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ABDOMINAL IMAGING

ORIGINAL ARTICLE

Grading portal vein stenosis following partial hepatectomy by high-frequency ultrasonography: an *in vivo* study of rats

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PURPOSE

To evaluate the diagnostic value of ultrasound in grading portal vein stenosis (PVS) in a rat model of 70% partial hepatectomy (PH).

METHODS

A total of 96 Sprague-Dawley rats were randomly divided into a PH group and PVS groups with mild, moderate, and severe PVS following PH. Hemodynamic parameters were measured using high-frequency ultrasound (5–12 MHz high-frequency linear transducer), including pre-stenotic, stenotic, and post-stenotic portal vein diameters (PVD_{pre}, PVD_{s}, PVD_{post}); pre-stenotic and stenotic portal vein velocity (PVV_{pre}, PVV_{s}); hepatic artery peak systolic velocity (PSV); end-diastolic velocity; and resistive index. The portal vein diameter ratio (PVDR) and portal vein velocity ratio (PVVR) were calculated using the following formulas: $PVDR=PVD_{pre}/PVD_{s}$ and $PVVR=PVV_{s}/PVV_{pre}$. The value of these parameters in grading PVS was assessed.

RESULTS

Portal vein hemodynamics showed gradient changes as PVS aggravated. For identifying >50% PVS, PVD_{s} and PVDR were the best parameters, with areas under the curve (AUC) of 0.85 and 0.86, respectively. For identifying >65% PVS, PVD_{s}, PVDR, and PVVR were relatively better, with AUCs of 0.94, 0.85, and 0.88, respectively. The AUC of hepatic artery PSV for identifying >65% PVS was 0.733.

CONCLUSION

High-frequency ultrasonography can be used to grade PVS in rats, with PVD_{s}, PVDR, and PVVR being particularly useful. Hepatic artery PSV may help in predicting >65% PVS. These findings provide valuable information for PVS rat model research and offer an experimental basis for further studies on PVS evaluation in living-donor liver transplantation (LDLT).

CLINICAL SIGNIFICANCE

Ultrasonography serves as a first-line technology for diagnosing PVS following LDLT. However, the grading criteria for PVS severity remain unclear. Investigating the use of ultrasonic hemodynamics in the early diagnosis of PVS and grading stenosis severity is important for early postoperative intervention and improving recipient survival rates.

KEYWORDS

Portal vein stenosis, high-frequency ultrasonography, hemodynamics, portal vein, hepatic artery, rat

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As organ transplantation techniques mature and new immunosuppressants are developed, living-donor liver transplantation (LDLT) is becoming an effective treatment for end-stage liver disease. Compared with whole-liver transplantation, a unique characteristic of LDLT is that postoperative regeneration allows the liver volume to increase, resulting in successful reconstruction even though the graft volume is relatively small.[1,2] Sufficient portal blood flow is a prerequisite for the transplanted liver to regenerate and survive. In LDLT, the recipient's portal vein trunk is usually anastomosed to the portal vein branch of the graft

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(left or right branch). Consequently, the donor's and recipient's portal vein diameters (PVD) often do not match, resulting in portal vein stenosis (PVS). Furthermore, portal vein angulation or torsion may lead to PVS after LDLT more frequently than after whole-liver transplantation, with an incidence rate of 0.5%–8.1%.[3-5] Mild PVS usually does not affect liver regeneration or function, but severe PVS can lead to portal hypertension, small-for-size syndrome, and acute liver failure. If PVS can be discovered early and clinical intervention is performed before liver regeneration and function are irreversibly affected, this defect may be reversed.[4-9]

The diagnosis of PVS mainly relies on imaging techniques such as ultrasonography, computed tomography, magnetic resonance imaging, and digital subtraction angiography. Among these techniques, ultrasonography can accurately assess PVD and hemodynamics and has advantages such as convenience, lack of radiation, repeatability, and bedside operation. Therefore, ultrasonography serves as a first-line imaging modality for diagnosing PVS in the early postoperative period and during long-term follow-up. Generally, a diagnosis of significant stenosis is made when the portal vein trunk diameter is <2.5–3.5 mm, the blood flow velocity at the stenotic site is >150 cm/s, or the velocity ratio between stenotic and pre-stenotic flow is ≥4.[10-13] However, to date, the grading criteria in ultrasonography for PVS severity remain unclear. In addition, when portal blood flow volume decreases, hepatic artery flow volume will show varying degrees of increase due to the hepatic arterial buffer response (HABR).[14,15] There are no reports on how hepatic artery flow changes under different severities of PVS or whether its hemodynamic parameters can aid in PVS evaluation. Therefore, studying the application of ultrasonic hemodynamics for the early diagnosis of PVS and the grading of stenosis severity is important for early postoperative intervention and for increasing the survival rate of liver transplant recipients.

Main points

- Portal vein hemodynamic parameters-portal vein diameter at stenosis (PVD_s), portal vein diameter ratio (PVDR), portal vein velocity at stenosis (PVV_s), and portal vein velocity ratio (PVVR)-show significant gradient changes among different degrees of portal vein stenosis (PVS), with stenosis rate (SR) ≤50%, 50%< SR ≤65%, and SR >65% (all P < 0.0001).
- PVD at stenosis and PVDR are the best parameters for PVS grading [all areas under the curve (AUCs) >0.80].
- PVV_s can effectively diagnose the presence/absence of PVS (AUC: 0.958), but the diagnostic performance in PVS grading is relatively low (AUC <0.80). The PVVR showed good performance in the identification of >65% PVS (AUC: 0.880).
- A significant increase in hepatic artery peak systolic velocity may be helpful for PVS evaluation, especially in predicting >65% PVS (AUC: 0.733).

Due to ethical constraints and the diversity of liver diseases, we conducted animal experiments in this study. The rat model of 70% partial hepatectomy (PH) is a classical model for studying liver regeneration,[16,17] and partial portal vein ligation is the most commonly used method for producing the PVS model.[18,19] In this study, varying degrees of partial portal vein ligation were performed based on the 70% PH rat model to simulate different degrees of PVS following LDLT. Ultrasonography was used to measure the hemodynamic parameters of the portal vein and hepatic artery to assess the effectiveness of ultrasonography in diagnosing and grading PVS, thereby providing an experimental basis for further studies on early PVS evaluation and intervention.

Methods

Study subjects

All rats and procedures used in this research were approved by the Animal Ethics Committee of West China Hospital, Sichuan University (no: 2020101A). Ninety-six healthy male Sprague-Dawley rats (7–14 weeks old, weighing 200–400 g, specific-pathogen-free grade) were purchased from Chengdu Dashuo Biotechnology Co., Ltd, and given ad libitum access to food and water at the animal experiment center of West China Hospital. All rats were housed at a constant temperature under a 12-h light–dark cycle to acclimate for at least 1 week before the experiment.

The rats were randomly divided into a PH group and PVS groups with mild, moderate, and severe PVS following PH (n = 24 for each group). The PH group was established as a model of 70% hepatectomy without portal vein ligation, whereas the PVS groups were created through varying degrees of partial portal vein ligation after PH. Mild, moderate, and severe PVS were respectively defined as ≤50% stenosis, 50%–65% stenosis, and >65% stenosis, approaching near occlusion.[19]

Construction of rat models

Construction of the 70% partial hepatectomy rat model

The standard method for 70% PH in rats developed by Higgins and Anderson[16] was used as a reference.[17] The specific procedure was as follows: (1) Continuous inhalational anesthesia with ether was administered before the rat was placed in the supine position. The rats were immobilized, and the abdomen was shaved using an electric hair remover. (2) Iodine was used to disinfect the surgical site, and an abdominal midline incision was made below the xiphoid process. The skin and muscles were dissected layer by layer to access the abdominal cavity, and the liver was exposed. (3) A suture was used to ligate and then resect the left lateral lobe and middle lobe. The resected liver accounted for approximately 70% of the entire liver. (4) The liver pedicle ligation site was inspected for bleeding, and the residual liver lobes were examined for congestion.

Construction of portal vein stenosis models with varying severity after partial hepatectomy

After PH, varying degrees of partial ligation of the portal vein trunk were performed to construct PVS models of different severity.[18,19] The specific steps were as follows: (1) The portal vein trunk was dissociated, and a microvascular caliper was used to measure the PVD. (2) Needles of different sizes were selected and placed parallel to the portal vein. A silk suture was used to ligate the portal vein and the needle together. At this point, significant congestion could be observed in the gastrointestinal tract. After ligation, the needle was slowly withdrawn, alleviating the congestion in the gastrointestinal tract. The PVD of the stenotic segment was equal to the external diameter of the needle. Needles of varying sizes were used for partial ligation of the portal vein to create PVS models of different severity. The sizes of needles used in this study were 18G, 19G, 20G, 21G, and 22G, with outer diameters of 1.2 mm, 1.0 mm, 0.9 mm, 0.8 mm, and 0.7 mm, respectively. The PV stenosis rate (SR) was calculated using the formula $SR=(1-D_{needle}/PVD) \times 100\%$.[3] After evaluating the intestinal congestion status and vital signs, 32,000 units of penicillin and 5 mL of NaCl (0.9%) were administered via peritoneal injection, and then the abdomen was sealed layer by layer.[4] The rats were labeled and housed in individual cages after surgery, kept warm, and given ad libitum access to food and water.

Ultrasonography examination

Duplex Doppler ultrasound examinations were performed using an IU22 US system (Philips Healthcare, Bothell, WA), equipped with a 5-12 MHz transducer. At 24 h post-surgery, scans were conducted with the rats ether-anesthetized and stably positioned in the supine position, using both grayscale and color Doppler imaging to identify vascular landmarks. Doppler tracings were acquired, and the best tracing was selected for analysis. In the PH group, the PVD and maximum portal vein velocity (PVV) were measured at a site approximately 5 mm below the bifurcation of the hilum. In the PVS groups, pre-stenotic, stenotic, and post-stenotic PVD (PVD_{pre}, PVD_{s}, PVD_{post}) and pre-stenotic and stenotic PVV (PVV_{pre}, PVV_{s}) were measured (Figure 1). The PVD ratio (PVDR) and the PVV ratio (PVVR) were calculated using the following formula: $PVDR=PVD_{pre}/PVD_{s}$ and $PVVR=PVV_{s}/PVV_{pre}$. Hepatic artery peak systolic velocity (PSV) and end-diastolic velocity (EDV) were measured in all rats, and the resistive index (RI) was calculated using the following formula: RI=(PSV–EDV)/PSV. The sampling volume was adjusted based on the course of the blood vessel and its inner diameter. The gain was adjusted to maximum sensitivity without noise, and the angle between the sound beam and blood flow was ≤60°. The aforementioned scanning and image storage were performed by an experienced physician who was blinded to the grouping. The mean of three measurements was calculated for all results.

Research ethics standards compliance

This study was carried out in accordance with the principles of the Basel Declaration and was approved by the Animal Ethics Committee of West China Hospital (decision no: 2020101A, date: March 24th, 2020).

Statistical analysis

SPSS 25.0 and GraphPad Prism 8 were used for statistical analysis. A value of $P < 0.05$ indicated a statistically significant difference. One-Way analysis of variance was used to compare the hemodynamic parameters among different groups for source data with a normal distribution. When inter-group differences were present, the least significant difference test was used for pairwise comparisons when variances were homogeneous, and Dunnett's T3 test was used for pairwise comparisons when variances were heterogeneous. Values are expressed as mean ± standard deviation ($\bar{x} \pm s$). Non-parametric rank tests were used to compare non-normally distributed source data, and pairwise comparisons were performed when inter-group differences were present. These values are expressed as medians.

The receiver operating characteristic (ROC) curve was plotted, and the area under the curve (AUC), standard error, asymptotic significance (b), asymptotic 95% confidence interval, best cut-off, sensitivity, and specificity were calculated to evaluate the value of the various ultrasound parameters in the diagnosis of PVS and in predicting stenosis severity.

Results

Model construction

In this study, the 70% PH models with no PVS were successfully constructed in 24 rats, whereas PVS models of different severities following PH were constructed in 72 rats. The SRs of the mild, moderate, and severe PVS groups were (45.16 ± 3.40)%, (59.21 ± 3.84)%, and (69.46 ± 2.17)%, respectively.

$D_{stenosis}$ (i.e., outer needle diameter) in PVS models with different severities showed significant gradient changes. When SR was >65%, the portal vein trunk diameter was extremely narrow, and the needle used for model construction was significantly thinner: mainly 21G (outer diameter: 0.8 mm). An 18G (outer diameter: 1.2 mm) needle was mostly used for model construction in rats with SR ≤50%, and an 18G (outer diameter: 1.2 mm) or 20G (outer diameter: 0.9 mm) needle was mostly used for model construction in rats with 50%< SR ≤65%. $D_{stenosis}$ in rats with SR >65% was significantly lower than that in the SR ≤50% and 50%< SR ≤65% groups, and the $D_{stenosis}$ of the 50%< SR ≤65% group was also significantly lower than that of the SR ≤50% group (Figure 2).

Hemodynamic changes

Portal vein hemodynamic changes

Residual liver and portal vein after 70% PH in rats can be observed using conventional ultrasound. In PVS rats, grayscale ultrasound clearly showed PVS, whereas Doppler ultrasound revealed turbulence of blood flow at the stenosis site, with the stenotic flow significantly faster and the pre-stenotic flow slower (Figure 1b, c). When PVS occurred, the lumen diameter of the stenotic site was significantly smaller, whereas the lumen diameters at two ends of the stenotic site showed varying degrees of expansion. As shown in Table 1 and Figure 3a-d, the PVD_{pre} of the moderate and severe PVS groups was significantly higher than that of the PH and mild PVS groups, and the PVD_{post} of the moderate PVS group was significantly higher than that of the PH group (all $P < 0.05$). The PVD_{s} among the mild, moderate, and severe PVS groups were significantly lower than that of

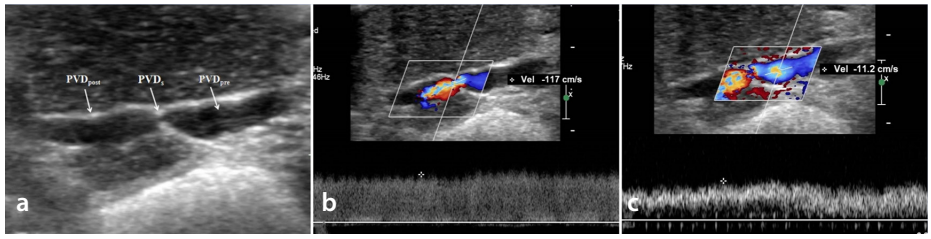

Figure 1. Measurement of portal vein blood flow parameters in the PVS group **(a)**. Pre-stenotic, stenotic, and post-stenotic PVD (PVD_{pre}, PVD_{s}, PVD_{post}) were measured using ultrasound (arrows). **(b, c)**. Stenotic and pre-stenotic PVV (PVV_{s}, PVV_{pre}) were measured using ultrasound. PVS, portal vein stenosis; PVD, portal vein diameter; PVV, portal vein velocity.

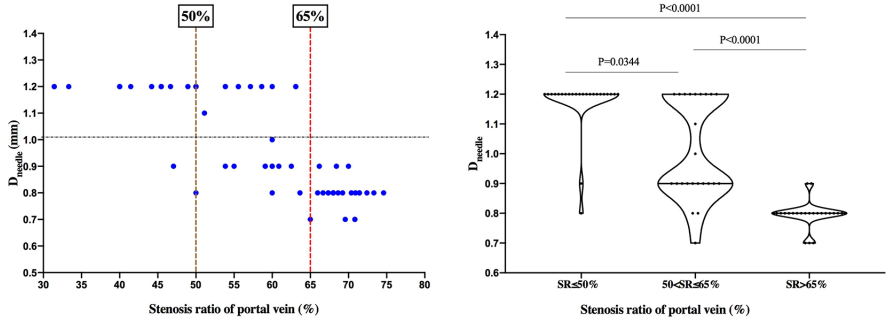

Figure 2. D_{needle} used in the PVS groups with different severities. D_{needle}, the diameter of the needle; PVS, portal vein stenosis.

the PH group (all $P < 0.05$). As PVS severity increased, PVD_s gradually decreased, and PVDR conversely increased. The differences in PVD_s and PVDR among the mild, moderate, and severe PVS groups were statistically significant (all $P < 0.05$).

When PVS occurred, the flow velocity at the stenotic site significantly increased, and pre-stenotic flow velocity showed varying magnitudes of decrease. As shown in Table 1 and Figure 3e-g, the PVV_{pre} of the moderate PVS group was significantly lower than the PVV of the PH group, and the PVV_{pre} of the severe PVS group was significantly lower than that of the PH and mild PVS groups (all $P < 0.05$). The PVV_s among the mild, moderate, and severe PVS groups were significantly higher than the PVV of the PH group (all $P < 0.05$). As PVS severity increased, PVV_s and PVVR increased. The differences in PVV_s and PVVR among the mild, moderate, and severe PVS groups were statistically significant (all $P < 0.05$).

Hepatic artery hemodynamic changes

When PVS occurred, hepatic artery PSV showed varying degrees of increase, and the PSV of the severe PVS group was significantly higher than that of the 70% PH group ($P < 0.05$, Table 1 and Figure 3h). There were no significant differences in EDV or RI among the various groups (all $P > 0.05$).

Evaluation of ultrasonography in portal vein stenosis diagnosis and grading of stenosis severity

Surgical PVS severity is the gold standard for PVS diagnosis. When diagnosing PVS, an ROC curve was plotted with the PH group as negative and the mild, moderate, and severe PVS groups as positive results. For identifying >50% PVS, the mild PVS group was used as the negative samples, and the moderate and severe PVS groups were used as positive samples for plotting the ROC curve. For identifying >65% PVS, the mild and moderate PVS groups were used as the negative samples, and the severe PVS group was used as the positive samples to plot the ROC curve.

The AUCs of PVD_{pre}, PVD_s, PVD_{post}, PVV_{pre}, and PVV_s in PVS diagnosis were significantly larger than the diagnostic reference AUC ($P < 0.05$ vs. AUC: 0.05, Table 2 and Figure 4a, b). The AUCs of PVD_s and PVV_s were 0.998 and 0.958, respectively. When PVD_s was <1.37 mm or PVV_s was >25.85 cm/s, their sensitivity and specificity were 98.61% and 100% or 83.33% and 100%, respectively.

Table 1. US parameters in different groups

US parameter	PH	Mild PVS	Moderate PVS	Severe PVS
PVD_s	1.94 ± 0.38	1.10 ± 0.17[a]	0.97 ± 0.16[a, b]	0.76 ± 0.06[a, b, c]
PVD_{pre}	1.94 ± 0.38	2.10 ± 0.40	2.58 ± 0.63[a, b]	2.60 ± 0.35[a, b]
PVD_{post}	1.94 ± 0.38	2.13 ± 0.37	2.30 ± 0.41[a]	2.13 ± 0.41
PVDR	-	1.97 ± 0.60	2.73 ± 0.85[b]	3.43 ± 0.51[b, c]
PVV_s	14.80 ± 4.70	43.15 ± 18.64[a]	51.86 ± 30.73[a]	80.50 ± 38.49[a, b, c]
PVV_{pre}	14.80 ± 4.70	11.56 ± 4.18	9.72 ± 3.48[a]	8.43 ± 3.67[a, b]
PVVR	-	4.03 ± 1.91	5.33 ± 3.09	10.33 ± 4.90[b, c]
HA PSV	42.65 ± 16.37	53.61 ± 16.55	56.86 ± 25.44	59.69 ± 17.37[a]

[a]$P < 0.05$ vs. PH group; [b]$P < 0.05$ vs. mild PVS group; [c]$P < 0.05$ vs. moderate group. US, ultrasound; PVS, portal vein stenosis; PH, partial hepatectomy; HA PSV, hepatic artery peak systolic velocity.

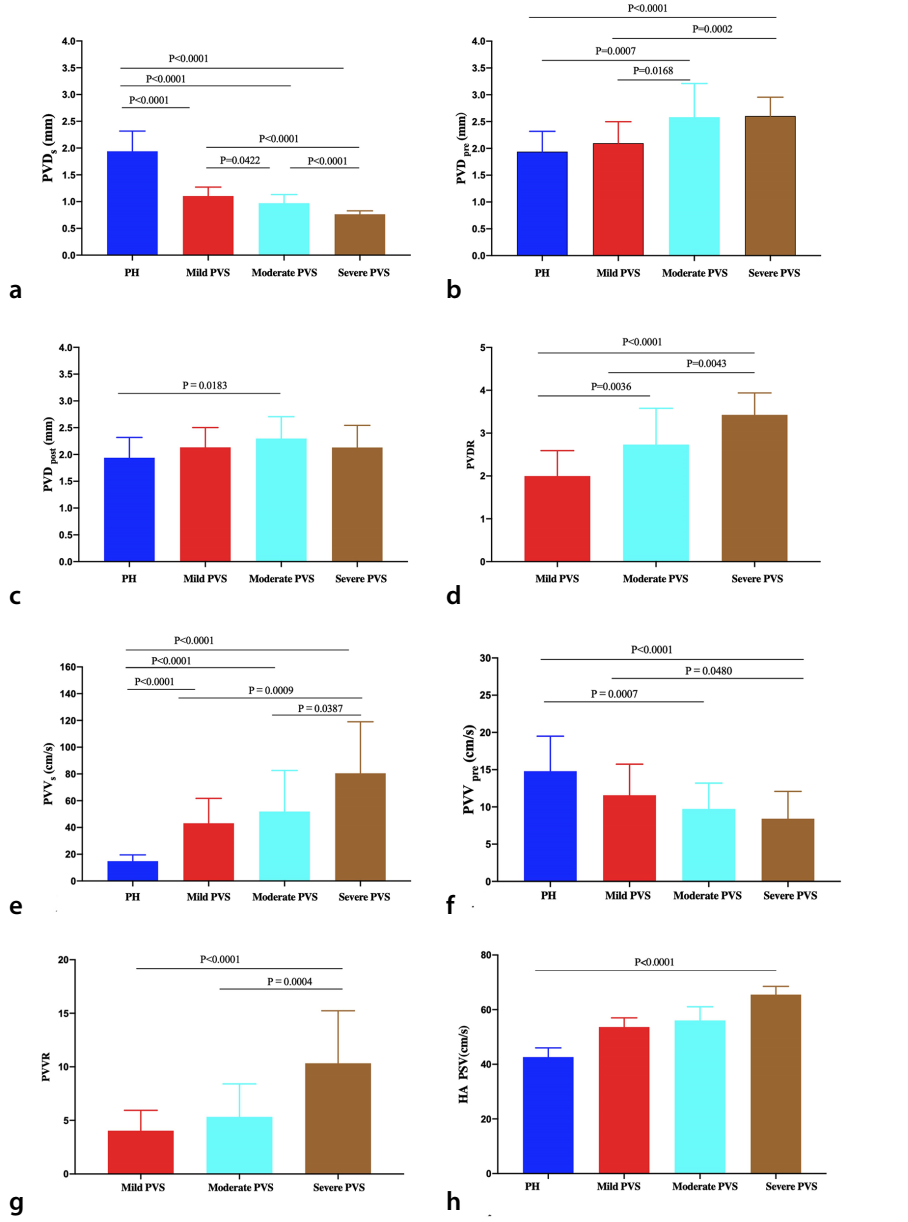

Figure 3. Ultrasound parameters in different groups. **(a)** Portal vein diameter at the stenotic site (PVD_s). **(b)** Portal vein diameter at the pre-stenotic site (PVD_{pre}). **(c)** Portal vein diameter at the post-stenotic site (PVD_{post}). **(d)** Portal vein diameter ratio (PVDR, PVD_{pre}/PVD_s). **(e)** Portal vein velocity at the stenotic site (PVV_s). **(f)** Portal vein velocity at the pre-stenotic site (PVV_{pre}). **(g)** Portal vein velocity ratio (PVVR, PVV_s/PVV_{pre}). **(h)** Hepatic artery peak systolic velocity (PSV).

With regards to PVS stenosis severity grading, the AUCs of PVD_s, PVD_{pre}, PVDR, PVV_s, PVV_{pre}, and PVVR were significantly higher than the diagnostic reference AUC when used to identify >50% PVS and >65% PVS. For identifying >50% PVS, PVD_s and PVDR were better than other parameters, with AUCs of 0.85 and 0.86, respectively. When PVD_s was <0.95 mm or PVDR >2.51, their sensitivity and specificity were 75.00% and 83.33% or 77.08% and 87.50%, respectively (Table 2 and Figure 4c, d). For identifying >65% PVS, PVD_s, PVDR, and PVVR were relatively better than other parameters, with AUCs of 0.94, 0.85, and 0.88, respectively. When PVD_s was <0.87 mm, PVDR was >2.82, or PVVR was >5.43, their sensitivity and specificity were 100% and 81.25%, 91.67% and 77.08%, or 87.50% and 72.92%, respectively (Table 2 and Figure 4e, f).

As shown in Table 2 and Figure 5, the AUC of hepatic artery PSV in predicting PVS was 0.711, and when used to identify >50% PVS and >65% PVS, the AUC of hepatic artery PSV was 0.666 and 0.733, respectively (all $P < 0.05$ vs. AUC: 0.05). When PSV was >51.15 cm/s, the sensitivity of identifying >65% PVS reached 87.50%, whereas the specificity was only 55.56%.

Discussion

Liver regeneration after LDLT is key to postoperative patient survival. Portal vein blood flow accounts for 75%–80% of the total blood flow volume in the liver. On one hand, this provides nutrient-rich blood from the intestines to liver tissues. On the other hand, this blood acts as a carrier of hepatocyte growth factors, hormones, and related receptors that play a vital role in liver regeneration. Therefore, sufficient portal vein blood supply is one of the prerequisites for the survival of the graft. PVS is one of the major vascular complications after LDLT. It may occur within 1 month after liver transplantation or may be late-onset (≥3 months after surgery).[20,21] Although PVS is not as acute as hepatic artery complications, its early clinical manifestations are not specific, and severe PVS significantly reduces liver blood supply and severely impairs the function of the transplanted liver, leading to graft failure.[3-6] In addition, the incidence of PVS is relatively high in pediatric LDLT due to factors such as small recipient portal vein size, dysplasia, and mismatched donor-recipient PVD.[4,5] In clinical practice, symptomatic treatment (such as balloon dilatation or stent implantation) is usually performed when there is significant hepatic dysfunction or portal hypertension.[7-9] However, hepatocyte structure and function may have undergone irreversible damage at this point, resulting in grafts being in a state of poor regeneration for a long time, even after treatments are applied. Therefore, early diagnosis of PVS and accurate grading of stenosis severity promote early intervention and thus increase the survival rate of patients.

Ultrasonography is the preferred imaging method for the early diagnosis of vascular complications after liver transplantation. Conventional grayscale ultrasound can clearly show the liver parenchyma and portal vein and accurately measure the PVD. Doppler ultrasound can monitor portal vein blood flow for disturbances, observe the blood flow direction, and obtain blood flow velocity infor-

Table 2. Results of ROC analysis in grading PVS by ultrasound

	US index	AUC	Standard error	*P* value	95% confidence interval		Best cut-off	Sensitivity (%)	Specificity (%)
					Lower bound	Upper bound			
PVS	PVD_s (mm)	0.998	0.002	<0.0001	0.994	1.000	<1.37	98.61	100.00
	PVD_{pre} (mm)	0.776	0.051	<0.0001	0.675	0.877	>2.13	68.06	79.17
	PVD_{post} (mm)	0.694	0.062	0.0045	0.574	0.815	>2.11	62.50	75.00
	PVV_s (cm/s)	0.958	0.018	<0.0001	0.922	0.994	>25.85	83.33	100.00
	PVV_{pre} (cm/s)	0.793	0.048	<0.0001	0.699	0.886	<11.60	69.44	79.17
	HA PSV (cm/s)	0.711	0.058	0.0020	0.5969	0.8250	>46.90	73.61	62.50
>50% PVS	PVD_s (mm)	0.850	0.050	<0.0001	0.760	0.940	<0.95	75.00	83.33
	PVD_{pre} (mm)	0.790	0.060	<0.0001	0.680	0.900	>2.54	62.50	87.50
	PVD_{post} (mm)	0.520	0.070	0.7335	0.380	0.670	-	-	-
	PVDR	0.860	0.050	<0.0001	0.760	0.950	>2.51	77.08	87.50
	PVV_s (cm/s)	0.690	0.060	0.0094	0.570	0.810	>52.60	62.50	75.00
	PVV_{pre} (cm/s)	0.670	0.070	0.0169	0.540	0.810	<8.00	45.83	83.33
	PVVR	0.770	0.050	0.0002	0.660	0.880	>4.79	72.92	75.00
	HA PSV (cm/s)	0.666	0.047	0.0010	0.574	0.759	>48.45	72.73	56.06
>65% PVS	PVD_s (mm)	0.940	0.030	<0.0001	0.880	1.000	<0.87	100.00	81.25
	PVD_{pre} (mm)	0.650	0.060	0.0417	0.520	0.770	>2.14	95.83	47.92
	PVD_{post} (mm)	0.580	0.070	0.2900	0.440	0.710	-	-	-
	PVDR	0.850	0.040	<0.0001	0.760	0.940	>2.82	91.67	77.08
	PVV_s (cm/s)	0.767	0.060	0.0002	0.650	0.880	>52.60	79.17	64.58
	PVV_{pre} (cm/s)	0.670	0.070	0.0169	0.540	0.800	<8.85	70.83	62.50
	PVVR	0.880	0.040	<0.0001	0.810	0.960	>5.43	87.50	72.92
	HA PSV (cm/s)	0.733	0.051	0.0007	0.633	0.832	>51.15	87.50	55.56

PVS, portal vein stenosis; US, ultrasound; PVD_s, portal vein diameter at the stenotic site; PVD_{pre}, portal vein diameter at the pre-stenotic site; PVD_{post}, portal vein diameter at the post-stenotic site; PVV_s, portal vein velocity at the stenotic site; PVV_{pre}, portal vein velocity at the pre-stenotic site; PVDR, portal vein diameter ratio (PVD_{pre}/PVD_s); PVVR, portal vein velocity ratio (PVV_s / PVV_{pre}); HA PSV, hepatic artery peak systolic velocity.

mation. Mild stenosis (SR <50%) at the portal vein anastomosis usually does not lead to significant hemodynamic changes. When significant PVS occurs, grayscale ultrasound will show local lumen narrowing, whereas Doppler ultrasound will demonstrate disturbance of blood flow at the stenotic site with a faster blood flow velocity. Currently, there are no unified ultrasonic diagnostic criteria for PVS in clinical practice. In China, a PVD of <2.5–3.5 mm at the stenotic site, a blood flow velocity at the stenotic site >150 cm/s, or a velocity ratio between stenotic and pre-stenotic flow ≥4 is regarded as the diagnostic criterion for PVS.[6,10-12] Mullan et al.[13] defined a maximal blood velocity >80 cm/s at the stenotic segment of the portal vein as the diagnostic criterion for PVS, with a sensitivity of 100% and a specificity of 84%. Chong et al.[22] used a maximal blood velocity >125 cm/s at the stenotic segment of the portal vein as the PVS diagnostic criterion, which had a specificity of 95% and a sensitivity of 73%. Moreover, the grading criteria in ultrasonography for PVS severity are not clear.

In this study, partial portal vein ligation was carried out based on the 70% PH rat model to simulate different degrees of PVS after LDLT. This model is easy to construct, stable, and facilitates hemodynamic monitoring. When PVS occurred, PVD decreased at the stenotic site, and PVD at the pre-stenotic and post-stenotic sites showed varying degrees of increase. Furthermore, stenotic PVV significantly increased, whereas pre-stenotic PVV showed varying degrees of decrease. The PVD_s, PVDR, PVV_s, and PVVR of the mild, moderate, and severe PVS groups showed significant gradient changes. More severe stenosis led to lower PVD_s, higher PVV_s, and larger PVDR and PVVR. Among the various portal vein hemodynamic parameters, PVD_s and PVV_s showed good performance in diagnosing PVS, followed by PVD_{pre} and PVV_{pre}, whereas PVD_{post} showed relatively poor performance. In grading PVS severity, PVD_s, PVD_{pre}, PVDR, PVV_s, PVV_{pre}, and PVVR demonstrated some diagnostic efficacy. Regarded as the standard with a high diagnostic value, an AUC >0.80 indicates that PVD_s and PVDR can effectively differentiate mild, moderate, and severe PVS, whereas PVVR showed good diagnostic performance in identifying >65% PVS. In contrast, PVD_{pre}, PVV_s, and PVV_{pre} showed relatively poor performance in grading PVS severity. After PH, the residual liver will be in a hyperdynamic circulatory state, and portal vein blood flow volume and velocity will increase. In this study, the construction of the surgical model and the grading and diagnostic criteria for PVS were all based on portal vein blood flow after PH. Additionally, there were inter-individual differences in parameters. Hence, the sample size should be expanded to further validate the PVS grading criteria.

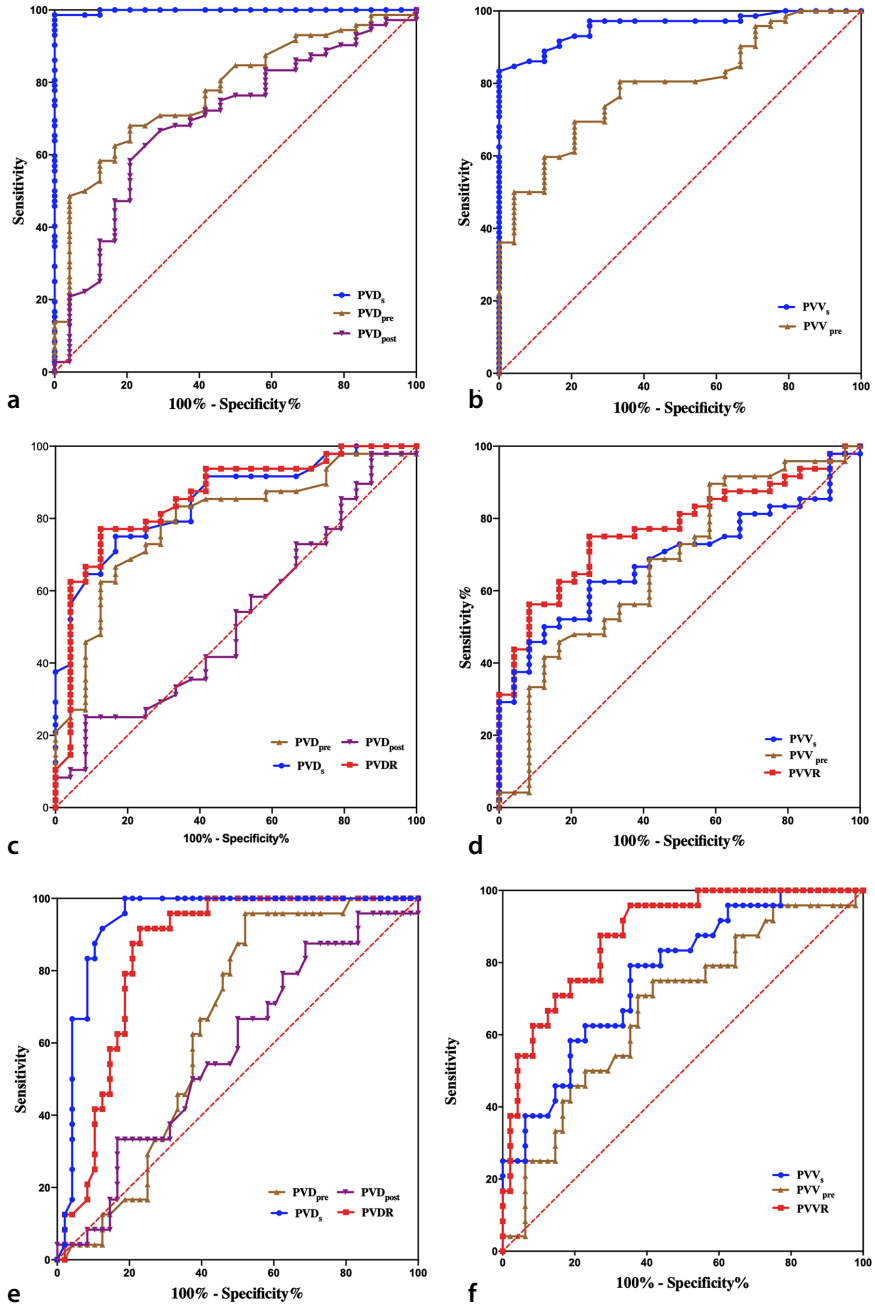

Figure 4. Receiver operating characteristic (ROC) curves of portal vein parameters in grading PVS. **(a, b)** ROC curves of PVD_s, PVD_{pre}, PVD_{post}, PVV_s, and PVV_{pre} in diagnosing PVS. **(c, d)** ROC curves of PVD_s, PVD_{pre}, PVD_{post}, PVDR, PVV_s, PVV_{pre}, and PVVR in identifying >50% PVS. **(e, f)** ROC curves of PVD_s, PVD_{pre}, PVD_{post}, PVDR, PVV_s, PVV_{pre}, and PVVR in identifying >65% PVS. PVS, portal vein stenosis; PVD_s, portal vein diameter at the stenotic site; PVD_{pre}, portal vein diameter at the pre-stenotic site; PVD_{post}, portal vein diameter at the post-stenotic site; PVV_s, portal vein velocity at the stenotic site; PVV_{pre}, portal vein velocity at the pre-stenotic site; PVDR, portal vein diameter ratio (PVD_{pre}/PVD_s); PVVR, portal vein velocity ratio (PVV_s/PVV_{pre}).

When significant changes in portal vein blood flow volume occur, the hepatic artery buffers these effects by adjusting the blood flow volume to maintain relative stability in the total blood flow volume of the liver. This phenomenon is known as the HABR. Under different severities of PVS, portal vein blood flow volume will exhibit varying degrees of decrease, and HABR can result in a compensatory increase in hepatic artery blood flow, leading to corresponding increases in blood flow volume and velocity.[14,15] In this study,

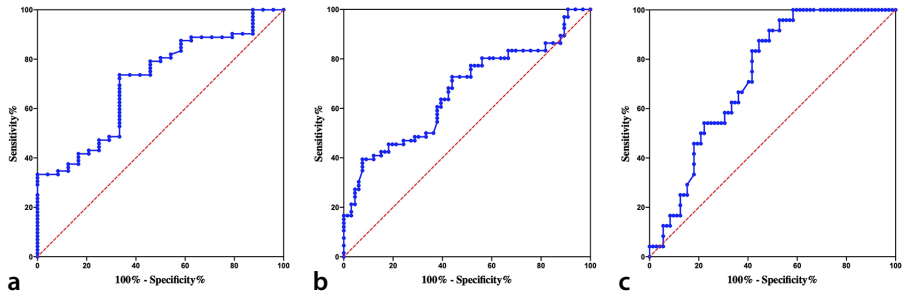

Figure 5. Receiver operating characteristic (ROC) curves of hepatic artery PSV in predicting PVS grade. **(a)** ROC curves of hepatic artery PSV in diagnosing PVS. **(b)** ROC curves of hepatic artery PSV in identifying >50% PVS. **(c)** ROC curves of hepatic artery PSV in identifying >65% PVS. PVS, portal vein stenosis; PSV, peak systolic velocity.

hepatic artery blood flow velocity in rats with different severities of PVS showed varying degrees of increase, with the most significant increase observed in cases of >65% PVS. The ROC analysis indicated that when hepatic artery PSV exceeded 51.15 cm/s, the sensitivity for identifying >65% PVS reached 87.50%. Therefore, significant increases in hepatic artery flow velocity can help predict >65% PVS. However, since the rat hepatic artery has a small inner diameter and a tortuous course, it tends to be influenced by heart rate and respiratory rate, leading to potential errors in the measurement of hemodynamic parameters by ultrasound. Consequently, the quantitative evaluation of hepatic artery compensation post-PVS requires further validation.

In conclusion, high-frequency greyscale and Doppler ultrasound can accurately demonstrate PVS and the hemodynamic changes it causes in rats. Portal vein hemodynamic parameters exhibit significant gradient changes among different degrees of PVS, classified as SR ≤50%, 50%< SR ≤65%, and SR >65%. PVDs and the PVDR are the best parameters for grading PVS. PVV can effectively diagnose the presence or absence of PVS, but its diagnostic performance in grading PVS is relatively low. The PVVR showed good performance in identifying >65% PVS. A significant increase in hepatic artery PSV may help evaluate PVS, particularly in predicting >65% PVS. These findings provide valuable information for PVS rat model research and an experimental basis for further studies on early PVS evaluation in LDLT.

Footnotes

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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