle correction during the spontaneous breath-hold at the end of normal expiration. "No demonstrable color flow" was defined as the absence of a color flow signal at recipient PV or anastomosis even with the velocity scale reduced to less than ± 10 cm/s [14].

Two radiologists retrospectively reviewed the DUS findings of 45 grafts in 41 recipients with significant PVS, on static images, by consensus. One reviewer had > 10 years of experience in the field of LT imaging, and the other reviewer had 5 years of experience in abdominal imaging.

First, for portal flow interpretation of spectral Doppler images, excluding those with "no demonstrable color flow," we evaluated time average velocity (TAV, cm/s) at the recipient PV and anastomosis. The TAV ratio (ΔTAV) between the recipient PV and anastomosis was calculated. Significant jet flow was defined as a TAV > 125 cm/s or a ≥ threefold ΔTAV [6]. We also gave special attention to indirect abnormalities such as the presence of post-anastomotic turbulence, defined as disorganized flow with pockets of flow moving at different velocities and in different directions and hepatofugal portal flow (HFPF), appearing as reversed flow or to-and-fro flow at any of 1st or 2nd order branches of graft PVs. Second, to interpret HA flow patterns as another indirect abnormality, we evaluated the peak systolic velocities (PSVs), end diastolic velocities (EDVs), resistive indices (RIs), and systolic acceleration times (SATs) of graft HAs. The PSV and EDV of HA were measured on the spectral wave showing optimal signal detection. The RIs were determined by the following formula: (PSV-EDV)/PSV. The SATs, which indicated the rapidity of the upstroke, were measured as the interval from end diastole to the fist systolic peak. Abnormal HA waveforms were defined as those with a low RI (< 0.5), prolonged SAT (> 0.08 s), or both (tardus–parvus pattern) [15].

Doppler ultrasound after treatment in portal vein stenosis group and in control group

In the PVS group, DUS follow-ups were performed 2 ± 2 (0–11) days after PVS treatment.

In the control group, the median interval time between LT and DUS examination was 92 days (9.5–325.5).

For PVS, balloon angioplasty was initially carried out, and stent placement was performed for residual PVS. In thrombotic PVS, thrombolysis with thrombectomy was performed either intravascularly or using surgical methods.

Table 1 Clinical characteristics of liver transplantation recipients with portal vein stenosis and without portal vein stenosis

Characteristic	PVS group	Control group	*p* values
Age (years)[a]	44.7 ± 11.3 (17.9–66.6)	45.09 ± 10.92 (20–67)	0.823
Sex			1.000
Male	27 (65.9)	27 (65.9)	
Female	14 (34.1)	14 (34.1)	
Weight (kg)[a]	64.3 ± 14.8 (40.0–111.4)	65.34 ± 10.60 (46.5-86.9)	0.696
Body mass index (kg/m^2)[a]	23.3 ± 4.5 (17.1–35.4)	23.08 ± 3.34 (17.8-32.2)	0.821
Graft weight of LDLT (g)[a]	794.1 ± 227.9 (550.0–1450.0)	933.55 ± 474.07 (510.0–2400.0)	0.905
Graft recipient weight ratio[a]	1.4 ± 0.6 (0.8–3.1)	1.45 ± 0.76 (0.8–4.4)	0.706
Indication for transplantation			0.161
HBV- or HCV-induced liver cirrhosis	15 (36.5)	14 (34.1)	
Alcohol-induced liver cirrhosis	5 (12.2)	2 (4.9)	
Hepatocellular carcinoma	12 (29.3)	11 (26.8)	
Primary or secondary biliary cirrhosis	3 (7.3)	1 (2.4)	
Primary sclerosing cholangitis	1 (2.4)	0 (0.0)	
Wilson's disease	1 (2.4)	4 (9.8)	
Caroli's disease	1 (2.4)	0 (0.0)	
Congenital portal vein thrombosis	1 (2.4)	0 (0.0)	
Autoimmune hepatitis	1 (2.4)	2 (4.9)	
Budd-Chiari syndrome	1 (2.4)	0 (0.0)	
Fulminant hepatic failure	0 (0.0)	6 (14.6)	
Congenital hepatic fibrosis	0 (0.0)	1 (2.4)	

Unless indicated otherwise, values are the number of patients, with percentages in parentheses

LDLT living donor liver transplantation, *PVS* portal vein stenosis, *HBV* hepatitis B virus, *HCV* hepatitis C virus

[a]Values are means ± standard deviations, with ranges in parentheses

Two radiologists reviewed the post-treatment DUS findings in the PVS group after PVS treatment and control group retrospectively in the same manner as described above.

Statistical analysis

All analyses were performed using commercially available software (SPSS version 21.0; SPSS, Chicago, Ill). The comparative analyses of categorical variables were performed using Chi square (χ^2) with Fisher's exact tests or McNemar's tests. The comparative analyses of continuous variables were performed using paired Student's *t* tests or independent *t* tests. Diagnostic values including sensitivity, specificity, positive likelihood ratio (PLR), and negative likelihood ratio (NLR) of each abnormal DUS finding and combinations were also evaluated. *p* values less than 0.05 were considered indicative of statistically significant differences.

Results

Doppler ultrasound findings

In the PVS group, DUS before PVS treatment revealed "no demonstrable color flow" at recipient PVs or anastomoses in 12 patients, consisting of five patients (41.7%) with non-thrombotic PVS and seven patients (58.3%) with PVS with thrombosis (Table 2). The frequency of turbulence in graft PVs was significantly higher in those with "demonstrable color flow" at recipient PVs or anastomoses (28/33 [84.8%]) than in the others (2/12 [16.7%], $p < 0.001$, Fig. 2). However, HFPF was more frequently observed in those with "no demonstrable color flow" at recipient PVs or anastomoses ($p = 0.006$); 6/12 (50.0%) with "no demonstrable color flow" versus 3/33 (9.0%) with "demonstrable color flow" (Fig. 3). Regarding HA, abnormal HA waveforms such as tardus–parvus waveforms, low RI, or prolonged SAT were more commonly observed in the "no demonstrable color flow" group (8/12 [66.7%]) than in the "demonstrable color flow" group

Table 2 Doppler parameters of portal veins before and after treatment in liver transplantation recipients with portal vein stenosis and in those without portal vein stenosis

	PVS group		*p* values[‡]	Control group	*p* values[¶]
	Before PVS treatment	After PVS treatment			
Group A, with "no demonstrable color flow"[a]	12 (26.7)	1 (0.02)[b]	0.003	0 (0.0)	< 0.001
Group B, with "demonstrable color flow"[a]	33 (73.3)	44 (97.8)		45 (100)	
Spectral Doppler parameters					
Recipient PV-TAV (cm/s)	35.8 ± 19.8 (7.9–112.3)	38.9 ± 17.3 (6.4–81.3)	0.053[c]	38.26 ± 18.55 (10.8–100.0)	0.572
Anastomosis–TAV (cm/s)	143.4 ± 71.1 (24.9–360.0)	73.8 ± 34.8 (7.0–171.0)	< 0.001[c]	59.18 ± 30.69 (16.39–158.0)	< 0.001
Velocity ratio	5.6 ± 7.7 (1.1–45.6)	2.3 ± 2.2 (0.6–15.4)	0.011[c]	1.60 ± 0.58 (0.8–3.1)	0.005
≥ threefold ΔTAV (%)	22 (66.7)	8 (17.8)	< 0.001[c]	2 (4.4)	< 0.001
CDI parameters[a]					
Turbulence	30 (66.7)	12 (26.7)	< 0.001	13 (28.9)	0.001
HFPF	9 (20.0)	2 (4.4)	0.039	0 (0.0)	0.003

Unless indicated otherwise, values are means ± standard deviations, with ranges in parentheses

PVS portal vein stenosis, *PV* portal vein, *TAV* time average velocity, *ΔTAV* ratio of time average velocity, *CDI* color Doppler imaging, *HFPF* hepatofugal portal flow

[a]Values are the number of patients, with percentages in parentheses

[b]Another graft showed newly developed "no demonstrable color flow" at graft and recipient PVs as well as anastomoses, confirming acute thrombotic occlusion on follow-up CT

[c]Comparisons before and after treatment were performed between those with Doppler-detectable portal flow both before and after treatment ($n = 32$)

[‡]*p* value was calculated by comparison between before and after treatment in recipients with PVS

[¶] *p* value was calculated by comparison between PVS group (before treatment) and control group

(8/33 [24.2%]), with a statistical significance ($p = 0.012$, Fig. 4).

In the PVS group after treatment, DUS of PV showed significantly decreased values of the TAV of anastomoses, ΔTAV, and the frequency of ≥ threefold ΔTAVs (Table 2; $p < 0.001$, $p = 0.011$, and $p < 0.001$, respectively). The frequencies of turbulence and HFPF were also significantly reduced (Table 2; $p < 0.001$ and $p = 0.031$, respectively). For HA, the proportion of patients with abnormal HA waveforms was significantly reduced from 16 patients (37.2%) to five patients (11.6%, Table 3, $p < 0.001$). In the control group, the TAV at anastomosis, ΔTAV, the frequency of ≥ threefold ΔTAV, and indirect DUS abnormalities such as turbulence, HFPF, and abnormal HA waveform were significantly lower than those values before treatment in the PVS group (Tables 2 and 3; $p < 0.001$, $p = 0.005$, $p < 0.001$, $p = 0.001$, $p = 0.003$, and $p = 0.008$, respectively).

Diagnostic value of DUS findings for diagnosing PVS

Of 45 grafts with PVS, 95.56% had at least one of the DUS abnormalities. When one of the PFV-related abnormalities or "no demonstrable color flow" were shown on DUS as well as one of the indirect DUS abnormalities, this combined panel approach yielded the sensitivity, specificity, PLR, and NLR of 71.1, 97.8, 32.00, and 0.30%, respectively, for diagnosing PVS (Table 4).

Discussion

Although DUS is the preferred post-transplantation screening method for identifying vascular complications, DUS diagnoses of significant PVS are controversial. While the role of DUS is clearly established for detecting postoperative PVS due to thrombosis [9, 10, 16, 17], there are no well-defined diagnostic criteria for significant PVS. Diagnostic DUS parameters used in the previous studies [18–22], including increased velocities > 125 cm/s and a greater than three- to fourfold velocity gradient between stenotic and pre-stenotic segments, are related to high false-positive PVS diagnoses, especially in recipients with severe preoperative portal hypertension [13]. Moreover, when it is difficult to measure velocities at PV anastomoses due to poor sonic windows, it is estimated by measuring post-anastomotic graft PVs. Meanwhile, when stenosis is present, PFV-related indices may not be accurate given that helical or turbulent flows in graft PVs renders determination of precise blood flow directions at DUS for angle corrections difficult [3, 23]. Thus, in this study, we have

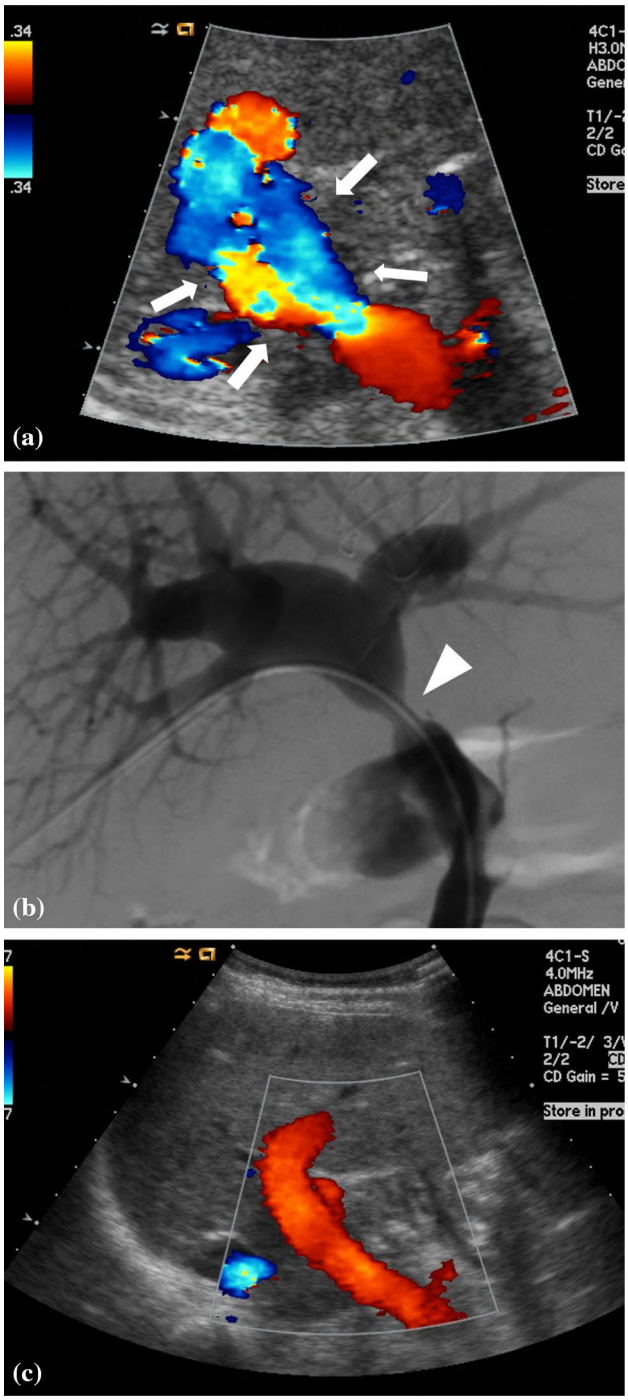

Fig. 2 A 27-year-old female with portal vein stenosis after whole liver transplantation from cadaveric donor. **a** Color Doppler sonogram shows turbulent flow, with alternating bands of red and blue flows within the graft portal vein (arrows). **b** Portal venography shows tight anastomotic stenosis (arrowhead). **c** After treatment with portal vein stenting, follow-up color Doppler sonogram shows disappearance of turbulent flow at the graft portal vein

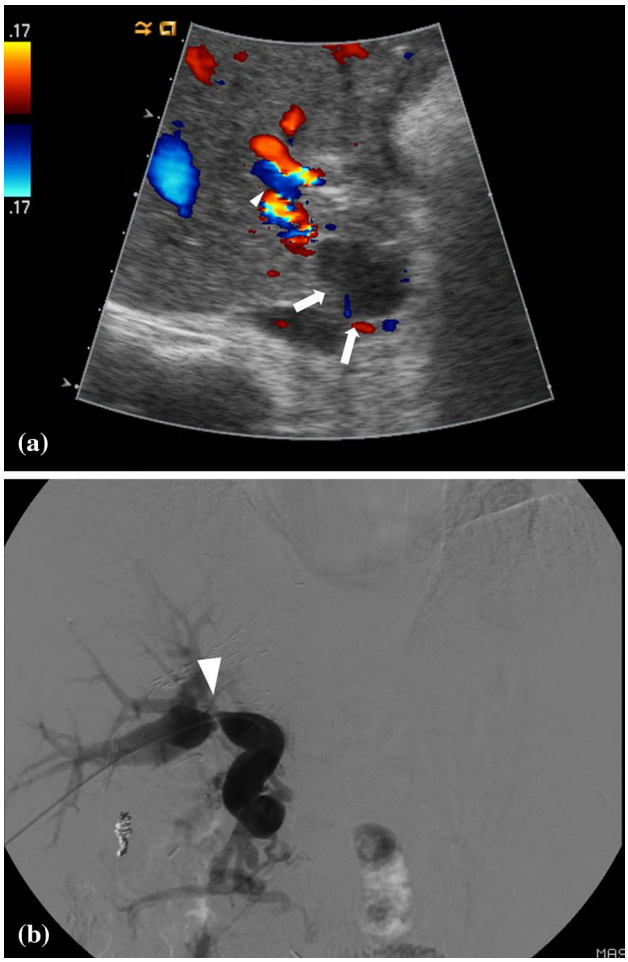

Fig. 3 A 50-year-old male with portal vein stenosis after living donor liver transplantation using right lobe graft. **a** Color Doppler sonogram reveals "no demonstrable color flow" at the recipient portal vein around the anastomosis (arrows), and hepatofugal portal flow at the graft portal vein exhibiting a blue signal (arrowhead), adjacent to the dilated hepatic artery. **b** Portal venography shows tight anastomotic stenosis (arrowhead). The patient was treated with portal vein stenting, and follow-up Doppler ultrasound revealed restoration of hepatopetal portal flow (not shown)

focused on not only PFV-related index abnormalities but also indirect abnormal features that can be associated with significant PVS.

Our results showing significant jet flow presenting as PFV-related index abnormalities in significant PVS were consistent with the previous studies [18–20, 22]. In addition, these PFV-related values decreased significantly following treatment. In addition to the significant jet flow, we found that 12 of 45 grafts with PVS presented with "no demonstrable color flow" at recipient PV or anastomosis. An earlier study by Spencer et al. [24] investigating carotid stenosis showed that as the stenotic diameter decreased, blood flow velocity increased initially; however, beyond the critical stenosis, blood flow velocities decreased. Findings from their

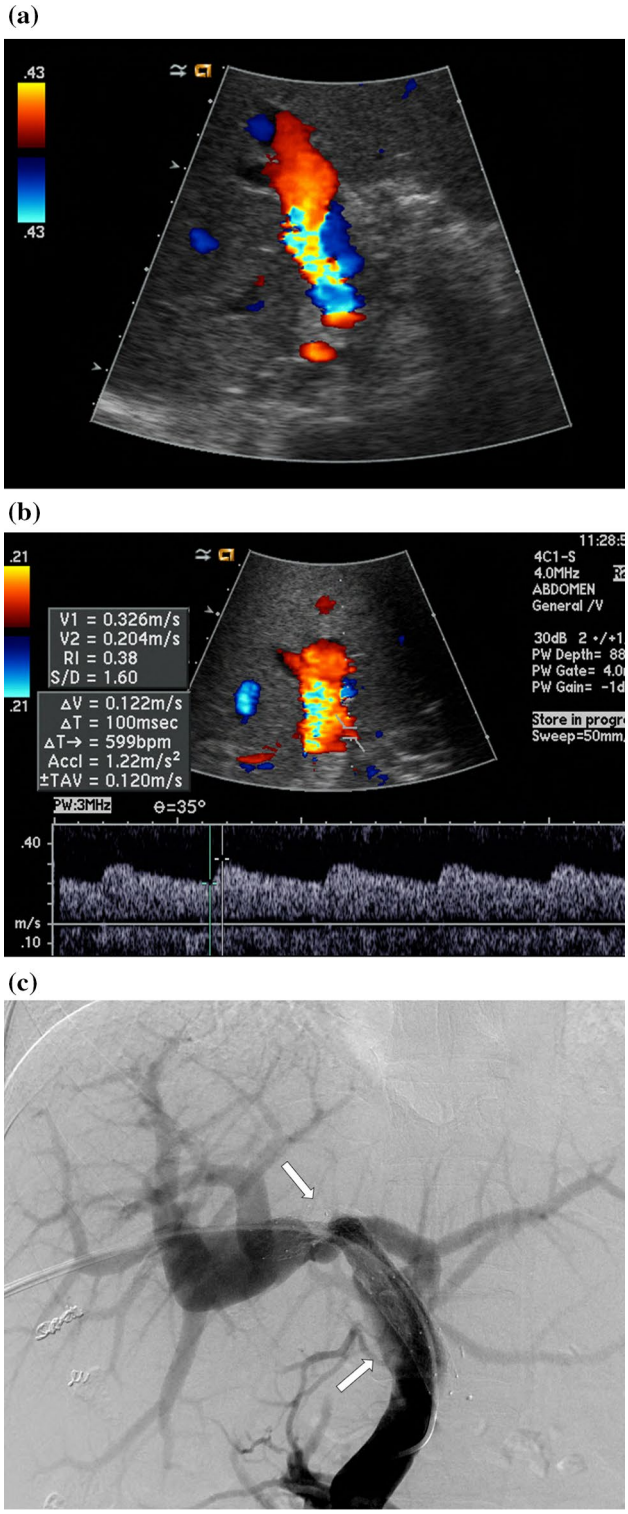

Fig. 4 A 36-year-old female with portal vein thrombosis after whole liver transplantation from cadaveric donor. **a** Color Doppler sonogram shows turbulent flow in the graft portal vein. **b** Spectral Doppler ultrasound shows a tardus–parvus waveform at the graft hepatic artery, with a prolonged systolic acceleration time and low resistive index. **c** Portal venography shows a large filling defect representing thrombosis in the main and right main portal vein. The patient underwent portal vein thrombectomy and stenting. Along with portal vein flow restoration, Doppler sonogram showed disappearance of the tardus–parvus waveform at the graft hepatic artery (not shown)

study might have consistently shown in our study as "no demonstrable color flow".

In our study, in addition to significant jet flow or "no demonstrable color flow" at recipient PVs or anastomoses, turbulence and HFPFs in graft PVs were frequently and occasionally found on color Doppler imaging of significant PVS. In particular, HFPFs at graft PVs were more commonly observed in patients with "no demonstrable color flow" at recipient PVs or anastomoses. These results may suggest that evaluating the graft PVs would be helpful in diagnosis of PVS in patients with suspected PVS, especially when PFVs cannot be measured in anastomoses or recipient PVs. However, HFPF may be attributed to various pathologic conditions such as overflow from the HAs to PVs (e.g., arterioportal fistula or peritumoral shunt) or reversal of the pressure gradients between the hepatic sinusoids and PVs (e.g., portal hypertension due to liver cirrhosis or acute rejection) [25]. For such HFPFs to be reliable findings of PVS, the aforementioned other causes should be excluded first.

Commonly, tardus–parvus waveforms in HAs are considered DUS criteria for substantial HA stenosis. However, a study by Park et al. [26] of false-positive diagnoses with tardus–parvus waveforms in HAs for HA stenosis showed that PV stenoses or thromboses could be one of the causes of false-positive diagnoses. Similarly, in our study, abnormal HA waveforms were occasionally detected in significant PVS, without any intrinsic HA abnormalities. An early study by Platt et al. [27], which included a small number of LT recipients, reported that obstructive PV thromboses after LT involved a decrease in HA RIs. In our series, not only decreased RIs but also prolonged SATs and tardus–parvus waveforms were frequently observed among significant PVS. This finding may be due to the ability of HAs to produce compensatory flow changes in response to portal-blood flow changes, termed the HA-buffer response [25]. As portal-blood flow decreases, HA flow increases (i.e., HA resistance decreases with an activated HA-buffer response). Several previous studies have reported that this mechanism is preserved, even in transplanted liver [28–30]. Thus, HA waveform abnormalities, such as tardus–parvus waveforms, decreased RIs, or prolonged SATs, as demonstrated by HA-buffer responses, could reflect PVS. As with abnormal flow directions of graft PVs, abnormal HA waveforms appeared more frequently in patients with "no demonstrable color flow" at recipient PVs or anastomoses, implying that these are useful when the PFV-related indices at recipient PV or anastomosis are not easily obtained.

Follow-up DUS after treatment of PVS showed that most of the indirect DUS abnormalities such as turbulence, HFPF, and abnormal HA waveforms disappeared and resolved. Therefore, the substantial decrease in frequencies of these indirect DUS abnormalities between treatments may indicate

Table 3 Doppler parameters of hepatic arteries before and after treatment of portal vein stenosis in liver transplantation recipients with portal vein stenosis and in those without portal vein stenosis

	PVS group		*p* values[c]	Control group (*n* = 45)	*p* values[§]
	Before PVS treatment (*n* = 43)	After PVS treatment (*n* = 43)			
PSV (cm/s)[a]	81.5 ± 38.7 (32.2–195.0)	94.9 ± 44.8 (44.0–205.0)	0.152	70.14 ± 30.60 (23.0–155.3)	0.081
EDV (cm/s)[a]	27.3 ± 16.4 (4.8–83.0)	26.3 ± 17.4 (0.7–78)	0.657	18.87 ± 12.98 (0.5–60.5)	0.009
RI[*]	0.66 ± 0.14 (0.33–0.87)	0.73 ± 0.11 (0.43–0.99)	0.007	0.7 ± 0.12 (0.48–0.99)	0.006
SAT (ms)[a]	69.7 ± 26.6 (23–144)	58.2 ± 21.9 (25–152)	0.003	62.24 ± 18.35 (32–100)	0.135
Abnormal wave[b]			0.001		0.008
TPW	9 (20.9)	0 (0.0)		0 (0.0)	
Low RI	0 (0.0)	1 (2.3)		1 (2.2)	
Prolonged SAT	7 (16.3)	4 (9.3)		5 (11.1)	

PVS portal vein stenosis, *PSV* peak systolic velocity, *EDV* end diastolic velocity, *RI* resistive index, *SAT* systolic acceleration time, *TPW* tardus–parvus waveform

[a]Numbers are means ± standard deviations, with ranges in parentheses

[b]Values are the number of grafts with available hepatic artery indices (43 grafts in PVS group and 45 grafts in control group), with percentages in parentheses

[c]Comparisons between hepatic artery indices before and after treatment were performed in 42 recipients with available hepatic artery indices both before and after treatment

[§]*p* value was calculated between PVS group and control group

Table 4 Diagnostic values of individual and combination of each Doppler ultrasound abnormalities for diagnosing portal vein stenosis

	Sensitivity	Specificity	PLR	NLR
I. Significant jet flow				
Anastomosis–TAV > 125 cm/s	46.7 (21/45)	95.6 (43/45)	10.5	0.56
≥ threefold ΔTAV	48.9 (22/45)	95.6 (43/45)	11.00	0.53
One of the two	57.8 (26/45)	95.6 (43/45)	13	0.44
II. No demonstrable color flow	26.7 (12/45)	100.0 (45/45)	NA	0.73
III. Indirect abnormalities				
Turbulence	66.7 (30/45)	71.1 (32/45)	2.31	0.47
HFPF	20 (9/45)	100.0 (45/45)	NA	0.80
Abnormal HA waveform pattern	35.6 (16/45)	86.7 (39/45)	2.67	0.74
One of the three findings	86.7 (39/45)	64.4 (29/45)	2.43	0.21
I or II and any of III	71.1 (32/45)	97.8 (44/45)	32.00	0.30
I or II or any of III	95.6 (43/45)	62.2 (28/45)	2.53	0.07

Data are presented as percentages. Data in parentheses are the number of subjects used to calculate the percentage

TAV time average velocity, *HFPF* hepatofugal portal flow, *HA* hepatic artery, *PLR* positive likelihood ratio, *NLR* negative likelihood ratio

that they are meaningfully associated with significant PVS. In addition, the frequencies of such findings in the PVS group were significantly higher than those in the control group.

We found that overall sensitivities of each DUS finding for diagnosing PVS were relatively poor. However, combination of PFV-related index abnormalities, "no demonstrable color flow" at recipient PV or anastomosis, and indirect DUS abnormalities including turbulence, HFPF, and abnormal HA waveforms improved sensitivity for diagnosing PVS. When one of the PFV-related index abnormalities or "no demonstrable color flow" were shown on DUS as well as one of the indirect DUS abnormalities, the probability of having PVS in the recipient markedly increased.

There are several limitations to our study. First, this study was a retrospective design, which potentially introduced selection bias and limited the generalizability of the findings, but we included a relatively large number of LT recipients with significant PVS on portal venography and attempted to exclude other elements potentially affecting

DUS findings of HAs and PVs by only including subjects with DUS data 1 week before and after endovascular or surgical interventions for PVs. Second, DUS quality depends on the operator, and interpretation of findings is subjective. As our study design involved analysis of DUS parameters on static images, the quality of DUS acquisition is an important factor for subsequent interpretation. Furthermore, as patients were enrolled over a relatively long period, DUS studies were performed by many abdominal radiologists, increasing the subjective heterogeneity of our study sample. Consequently, inter- and intra-operator variability for measuring DUS parameters could be one of the limitations. However, there were no substantial changes in the DUS protocol during the study period, and all radiologists were trained using a standard and strict DUS protocol for LT recipients under the supervision of a dedicated radiologist experienced in LT imaging. Finally, due to inherent limitations of 1:1 matched case–control studies, positive predictive value, negative predictive value, and accuracy could not be derived from our study, as being dependent upon prevalence. Thus, future validation using a consecutive study population is needed.

Conclusions

Besides abnormalities of PFV-related indices, DUS occasionally shows "no demonstrable color flow" either at recipient PVs or anastomoses. In addition, indirect Doppler abnormalities such as turbulence and HFPF at graft PVs, and abnormal waveforms of graft Has, can be found in LT recipients with significant PVS. The combination of PFV-related abnormalities and indirect DUS abnormalities would be helpful for diagnosis of PVS.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical statements All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

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