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Splenectomy Causes 10-Fold Increased Risk of Portal Venous System Thrombosis in Liver Cirrhosis Patients

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Background: Portal venous system thrombosis (PVST) is a life-threatening complication of liver cirrhosis. We conducted a retrospective study to comprehensively analyze the prevalence and risk factors of PVST in liver cirrhosis.

Material/Methods: All cirrhotic patients without malignancy admitted between June 2012 and December 2013 were eligible if they underwent contrast-enhanced CT or MRI scans. Independent predictors of PVST in liver cirrhosis were calculated in multivariate analyses. Subgroup analyses were performed according to the severity of PVST (any PVST, main portal vein [MPV] thrombosis >50%, and clinically significant PVST) and splenectomy. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported.

Results: Overall, 113 cirrhotic patients were enrolled. The prevalence of PVST was 16.8% (19/113). Splenectomy (any PVST: OR=11.494, 95%CI=2.152–61.395; MPV thrombosis >50%: OR=29.987, 95%CI=3.247–276.949; clinically significant PVST: OR=40.415, 95%CI=3.895–419.295) and higher hemoglobin (any PVST: OR=0.974, 95%CI=0.953–0.996; MPV thrombosis >50%: OR=0.936, 95%CI=0.895–0.980; clinically significant PVST: OR=0.935, 95%CI=0.891–0.982) were the independent predictors of PVST. The prevalence of PVST was 13.3% (14/105) after excluding splenectomy. Higher hemoglobin was the only independent predictor of MPV thrombosis >50% (OR=0.952, 95%CI=0.909–0.997). No independent predictors of any PVST or clinically significant PVST were identified in multivariate analyses. Additionally, PVST patients who underwent splenectomy had a significantly higher proportion of clinically significant PVST but lower MELD score than those who did not undergo splenectomy. In all analyses, the in-hospital mortality was not significantly different between cirrhotic patient with and without PVST.

Conclusions: Splenectomy may increase by at least 10-fold the risk of PVST in liver cirrhosis independent of severity of liver dysfunction.

MeSH Keywords: Liver Cirrhosis • Portal Vein • Venous Thrombosis

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Background

Portal venous system thrombosis (PVST) refers to the formation of a thrombus within the intrahepatic portal vein branches, main portal vein (MPV), splenic vein (SV), and superior mesenteric vein (SMV) [1,2]. Given the relatively high prevalence and negative prognostic impact of PVST in liver cirrhosis [3–6], understanding the risk factors of PVST is important to optimize the prevention strategy in clinical practice.

Portal vessel wall injury caused by splenectomy may be one of the most important local risk factors of PVST [7–15]. Numerous studies confirmed that the incidence of PVST after splenectomy was up to about 50% [15]. Notably, splenectomy is widely used for the treatment of cirrhotic portal hypertension and hypersplenism in China [16], but not in the West. However, few studies have explored the extent to which the risk of PVST is increased by splenectomy in liver cirrhosis. On the other hand, factor V Leiden and prothrombin G20210A mutations are the major systemic risk factors of PVST in liver cirrhosis [17]. Notably, these 2 gene mutations are frequently observed in Western populations [18], but rarely in Chinese populations [19,20]. Taken together, the distribution of risk factors of PVST in liver cirrhosis may be largely different between Western countries and China.

Herein, we analyzed the prevalence and risk factors of PVST in a retrospective cohort of Chinese patients with liver cirrhosis based on contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) scans. Additionally, the effect of PVST on the in-hospital mortality of liver cirrhosis was explored.

Material and Methods

Patients

All patients with a diagnosis of liver cirrhosis who were admitted to our hospital between June 2012 and December 2013 were retrospectively reviewed in this study. At our hospital, the diagnosis of liver cirrhosis was made according to the history of chronic liver diseases, clinical symptoms (i.e., decompensated events) and signs, laboratory tests (i.e., liver function and coagulation tests), and abdominal images (i.e., liver and spleen morphology). If necessary, liver biopsy was performed. All eligible patients underwent contrast-enhanced CT and/or MRI scans to evaluate the patency of portal venous system vessels. Malignancy was excluded. The study protocol was approved by the Medical Ethics Committee of our hospital, approval number (k2014)07.

Clinical and laboratory data

As previously mentioned, our study group had continuously collected the data of cirrhotic patients from our hospital [21–26]. Some of them had been included in our previous studies. The primary data were as follows: age, sex, etiology of liver cirrhosis, other diseases, previous history of surgery, abdominal trauma, main clinical presentations (i.e., acute upper gastrointestinal bleeding [AUGIB], ascites, and hepatic encephalopathy [HE]), red blood cell (RBC), hemoglobin (Hb), white blood cell (WBC), platelet count (PLT), total bilirubin (TBIL), albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), blood urea nitrogen (BUN), creatinine (Cr), potassium, sodium, prothrombin time (PT), activated partial thromboplastin time (APTT), and international normalized ratio (INR). Notably, the major indications for splenectomy with or without portal azygous devascularization in our patients were splenomegaly and hypersplenism and prevention of portal hypertension-related bleeding. Endoscopic examinations, if any, were reviewed. Severity of esophageal varices at endoscopy was evaluated [16]. Several scores/indexes related to the prognosis of liver diseases were also calculated, including Child-Pugh [27], model for end-stage of liver disease (MELD) [28], AST to PLT ratio index (APRI) [29], AST to ALT ratio (AAR) [30], FIB-4 [31], fibrosis index (FI) [32], and King scores [33].

Imaging data

Extension of portal venous system vessels referred to the left portal vein branch (LPV), right portal vein branch (RPV), MPV, SV, and SMV. Degree of MPV thrombosis was divided into mural (thrombus occupation <50%), partial (thrombus occupation >50%), total (thrombus occupation=100%), and obliterative (MPV became fibrotic cord) [34]. Cavernous transformation of the portal vein (CTPV) was also identified. Clinically significant PVST was defined as any 1 of the following conditions: 1) partial MPV thrombosis with SMV thrombosis; or 2) total MPV thrombosis with or without SMV thrombosis [35]. Additionally, the maximal diameters of spleen, SV, and MPV, and ascites were also evaluated.

Data analysis

Continuous data were expressed as mean ± standard deviation (SD) and median (range) and were compared by the independent-sample *t* test. Categorical data were expressed as frequency (percentage) and were compared by the chi-square test or Fisher's exact test. Comparative analyses were performed according to the severity of thrombosis (PVST versus no PVST, partial and total MPV thrombosis versus mural MPV thrombosis and patency, and clinically significant PVST versus no clinically significant PVST). Comparative analyses were

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further performed after excluding patients who underwent splenectomy. All variables that were statistically significant in the univariate analyses were also entered into the multivariate logistic regression analyses. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to express the association of different variables with PVST. Clinical, laboratory, and imaging data were also compared between PVST patients with and without splenectomy. P value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS statistical software version 16.0.0.

Results

Patients

A total of 113 cirrhotic patients were included in our study. Patient characteristics are shown in Table 1. A majority of patients were male (66.4%) and had Child-Pugh class A and B (79.6%). Major etiologies of liver cirrhosis were hepatitis B virus and alcohol abuse. The prevalence of PVST was 16.8% (19/113). MPV thrombosis was observed in 12.4% (14/113) of patients, including mural (n=5, 4.4%), partial (n=6, 5.3%), and total (n=3, 2.7%) thrombosis. Eight (7.1%) patients had a history of splenectomy. Characteristics of patients without splenectomy are shown in Supplementary Table 1. After excluding splenectomy, the prevalence of PVST was 13.3% (14/105).

Risk factors in all patients

PVST

Patients with PVST had significantly higher proportions of splenectomy and severe esophageal varices, lower RBC, Hb, ALB, and sodium, and higher FI score than those without (Table 2). Only Hb, but not RBC, was entered into the multivariate analysis, because there was a collinearity between RBC and Hb. The statistical significance was observed as esophageal varices were categorized into 4 grades, but disappeared as it was categorized into 2 grades. Thus, this variable was not entered into the multivariate analysis. Because ALB was 1 component of the FI score, FI score was not entered. Finally, splenectomy (OR=11.494, 95%CI=2.152–61.395, p=0.004) and higher Hb (OR=0.974, 95%CI=0.953–0.996, p=0.019) were the independent predictors of PVST.

MPV thrombosis >50%

Patients with MPV thrombosis >50% had a significantly higher proportion of splenectomy and lower RBC and Hb than those without (Table 3). Severity of liver dysfunction was not significantly different between them. Only Hb, but not RBC, was entered into the multivariate analysis, because there was a collinearity between RBC and Hb. Finally, both splenectomy (OR=29.987, 95%CI=3.247–276.949, p=0.003) and higher Hb (OR=0.936, 95%CI=0.895–0.980, p=0.004) were the independent predictors of MPV thrombosis >50%.

Clinically significant PVST

Patients with clinically significant PVST had significantly higher proportions of splenectomy and ascites and lower RBC and Hb than those without (Table 4). Only Hb, but not RBC, was entered into the multivariate analysis, because there was a collinearity between RBC and Hb. The statistical significance was observed as ascites were categorized into 3 grades, but disappeared as it was categorized into 2 grades. Thus, this variable was not entered into the multivariate analysis. Finally, both splenectomy (OR=40.415, 95%CI=3.895–419.295, p=0.002) and higher Hb (OR=0.935, 95%CI=0.891–0.982, p=0.007) were the independent predictors of clinically significant PVST.

Risk factors after excluding splenectomy

PVST

After excluding splenectomy, patients with PVST had significantly lower RBC, Hb, ALB, sodium, PT, APTT, INR, MELD score, and FI score, and higher Cr than those without (Table 5). Given the potential collinearity among variables, only Hb and INR, but not RBC or PT, were entered into the multivariate analysis. Additionally, because Cr and INR were 2 components of the MELD score, MELD score was not entered. Similarly, because ALB was 1 component of the FI score, FI score was not entered. Finally, no variables were identified as independent predictors of PVST.

MPV thrombosis >50%

After excluding splenectomy, patients with MPV thrombosis >50% had significantly lower Hb and higher BUN than those without (Table 6). Severity of liver dysfunction was not significantly different between them. In the multivariate analysis, only Hb (OR=0.952, 95%CI=0.909–0.997, p=0.035) was an independent predictor of MPV thrombosis >50%.

Clinically significant PVST

After excluding splenectomy, patients with clinically significant PVST had a significantly higher proportion of ascites, lower Hb, and higher BUN and FI score than those without (Table 7). The statistical significance was observed as ascites were categorized into 3 grades, but disappeared as it was categorized into 2 grades. Thus, this variable was not entered into the multivariate analysis. Because ALB was 1 component of the FI score, FI

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Table 1. Characteristics of all patients.

Variables	N	Values
Age (years)	113	55.15±12.87; 55.18 (22.14–85.46)
Sex (Male/Female) – n.	113	75 (66.4%)/38 (33.6%)
Etiology of liver diseases – n.	113	
– Hepatitis B virus alone		34 (30.1%)
– Hepatitis C virus alone		7 (6.2%)
– Hepatitis B + C virus		4 (3.5%)
– Alcohol		30 (26.5%)
– Hepatitis B virus + Alcohol		9 (8.0%)
– Hepatitis C virus + Alcohol		1 (0.9%)
– Hepatitis B + C virus + Alcohol		1 (0.9%)
– Autoimmunity		6 (5.3%)
– Drug related		2 (1.8%)
– Unknown		20 (17.7%)
Disease history – n.	113	
– Diabetes		15 (13.3%)
– Coronary heart disease		8 (7.1%)
– Ischemic stroke		5 (4.4%)
– Arterial hypertension		9 (8.0%)
– Deep vein thrombosis		1 (0.9%)
Surgery history – n.	113	
– Splenectomy		8 (7.1%)
– Appendicectomy		3 (2.7%)
– Gastric surgery		2 (1.8%)
– Colonic surgery		1 (0.9%)
– Orthopedic surgery		3 (2.7%)
Abdominal trauma history – n.	113	1 (0.9%)
Acute upper gastrointestinal bleeding – n.	113	19 (16.8%)
Ascites at CT scans – n.	113	
– No		49 (43.4%)
– Mild		30 (26.5%)
– Moderate-Severe		34 (30.1%)
Hepatic encephalopathy – n.	112	6 (5.4%)
Esophageal varices at endoscopy – n.	48	
– No		10 (20.8%)
– Mild		3 (6.2%)
– Moderate		10 (20.8%)
– Severe		25 (52.1%)
Red blood cell (10^{12}/L)	110	3.39±0.88; 3.36 (1.19–5.27)
Hemoglobin (g/L)	110	105.15±30.48; 106.00 (42.00–170.00)
White blood cell (10^9/L)	110	5.10±3.22; 4.40 (1.50–20.50)
Platelet count (10^9/L)	110	101.37±82.67; 75.00 (11.00–545.00)

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Table 1 continued. Characteristics of all patients.

Variables	N	Values
Total bilirubin (umol/L)	112	46.79±69.82; 22.50 (5.10–436.50)
Albumin (g/L)	111	32.27±6.53; 31.70 (11.70–44.30)
Alanine aminotransferase (U/L)	112	51.74±61.61; 33.00 (8.00–429.00)
Aspartate aminotransferase (U/L)	112	74.18±95.92; 47.00 (10.00–889.00)
Alakaline phosphatate (U/L)	112	120.88±86.96; 92.00 (34.00–524.40)
Gamma-glutamyl transpeptidase (U/L)	112	154.86±216.00; 66.00 (12.00–1130.00)
Blood urea nitrogen (mmol/L)	110	5.70±2.58; 5.09 (1.73–17.18)
Creatinine (umol/L)	110	58.85±21.00; 55.65 (29.00–151.00)
Potassium (mmol/L)	110	4.04±0.47; 4.00 (3.01–5.43)
Sodium (mmol/L)	110	138.07±6.32; 138.80 (83.00–144.50)
Prothrombin time (seconds)	111	16.21±6.35; 14.70 (11.40–62.80)
Activated partial thromboplastin time (seconds)	111	44.56±16.09; 42.00 (29.90–180.00)
International normalized ratio	111	1.34±0.81; 1.16 (0.77–7.96)
Child-Pugh score	108	7.61±2.02; 7.50 (5.00–12.00)
Child-Pugh class A/B/C	108	40 (37.0%)/45 (41.7%)/23 (21.3%)
MELD score	108	5.93±6.95; 4.73 (–5.20–34.52)
APRI score	110	3.12±5.98; 1.67 (0.10–56.99)
AAR score	112	1.27±1.66; 0.69 (0.20–10.08)
FIB-4 score	110	8.94±9.49; 5.85 (0.38–61.59)
FI score	109	–25.33±6.73; –25.24 (–39.25 – –3.85)
King score	109	115.74±299.39; 43.31 (1.77–2589.47)
Portal vein system thrombosis – n.	113	19 (16.8%)
According to the location of thrombosis		
– Left portal vein branch thrombosis – n.	113	7 (6.2%)
– Right portal vein branch thrombosis – n.	113	6 (5.3%)
– Main portal vein thrombosis – n.	113	14 (12.4%)
– Superior mesenteric vein thrombosis – n.	113	9 (8.0%)
– Splenic vein thrombosis – n.	113	4 (3.5%)
According to the degree of MPV thrombosis		
– Mural thrombosis (<50%) – n.	113	5 (4.4%)
– Partial thrombosis (>50%) – n.	113	6 (5.3%)
– Total thrombosis (100%) – n.	113	3 (2.7%)
Cavernous transformation of the portal vein – n.	113	5 (4.4%)
Clinically significant PVST – n.	113	8 (7.1%)
Maximal diameter of spleen (mm)	105	140.27±30.77; 138.20 (83.8–240.9)
Maximal diameter of splenic vein (mm)	105	10.68±3.83; 10.3 (4.3–29.6)
Maximal diameter of main portal vein (mm)	113	18.38±5.44; 17.90 (0–35.4)
In-hospital mortality – n.	113	4 (3.5%)

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Table 2. Overall comparison between patients with and without PVST.

Variables	PVST		No PVST		P value
	N	Values	N	Values	
Age (years)	19	53.14±12.21	94	55.56±13.02	0.457
Sex (Male/Female) – n.	19	13 (68.4%)/6 (31.6%)	94	62 (66%)/32 (34%)	0.836
Etiology of liver diseases – n.	19		94		0.916
– Hepatitis B virus alone		5 (26.3%)		29 (30.9%)	
– Hepatitis C virus alone		1 (5.3%)		6 (6.4%)	
– Hepatitis B + C virus		1 (5.3%)		3 (3.2%)	
– Alcohol		5 (26.3%)		24 (26.6%)	
– Hepatitis B virus + Alcohol		3 (15.8%)		6 (6.4%)	
– Hepatitis C virus + Alcohol		0 (0%)		1 (1.1%)	
– Autoimmunity		1 (5.3%)		5 (5.3%)	
– Drug related		0 (0%)		2 (2.1%)	
– Unknown		3 (15.8%)		17 (18.1%)	
Disease history – n.	19		94		
– Diabetes		3 (15.8%)		12 (12.8%)	0.723
– Coronary heart disease		0 (0%)		8 (8.5%)	0.187
– Ischemic stroke		1 (5.3%)		4 (4.3%)	0.846
– Arterial hypertension		0 (0%)		9 (9.6%)	0.160
– Deep vein thrombosis		0 (0%)		1 (1.1%)	0.652
Surgery history – n.	19		94		
– Splenectomy		5 (26.3%)		3 (3.2%)	**<0.001**
– Appendicectomy		0 (0%)		3 (3.2%)	1.000
– Gastric surgery		0 (0%)		2 (2.1%)	1.000
– Colonic surgery		0 (0%)		1 (1.1%)	1.000
– Orthopedic surgery		0 (0%)		3 (3.2%)	1.000
Abdominal trauma history – n.	19	0 (0%)	94	1 (1.1%)	0.652
Acute upper gastrointestinal bleeding – n.	19	3 (15.8%)	94	16 (17.0%)	0.896
Ascites at CT scans – n.	19		94		0.068
– No		5 (26.3%)		44 (46.8%)	
– Mild		9 (47.4%)		21 (22.3%)	
– Moderate-Severe		5 (26.3%)		29 (30.9%)	
Hepatic encephalopathy – n.	19	2 (10.5%)	93	4 (4.3%)	0.272
Esophageal varices at endoscopy – n.	10		38		**0.047**
– No		0 (0%)		10 (26.3%)	
– Mild		2 (20.0%)		1 (2.6%)	
– Moderate		1 (10.0%)		9 (23.7%)	
– Severe		7 (70.0%)		18 (47.4%)	
Red blood cell (10^{12}/L)	18	2.86±0.64	92	3.49±0.88	**0.004**
Hemoglobin (g/L)	18	84.39±26.89	92	109.21±29.59	**0.001**
White blood cell (10^9/L)	18	5.24±3.07	92	5.08±3.26	0.844
Platelet count (10^9/L)	18	110.33±102.15	92	99.62±78.85	0.617

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Table 2 continued. Overall comparison between patients with and without PVST.

Variables	PVST		No PVST		P value
	N	Values	N	Values	
Total bilirubin (umol/L)	19	55.52±97.61	93	45.01±63.23	0.552
Albumin (g/L)	19	29.41±6.64	92	32.87±6.39	**0.035**
Alanine aminotransferase (U/L)	19	49.84±58.83	93	52.13±62.46	0.884
Aspartate aminotransferase (U/L)	19	63.74±55.91	93	76.31±102.29	0.605
Alakaline phosphatate (U/L)	19	132.92±124.27	93	118.42±77.88	0.510
Gamma-glutamyl transpeptidase (U/L)	19	132.11±185.47	93	159.51±222.33	0.617
Blood urea nitrogen (mmol/L)	18	6.20±3.30	92	5.61±2.42	0.377
Creatinine (umol/L)	18	65.06±26.90	92	57.64±19.60	0.171
Potassium (mmol/L)	18	4.04±0.46	92	4.04±0.46	0.954
Sodium (mmol/L)	18	135.03±13.43	92	138.66±3.50	**0.025**
Prothrombin time (seconds)	18	18.71±11.39	93	15.73±4.77	0.068
Activated partial thromboplastin time (seconds)	18	49.36±33.45	93	43.63±9.87	0.168
International normalized ratio	18	1.68±1.60	93	1.27±0.54	0.052
Child-Pugh score	18	8.28±1.74	90	7.48±2.06	0.126
Child-Pugh class A/B/C	18	4 (22.2%)/9 (50.0%)/5 (27.8%)	90	36 (40%)/36 (40%)/18 (20%)	0.356
MELD score	18	7.94±8.70	90	5.53±6.54	0.181
APRI score	18	2.21±2.07	92	3.29±6.47	0.487
AAR score	19	1.16±2.20	93	1.30±1.54	0.740
FIB-4 score	18	7.39±5.04	92	9.25±10.13	0.451
FI score	18	–22.19±7.05	91	–25.96±6.53	**0.029**
King score	18	100.93±218.90	91	118.67±313.78	0.820
Maximal diameter of spleen (mm)	14	153.19±37.98	91	138.28±29.25	0.092
Maximal diameter of splenic vein (mm)	14	11.05±4.44	91	10.63±3.76	0.703
Maximal diameter of main portal vein (mm)	19	17.68±6.86	94	18.52±5.13	0.542
In-hospital mortality – n.	19	1 (5.3%)	94	3 (3.2%)	0.656

Table 3. Overall comparison between patients with and without MPV thrombosis >50%.

Variables	MPV thrombosis >50%		MPV thrombosis <50% and MPV patency		P value
	N	Values	N	Values	
Age (years)	9	57.68±13.95	104	54.93±12.82	0.542
Sex (Male/Female) – n.	9	5 (55.6%)/4 (44.4%)	104	70 (67.3%)/34 (32.7%)	0.474
Etiology of liver diseases – n.	9		104		0.740
– Hepatitis B virus alone		2 (22.2%)		32 (30.8%)	
– Hepatitis C virus alone		0 (0%)		7 (6.7%)	
– Hepatitis B + C virus		1 (1.1%)		3 (2.9%)	
– Alcohol		2 (22.2%)		28 (26.9%)	
– Hepatitis B virus + Alcohol		2 (22.2%)		7 (6.7%)	
– Hepatitis C virus + Alcohol		0 (0%)		1 (1.0%)	

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Table 3 continued. Overall comparison between patients with and without MPV thrombosis >50%.

Variables	MPV thrombosis >50%		MPV thrombosis <50% and MPV patency		P value
	N	Values	N	Values	
– Autoimmunity		0 (0%)		6 (5.8%)	
– Drug related		0 (0%)		2 (1.9%)	
– Unknown		2 (22.2%)		18 (17.3%)	
Disease history – n.	9		104		
– Diabetes		2 (22.2%)		13 (12.5%)	0.410
– Coronary heart disease		0 (0%)		8 (7.7%)	0.388
– Ischemic stroke		1 (11.1%)		4 (4.6%)	0.309
– Arterial hypertension		0 (0%)		9 (8.7%)	0.358
– Deep vein thrombosis		0 (0%)		1 (1.0%)	0.768
Surgery history – n.	9		104		
– Splenectomy		4 (44.4%)		4 (3.8%)	**<0.001**
– Appendicectomy		0 (0%)		3 (2.9%)	0.606
– Gastric surgery		0 (0%)		2 (1.9%)	0.675
– Colonic surgery		0 (0%)		1 (1.0%)	0.768
– Orthopedic surgery		0 (0%)		3 (2.9%)	0.606
Abdominal trauma history – n.	9	0 (0%)	104	1 (1.0%)	0.768
Acute upper gastrointestinal bleeding – n.	9	1 (11.1%)	104	18 (17.3%)	0.633
Ascites at CT scans – n.	9		104		0.065
– No		1 (11.1%)		48 (46.2%)	
– Mild		5 (55.6%)		25 (24.0%)	
– Moderate-Severe		3 (33.3%)		31 (29.8%)	
Hepatic encephalopathy – n.	9	0 (0%)	103	6 (5.8%)	0.457
Esophageal varices at endoscopy – n.	7		41		0.057
– No		0 (0%)		10 (24.4%)	
– Mild		0 (0%)		3 (7.3%)	
– Moderate		0 (0%)		10 (24.4%)	
– Severe		7 (100%)		18 (43.9%)	
Red blood cell (10^{12}/L)	9	2.70±0.37	101	3.45±0.88	**0.013**
Hemoglobin (g/L)	9	70.22±12.85	101	108.26±29.66	**<0.001**
White blood cell (10^9/L)	9	4.70±3.17	101	5.14±3.23	0.698
Platelet count (10^9/L)	9	136.33±122.15	101	98.26±78.33	0.187
Total bilirubin (umol/L)	9	17.77±15.02	103	49.33±72.15	0.195
Albumin (g/L)	9	29.94±7.21	102	32.48±6.47	0.266
Alanine aminotransferase (U/L)	9	28.33±26.81	103	53.79±63.42	0.236
Aspartate aminotransferase (U/L)	9	39.11±43.24	103	77.24±98.74	0.255
Alakaline phosphatate (U/L)	9	74.82±42.70	103	124.90±88.78	0.098
Gamma-glutamyl transpeptidase (U/L)	9	33.78±23.30	103	165.44±222.09	0.079
Blood urea nitrogen (mmol/L)	9	6.43±4.57	101	5.64±2.35	0.380
Creatinine (umol/L)	9	56.24±15.84	101	59.08±21.45	0.699
Potassium (mmol/L)	9	4.01±0.35	101	4.05±0.47	0.842

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Table 3 continued. Overall comparison between patients with and without MPV thrombosis >50%.

Variables	MPV thrombosis >50%		MPV thrombosis <50% and MPV patency		P value
	N	Values	N	Values	
Sodium (mmol/L)	9	138.64±2.85	101	138.02±6.54	0.778
Prothrombin time (seconds)	9	15.78±3.02	102	16.25±6.57	0.832
Activated partial thromboplastin time (seconds)	9	39.22±7.22	102	45.03±16.59	0.302
International normalized ratio	9	1.28±0.33	102	1.34±0.84	0.824
Child-Pugh score	9	7.67±1.41	99	7.61±2.07	0.932
Child-Pugh class A/B/C	9	2 (22.2%)/6 (66.7%)/1 (11.1%)	99	38 (38.4%) 39 (39.4%)/22 (22.2%)	0.282
MELD score	9	3.11±5.58	99	6.19±7.03	0.205
APRI score	9	1.14±0.92	101	3.29±6.21	0.303
AAR score	9	0.48±0.31	103	1.34±1.71	0.543
FIB-4 score	9	5.37±3.89	101	9.26±9.78	0.240
FI score	9	–23.31±7.63	100	–25.52±6.66	0.348
King score	9	34.26±28.62	100	123.08±311.55	0.396
Maximal diameter of spleen (mm)	5	158.50±48.02	100	139.36±29.73	0.176
Maximal diameter of splenic vein (mm)	5	11.74±4.04	100	10.63±3.84	0.530
Maximal diameter of main portal vein (mm)	9	18.64±8.98	104	18.36±5.09	0.881
In-hospital mortality – n.	9	0 (0%)	104	4 (3.8%)	0.549

Table 4. Overall comparison between patients with and without clinically significant PVST.

Variables	Clinically significant PVST		No clinically significant PVST		P value
	N	Values	N	Values	
Age (years)	8	58.47±14.69	105	54.90±12.76	0.451
Sex (Male/Female) – n.	8	4 (50%)/4 (50%)	105	71 (67.6%)/34 (32.4%)	0.309
Etiology of liver diseases – n.	8		105		0.595
– Hepatitis B virus alone		2 (25%)		32 (30.5%)	
– Hepatitis C virus alone		0 (0%)		7 (6.7%)	
– Hepatitis B + C virus		1 (12.5%)		3 (2.9%)	
– Alcohol		1 (12.5%)		29 (27.6%)	
– Hepatitis B virus + Alcohol		2 (25%)		7 (6.7%)	
– Hepatitis C virus + Alcohol		0 (0%)		1 (1.0%)	
– Autoimmunity		0 (0%)		6 (5.6%)	
– Drug related		0 (0%)		2 (1.9%)	
– Unknown		2 (25%)		18 (17.1%)	
Disease history – n.	8		105		
– Diabetes		2 (25%)		13 (12.4%)	0.311
– Coronary heart disease		0 (0%)		8 (7.6%)	1.000
– Ischemic stroke		1 (12.5%)		4 (3.8%)	0.312
– Arterial hypertension		0 (0%)		9 (8.6%)	1.000
– Deep vein thrombosis		0 (0%)		1 (1.1%)	1.000

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Table 4 continued. Overall comparison between patients with and without clinically significant PVST.

Variables	Clinically significant PVST		No clinically significant PVST		p value
	N	Values	N	Values	
Surgery history – n.	8		105		
– Splenectomy		4 (50%)		4 (3.8%)	**<0.001**
– Appendicectomy		0 (0%)		3 (2.9%)	1.000
– Gastric surgery		0 (0%)		2 (1.9%)	1.000
– Colonic surgery		0 (0%)		1 (1.0%)	1.000
– Orthopedic surgery		0 (0%)		3 (3.2%)	1.000
Abdominal trauma history – n.	8	0 (0%)	105	1 (1.1%)	1.000
Acute upper gastrointestinal bleeding – n.	8	1 (12.5%)	105	18 (17.1%)	1.000
Ascites at CT scans – n.	8		105		**0.046**
– No		1 (12.5%)		48 (45.7%)	
– Mild		5 (62.5%)		25 (23.8%)	
– Moderate-Severe		2 (25%)		32 (30.5%)	
Hepatic encephalopathy – n.	8	0 (0%)	105	6 (5.8%)	1.000
Esophageal varices at endoscopy – n.	6		42		0.098
– No		0 (0%)		10 (23.8%)	
– Mild		0 (0%)		3 (7.1%)	
– Moderate		0 (0%)		10 (23.8%)	
– Severe		6 (100%)		19 (45.2%)	
Red blood cell (10^{12}/L)	8	2.71±0.39	102	3.44±0.88	**0.022**
Hemoglobin (g/L)	8	70±13.72	102	107.90±29.73	**0.001**
White blood cell (10^9/L)	8	5.06±3.18	102	65.10±3.23	0.972
Platelet count (10^9/L)	8	151.38±121.35	102	97.45±78.37	0.076
Total bilirubin (umol/L)	8	18.78±15.73	104	48.95±71.91	0.241
Albumin (g/L)	8	28.89±6.92	103	32.54±6.46	0.129
Alanine aminotransferase (U/L)	8	30.5±27.81	104	53.38±63.25	0.314
Aspartate aminotransferase (U/L)	8	42.25±45.11	104	76.63±98.45	0.331
Alakaline phosphatate (U/L)	8	78.18±44.36	104	124.17±88.67	0.150
Gamma-glutamyl transpeptidase (U/L)	8	34.88±24.65	104	164.09±221.44	0.103
Blood urea nitrogen (mmol/L)	8	6.58±4.86	102	5.64±2.34	0.322
Creatinine (umol/L)	8	56.9±16.81	102	59.00±21.36	0.786
Potassium (mmol/L)	8	3.95±0.31	102	4.05±0.47	0.541
Sodium (mmol/L)	8	138.45±2.98	102	138.04±6.51	0.861
Prothrombin time (seconds)	8	15.9±3.21	103	16.23±6.54	0.887
Activated partial thromboplastin time (seconds)	8	38.31±7.14	103	45.04±16.50	0.256
International normalized ratio	8	1.29±0.35	103	1.34±0.84	0.877
Child-Pugh score	8	7.75±1.49	100	7.6±2.06	0.841
Child-Pugh class A/B/C	8	2 (25.0%)/5 (62.5%)/1 (12.5%)	100	38 (38%)/40 (40%)/22 (22%)	0.460
MELD score	8	3.45±5.86	100	6.13±7.02	0.296
APRI score	8	1.01±0.89	102	3.28±6.18	0.302
AAR score	8	0.48±0.33	104	1.33±1.70	0.160

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Table 4 continued. Overall comparison between patients with and without clinically significant PVST.

Variables	Clinically significant PVST		No clinically significant PVST		P value
	N	Values	N	Values	
FIB-4 score	8	4.34±2.57	102	9.30±9.75	0.156
FI score	8	–22.40±7.63	101	–25.57±6.64	0.202
King score	8	32.03±29.75	101	122.37±310.06	0.414
Maximal diameter of spleen (mm)	4	137.9±15.66	101	140.36±31.26	0.876
Maximal diameter of splenic vein (mm)	4	11.68±4.67	101	10.64±3.82	0.600
Maximal diameter of main portal vein (mm)	8	19.11±9.48	105	18.33±5.07	0.695
In-hospital mortality – n.	8	0 (0%)	105	4 (3.7%)	1.000

Table 5. Comparison between patients with and without PVST after excluding splenectomy.

Variables	PVST		No PVST		P value
	N	Values	N	Values	
Age (years)	14	52.67±11.69	91	55.60±13.22	0.435
Sex (Male/Female) – n.	14	11 (78.64%)/3 (21.4%)	91	60 (65.9%)/31 (34.1%)	0.347
Etiology of liver diseases – n.	14		91		0.988
– Hepatitis B virus alone		5 (35.7%)		27 (29.7%)	
– Hepatitis C virus alone		1 (7.1%)		6 (6.6%)	
– Hepatitis B + C virus		0 (0%)		3 (3.3%)	
– Alcohol		5 (35.7%)		25 (27.5%)	
– Hepatitis B virus + Alcohol		1 (7.1%)		6 (6.6%)	
– Hepatitis C virus + Alcohol		0 (0%)		1 (1.1%)	
– Autoimmunity		0 (0%)		5 (5.5%)	
– Drug related		0 (0%)		2 (2.0%)	
– Unknown		2 (14.3%)		16 (17.6%)	
Disease history – n.	14		91		
– Diabetes		2 (14.3%)		11 (12.1%)	0.816
– Coronary heart disease		0 (0%)		8 (8.8%)	0.594
– Ischemic stroke		1 (7.1%)		4 (4.4%)	0.518
– Arterial hypertension		0 (0%)		9 (9.9%)	0.604
– Deep vein thrombosis		0 (0%)		1 (1.1%)	1.000
Surgery history – n.	14		91		
– Splenectomy		0 (0%)		0 (0%)	NA
– Appendicectomy		0 (0%)		3 (3.3%)	1.000
– Gastric surgery		0 (0%)		2 (2.2%)	1.000
– Colonic surgery		0 (0%)		1 (1.1%)	1.000
– Orthopedic surgery		0 (0%)		3 (3.3%)	1.000
Abdominal trauma history – n.	14	0 (0%)	91	1 (1.1%)	1.000
Acute upper gastrointestinal bleeding – n.	14	2 (14.3%)	91	15 (16.5%)	0.835
Ascites at CT scans – n.	14		91		0.219

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Table 5 continued. Comparison between patients with and without PVST after excluding splenectomy.

Variables	PVST		No PVST		P value
	N	Values	N	Values	
– No		4 (28.6%)		42 (46.2%)	
– Mild		6 (42.9%)		20 (22.0%)	
– Moderate-Severe		4 (28.6%)		29 (31.9%)	
Hepatic encephalopathy – n.	14	2 (14.3%)	90	4 (4.4%)	0.142
Esophageal varices at endoscopy – n.	5		37		0.237
– No		0 (0%)		10 (27.0%)	
– Mild		1 (20%)		1 (2.7%)	
– Moderate		1 (20%)		8 (21.6%)	
– Severe		3 (60%)		18 (48.6%)	
Red blood cell (10^{12}/L)	13	2.92±0.71	89	3.49±0.89	**0.028**
Hemoglobin (g/L)	13	88.69±28.60	89	108.73±29.84	**0.025**
White blood cell (10^9/L)	13	4.85±3.19	89	4.98±3.23	0.897
Platelet count (10^9/L)	13	58.77±38.48	89	97.97±79.65	0.085
Total bilirubin (umol/L)	14	68.26±111.35	90	45.36±63.99	0.269
Albumin (g/L)	14	28.65±7.28	89	32.91±6.48	**0.027**
Alanine aminotransferase (U/L)	14	46.71±64.26	90	52.37±63.22	0.757
Aspartate aminotransferase (U/L)	14	56.79±49.92	90	76.82±103.56	0.480
Alakaline phosphatate (U/L)	14	123.12±94.37	90	116.82±78.22	0.786
Gamma-glutamyl transpeptidase (U/L)	14	145.00±202.98	90	162.02±225.43	0.791
Blood urea nitrogen (mmol/L)	13	6.97±3.39	89	5.63±2.45	0.083
Creatinine (umol/L)	13	71.12±29.62	89	57.71±19.83	**0.036**
Potassium (mmol/L)	13	4.05±0.51	89	4.03±0.46	0.880
Sodium (mmol/L)	13	133.73±15.66	89	138.64±3.51	**0.010**
Prothrombin time (seconds)	13	20.25±13.12	90	15.77±4.84	**0.021**
Activated partial thromboplastin time (seconds)	13	54.82±38.25	90	43.73±10.01	**0.023**
International normalized ratio	13	1.87±1.86	90	1.28±0.55	**0.016**
Child-Pugh score	13	8.62±1.76	87	7.49±2.08	0.069
Child-Pugh class A/B/C	13	2 (15.4%)/6 (46.2%)/5 (38.5%)	87	35 (40.2%)/34 (39.1%)/18 (20.7%)	0.167
MELD score	13	10.48±8.57	87	5.60±6.62	**0.019**
APRI score	13	2.64±2.22	89	3.37±6.56	0.694
AAR score	14	1.38±2.54	90	1.32±1.56	0.903
FIB-4 score	13	9.19±4.71	89	9.45±10.23	0.928
FI score	13	–20.73±7.39	88	–25.99±6.62	**0.010**
King score	13	128.23±254.16	88	121.70±318.66	0.944
Maximal diameter of spleen (mm)	14	153.19±37.98	91	138.28±29.25	0.092
Maximal diameter of splenic vein (mm)	14	11.05±4.44	91	10.63±3.76	0.703
Maximal diameter of main portal vein (mm)	14	17.51±7.27	91	18.47±4.82	0.521
In-hospital mortality – n.	14	1 (7.1%)	91	3 (3.3%)	0.441

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Table 6. Comparison between patients with and without MPV thrombosis >50% after excluding splenectomy.

Variables	MPV thrombosis >50%		MPV thrombosis <50% and MPV patency		P value
	N	Values	N	Values	
Age (years)	5	61.13±11.72	100	54.92±13.06	0.300
Sex (Male/Female) – n.	5	3 (60%)/2 (40%)	100	68 (68.0%)/32 (32.0%)	0.658
Etiology of liver diseases – n.	5		100		0.996
– Hepatitis B virus alone		2 (40%)		30 (30.0%)	
– Hepatitis C virus alone		0 (0%)		7 (7.0%)	
– Hepatitis B + C virus		0 (0%)		3 (3.0%)	
– Alcohol		2 (40%)		28 (28.0%)	
– Hepatitis B virus + Alcohol		0 (0%)		7 (7.0%)	
– Hepatitis C virus + Alcohol		0 (0%)		1 (1.0%)	
– Autoimmunity		0 (0%)		5 (5.0%)	
– Drug related		0 (0%)		2 (2.0%)	
– Unknown		1 (20%)		17 (17.0%)	
Disease history – n.	5		100		
– Diabetes		1 (20%)		12 (12.0%)	0.491
– Coronary heart disease		0 (0%)		8 (8.0%)	1.000
– Ischemic stroke		1 (20%)		4 (4.0%)	0.220
– Arterial hypertension		0 (0%)		9 (9.0%)	1.000
– Deep vein thrombosis		0 (0%)		1 (1.0%)	1.000
Surgery history – n.	5		100		
– Splenectomy		0 (0%)		0 (0%)	NA
– Appendicectomy		0 (0%)		3 (3.0%)	1.000
– Gastric surgery		0 (0%)		2 (2.0%)	1.000
– Colonic surgery		0 (0%)		1 (1.0%)	1.000
– Orthopedic surgery		0 (0%)		3 (3%)	1.000
Abdominal trauma history – n.	5	0 (0%)	100	1 (1.0%)	1.000
Acute upper gastrointestinal bleeding – n.	5	1 (0%)	100	17 (17.0%)	0.589
Ascites at CT scans – n.	5		100		0.080
– No		0 (0%)		46 (46.0%)	
– Mild		3 (60%)		23 (23.0%)	
– Moderate-Severe		2 (40%)		31 (31.0%)	
Hepatic encephalopathy – n.	5	0 (0%)	99	6 (6.1%)	1.000
Esophageal varices at endoscopy – n.	3		38		0.357
– No		0 (0%)		10 (25.6%)	
– Mild		0 (0%)		2 (5.1%)	
– Moderate		0 (0%)		8 (23.1%)	
– Severe		3 (100%)		18 (46.2%)	
Red blood cell (10^{12}/L)	5	2.75±0.29	97	3.46±0.89	0.081
Hemoglobin (g/L)	5	72.40±8.73	97	107.92±30.00	**0.010**
White blood cell (10^9/L)	5	4.36±4.25	97	4.99±3.17	0.669
Platelet count (10^9/L)	5	52.00±32.85	97	95.08±77.75	0.222

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Table 6 continued. Comparison between patients with and without MPV thrombosis >50% after excluding splenectomy.

Variables	MPV thrombosis >50%		MPV thrombosis <50% and MPV patency		P value
	N	Values	N	Values	
Total bilirubin (umol/L)	5	23.12±18.39	99	49.72±73.35	0.422
Albumin (g/L)	5	28.40±8.92	98	32.53±6.59	0.181
Alanine aminotransferase (U/L)	5	15.80±6.14	99	53.41±64.12	0.195
Aspartate aminotransferase (U/L)	5	21.80±9.50	99	76.77±99.85	0.223
Alakaline phosphatate (U/L)	5	77.28±60.19	99	119.71±80.67	0.250
Gamma-glutamyl transpeptidase (U/L)	5	32.00±19.66	99	166.18±225.31	0.188
Blood urea nitrogen (mmol/L)	5	8.22±5.30	97	5.68±2.40	**0.033**
Creatinine (umol/L)	5	62.94±19.34	97	59.24±21.80	0.711
Potassium (mmol/L)	5	4.13±0.40	97	4.05±0.47	0.640
Sodium (mmol/L)	5	138.84±2.15	97	137.98±6.65	0.773
Prothrombin time (seconds)	5	16.24±3.40	98	16.34±6.68	0.973
Activated partial thromboplastin time (seconds)	5	42.02±8.12	98	45.28±16.86	0.669
International normalized ratio	5	1.32±0.38	98	1.35±0.86	0.933
Child-Pugh score	5	8.20±1.30	95	7.61±2.11	0.538
Child-Pugh class A/B/C	5	0 (0%)/4 (80%)/1 (20%)	95	37 (38.9%)/36 (37.8%)/22 (23.2%)	0.130
MELD score	5	5.43±5.30	95	6.27±7.15	0.796
APRI score	5	1.28±0.69	97	3.38±6.32	0.462
AAR score	5	0.48±0.27	99	1.38±1.74	0.253
FIB-4 score	5	7.68±3.45	97	9.51±9.90	0.683
FI score	5	–20.92±8.87	96	–25.54±6.78	0.147
King score	5	39.52±21.38	96	126.87±317.42	0.542
Maximal diameter of spleen (mm)	5	158.50±48.02	100	139.36±29.73	0.176
Maximal diameter of splenic vein (mm)	5	11.74±4.04	100	10.63±3.84	0.530
Maximal diameter of main portal vein (mm)	5	17.86±11.43	100	18.36±5.09	0.833
In-hospital mortality – n.	5	0 (0%)	100	4 (4.0%)	1.000

Table 7. Comparison between patients with and without clinically significant PVST after excluding splenectomy.

Variables	Clinically significant PVST		No clinically significant PVST		P value
	N	Values	N	Values	
Age (years)	4	63.59±11.96	101	54.88±12.99	0.191
Sex (Male/Female) – n.	4	2 (50%)/2 (50%)	101	69 (68.3%)/32 (31.7%)	0.593
Etiology of liver diseases – n.	4		101		0.996
– Hepatitis B virus alone		2 (50%)		30 (29.7%)	
– Hepatitis C virus alone		0 (0%)		7 (6.9%)	
– Hepatitis B + C virus		0 (0%)		3 (3.0%)	
– Alcohol		1 (25%)		28 (27.7%)	
– Hepatitis B virus + Alcohol		0 (0%)		7 (6.9%)	

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Table 7 continued. Comparison between patients with and without clinically significant PVST after excluding splenectomy.

Variables	Clinically significant PVST			No clinically significant PVST			P value
	N	Values		N	Values		
– Hepatitis C virus + Alcohol		0	(0%)		1	(1.0%)	
– Autoimmunity		0	(0%)		5	(5.0%)	
– Drug related		0	(0%)		2	(2.0%)	
– Unknown		1	(25%)		17	(16.8%)	
Disease history – n.	4			101			
– Diabetes		1	(25%)		12	(11.9%)	0.415
– Coronary heart disease		0	(0%)		8	(7.9%)	1.000
– Ischemic stroke		1	(25%)		4	(4.0%)	0.180
– Arterial hypertension		0	(0%)		9	(8.9%)	1.000
– Deep vein thrombosis		0	(0%)		1	(1.0%)	1.000
Surgery history – n.	4			101			
– Splenectomy		0	(0%)		0	(0%)	NA
– Appendicectomy		0	(0%)		3	(3.0%)	1.000
– Gastric surgery		0	(0%)		2	(2.0%)	1.000
– Colonic surgery		0	(0%)		1	(1.0%)	1.000
– Orthopedic surgery		0	(0%)		3	(3.0%)	1.000
Abdominal trauma history – n.	4	0	(0%)	101	1	(1.0%)	1.000
Acute upper gastrointestinal bleeding – n.	4	1	(12.5%)	101	17	(16.8%)	1.000
Ascites at CT scans – n.	4			101			**0.047**
– No		0	(0%)		46	(45.5%)	
– Mild		3	(75%)		23	(22.8%)	
– Moderate-Severe		1	(25%)		32	(31.7%)	
Hepatic encephalopathy – n.	4	0	(0%)	101	6	(6.0%)	1.000
Esophageal varices at endoscopy – n.	2			40			0.552
– No		0	(0%)		10	(25%)	
– Mild		0	(0%)		2	(5%)	
– Moderate		0	(0%)		9	(22.5%)	
– Severe		2	(100%)		19	(47.5%)	
Red blood cell (10^{12}/L)	4	2.79±0.32		98	3.45±0.89		0.145
Hemoglobin (g/L)	4	72.5±10.08		98	107.55±30.07		**0.023**
White blood cell (10^9/L)	4	5±4.62		98	4.96±3.17		0.981
Platelet count (10^9/L)	4	61±29.98		98	94.28±77.77		0.397
Total bilirubin (umol/L)	4	26.48±19.38		100	49.32±73.09		0.536
Albumin (g/L)	4	25.9±8.03		99	32.59±6.58		0.050
Alanine aminotransferase (U/L)	4	17±6.38		100	52.99±63.94		0.265
Aspartate aminotransferase (U/L)	4	23.75±9.74		100	76.14±99.54		0.297
Alakaline phosphatate (U/L)	4	84.6±66.88		100	118.99±80.58		0.402
Gamma-glutamyl transpeptidase (U/L)	4	33.75±22.25		100	164.77±224.61		0.248
Blood urea nitrogen (mmol/L)	4	8.96±5.81		98	5.67±2.37		**0.013**
Creatinine (umol/L)	4	65.93±20.97		98	59.16±21.70		0.542

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Table 7 continued. Comparison between patients with and without clinically significant PVST after excluding splenectomy.

Variables	Clinically significant PVST		No clinically significant PVST		P value
	N	Values	N	Values	
Potassium (mmol/L)	4	4.03±0.38	98	4.04±0.47	0.969
Sodium (mmol/L)	4	138.5±2.32	98	138.00±6.62	0.881
Prothrombin time (seconds)	4	16.6±3.81	99	16.33±6.65	0.935
Activated partial thromboplastin time (seconds)	4	40.9±8.92	99	45.30±16.77	0.605
International normalized ratio	4	1.36±0.43	99	1.35±0.85	0.983
Child-Pugh score	4	8.5±1.29	96	7.60±2.10	0.400
Child-Pugh class A/B/C	4	0 (0%)/3 (75%)/1 (25%)	96	37 (38.5%)/37 (38.5%)/22 (22.9%)	0.244
MELD score	4	6.69±5.18	96	6.21±7.13	0.895
APRI score	4	1.06±0.54	98	3.37±6.29	0.466
AAR score	4	0.47±0.32	100	1.37±1.73	0.303
FIB-4 score	4	6.22±1.25	98	9.58±9.86	0.503
FI score	4	–18.51±8.14	97	–25.59±6.77	**0.044**
King score	4	36.38±23.32	97	126.10±315.86	0.573
Maximal diameter of spleen (mm)	4	137.9±15.66	101	140.36±31.26	0.876
Maximal diameter of splenic vein (mm)	4	11.68±4.67	101	10.64±3.82	0.600
Maximal diameter of main portal vein (mm)	4	18.6±13.06	101	18.33±4.78	0.919
In-hospital mortality – n.	4	0 (0%)	101	4 (4.0%)	1.000

score was not entered. Finally, no variables were identified as independent predictors of clinically significant PVST.

Comparison of characteristics between PVST patients with and without splenectomy

PVST patients with splenectomy had significantly higher proportions of clinically significant PVST and RPV thrombosis, higher PLT, and lower MELD and FIB-4 scores than those without (Table 8).

Discussion

Our study found that the prevalence of PVST was 16.8% (19/113) in all patients with liver cirrhosis and was 13.3% (14/105) in cirrhotic patients after excluding splenectomy. We are confident about the data, because axial contrast-enhanced CT scans were used to more objectively detect the presence of PVST. Our data are consistent with a review by Fimognari et al. (5–20%) [4] and suggest that PVST should be a relatively frequent complication of liver cirrhosis.

The most important finding of our study was that splenectomy was a very strong risk factor for the development of PVST in liver cirrhosis. Their association became closer as PVST was more severe (Supplementary Figure 1). In detail, if the severity of PVST was not restricted, the OR for splenectomy was 10.833 and 11.494 in univariate and multivariate analysis, respectively; if only patients with MPV thrombosis >50% were analyzed, the OR for splenectomy was 20.000 and 29.987 in univariate and multivariate analysis, respectively; and if only patients with clinically significant PVST were analyzed, the OR for splenectomy was 25.250 and 40.415 in univariate and multivariate analysis, respectively. In addition, our study demonstrated that cirrhotic patients with splenectomy had more severe PVST but less severe liver dysfunction than those without. Thus, splenectomy might be more independent of liver dysfunction in the development of PVST in liver cirrhosis.

Based on these findings, we should fully balance the clinical benefits and adverse effects of splenectomy in liver cirrhosis. The indications for splenectomy in cirrhosis should be clearly specified. On the other hand, low-quality evidence suggested that the pharmacological prophylaxis of PVST in liver cirrhosis should be effective [36]. Thus, well-designed randomized studies are needed to accurately identify the candidates for and timing of pharmacological prophylaxis of PVST in cirrhotic patients treated with splenectomy. Certainly, when its clinical significance is explained, the regions should be also taken

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Table 8. Comparison between PVST patients with and without splenectomy.

Variables	Splenectomy		No splenectomy		P value
	N	Values	N	Values	
Age (years)	5	54.46±14.98	14	52.67±11.69	0.787
Sex (Male/Female) – n.	5	2 (40%)/3 (60%)	14	11 (78.6%)/3 (21.4%)	0.111
Etiology of liver diseases – n.	5		14		0.059
– Hepatitis B virus alone		0 (0%)		5 (35.7%)	
– Hepatitis C virus alone		0 (0%)		1 (7.1%)	
– Hepatitis B + C virus		1 (20%)		0 (0%)	
– Alcohol		0 (0%)		5 (35.7%)	
– Hepatitis B virus + Alcohol		2 (40%)		1 (7.1%)	
– Hepatitis C virus + Alcohol		0 (0%)		0 (0%)	
– Hepatitis B + C virus + Alcohol		0 (0%)		0 (0%)	
– Autoimmunity		1 (20%)		0 (0%)	
– Drug related		0 (0%)		0 (0%)	
– Unknown		1 (20%)		2 (14.3%)	
Disease history – n.	5		14		
– Diabetes		1 (20%)		2 (14.3%)	0.764
– Coronary heart disease		0 (0%)		0 (0%)	NA
– Ischemic stroke		0 (0%)		1 (7.1%)	1.000
– Arterial hypertension		0 (0%)		0 (0%)	NA
– Deep vein thrombosis		0 (0%)		0 (0%)	NA
Surgery history – n.	5		14		
– Appendicectomy		0 (0%)		0 (0%)	NA
– Gastric surgery		0 (0%)		0 (0%)	NA
– Colonic surgery		0 (0%)		0 (0%)	NA
– Orthopedic surgery		0 (0%)		0 (0%)	NA
Abdominal trauma history – n.	5	0 (0%)	14	0 (0%)	NA
Acute upper gastrointestinal bleeding – n.	5	1 (20%)	14	2 (14.3%)	0.764
Ascites at CT scans – n.	5		14		0.805
– No		1 (20%)		4 (28.6%)	
– Mild		3 (60%)		6 (42.9%)	
– Moderate-Severe		1 (20%)		4 (28.6%)	
Hepatic encephalopathy – n.	5	0 (0%)	14	2 (14.3%)	0.372
Esophageal varices at endoscopy – n.	5		5		0.565
– No		0 (0%)		0 (0%)	
– Mild		1 (20%)		1 (20%)	
– Moderate		0 (0%)		1 (20%)	
– Severe		4 (80%)		2 (60%)	
Red blood cell (10^{12}/L)	5	2.7±0.45	13	2.92±0.71	0.532
Hemoglobin (g/L)	5	73.2±20.08	13	88.69±28.60	0.287
White blood cell (10^9/L)	5	6.24±2.82	13	4.85±3.19	0.408
Platelet count (10^9/L)	5	244.4±93.79	13	58.77±38.48	**<0.001**

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Table 8 continued. Comparison between PVST patients with and without splenectomy.

Variables	Splenectomy		No splenectomy		P value
	N	Values	N	Values	
Total bilirubin (umol/L)	5	19.84±20.41	14	68.26±111.35	0.356
Albumin (g/L)	5	31.54±4.27	14	28.65±7.28	0.419
Alanine aminotransferase (U/L)	5	58.6±44.99	14	46.71±64.26	0.710
Aspartate aminotransferase (U/L)	5	83.2±72.98	14	56.79±49.92	0.380
Alakaline phosphatate (U/L)	5	160.36±198.16	14	123.12±94.37	0.580
Gamma-glutamyl transpeptidase (U/L)	5	96±136.71	14	145±202.98	0.626
Blood urea nitrogen (mmol/L)	5	4.18±2.16	13	6.97±3.39	0.109
Creatinine (umol/L)	5	49.3±3.46	13	71.12±29.62	0.126
Potassium (mmol/L)	5	3.99±0.35	13	4.05±0.51	0.804
Sodium (mmol/L)	5	138.4±3.40	13	133.73±15.66	0.525
Prothrombin time (seconds)	5	14.7±2.71	13	20.25±13.12	0.371
Activated partial thromboplastin time (seconds)	5	35.16±4.22	13	54.82±38.25	0.277
International normalized ratio	5	1.18±0.28	13	1.87±1.86	0.427
Child-Pugh score	5	7.4±1.52	13	8.62±1.76	0.193
Child-Pugh class A/B/C	5	2 (40%)/3 (60%)/0 (0%)	13	2 (15.4%)/7 (53.8%)/4 (30.8%)	0.280
MELD score	5	1.32±5.02	13	10.48±8.57	**0.041**
APRI score	5	1.11±1.12	13	2.64±2.22	0.165
AAR score	5	0.52±0.35	14	1.38±2.54	0.468
FIB-4 score	5	2.72±1.91	13	9.19±4.71	**0.010**
FI score	5	–25.98±4.72	13	–20.73±7.39	0.163
King score	5	29.97±33.61	13	128.23±254.16	0.410
According to the location of thrombosis	5		14		
– Left portal vein branch thrombosis – n.		3 (60%)		4 (28.6%)	0.211
– Right portal vein branch thrombosis – n.		4 (80%)		2 (14.3%)	**0.007**
– Main portal vein thrombosis – n.		5 (100%)		9 (64.3%)	0.120
– Superior mesenteric vein thrombosis – n.		5 (4.8%)		4 (28.6%)	0.089
– Splenic vein thrombosis – n.		NA		4 (28.6%)	NA
According to the degree of MPV thrombosis	5		14		0.207
– Mural thrombosis (<50%) – n.		1 (20%)		4 (28.6%)	
– Partial thrombosis (>50%) – n.		2 (40%)		4 (28.6%)	
– Total thrombosis (100%) – n.		2 (40%)		1 (7.1%)	
Cavernous transformation of the portal vein – n.	5	2 (40%)	14	3 (21.4%)	0.418
Clinically significant PVST – n.	5	4 (80%)	14	4 (28.6%)	**0.046**
Maximal diameter of spleen (mm)	5	NA	14	153.19±37.98	NA
Maximal diameter of splenic vein (mm)	5	NA	14	11.05±4.39	NA
Maximal diameter of main portal vein (mm)	5	18.18±6.27	14	17.51±7.27	0.857
In-hospital mortality – n.	5	0 (0%)	14	1 (7.1%)	0.539

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into account. Splenectomy with porta-azygous devascularization is a major treatment option for portal hypertension and hypersplenism in China and Japan [7,10,11,16,37]. By comparison, it is rarely recommended by the practice guidelines and consensus from Western countries [38–40]. Thus, this finding may be relevant in Western populations.

Theoretically, the portal pressure and risk of portal hypertension-related bleeding may be higher in cirrhotic patients with PVST than in those without. If so, the preventive and therapeutic strategy of variceal bleeding should be actively applied in patients with PVST. In agreement with this, we found a significantly higher proportion of high-risk varices in patients with PVST than in those without, but the statistical significance disappeared in other subgroup analyses due to the relatively small number of patients with MPV thrombosis >50% and clinically significant PVST (Supplementary Figure 2). On the other hand, all patients with clinically significant PVST who underwent endoscopic examinations had high-risk varices. Therefore, they should undergo careful variceal eradication before anticoagulation is initiated for the treatment of PVST in cirrhosis [41–45]. All analyses demonstrated that cirrhotic patients with PVST had significantly lower Hb than those without, which suggested a larger amount of upper gastrointestinal bleeding in patients with PVST. However, the prevalence of AUGIB was statistically similar between patients with and without PVST.

Regardless of splenectomy, all analyses showed no statistically significant association between Child-Pugh score and PVST in liver cirrhosis. Notably, after excluding patients with splenectomy, cirrhotic patients with PVST might have a higher Child-Pugh score than those without. Similarly, all but 1 analyses showed no significant association of MELD score with PVST. Notably, after excluding patients with splenectomy, MELD score was higher in cirrhotic patients PVST than in those without. Taken together, we should not neglect the role of liver dysfunction in the development of PVST in liver cirrhosis.

A previous study by D'Amico et al. found that PVST is significantly associated with worse short-term prognosis of cirrhotic patients with AUGIB [46]. By comparison, our study population was not restricted to AUGIB. In this setting, the in-hospital mortality was not significantly different between patients with and without PVST. Additionally, long-term outcome was lacking in our study.

Several other limitations should be clarified. First, the concentrations of coagulation and anticoagulation factors were not tested in any patients. Second, several studies suggested that abdominal surgery, such as colon and rectal surgery and sleeve gastrectomy, might increase the risk of PVST [47,48]. However, we did not identify any statistically significant association of appendicectomy and gastric and colonic surgery with the development of PVST in liver cirrhosis. It should be noted that very few patients underwent such abdominal surgery. Finally, the statistical power of our study may have been inadequate.

Conclusions

Splenectomy increases by at least 10-fold the risk of PVST in liver cirrhosis. Given the effect of PVST on the outcomes of liver cirrhosis, physicians should fully balance the benefits and risks of splenectomy for the treatment of portal hypertension and hypersplenism in liver cirrhosis. Further studies are warranted to explore the prevention of PVST after splenectomy.

Conflict of interest

None.

Supplementary Material

Supplementary Table 1. Characteristics of patients after excluding splenectomy.

Variables	N	Values
Age (years)	105	55.21±13.01; 55.19 (22.14–85.46)
Sex (Male/Female) – n.	105	71 (67.6%)/34 (32.4%)
Etiology of liver diseases – n.	105	
– Hepatitis B virus alone		32 (30.5%)
– Hepatitis C virus alone		7 (6.7%)
– Hepatitis B + C virus		3 (2.9%)
– Alcohol		30 (28.6%)
– Hepatitis B virus + Alcohol		7 (6.7%)

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Supplementary Table 1 continued. Characteristics of patients after excluding splenectomy.

Variables	N	Values
– Hepatitis C virus + Alcohol		1 (1%)
– Autoimmunity		5 (4.8%)
– Drug related		2 (1.9%)
– Unknown		18 (17.1%)
Disease history – n.	105	
– Diabetes		13 (12.4%)
– Coronary heart disease		8 (7.6%)
– Ischemic stroke		5 (4.8%)
– Arterial hypertension		9 (8.6%)
– Deep vein thrombosis		1 (1.0%)
Surgery history – n.	105	
– Splenectomy		0 (0%)
– Appendicectomy		3 (2.9%)
– Gastric surgery		2 (1.8%)
– Colonic surgery		1 (1%)
– Orthopedic surgery		3 (2.9%)
Abdominal trauma history – n.	105	1 (1%)
Acute upper gastrointestinal bleeding – n.	105	17 (16.2%)
Ascites at CT scans – n.	105	
– No		46 (43.8%)
– Mild		26 (24.8%)
– Moderate-Severe		33 (31.4%)
Hepatic encephalopathy – n.	104	6 (5.8%)
Esophageal varices at endoscopy – n.	42	
– No		10 (23.8%)
– Mild		2 (4.8%)
– Moderate		9 (21.4%)
– Severe		21 (50.0%)
Red blood cell (10^{12}/L)	102	3.42±0.88; 3.38 (1.19–5.27)
Hemoglobin (g/L)	102	106.18±30.30; 107 (42–170)
White blood cell (10^9/L)	102	4.96±3.21; 4.15 (1.5–20.5)
Platelet count (10^9/L)	102	92.97±76.65; 73.5 (11–545)
Total bilirubin (umol/L)	104	48.44±71.87; 23.8 (5.1–436.5)
Albumin (g/L)	103	32.33±6.67; 32.2 (11.7–44.3)
Alanine aminotransferase (U/L)	104	51.61±63.08; 33 (8–429)
Aspartate aminotransferase (U/L)	104	74.13±98.12; 47 (10–889)
Alakaline phosphatate (U/L)	104	117.67±80.09; 92 (34–524.4)
Gamma-glutamyl transpeptidase (U/L)	104	159.73±222.69; 68.5 (12–1130)
Blood urea nitrogen (mmol/L)	102	5.80±2.60; 5.26 (1.73–17.18)
Creatinine (umol/L)	102	59.42±21.61; 57 (29–151)
Potassium (mmol/L)	103	4.04±0.47; 4 (3.01–5.43)
Sodium (mmol/L)	103	138.02±6.50; 139.2 (83–144.5)

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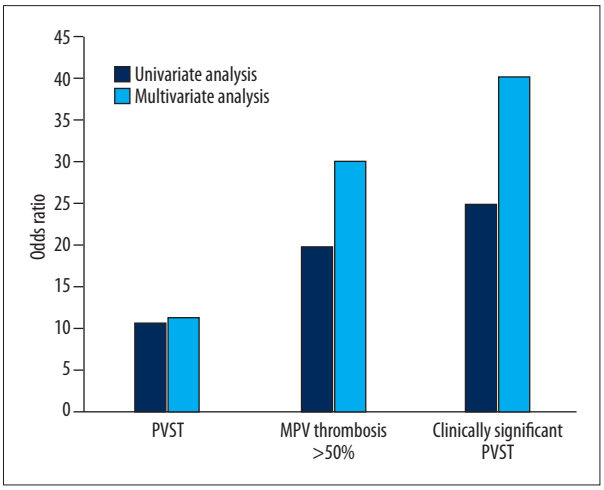
Supplementary Table 1 continued. Characteristics of patients after excluding splenectomy.

Variables	N	Values
Prothrombin time (seconds)	103	16.34±6.55; 14.8 (11.4–62.8)
Activated partial thromboplastin time (seconds)	103	45.13±16.53; 42.1 (29.9–180)
International normalized ratio	103	1.35±0.84; 1.16 (0.77–7.96)
Child-Pugh score	100	7.64±2.07; 8 (5–12)
Child-Pugh class A/B/C	100	37 (37%)/40 (40%)/23 (23%)
MELD score	100	6.23±7.04; 4.86 (–5.20–34.52)
APRI score	102	3.28±6.18; 1.69 (0.10–56.99)
AAR score	104	1.33±1.70; 0.72 (0.22–10.08)
FIB-4 score	102	9.42±9.68; 6.97 (0.38–61.59)
FI score	101	–25.31±6.91; –25.24 (–39.25 – –3.85)
King score	101	122.54±310.00; 46.97 (1.77–2589.47)
Portal vein system thrombosis – n.	105	14 (13.3%)
According to the location of thrombosis		
– Left portal vein branch thrombosis – n.	105	4 (3.8%)
– Right portal vein branch thrombosis – n.	105	2 (1.9%)
– Main portal vein thrombosis – n.	105	9 (8.6%)
– Superior mesenteric vein thrombosis – n.	105	5 (4.8%)
– Splenic vein thrombosis – n.	105	4 (3.8%)
According to the degree of MPV thrombosis		
– Mural thrombosis (<50%) – n.	105	4 (3.8%)
– Partial thrombosis (>50%) – n.	105	4 (3.8%)
– Total thrombosis (100%) – n.	105	1 (11.1%)
Cavernous transformation of the portal vein – n.	105	3 (2.9%)
Clinically significant PVST – n.	105	4 (3.8%)
Maximal diameter of spleen (mm)	105	140.27±30.77; 138.2 (83.8–240.9)
Maximal diameter of splenic vein (mm)	105	10.68±3.83; 10.3 (4.3–29.6)
Maximal diameter of main portal vein (mm)	105	18.34±5.18; 18 (0–31)
In-hospital mortality – n.	105	4 (3.8%)



Supplementary Figure 1. The ORs for splenectomy in the development of PVST according to the severity of PVST.

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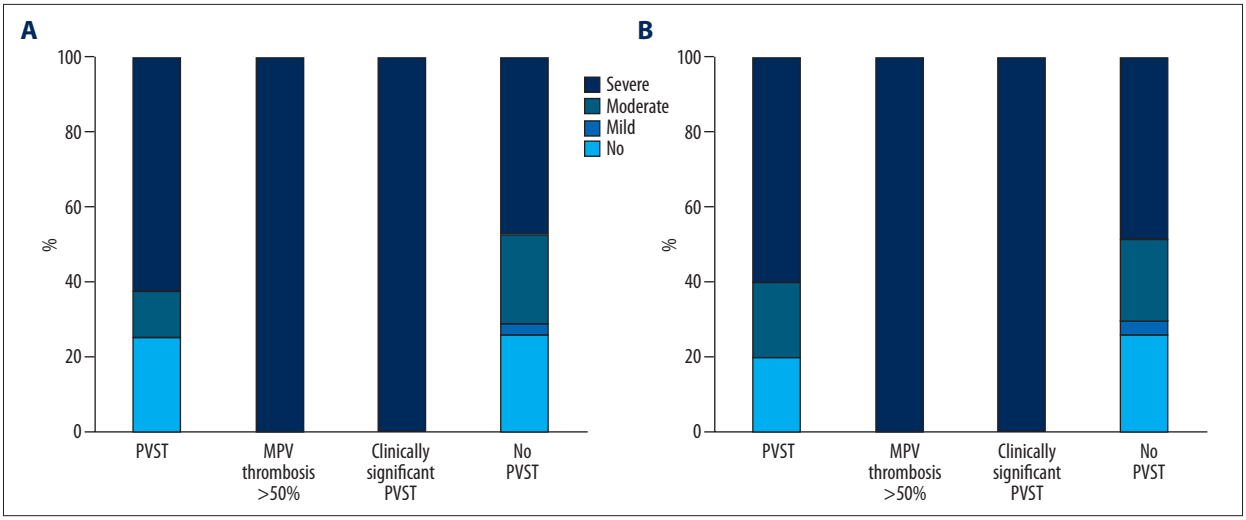

Supplementary Figure 2. The proportions of degree of esophageal varices in cirrhotic patients with and without PVST. (A) All patients. (B) Patients after excluding splenectomy.

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