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Original Article

Clinical Characteristics and Outcomes of Portal Vein Thrombosis in Patients with Porto-sinusoidal Vascular Disease: A Cohort Study

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Abstract

Background and Aims: Portal vein thrombosis (PVT) frequently occurs in patients with porto-sinusoidal vascular disease (PSVD), but its clinical characteristics and outcomes remain poorly understood. This study aimed to investigate the clinical features and outcomes of PVT in PSVD. ***Methods:*** A total of 169 patients with PSVD confirmed by hepatic histology were included. PVT was diagnosed using contrast-enhanced magnetic resonance imaging or computed tomography. Demographic, clinical, and laboratory data, portal hypertension-related complications, comorbidities, and mortality were collected and compared between patients with and without PVT. The primary outcomes were baseline clinical characteristics and liver-transplantation-free mortality; the secondary outcome was the dynamic changes of PVT during follow-up. ***Results:*** At baseline, 45 (26.6%) PSVD patients had PVT. Compared to those without PVT, patients with PVT had significantly higher rates of esophageal variceal bleeding (62.2% *vs.* 29.0%), ascites (73.3% *vs*. 35.5%), antithrombin III deficiency (78.1% *vs.* 38.4%) (all $p < 0.001$), and a history of hematological disorders (11.1% *vs.* 0.8%, $p = 0.005$). After a median follow-up of 40.1 (23.4–62.3) months, liver-transplantation-free mortality rates were 7.9% (3/38) and 1.8% (2/112) in patients with and without PVT, respectively (log-rank $p = 0.110$). Among 41 patients followed for a median of 17.1 (7.4–39.3) months, PVT resolved in 9.1% (1/11) of those with baseline PVT and developed in 13.3% (4/30) of those without PVT at baseline. The one- and two-year cumulative incidence rates of PVT were 3.3% and 6.7%, respectively. ***Conclusions:*** PSVD patients with PVT experience more portal hypertension-related complications, complex coagulation profiles, hematological disorders, and a higher risk of death compared to those without PVT.

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Keywords: Portal vein thrombosis; Porto-sinusoidal vascular disease; Portal hypertension; Ascites; Variceal bleeding; Idiopathic non-cirrhotic portal hypertension; Superior mesenteric vein; Splenic vein; Mortality.

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Introduction

Porto-sinusoidal vascular disease (PSVD) refers to a group of hepatic vascular disorders that occur with or without portal hypertension in the absence of cirrhosis.[1] The etiology and pathogenesis of PSVD remain unclear.[2] PSVD may be associated with systemic conditions, including immunological disorders, hematologic diseases, infections, drug exposure, and hereditary or genetic disorders.[2–4] In some PSVD patients, the underlying cause remains unidentified.[5] Clinically, PSVD with portal hypertension is termed idiopathic non-cirrhotic portal hypertension, characterized by presinusoidal portal hypertension and a prothrombotic tendency, which may contribute to the development of portal vein thrombosis (PVT).[1]

PVT is defined as the obstruction or cavernous transformation of the main portal vein or its branches due to thrombus formation, which may extend to the superior mesenteric vein (SMV) and splenic vein (SV).[6] PVT can occur in both cirrhotic and non-cirrhotic portal hypertension.[7,8] A multicenter European cohort study reported that 29.5% (173/587) of PSVD patients had PVT,[9] while a Chinese study found a PVT prevalence of 25.0%.[10]

PVT is associated with several portal hypertension-related complications, including esophageal-gastric varices, esophageal variceal bleeding (EVB), hepatic encephalopathy, splenomegaly, ascites, and hepatorenal syndrome, which contribute to substantial morbidity and mortality in cirrhotic patients.[7,11,12] However, the clinical characteristics and outcomes of PVT in PSVD patients remain poorly understood. Therefore, the present study aimed to investigate the clinical characteristics and outcomes of PVT in patients with PSVD.

Methods

Patients

This was a retrospective-prospective cohort study. The PSVD

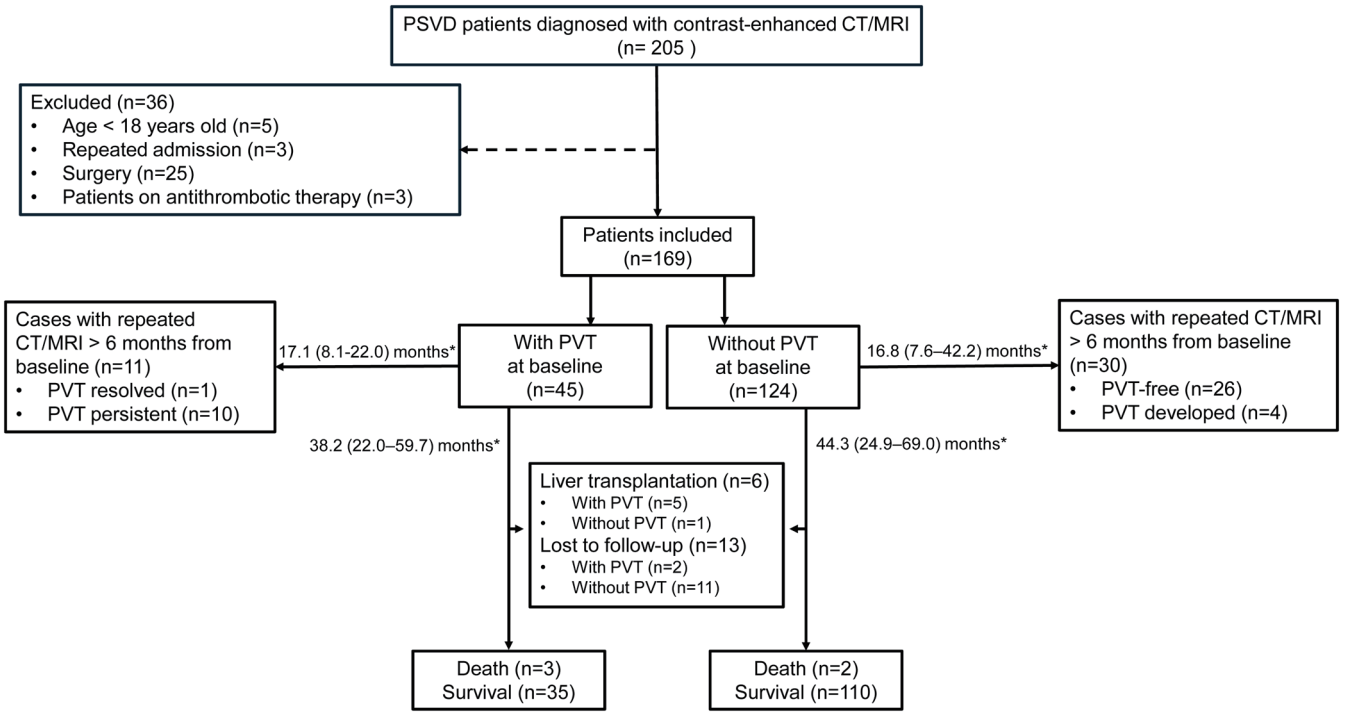

Fig. 1. Flowchart of enrolled patients with porto-sinusoidal vascular disease (PSVD) in the study. *, median (interquartile) duration of follow-up. PVT, portal vein thrombosis; CT, computed tomography; MRI, magnetic resonance imaging.

cohort was established at Beijing Youan Hospital between January 2010 and November 2023.

Patients were enrolled if they met the following inclusion criteria: 1) a definitive diagnosis of PSVD confirmed by hepatic histology and 2) routine evaluation with contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI). PSVD was diagnosed based on the criteria outlined in Baveno VII: 1) a good-quality liver biopsy without cirrhosis; 2) at least one specific histological lesion associated with PSVD (such as obliterative portal venopathy, nodular regenerative hyperplasia, or incomplete septal fibrosis) or one specific sign of portal hypertension (such as esophageal-gastric or ectopic varices, portal hypertensive gastropathy bleeding, or porto-systemic collaterals); and 3) at least one nonspecific histological feature (*e.g.*, portal tract abnormalities, irregular distribution of portal tracts and central veins, non-zonal sinusoidal dilation, or mild perisinusoidal fibrosis) and one nonspecific sign of portal hypertension (such as ascites, platelet count < 150 × 10^9/L, or spleen size > 13 cm).[2] Liver biopsies were performed via transjugular or percutaneous routes or as wedge biopsies during splenectomy or liver surgery. Exclusion criteria were as follows: 1) age under 18 years; 2) repeated admission; 3) previous surgeries or procedures associated with increased thrombotic risk, including splenectomy, transjugular intrahepatic portosystemic shunt, partial splenic embolization, or liver transplantation; and 4) previous use of anticoagulation therapy. The flowchart for patient enrollment is shown in Figure 1.

Baseline data

Baseline data included demographics, medical history, clinical manifestations and comorbidities, laboratory and endoscopic findings, liver stiffness measurement (LSM) assessed by ultrasound elastography, and CT or MRI performed at the time of pathological confirmation of PSVD. Clinical manifestations included portal hypertension-related complications, such as esophageal-gastric varices, EVB, splenomegaly, ascites, *etc.* Comorbidities were categorized as follows: 1) systemic diseases associated with PSVD, including immunological disorders, hematologic disorders, infections, drug exposure, and hereditary or genetic conditions; 2) chronic liver-related factors, including alcohol abuse and hepatitis B virus (HBV) infection; and 3) other comorbidities, such as hypertension and diabetes. HBV infection was defined as HBsAg positivity. Protein C, protein S, and antithrombin III (AT-III) levels were measured using coagulation-based functional assays to diagnose corresponding deficiencies. Thromboelastography (TEG) was performed using a TEG-5000 device (Haemoscope Corporation, USA) according to the manufacturer's instructions. LSM was measured using FibroScan® (France Ikoson Medical Technology Co., Ltd). High-risk varices (HRV) were defined endoscopically as: 1) medium or large varices (≥5 mm), or 2) small varices with red signs. Specific and nonspecific histological lesions of PSVD (as defined by consensus),[1] stenosis, and the stage of fibrosis and hepatic inflammatory activity (assessed using the METAVIR scoring system) were independently re-assessed by an experienced pathologist (H.L., with more than 20 years of experience).[13]

Diagnosis of PVT and evaluation of its characteristics

PVT was diagnosed and assessed using contrast-enhanced CT or MRI images. PVT was defined as thrombosis within the left or right branch of the portal vein (intrahepatic PVT), the main portal vein (extrahepatic PVT), the SMV, or the SV.[14] The severity of PVT was classified according to the Yerdel grading system.[15]

Follow-up of patients

All patients were followed up by telephone or through out-

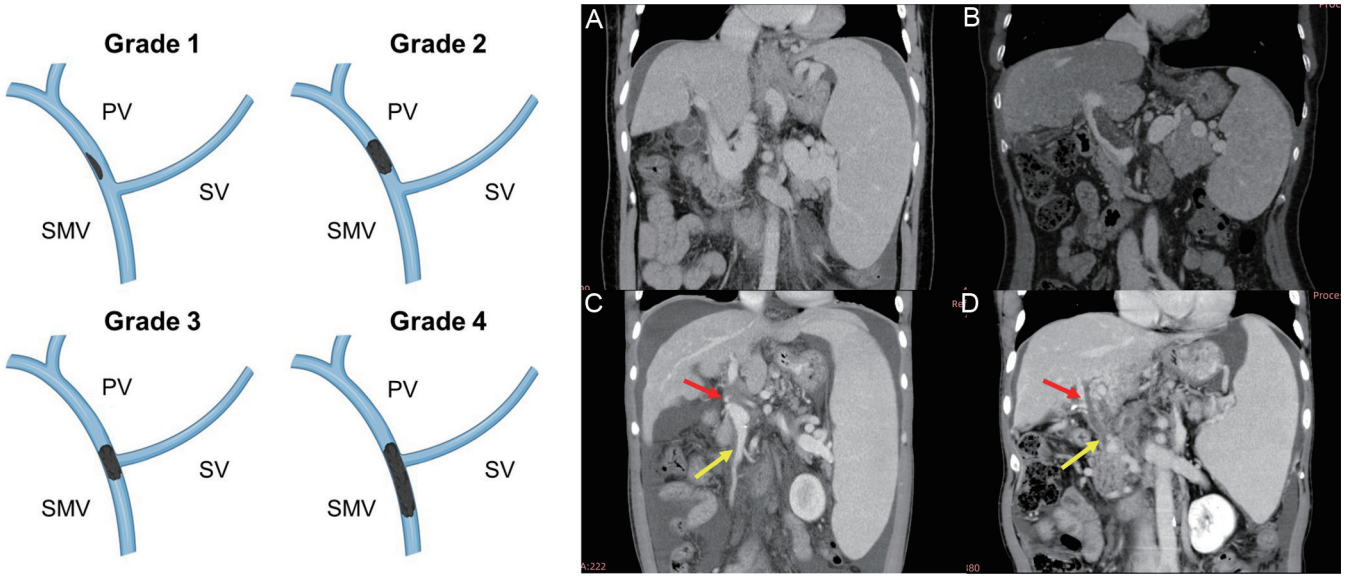

Fig. 2. Yerdel classification of portal vein thrombosis. A: grade 1, < 50% occlusion of the main portal vein (PV) with no or minimal obstruction of the superior mesenteric vein (SMV, top left of left panel); B: grade 2, > 50% obstruction of main PV, including total obstruction (top right of left panel); C: grade 3, complete obstruction of main PV and proximal SMV (bottom left of left panel); D: grade 4, complete obstruction of the PV and SMV (bottom right of left panel). Red arrow: thrombosis in the PV; yellow arrow: thrombosis in the SMV. SV, splenic vein.

patient/inpatient records until 1) death, liver transplantation, or loss to follow-up; 2) undergoing any surgical or radiological interventional procedures; or 3) December 30, 2024. Patients who underwent CT or MRI at least six months after baseline without thrombosis-related surgical interventions during follow-up were assessed for PVT evolution.[16] Additionally, data on concurrent medications, including anticoagulants and non-selective beta-blockers (NSBBs), were collected at baseline and during follow-up.

Primary and secondary outcomes

The study outcomes were defined to assess baseline clinical characteristics, prognostic impact, and incidence of PVT in PSVD patients. Primary outcomes included baseline clinical characteristics (such as demographics, portal hypertension-related complications, complex coagulation profiles, and hematological disorders) and liver-transplantation-free mortality. The secondary outcome was the evaluation of PVT status during follow-up, including persistence or resolution (*i.e.*, disappearance of previous thrombus) in patients with baseline PVT, and PVT-free status or development of PVT in those without PVT at baseline throughout the follow-up period.[16]

Statistical analysis

For statistical analysis, normally distributed continuous variables were summarized using mean ± standard deviation, while non-normally distributed continuous variables were expressed as median (IQR). Categorical variables were reported as frequencies and percentages. Normality of continuous variables was assessed using normality tests and Q-Q plots, and appropriate statistical methods were applied based on data distribution. For comparisons of continuous variables, Welch's t-test or ANOVA was used for normally distributed data, and the Wilcoxon rank-sum test or Kruskal-Wallis test was used for non-normally distributed data. For categorical data, Fisher's exact test was applied when expected frequencies were less than 5; otherwise, the Chi-square test was used. Kaplan–Meier survival curves were generated to evaluate liver-transplantation-free survival relative to the presence of PVT, as well as across different PVT locations (intrahepatic, extrahepatic, SV, and SMV) and Yerdel grades. Cox proportional hazards regression was used to examine potential multivariable confounders. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated for all covariates. The illustration of Yerdel's classification was created using BioRender software (BioRender, Toronto, ON, Canada). All statistical analyses were performed using R software (version 4.2.2) and Stata software (www.stata.com). A p-value < 0.05 was considered statistically significant.

Results

Study population

A total of 205 PSVD patients who underwent contrast-enhanced CT or MRI were initially included in this study. Thirty-six patients were excluded due to age under 18 years (n = 5), repeated admissions (n = 3), previous surgical procedures (n = 25), and anticoagulant therapy (n = 3). Thus, 169 patients, 83 males and 86 females, with a median age of 51 (37–60) years, were finally included (Fig. 1). Two PSVD patients did not exhibit specific or nonspecific signs of portal hypertension at diagnosis. Eighteen patients had immune-related diseases, four received targeted tyrosine kinase inhibitors or immunotherapy for gastrointestinal cancers, seven had hematological disorders, and 39 had no identifiable underlying disease or etiology associated with PSVD. Five patients had a history of alcohol abuse, and one patient was positive for active HBsAg.

Among the 169 patients, 156 (92.3%) underwent contrast-enhanced CT, and 13 (7.7%) underwent MRI. PVT was diagnosed in 45 (26.6%) patients at baseline. Of these, 10 (22.2%), 17 (37.8%), two (4.4%), and six (13.3%) had Yerdel grades 1, 2, 3, and 4, respectively (Fig. 2). The remaining 10 patients could not be classified using the Yerdel system because thrombosis was limited to branches of the portal vein, SV, or SMV.

Clinical characteristics

Table 1 compares demographic and baseline clinical data between PSVD patients with and without PVT. Patients with PVT were significantly older than those without PVT (55 [48–63] *vs.* 49 [34–59] years, $p < 0.05$). No significant difference in gender distribution was observed between groups ($p = 0.754$). Compared to patients without PVT, those with PVT had significantly higher proportions of portal hypertension-related complications, including EVB (29.0% *vs.* 62.2%, $p < 0.001$), ascites (35.5% *vs.* 73.3%, $p < 0.001$), and HRV (71.1% *vs.* 97.1%, $p = 0.003$). Additionally, patients with PVT had significantly lower levels of white blood cells, red blood cells, hemoglobin, platelets, albumin, and cholinesterase, but higher prothrombin time, international normalized ratio, and greater prevalence of AT-III deficiency. No significant differences were noted in protein C or S deficiency or TEG parameters, including R, K, MA, angle, CI, G, and LY30.

Regarding medical history, PSVD patients with PVT had a higher prevalence of hematologic diseases ($p = 0.005$) and hypertension ($p = 0.037$) compared to those without PVT. There were no significant differences in alcohol abuse or HBV infection between groups (Table 2), nor in liver fibrosis stage, inflammatory cell infiltration, or steatosis (Table 3). Compared to patients without PVT, those with PVT had higher rates of nodular regenerative hyperplasia ($p = 0.043$) and thickening of the portal vessel wall ($p < 0.001$, Table 3 and Fig. 3).

PVT at baseline and outcomes

Of the 169 patients, 156 (92.3%) were followed up by telephone or medical records for a median of 39.8 (23.1–62.4) months. Thirteen (7.7%) patients were lost to follow-up. Follow-up duration did not significantly differ between patients with and without PVT (38.2 [22.0–59.7] *vs.* 44.3 [24.9–69.0] months). After excluding six patients who underwent liver transplantation, 150 patients remained for survival analysis, including five deaths and 145 survivors, over a median follow-up of 40.1 (23.4–62.3) months. Liver-transplantation-free mortality rates were 7.9% (3/38) for patients with PVT and 1.8% (2/112) for those without PVT. Although mortality was higher in patients with PVT, Kaplan–Meier analysis showed no statistically significant difference in liver transplantation-free survival between the groups (log-rank $p = 0.110$; Fig. 4A). However, subgroup analysis by Yerdel grade revealed significantly higher mortality in patients with grade 1 PVT (22.2%, 2/9) compared to those without PVT (1.8%, 2/112; log-rank $p = 0.006$; Fig. 4B). No significant mortality differences were observed among patients with intrahepatic PVT (1/30 [3.3%], $p = 0.69$), extrahepatic PVT (2/29 [6.9%], $p = 0.69$), SV thrombosis (1/11 [9.1%], $p = 0.18$), or SMV thrombosis (1/11 [9.1%], $p = 0.69$) (Supplementary Fig. 1).

Cox proportional hazards regression indicated that PSVD patients with PVT had a fourfold increased risk of liver transplantation-free mortality (HR = 3.98; 95% CI: 0.66–23.96; $p = 0.131$; Table 4). In multivariable models adjusting for age and one additional covariate, HRs for PVT ranged from 1.93 to 5.10, none reaching statistical significance (all $p > 0.1$) (Supplementary Table 1). Conversely, patients with grade 1 PVT had a tenfold increased risk of liver transplantation-free mortality (HR = 9.5; 95% CI: 1.33–67.94; $p = 0.025$; Table 4). After adjusting for age, this risk remained elevated (HR = 7.32; 95% CI: 0.99–54.30; $p = 0.051$). In multivariable Cox models controlling for age and one additional covariate, the HR for grade 1 PVT predicting liver transplantation-free mortality ranged from 2.61 to 15.71, with significant associations observed in models including ascites (HR = 8.00; 95% CI: 1.08–58.97; $p = 0.041$) and comorbidities (HR = 15.71; 95% CI: 1.28–192.55; $p = 0.031$) (Supplementary Table 2).

Evolution of PVT during the follow-up

Overall, 41 PSVD patients (11 with PVT and 30 without PVT at baseline) underwent a second contrast-enhanced CT or MRI at least six months after baseline. Among the 11 patients with PVT, three received anticoagulation therapy: one with low-molecular-weight heparin and two with direct oral anticoagulants. The thrombus resolved in the patient treated with low-molecular-weight heparin and remained stable in the other 10 patients over a median follow-up of 17.1 (8.1–22.0) months (Fig. 1). Among the 30 patients without PVT, four (13.3%) developed PVT during a median follow-up of 16.8 (7.6–42.2) months; three of these had been treated with NSBBs. The remaining 26 patients did not develop PVT, of whom three had received NSBBs (propranolol or carvedilol). The cumulative incidence of PVT was 3.3% at one year and 6.7% at two years.

Discussion

This study provides comprehensive insights into the burden, risk factors, and clinical outcomes of PVT in patients with PSVD. Three primary findings were identified: 1) at baseline, 26.6% of PSVD patients had PVT, and this group exhibited more severe clinical features, including a higher prevalence of portal hypertension-related complications, abnormal coagulation profiles, and a greater proportion of underlying hematologic or prothrombotic disorders; 2) regarding prognosis, PSVD patients with baseline PVT had higher liver-transplantation-free mortality (7.9% vs. 1.8%), although this difference did not reach statistical significance; 3) among 30 patients without PVT at baseline, four (12.9%) developed new-onset PVT during follow-up. In contrast, most patients with baseline PVT had persistent thrombosis, with recanalization being uncommon.

The observed prevalence of PVT in this PSVD cohort was 26.6%, comparable to the 25% reported by Ma *et al.* in another Chinese cohort,[10] but notably higher than the 6.0% reported in a European cohort.[9] This discrepancy may reflect differences in diagnostic timing and awareness of PSVD. Our cohort included patients diagnosed between 2010 and 2023, a period during which PSVD was not widely recognized in clinical practice, especially in the earlier years. Moreover, the diagnosis of PSVD relies on liver pathology, often leading to delays in clinical diagnosis. In our cohort, the average time from onset of clinical symptoms (*e.g.*, abnormal liver function, splenomegaly, thrombocytopenia, or variceal bleeding) to confirmed diagnosis was 30 months, similar to the 20-month delay reported in Ma's study.[10] Additionally, the one-year and two-year cumulative incidence rates of PVT in our cohort were 3.3% and 6.7%, respectively, aligning with previous findings of 5% and 7%.[9]

This study found that PSVD patients with PVT exhibited more severe portal hypertension, as evidenced by significantly higher proportions of EVB, ascites, and HRV, as well as significantly lower levels of white blood cells, red blood cells, and platelets. They also presented with more impaired hepatic synthetic function, indicated by significantly lower levels of cholinesterase and albumin. This may reflect the impact of reduced portal venous inflow on hepatic metabolic capacity and regeneration.[17] Although alanine aminotransferase and aspartate aminotransferase levels were lower in PSVD patients with PVT, median values in both groups remained within normal reference ranges. Furthermore, liver pathology showed no evidence of inflammatory cell infiltration regard-

Table 1. Comparison of baseline demographic, clinical, and laboratory characteristics between PSVD patients with and without PVT

Variables	PSVD with PVT (n = 45)	PSVD without PVT (n = 124)	*p*-value
Age (years)	55 (48–61)	49 (34–59)	0.016
male	23 (51.1)	60 (48.4)	0.754
EVB	28 (62.2)	36 (29.0)	<0.001
Ascites	33 (73.3)	44 (35.5)	<0.001
HRV	34 (97.1)	64 (71.1)	0.003
LSM (kPa)	9.70 (7.90–17.50)	9.10 (6.60–11.90)	0.067
WBC (10^9/L)	2.41 (1.70–3.07)	3.15 (2.12–4.73)	0.024
RBC (10^{12}/L)	3.49 ± 1.13	3.89 ± 0.86	0.035
HGB (g/L)	96 ± 31	109 ± 29	0.014
PLT (10^9/L)	60 (37–106)	82 (54–130)	0.023
ALT (U/L)	16 (12–24)	22 (15–33)	0.004
AST (U/L)	21 (17–27)	27 (19–35)	0.007
TBil (μmol/L)	23 (14–32)	17 (13–25)	0.077
ALB (g/L)	35 (33–40)	39 (36–42)	0.005
GGT (U/L)	21 (13–29)	38 (23–59)	<0.001
CHE (U/L)	4,607 ± 1,777	5,700 ± 1,808	0.003
Cr (μmol/L)	61 (50–77)	58 (50–67)	0.148
PT (s)	13.30 (12.30–14.60)	12.00 (11.05–13.15)	<0.001
PTA (%)	74 ± 15	83 ± 12	<0.001
INR	1.21 (1.11–1.32)	1.11 (1.05–1.19)	<0.001
APTT (s)	1.93 (1.56–2.30)	2.34 (1.98–2.73)	<0.001
Fib (g/L)	1.95 (1.56–2.32)	2.34 (1.97–2.74)	<0.001
D-dimer (Elevated)	22 (68.8)	33 (37.9)	0.003
FDP (Elevated)	12 (37.5)	13 (15.1)	0.008
MELD	9.77 (8.58–11.48)	8.14 (7.20–9.85)	<0.001
Child-Pugh scores	7 (6–8)	5 (5–7)	<0.001
Thromboelastography			
R (m)	5.70 (4.80–7.05)	5.50 (5.18–6.60)	0.95
K (m)	3.20 (2.15–3.95)	2.65 (2.20–3.15)	0.872
Angle (degree)	53 (46–60)	53 (46–58)	0.695
MA (mm)	47 ± 13	50 ± 7	0.303
G (dyn/cm^2)	4.30 (3.43–6.48)	4.85 (4.08–6.05)	0.255
CI	−2.66 ± 2.91	−2.57 ± 2.04	0.902
LY30 (%)	0.10 (0.10–0.10)	0.10 (0.10–0.10)	0.058
Test for thrombophilia			
AT-III deficiency	25 (78.1)	33 (38.4)	<0.001
Protein C deficiency	6 (66.7)	14 (60.9)	>0.999
Protein S deficiency	2 (25.0)	9 (42.9)	0.671

Data are expressed as numbers (%), means ± standard deviations, or medians (IQR), where appropriate. PSVD, porto-sinusoidal vascular disease; PVT, portal vein thrombosis; EVB, esophagogastric variceal bleeding; HRV, high-risk varices; LSM, liver stiffness measurement; WBC, white blood cell count; RBC, red blood cell count; HGB, hemoglobin; PLT, platelet count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin; ALB, albumin; GGT, gamma-glutamyl transferase; CHE, cholinesterase; Cr, creatinine; PT, prothrombin time; PTA, prothrombin activity; INR, international normalized ratio; APTT, activated partial thromboplastin time; Fib, fibrinogen; FDP, fibrin degradation product; MELD, model for end-stage liver disease; MA, maximum amplitude; G, clot strength; CI, coagulation index; LY30, clot lysis at 30 m; AT-III, antithrombin III.

Table 2. Comparison of comorbidities between PSVD patients with and without PVT

Comorbidities	PSVD with PVT (n = 45)	PSVD without PVT (n = 124)	*p*-value
Immunological disorders	6 (13.3)	20 (16.2)	0.656
HIV infection	NA	1 (0.8)	
Connective tissue disease	NA	1 (0.8)	
Psoriasis	1 (2.2)	6 (4.9)	
Rheumatoid arthritis	-	1 (0.8)	
Systemic lupus erythematosus	1 (2.2)	2 (1.6)	
Primary Sjögren's syndrome	NA	1 (0.8)	
Neurodermatitis	NA	1 (0.8)	
Connective tissue disease	1 (2.2)	NA-	
Primary sclerosing cholangitis	1 (2.2)	NA	
Hydatidiform mole	NA	1 (0.8)	
POEMS	1 (2.2)	NA	
Hypothyroidism or hyperthyroidism	1 (2.2)	6 (4.9)	
Chemotherapy for cancer treatment	0 (0.0)	4 (3.2)	0.574
Hematological diseases	5 (11.1)	1 (0.8)	0.005
JAK2V617F positive	1 (2.2)	-	
Castleman	1 (2.2)	1 (0.8)	
Myeloproliferative neoplasm	3 (6.5)	-	
Hypertension	5 (13.0)	5 (4.0)	0.037
Diabetes	4 (8.7)	8 (6.5)	0.286
Known chronic liver diseases			
Alcohol abuse	1 (2.2)	4 (3.2)	>0.999
HBsAg (+)	1 (2.2)	0	0.271

Data are expressed as numbers (%). PSVD, porto-sinusoidal vascular disease; PVT, portal vein thrombosis; HIV, human immunodeficiency virus; POEMS, polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes syndrome; HBsAg, hepatitis B surface antigen; NA, not available.

Table 3. Comparison of histological features between PSVD patients with and without PVT

Variables	PSVD with PVT (n = 21)	PSVD without PVT (n = 55)	*p*-value
Specific histological changes			
Obliterative portal venopathy	18 (85.7)	43 (78.2)	0.538
Incomplete septal fibrosis	4 (19.0)	10 (18.2)	>0.999
Nodular regenerative hyperplasia	15 (71.4)	25 (45.5)	0.043
Non-specific histological changes			
Portal vein dilatation	11 (52.4)	37 (67.3)	0.229
Periportal abnormal vessels	5 (23.8)	18 (32.7)	0.449
Thickening of the portal vessel wall	18 (85.7)	23 (41.8)	<0.001
Herniated portal venules	6 (28.6)	5 (9.1)	0.062
Sinusoidal dilatation	10 (47.6)	31 (56.4)	0.494
Peri-venular fibrosis	16 (76.2)	40 (72.7)	0.759
Fibrosis stage (F2–3)	11 (52.4)	30 (54.5)	0.866
Inflammatory stage (G2–3)	5 (23.8)	9 (16.7)	0.517
Hepatic steatosis	2 (9.5)	2 (3.6)	0.304

Data are expressed as numbers (%). PSVD, porto-sinusoidal vascular disease; PVT, portal vein thrombosis.

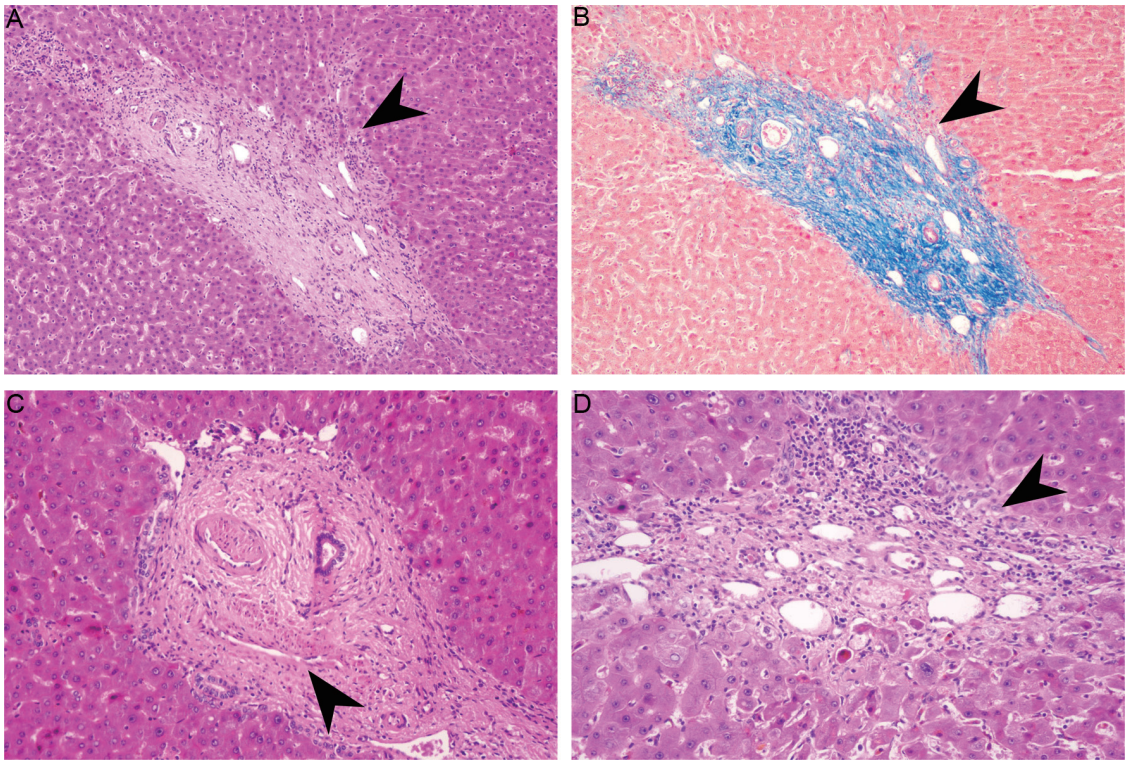

Fig. 3. Representative histological features of a 56-year-old female PSVD patient with PVT. A: Hematoxylin and eosin (HE)–stained image showing obliterative portal venopathy (OPV) (×100, black arrowhead); B: Masson's staining of OPV (×100, black arrowhead); C: HE-stained section highlighting OPV under higher magnification (×200, black arrowhead); D: HE-stained image demonstrating thickening of the portal vein wall (black arrowhead). PSVD, porto-sinusoidal vascular disease; PVT, portal vein thrombosis.

less of PVT presence. These findings suggest limited clinical and pathological relevance of hepatocellular injury in PSVD patients with PVT. The lack of significant differences in LSM and fibrosis stage indicates that PVT does not affect fibrosis progression but worsens portal hypertension.[18]

Our analysis of comorbidities and hemostatic parameters revealed that PSVD was frequently associated with thrombophilia. Consistent with a previous Chinese study,[10] we found that PSVD patients commonly presented with prothrombotic conditions (*e.g.*, myeloproliferative neoplasms), immunological disorders (*e.g.*, systemic lupus erythematosus), and histories of drug exposure (*e.g.*, glucocorticoids, oxaliplatin, chemotherapy agents). The prevalence of AT-III and protein C or S deficiencies in PSVD patients, especially those with

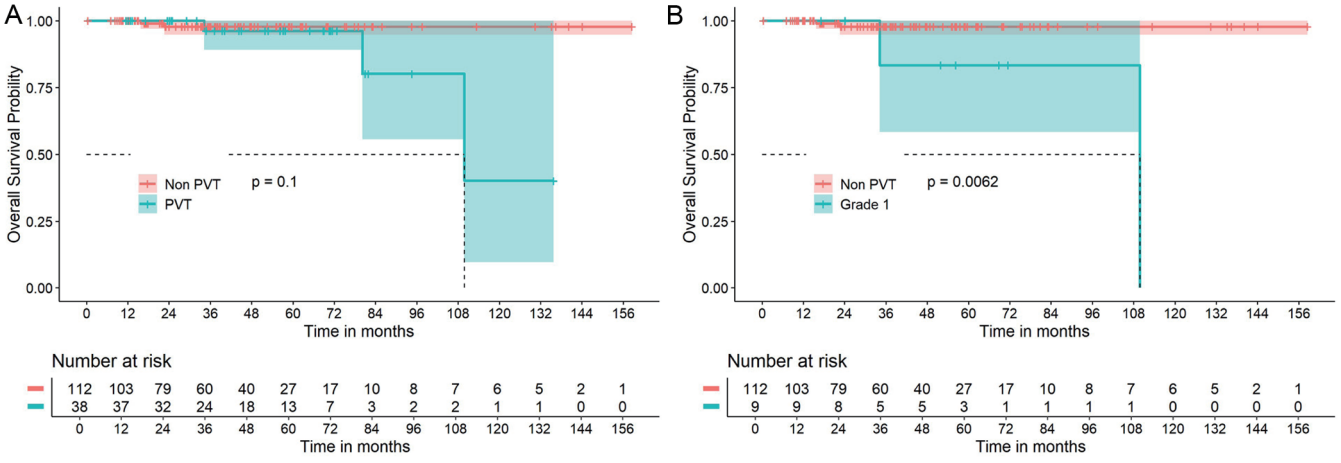

Fig. 4. Kaplan-Meier curves for overall survival in PSVD patients with PVT and Yerdel grade 1 PVT. A: Kaplan-Meier survival curves comparing overall survival between PSVD patients with and without PVT. Although patients with PVT tend to have lower survival rates, the difference is not statistically significant (p = 0.100). B: Kaplan-Meier survival curves comparing PSVD patients with Yerdel grade 1 PVT and those without PVT. Patients with Yerdel grade 1 PVT show significantly worse survival outcomes (p = 0.006). Shaded areas represent 95% confidence intervals (CI). The number at risk at each time point is shown below each panel. PSVD, porto-sinusoidal vascular disease; PVT, portal vein thrombosis.

Table 4. Cox regression analyses of the risk of mortality in PSVD patients

Variables	Univariate HR (95% CI)	*p*-value	Model 1 HR (95% CI)	*p*-value	Model 2 HR (95% CI)	*p*-value
Age (years)	1.11 (1.01–1.22)	0.037	1.11 (1.00–1.23)	0.051	1.13 (0.98–1.30)	0.096
Gender $_{(Female\ vs.\ Male)}$	5.54 $\times 10^8$ (0.00–Inf)	0.999				
Comorbidities $_{(Yes\ vs.\ No)}$	2.80 (0.46–17.14)	0.266				
EVB $_{(Yes\ vs.\ No)}$	3.29 (0.54–19.84)	0.195				
Ascites $_{(Yes\ vs.\ No)}$	0.78 (0.13–4.65)	0.781				
PVT $_{(Yes\ vs.\ No)}$	3.98 (0.66–23.96)	0.131	2.71 (0.45–16.32)	0.276		
PVT Grade 1 $_{(Yes\ vs.\ non\text{-}PVT)}$	9.50 (1.33–67.94)	0.025			7.32 (0.99–54.30)	0.051
WBC (10^9/L)	0.56 (0.24–1.31)	0.180				
RBC (10^{12}/L)	0.18 (0.06–0.55)	0.002				
HGB (g/L)	0.95 (0.91–0.99)	0.011				
PLT (10^9/L)	0.99 (0.97–1.01)	0.375				
ALT (U/L)	0.93 (0.84, 1.04)	0.204				
AST (U/L)	0.99 (0.93–1.04)	0.636				
TBil (μmol/L)	1.05 (1.01–1.09)	0.023				
ALB (g/L)	0.89 (0.79–1.00)	0.052				
GGT (U/L)	0.97 (0.92–1.03)	0.371				
CHE (U/L)	1.00 (1.00–1.00)	0.028				
Cr (μmol/L)	1.00 (0.94–1.06)	0.970				
PT (s)	1.49 (1.03–2.15)	0.032				
PTA (%)	0.93 (0.87–0.99)	0.019				
INR	209.09 (3.85–11,362.92)	0.009				
Child-Pugh class $_{(B+C\ vs.\ A)}$	1.37 (0.23–8.22)	0.734				

Data are expressed as median (IQR). Univariate Cox regression was performed for each variable. Two separate multivariate models were constructed: Model 1 included PVT and age; Model 2 included Yerdel grade 1 PVT and age. PSVD, porto-sinusoidal vascular disease; HR, hazard ratio; CI, confidence interval; EVB, esophagogastric variceal bleeding; PVT, portal vein thrombosis; WBC, white blood cell count; RBC, red blood cell count; HGB, hemoglobin; PLT, platelet count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin; ALB, albumin; GGT, gamma-glutamyltransferase; CHE, cholinesterase; Cr, creatinine; PT, prothrombin time; PTA, prothrombin activity; INR, international normalized ratio.

PVT, has been reported to be significantly higher than in the general Chinese Han population.[19] In our study, AT-III deficiency, but not protein C or S deficiency, was more prevalent in patients with PVT, supporting the notion that AT-III deficiency may be a critical prothrombotic factor in PVT development among PSVD patients. These findings align with the concept that underlying hematological conditions may contribute to PVT in PSVD patients.[20,21] Although some studies have reported an association between HIV infection and PVT,[22,23] our cohort included only one HIV-positive patient, suggesting HIV infection is not a major comorbidity in PSVD patients in China.[10]

Hereditary and acquired thrombophilias associated with these comorbidities may contribute to local microenvironment alterations, such as portal hemodynamic abnormalities that lead to the preferential consumption of specific coagulation factors or the induction of a prothrombotic endothelial phenotype.[24] In our cohort, compared to PSVD patients without PVT, those with PVT exhibited a more complex hemostatic profile characterized by elevated serum D-dimer and fibrin degradation product levels, as well as prolonged prothrombin time and international normalized ratio, while TEG parameters showed no significant differences.

The histopathological characteristics of PSVD with PVT remain poorly understood.[21] Previous studies have suggested that the hypercoagulable state in PSVD may lead to occlusion of small branches of the portal vein,[21,25] which is considered the primary histological lesion of PSVD.[25] Similar to a previous study,[26] our findings show that patients with PVT had a higher prevalence of portal vein wall thickening and nodular regenerative hyperplasia compared to those without PVT.

In the present study, overall mortality was five out of 150 patients (3.3%), notably lower than rates reported in previous studies: 10% in a Japanese study,[22] 19% in a multicenter European study,[9] 37% in a two-center study,[27] and 42% in an American study.[28] One possible explanation is the relatively shorter median follow-up duration in our cohort (40 months) compared to six, 6.7, and eight years, respectively, in the European, Japanese, and American studies. Nevertheless, we observed a trend toward increased mortality in PSVD patients with PVT, although this association did not reach statistical significance ($p = 0.110$). Given this borderline *p*-value, these results should be interpreted with caution. Multivariable Cox regression models showed that the HR remained elevated. These findings suggest a potential association between PVT and mortality in PSVD patients, warranting confirmation in larger cohorts with longer follow-up. Ma *et al.* found that patients with comorbidities had higher mortality,[10] consistent with the clinical features

of PSVD patients with PVT in our study. In contrast to the high incidence of hepatocellular carcinoma in cirrhotic patients with PVT,[28] no patient developed hepatocellular carcinoma during follow-up in our PSVD cohort, irrespective of PVT status.

Furthermore, the potential impact of medical therapy on PVT progression warrants further investigation. In our cohort, most patients with baseline PVT showed persistent thrombosis on follow-up imaging, with improvement seen only following anticoagulation therapy. This reflects current clinical practice, where anticoagulation or thrombolytic therapy is used cautiously in PSVD due to limited strong evidence or established guideline recommendations.[29] Among patients without PVT at baseline, three of the four who subsequently developed PVT had received NSBBs. Although limited by sample size, this observation aligns with findings from a meta-analysis in cirrhotic populations suggesting that NSBBs may increase the risk of PVT.[30]

This study has several limitations. First, it included a reasonable but relatively small number of patients from a single medical center, and some subgroup analyses, such as those involving Yerdel classification or hematologic disorders, may have been underpowered. Second, data on surgical or interventional treatments, such as transjugular intrahepatic portosystemic shunt, were not the focus of this analysis, and changes in PVT status following such procedures were not systematically evaluated. Additionally, surgical history was not included as a covariate in the Cox regression model due to the limited number of outcome events and the need to avoid model overfitting. We acknowledge that the impact of surgery on mortality and PVT progression merits further investigation in larger prospective cohort studies. Finally, spleen stiffness measurement, a promising tool in PSVD evaluation,[31] was not routinely performed in our clinical practice, resulting in missing data on spleen stiffness measurement.

Conclusions

PSVD patients exhibit a high prevalence of PVT, which is associated with increased mortality. Notably, PSVD patients with PVT experience more portal hypertension-related complications, complex coagulation abnormalities, hematological disorders, and a higher risk of death compared to those without PVT. These findings highlight the need for a comprehensive understanding of the etiology, pathogenesis, and clinical management of PSVD. Further large-scale, prospective, multicenter cohort studies are warranted to assess the value of routine screening for PVT and early anticoagulation therapy in PSVD patients, as well as to determine their impact on long-term prognosis.

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Conflict of interest

None to declare.

Author contributions

Conceptualization (HD), formal analysis (YHe, HL), investigation (YHe, YL), resources (YHe, HL), writing–original draft (YHe, HD), writing–review and editing (YHan, CF, XL, HD), visualization (YHe, XL), supervision (YW, YHan, CF, LL, XL), project administration (HD). All authors have made intellectual contributions to the manuscript and approved the submission.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2024), and was approved by the institutional ethical committee (approval number: LL-2024-083-K). All participants provided informed consent for the use of their clinical data in research.

Data sharing statement

Data in this article can be requested by contacting HD (E-mail: dinghuiguo@ccmu.edu.cn). Data anonymized to protect patient characteristics will be provided for studies whose aims and objectives align with the study protocols. Only proposals in which data will be used for statistical and scientific studies will be considered. Data will be shared through Excel electronic forms after the signing of a data access agreement.

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