

Impact of thrombocytopenia on failure of endoscopic variceal treatment in cirrhotic patients with acute variceal bleeding

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Abstract

Background: Acute variceal bleeding (AVB), a life-threatening complication of liver cirrhosis, can be effectively treated by endoscopy, but there is a risk of early rebleeding after endoscopic variceal treatment (EVT). Thrombocytopenia is the most common hemostatic abnormality in liver cirrhosis. However, it is still unclear about whether thrombocytopenia increases the failure of EVT in cirrhotic patients with AVB.

Objectives: We investigated the association between thrombocytopenia and the failure of EVT in cirrhotic patients with AVB.

Design: International multicenter, retrospective study.

Methods: Overall, 2467 cirrhotic patients with acute gastrointestinal bleeding who were enrolled into an international multicenter study between September 30, 2020 and June 30, 2023 were retrospectively screened. Thrombocytopenia was defined as platelet count below $150 \times 10^9/L$ and further classified as mild ($100 \times 10^9/L - 150 \times 10^9/L$), moderate ($50 \times 10^9/L - 100 \times 10^9/L$), and severe ($<50 \times 10^9/L$). A 1:1 propensity score matching (PSM) analysis was performed. Five-day failure to control bleeding was evaluated.

Results: Overall, 1079 patients were included, of whom 923 (85.5%) had thrombocytopenia, including mild ($n=241$), moderate ($n=445$), and severe ($n=237$) thrombocytopenia. PSM analysis demonstrated that the rate of 5-day failure to control bleeding was not significantly different between patients with and without thrombocytopenia (mild: [12/153] 7.8% vs [7/153] 4.6%, $p=0.236$; moderate: [9/155] 5.8% vs [7/155] 4.5%, $p=0.608$; or severe: [5/132] 3.8% vs [7/132] 5.3%, $p=0.555$).

Conclusion: Thrombocytopenia may not influence the efficacy of EVT in cirrhotic patients with AVB.

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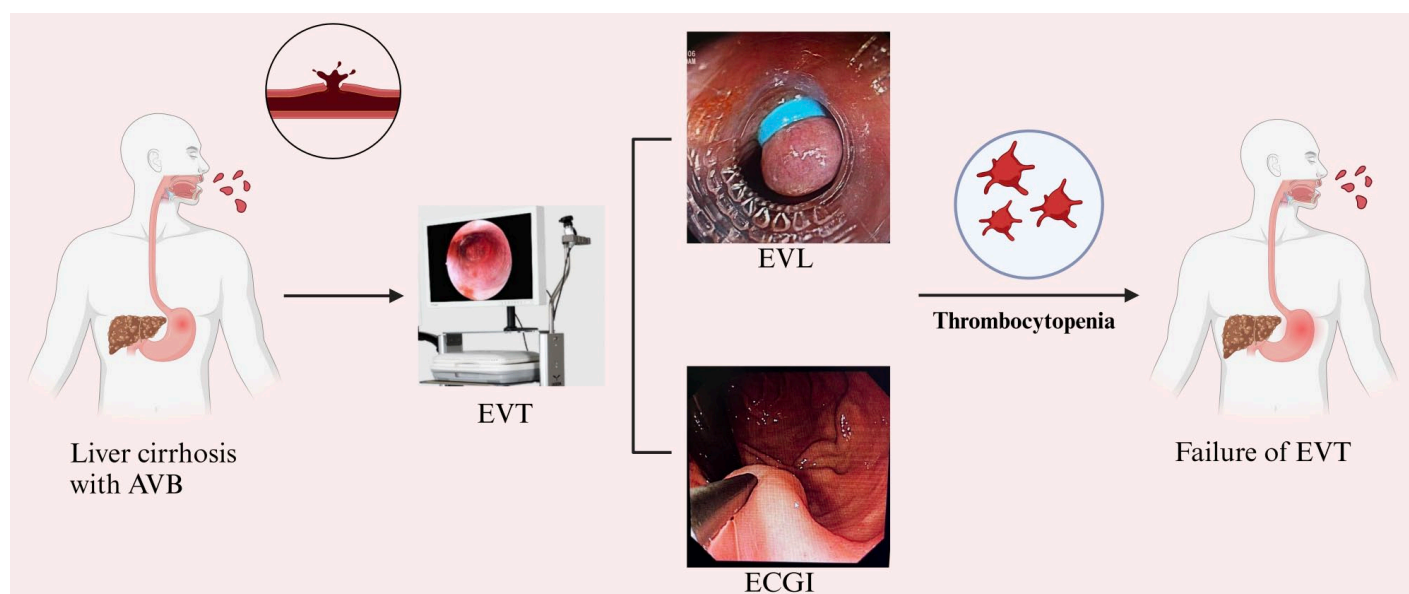
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Graphical abstract



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Plain language summary

Effect of decreased platelet count on the failure to control bleeding after endoscopic therapy in cirrhotic patients presenting with hematemesis or melena

Why was the study done? Patients with cirrhosis who have hematemesis or melena are usually treated by endoscopy. However, in some patients, endoscopic therapy cannot completely control bleeding. Notably, cirrhotic patients may experience varying degrees of decreased platelet count, which may be associated with increased risk of bleeding. Until now, it is still unclear about whether decreased platelet count is associated with the failure to control bleeding after endoscopic therapy.

What did the researchers do? Cirrhotic patients with acute gastrointestinal bleeding from an international multicenter database were screened. We adjusted confounding factors that may potentially influence the efficacy of endoscopic therapy to further clarify the effect of decreased platelet count on the failure of endoscopic therapy.

What did the researchers find? Overall, 1079 patients were included, of whom 923 had decreased platelet count. Among them, platelet count was mildly, moderately, and severely decreased in 241, 445, and 237 patients, respectively. After eliminating the confounding factors, the incidence of failure of endoscopic therapy was not significantly different between patients with and without decreased platelet count.

What do the findings mean? Decreased platelet count may not influence the efficacy of endoscopic therapy in cirrhotic patients presenting with hematemesis or melena.

Keywords: endoscopy, failure to control bleeding, liver cirrhosis, thrombocytopenia, variceal bleeding

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Introduction

Acute variceal bleeding (AVB) is a common and life-threatening complication of liver cirrhosis, which accounts for approximately 70% of acute gastrointestinal bleeding (AGIB) events.^{1,2} AVB is attributed to the rupture of gastroesophageal varices secondary to portal hypertension.³ In spite of advances in diagnosis and treatment, the 6-week mortality of cirrhotic patients with AVB remains 15%–20%.⁴ Additionally, recurrent bleeding is frequent, ranging from 30% to 40% within the subsequent 6 weeks after an initial AVB episode, especially the first 5 days.⁵ Currently, endoscopic variceal treatment (EVT), together with medical therapy, is the golden standard for the management of AVB,⁶ but the incidence of failure to control bleeding within the initial 5 days after EVT is as high as 10%–15%.^{7,8}

Thrombocytopenia is the most common hemostatic abnormality occurring in cirrhosis. The pathogenesis of thrombocytopenia is multifactorial, including decreased synthesis of thrombopoietin, splenic sequestration of platelets secondary to portal hypertension, myelosuppression, and increased destruction of platelets.⁹ The prevalence and degree of thrombocytopenia is in parallel with the severity of cirrhosis. Approximately 80% of cirrhotic patients with Child-Pugh class B and C have thrombocytopenia, with a majority presenting with moderate thrombocytopenia.¹⁰

Current evidence remains very scarce about the association of thrombocytopenia with treatment failure of EVT in cirrhotic patients with AVB. To the best of our knowledge, only three previous studies have explored the association between platelet (PLT) count and short-term outcomes of cirrhotic patients with AVB after EVT. A prospective cohort study found that PLT was not significantly different between patients who failed to control bleeding after endoscopy and those who did not.¹¹ But the confounding factors were not adjusted in this study, which may influence the statistical validity of the results. Similarly, another two previous studies also demonstrated that PLT was not significantly different between patients who developed early rebleeding and those who did not.^{12,13} However, the number of patients included in a study by Chau *et al.*¹² was very limited. Furthermore, all of them did not stratify the patients according to the severity of thrombocytopenia.^{11–13}

Herein, we aimed to further explore the association of thrombocytopenia with 5-day failure to control bleeding after EVT in cirrhotic patients with AVB, based on the data from an international multicenter study.

Methods

Study design

We retrospectively screened the data of cirrhotic patients with AGIB who were enrolled into an international multicenter observational study between September 30, 2020 and June 30, 2023 (NCT04662918).¹⁴ Exclusion criteria were as follows: (i) patients who did not undergo endoscopy; (ii) patients who were not diagnosed with variceal bleeding on endoscopy; (iii) patients who did not undergo EVT; and (iv) patients who underwent splenectomy, liver transplantation, or transjugular intrahepatic portosystemic shunt. The study protocol was approved by the Medical Ethical Committee of the General Hospital of Northern Theater Command with an ethical approval number (Y (2024) 139) and was carried out following the rules of the 1975 Declaration of Helsinki. Patients' informed consents were waived. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology statement.¹⁵

The following baseline data were collected: demographics, etiology of liver cirrhosis, decompensated complications at admission, and laboratory tests (i.e., white blood cell (WBC), PLT, prothrombin time (PT), and international normalized ratio (INR)). Child-Pugh score and Model for End-Stage Liver Disease (MELD) score at admission were calculated. According to the data collected in this study, EVT primarily included endoscopic variceal ligation (EVL), endoscopic cyanoacrylate glue injection (ECGI), and endoscopic injection sclerotherapy (EIS). Drugs mainly included vasoactive drugs (i.e., octreotide, somatostatin, and terlipressin), proton pump inhibitors, and antibiotics. Blood transfusions mainly included PLT, red blood cell (RBC), and fresh frozen plasma (FFP).

Patients were divided according to the presence of thrombocytopenia. Thrombocytopenia was defined as $PLT < 150 \times 10^9/L$ and further classified as mild ($100 \times 10^9/L$ – $150 \times 10^9/L$), moderate ($50 \times 10^9/L$ – $100 \times 10^9/L$), and severe

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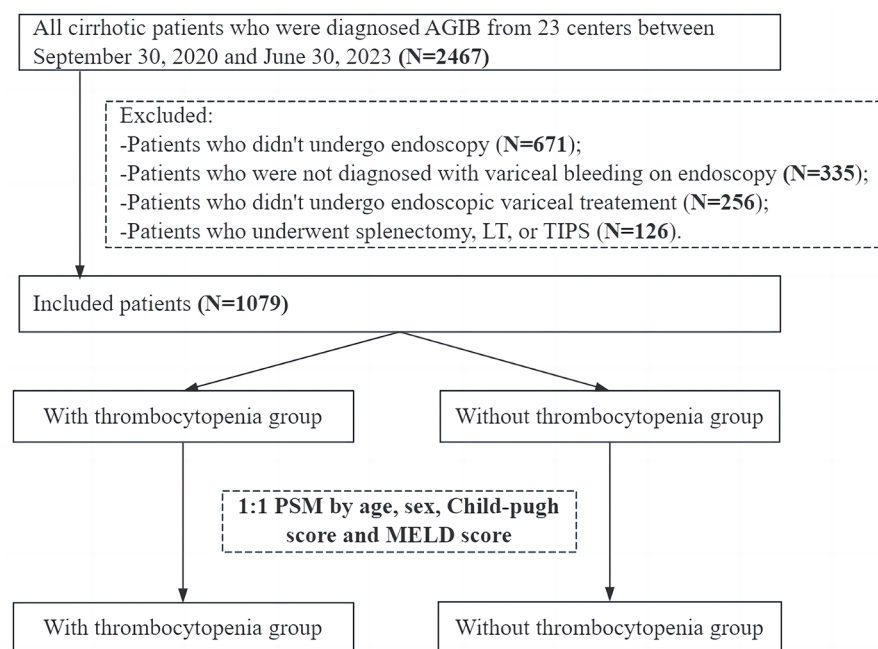


Figure 1. Flowchart of patients' screening and grouping.

AGIB, acute gastrointestinal bleeding; LT, liver transplantation; MELD, model for end-stage liver disease; PSM, propensity score matching; TIPS, transjugular intrahepatic portosystemic shunt.

(<50 × 10⁹/L).^{10,16} The outcome of interest in this study was the rate of 5-day failure to control bleeding, which was defined according to the Baveno VII consensus.⁶

Statistical analyses

All statistical analyses were performed with IBM SPSS 25.0 (IBM Corp., Armonk, NY, USA) and Stata/SE 12.0 (Stata Corp., College Station, TX, USA). Continuous variables were expressed as mean ± standard deviation and median (range) and compared using the independent sample *t*-test or nonparametric Mann–Whitney *U* test. Categorical variables were expressed as frequency (percentage) and were compared using the Chi-squared test or Fisher's exact test. Logistic regression analyses were conducted to explore whether thrombocytopenia was significantly associated with the risk of 5-day failure to control bleeding after EVT. Crude odd ratios (cORs) with their 95% confidence intervals (CIs) were calculated in univariate analyses. Adjusted odd ratios (aORs) with their 95% CIs were calculated in multivariate analyses after adjusting for age, gender, blood transfusions (i.e., PLT, RBC, and FFP), Child-Pugh score, and MELD score. A 1:1 propensity score

matching (PSM) analysis was performed to match baseline characteristics between patients with and without thrombocytopenia. Matching factors included age, gender, blood transfusions (i.e., PLT, RBC, and FFP), Child-Pugh score, and MELD score. A two-tailed *p* < 0.05 was considered statistically significant.

Results

Patients

A total of 1079 patients were included (Figure 1), of whom 923 (85.5%) had thrombocytopenia, including mild (*n* = 241), moderate (*n* = 445), and severe (*n* = 237) thrombocytopenia. Patient characteristics are summarized in Table 1. The median age was 57 years (range: 19–92), and 762 (70.6%) patients were male. Hepatitis B virus infection (52.9%) was the most common etiology of liver cirrhosis followed by alcohol abuse (16.6%). Among them, 684 (63.4%) patients had ascites at admission, and 635 (58.9%) had history of variceal bleeding. The median Child-Pugh score and MELD score were 7.00 (range: 5.00–15.00) and 12.14 (range: 6.43–40.00), respectively. The rate of 5-day failure to control bleeding was 5.2% (*n* = 56/1079).

Table 1. Baseline characteristics of the study cohort.

Variables	Overall	
	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)
Demographics		
Age (years)	1079	56.94 $\pm$ 12.27 57.00 (19.00–92.00)
Male (%)	1079	762 (70.6%)
Etiology of liver cirrhosis		
HBV (%)	1079	571 (52.9%)
HCV (%)	1079	74 (6.9%)
Alcohol (%)	1079	179 (16.6%)
Diabetes	1079	285 (26.4%)
Complications of liver cirrhosis (past and current)		
Ascites (%)	1079	684 (63.4%)
HE (%)	1079	108 (10.0%)
History of variceal bleeding (%)	1079	635 (58.9%)
ACLF (%)	1079	56 (5.2%)
HCC (%)	1079	184 (17.1%)
Laboratory tests		
WBC ($10^9/L$)	1079	5.97 $\pm$ 3.97 4.92 (0.37–28.48)
HB (g/L)	1079	82.91 $\pm$ 23.56 81.00 (16.00–161.00)
PLT ($10^9/L$)	1079	96.35 $\pm$ 69.65 78.00 (3.00–836.00)
TBIL ($\mu\text{mol/L}$)	1079	34.92 $\pm$ 41.71 23.90 (2.30–408.00)
ALB (g/L)	1079	31.12 $\pm$ 5.67 30.80 (12.40–55.00)
Scr ($\mu\text{mol/L}$)	1079	74.65 $\pm$ 49.98 64.80 (7.00–859.25)
PT (s)	1077	15.88 $\pm$ 3.49 15.20 (10.00–39.90)
INR	1079	1.38 $\pm$ 0.32 1.31 (0.90–4.13)
INR $\geq$ 1.5 (%)	1079	251 (23.3%)

(Continued)

Table 1. (Continued)

Variables	Overall	
	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)
Child-Pugh score	1079	7.63 $\pm$ 1.78 7.00 (5.00–15.00)
MELD score	1079	13.40 $\pm$ 5.08 12.14 (6.43–40.00)
Endoscopy		
EV (%)	1079	1055 (97.8%)
GV (%)	1079	752 (69.7%)
Medical therapy		
Vasoconstrictors	1079	1029 (95.3%)
PPIs	1079	1049 (97.2%)
Antibiotics	1079	885 (82.0%)
Blood transfusions		
PLT	1079	27 (2.5%)
RBC	1079	476 (44.1%)
FFP	1079	227 (21.0%)
Endoscopic variceal therapy		
EVL	1079	454 (42.1%)
EIS	1079	52 (4.8%)
ECGI	1079	114 (10.6%)
EVL + EIS	1079	23 (2.1%)
EVL + ECGI	1079	169 (15.7%)
EIS + ECGI	1079	174 (16.1%)
EVL + EIS + ECGI	1079	76 (7.0%)
Others	1079	17 (1.6%)
5-Day failure to control bleeding (%)	1079	56 (5.2%)

ACLF, acute-on-chronic liver failure; ALB, albumin; ECGI, endoscopic cyanoacrylate glue injection; EIS, endoscopic injection sclerotherapy; EV, esophageal varices; EVL, endoscopic variceal ligation; FFP, fresh frozen plasma; GV, gastric varices; HB, hemoglobin; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HE, hepatic encephalopathy; INR, international normalized ratio; MELD, model for end-stage liver disease; No. Pts, number of patients; PLT, platelet; PPIs, proton pump inhibitors; PT, prothrombin time; RBC, red blood cell; Scr, serum creatinine; SD, standard deviation; TBIL, total bilirubin; WBC, white blood cell.

Mild thrombocytopenia versus normal PLT

In the overall analysis, patients with mild thrombocytopenia had significantly higher prevalence of esophageal varices (EV) (98.3% vs 94.9%, $p=0.049$), but lower WBC ($7.06 \times 10^9/L$ vs $9.44 \times 10^9/L$, $p<0.001$) than those with normal PLT. However, the rate of 5-day failure to control bleeding was not significantly different between the two groups (5.4% vs 4.5%, $p=0.687$; Table 2). Univariate logistic regression analysis showed that the presence of mild thrombocytopenia was not independently associated with the rate of 5-day failure to control bleeding (cOR=1.214, 95% CI=0.473–3.112, $p=0.687$). Multivariate logistic regression analysis showed that the presence of mild thrombocytopenia was not independently associated with the rate of 5-day failure to control bleeding (aOR=1.713, 95% CI=0.618–4.748, $p=0.300$).

In the PSM analysis, 153 patients were matched to each group. Patients with mild thrombocytopenia had significantly lower WBC ($7.42 \times 10^9/L$ vs $9.46 \times 10^9/L$, $p<0.001$) than those with normal PLT. However, the rate of 5-day failure to control bleeding was not significantly different between the two groups (7.8% vs 4.6%, $p=0.236$; Table 2).

Moderate thrombocytopenia versus normal PLT

In the overall analysis, patients with moderate thrombocytopenia had significantly higher total bilirubin (TBIL) ($35.53 \mu\text{mol/L}$ vs $29.72 \mu\text{mol/L}$, $p<0.001$), PT (15.98s vs 15.39s, $p=0.023$), INR (1.39 vs 1.34, $p=0.011$), prevalence of EV (98.0% vs 94.9%, $p=0.044$), and gastric varices (GV) (73.9% vs 59.0%, $p<0.001$), but lower WBC ($5.35 \times 10^9/L$ vs $9.44 \times 10^9/L$, $p<0.001$) than those with normal PLT (Table 3). However, the rate of 5-day failure to control bleeding was not significantly different between the two groups (5.8% vs 4.5%, $p=0.522$). Univariate logistic regression analysis showed that the presence of moderate thrombocytopenia was not independently associated with the rate of 5-day failure to control bleeding (cOR=1.321, 95% CI=0.562–3.107, $p=0.524$). Multivariate logistic regression analysis showed that the presence of moderate thrombocytopenia was not independently associated with the rate of 5-day failure to control bleeding (aOR=1.384, 95% CI=0.567–3.380, $p=0.476$).

In the PSM analysis, 155 patients were matched to each group. Patients with moderate thrombocytopenia had significantly higher TBIL ($40.05 \mu\text{mol/L}$ vs $29.87 \mu\text{mol/L}$, $p=0.004$), prevalence of GV (70.3% vs 59.4%, $p=0.043$), but lower WBC ($5.48 \times 10^9/L$ vs $9.44 \times 10^9/L$, $p<0.001$) than those with normal PLT. However, the rate of 5-day failure to control bleeding was not significantly different between the two groups (5.8% vs 4.5%, $p=0.608$; Table 3).

Severe thrombocytopenia versus normal PLT

In the overall analysis, patients with severe thrombocytopenia had significantly higher TBIL ($35.83 \mu\text{mol/L}$ vs $29.72 \mu\text{mol/L}$, $p<0.001$), PT (16.49s vs 15.39s, $p<0.001$), INR (1.44 vs 1.34, $p<0.001$), and prevalence of GV (77.2% vs 59.0%, $p<0.001$), but lower WBC ($3.71 \times 10^9/L$ vs $9.44 \times 10^9/L$, $p<0.001$). However, the rate of 5-day failure to control bleeding was not significantly different between the two groups (4.2% vs 4.5%, $p=0.898$; Table 4). Univariate logistic regression analysis showed that the presence of severe thrombocytopenia was not independently associated with the rate of 5-day failure to control bleeding (cOR=0.938, 95% CI=0.349–2.518, $p=0.898$). Multivariate logistic regression analysis showed that the presence of severe thrombocytopenia was not independently associated with the rate of 5-day failure to control bleeding (aOR=0.771, 95% CI=0.256–2.315, $p=0.642$).

In the PSM analysis, 132 patients were matched to each group. Patients with severe thrombocytopenia had significantly higher TBIL ($33.64 \mu\text{mol/L}$ vs $27.60 \mu\text{mol/L}$, $p<0.001$), PT (16.33s vs 15.42s, $p=0.001$), INR (1.42 vs 1.34, $p<0.001$), and prevalence of GV (78.8% vs 62.1%, $p=0.003$), but lower WBC ($3.93 \times 10^9/L$ vs $9.56 \times 10^9/L$, $p<0.001$) than those with normal PLT. However, the rate of 5-day failure to control bleeding was not significantly different between the two groups (3.8% vs 5.3%, $p=0.555$; Table 4).

Discussion

Hepatic venous pressure gradient (HVPG) $>20 \text{ mmHg}$ is the most widely recognized predictor of 5-day failure after EVT.⁷ However, the applicability of HVPG measurement in patients with AVB is limited, because it is invasive and

Table 2. Overall analysis and PSM analysis between patients with mild thrombocytopenia and normal PLT.

Variables	Overall analysis			PSM analysis						
	With mild thrombocytopenia		p Value	With mild thrombocytopenia		p Value				
	No. Pts	Mean ± SD, median (range) or frequency (percentage)		No. Pts	Mean ± SD, median (range) or frequency (percentage)					
Demographics										
Age (years)	241	58.73 ± 11.95 58.00 [31.00–89.00]	156	58.66 ± 13.40 58.00 [25.00–92.00]	0.959	153	58.62 ± 12.44 59.00 [31.00–89.00]	153	58.69 ± 13.53 58.00 [25.00–92.00]	0.965
Male (%)	241	163 [67.6%]	156	122 [78.2%]	0.022	153	115 [75.2%]	153	119 [77.8%]	0.590
Etiology of liver cirrhosis										
HBV (%)	241	98 [40.7%]	156	79 [50.6%]	0.051	153	67 [43.8%]	153	78 [51.0%]	0.208
HCV (%)	241	17 [7.1%]	156	6 [3.8%]	0.181	153	12 [7.8%]	153	6 [3.9%]	0.145
Alcohol (%)	241	48 [19.9%]	156	27 [17.3%]	0.517	153	31 [20.3%]	153	25 [16.3%]	0.375
Diabetes	241	81 [33.6%]	156	49 [31.4%]	0.648	153	54 [35.5%]	153	48 [31.4%]	0.467
Complications of liver cirrhosis (past and current)										
Ascites (%)	241	148 [61.4%]	156	94 [60.3%]	0.818	153	89 [58.2%]	153	92 [60.1%]	0.727
HE (%)	241	23 [9.5%]	156	25 [16.0%]	0.053	153	15 [9.8%]	153	25 [16.3%]	0.090
History of variceal bleeding (%)	241	122 [50.6%]	156	90 [57.7%]	0.168	153	82 [53.6%]	153	89 [58.2%]	0.420
ACLF (%)	241	16 [6.6%]	156	9 [5.8%]	0.728	153	9 [5.9%]	153	9 [5.9%]	1.000
HCC (%)	241	57 [23.7%]	156	32 [20.5%]	0.464	153	46 [30.1%]	153	32 [20.9%]	0.066
Laboratory tests										
WBC (10 ⁹ /L)	241	7.06 ± 3.73 6.33 [1.70–22.27]	156	9.44 ± 4.30 8.82 [1.47–22.20]	<0.001	153	7.42 ± 4.02 6.90 [1.95–22.27]	153	9.46 ± 4.33 8.80 [1.47–22.20]	<0.001
HB (g/L)	241	85.56 ± 22.06 84.00 [22.00–161.00]	156	81.80 ± 27.09 80.50 [16.00–151.00]	0.149	153	85.28 ± 22.31 83.00 [34.00–161.00]	153	81.92 ± 27.33 81.00 [16.00–151.00]	0.239
PLT (10 ⁹ /L)	241	121.34 ± 14.20 120.00 [100.00–149.00]	156	222.06 ± 91.67 193.00 [150.00–836.00]	<0.001	153	120.99 ± 14.66 119.00 [100.00–149.00]	153	222.50 ± 92.49 192.00 [150.00–836.00]	<0.001

(Continued)

Table 2. (Continued)

Variables	Overall analysis			PSM analysis		
	With mild thrombocytopenia		p Value	With mild thrombocytopenia		p Value
	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)		No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)	
With normal PLT	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)		No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)	
TBIL ($\mu\text{mol/L}$)	241	36.29 $\pm$ 51.96 21.50 [6.70–391.50]	0.173	153	41.38 $\pm$ 62.61 23.10 [6.70–391.59]	0.093
ALB (g/L)	241	30.96 $\pm$ 5.64 30.30 [18.00–50.40]	0.922	153	30.60 $\pm$ 5.77 30.00 [18.00–50.40]	0.882
Scr ($\mu\text{mol/L}$)	241	72.57 $\pm$ 40.26 63.69 [26.52–477.36]	0.062	153	75.21 $\pm$ 45.00 66.00 [28.00–477.36]	0.316
PT (s)	241	15.42 $\pm$ 3.54 14.60 [10.00–32.90]	0.840	153	15.68 $\pm$ 3.55 14.70 [11.20–32.90]	0.561
INR	241	1.34 $\pm$ 0.31 1.27 [0.90–3.10]	0.837	153	1.36 $\pm$ 0.31 1.28 [1.00–3.10]	0.380
INR $\geq$ 1.5 (%)	241	43 [17.8%]	0.978	153	28 [18.3%]	1.000
Child-Pugh score	241	7.60 $\pm$ 1.76 7.00 [5.00–13.00]	0.888	153	7.63 $\pm$ 1.77 7.00 [5.00–12.00]	0.959
MELD score	241	12.86 $\pm$ 5.49 11.02 [6.43–33.36]	0.144	153	13.50 $\pm$ 5.88 11.17 [6.67–33.36]	0.849
Endoscopy						
EV (%)	241	237 [98.3%]	0.049	153	151 [98.7%]	0.054
GV (%)	241	148 [61.4%]	0.628	153	90 [58.8%]	0.907
Medical therapy						
Vasopressors	241	226 [93.8%]	0.460	153	141 [92.2%]	0.145
PPIs	241	226 [93.8%]	0.460	153	145 [94.8%]	0.791
Antibiotics	241	190 [78.8%]	0.269	153	128 [83.7%]	0.878
Blood transfusions						
PLT	241	2 [0.8%]	1.000	153	1 [0.7%]	1.000
RBC	241	109 [45.2%]	0.192	153	79 [51.6%]	1.000

(Continued)

Table 2. (Continued)

Variables	Overall analysis				PSM analysis					
	With mild thrombocytopenia		With normal PLT		p Value	With mild thrombocytopenia		With normal PLT		
	No. Pts	Mean ± SD, median (range) or frequency (percentage)	No. Pts	Mean ± SD, median (range) or frequency (percentage)		No. Pts	Mean ± SD, median (range) or frequency (percentage)	No. Pts	Mean ± SD, median (range) or frequency (percentage)	
FFP	241	34 (14.1%)	156	28 (17.9%)	0.303	153	31 (20.3%)	153	28 (18.3%)	0.664
Endoscopic variceal therapy										
EVL	241	114 (47.3%)	156	81 (51.9%)	0.368	153	75 (49.0%)	153	79 (51.6%)	0.647
EIS	241	10 (4.1%)	156	6 (3.8%)	0.881	153	6 (3.9%)	153	6 (3.9%)	1.000
ECGI	241	26 (10.8%)	156	20 (12.8%)	0.537	153	16 (10.5%)	153	20 (13.1%)	0.478
EVL + EIS	241	7 (2.9%)	156	2 (1.3%)	0.474	153	4 (2.6%)	153	2 (1.3%)	0.680
EVL + ECGI	241	33 (13.7%)	156	21 (13.5%)	0.948	153	19 (12.4%)	153	21 (13.7%)	0.734
EIS + ECGI	241	34 (14.1%)	156	20 (12.8%)	0.715	153	22 (14.4%)	153	20 (13.1%)	0.740
EVL + EIS + ECGI	241	13 (5.4%)	156	3 (1.9%)	0.086	153	8 (5.2%)	153	3 (2.0%)	0.125
Others	241	4 (1.7%)	156	3 (1.9%)	1.000	153	3 (2.0%)	153	2 (1.3%)	1.000
5-Day failure to control bleeding (%)	241	13 (5.4%)	156	7 (4.5%)	0.687	153	12 (7.8%)	153	7 (4.6%)	0.236
The values in bold mean statistically significant. ACLF, acute-on-chronic liver failure; ALB, albumin; ECGI, endoscopic cyanoacrylate glue injection; EIS, endoscopic injection sclerotherapy; EV, esophageal varices; EVL, endoscopic variceal ligation; FFP, fresh frozen plasma; GV, gastric varices; HB, hemoglobin; HBV, Hepatitis B Virus; HCC, hepatocellular carcinoma; HCV, Hepatitis C Virus; HE, hepatic encephalopathy; INR, international normalized ratio; MELD, model for end-stage liver disease; No. Pts, number of patients; PLT, platelet; PPIs, proton pump inhibitors; PSM, propensity score matching; PT, prothrombin time; RBC, red blood cell; Scr, serum creatinine; SD, standard deviation; TBIL, total bilirubin; WBC, white blood cell.										

The values in bold mean statistically significant.

ACLF, acute-on-chronic liver failure; ALB, albumin; ECGI, endoscopic cyanoacrylate glue injection; EIS, endoscopic injection sclerotherapy; EV, esophageal varices; EVL, endoscopic variceal ligation; FFP, fresh frozen plasma; GV, gastric varices; HB, hemoglobin; HBV, Hepatitis B Virus; HCC, hepatocellular carcinoma; HCV, Hepatitis C Virus; HE, hepatic encephalopathy; INR, international normalized ratio; MELD, model for end-stage liver disease; No. Pts, number of patients; PLT, platelet; PPIs, proton pump inhibitors; PSM, propensity score matching; PT, prothrombin time; RBC, red blood cell; Scr, serum creatinine; SD, standard deviation; TBIL, total bilirubin; WBC, white blood cell.

Table 3. Overall analysis and PSM analysis between patients with moderate thrombocytopenia and normal PLT.

Variables	Overall analysis			PSM analysis			p Value	PSM analysis			p Value	
	With moderate thrombocytopenia		p Value	With moderate thrombocytopenia		p Value						
	No. Pts	Mean ± SD, median (range) or frequency (percentage)		No. Pts	Mean ± SD, median (range) or frequency (percentage)							
Demographics												
Age (years)	445	56.85 ± 11.80 57.00 (19.00–90.00)	156	58.66 ± 13.40 58.00 (25.00–92.00)	155	59.86 ± 12.11 59.00 (32.00–90.00)	0.112	155	59.86 ± 12.11 59.00 (32.00–90.00)	155	58.49 ± 13.27 58.00 (25.00–92.00)	0.342
Male (%)	445	308 (69.2%)	156	122 (78.2%)	155	119 (76.8%)	0.032	155	119 (76.8%)	155	121 (78.1%)	0.786
Etiology of liver cirrhosis												
HBV (%)	445	243 (54.6%)	156	79 (50.6%)	155	79 (51.0%)	0.393	155	79 (51.0%)	155	79 (51.0%)	1.000
HCV (%)	445	33 (7.4%)	156	6 (3.8%)	155	12 (7.7%)	0.119	155	12 (7.7%)	155	6 (3.9%)	0.145
Alcohol (%)	445	73 (16.4%)	156	27 (17.3%)	155	24 (15.5%)	0.794	155	24 (15.5%)	155	27 (17.4%)	0.646
Diabetes	445	111 (24.9%)	156	49 (31.4%)	155	44 (28.4%)	0.116	155	44 (28.4%)	155	49 (31.6%)	0.535
Complications of liver cirrhosis (past and current)												
Ascites (%)	445	279 (62.7%)	156	94 (60.3%)	155	102 (65.8%)	0.589	155	102 (65.8%)	155	94 (60.6%)	0.346
HE (%)	445	43 (9.7%)	156	25 (16.0%)	155	17 (11.0%)	0.031	155	17 (11.0%)	155	25 (16.1%)	0.184
History of variceal bleeding (%)	445	265 (59.6%)	156	90 (57.7%)	155	92 (59.4%)	0.685	155	92 (59.4%)	155	90 (58.1%)	0.818
ACLF (%)	445	19 (4.3%)	156	9 (5.8%)	155	10 (6.5%)	0.444	155	10 (6.5%)	155	9 (5.8%)	0.813
HCC (%)	445	63 (14.2%)	156	32 (20.5%)	155	32 (20.6%)	0.061	155	32 (20.6%)	155	31 (20.0%)	0.888
Laboratory tests												
WBC (10 ⁹ /L)	445	5.35 ± 3.52 4.56 (0.89–28.48)	156	9.44 ± 4.30 8.82 (1.47–22.20)	155	5.48 ± 3.55 4.59 (1.20–24.30)	< 0.001	155	5.48 ± 3.55 4.59 (1.20–24.30)	155	9.44 ± 4.32 8.80 (1.47–22.20)	< 0.001
HB (g/L)	445	83.01 ± 23.30 81.00 (26.00–161.00)	156	81.80 ± 27.09 80.50 (16.00–151.00)	155	82.05 ± 20.78 81.00 (41.00–161.00)	0.688	155	82.05 ± 20.78 81.00 (41.00–161.00)	155	81.90 ± 27.14 81.00 (16.00–151.00)	0.974
PLT (10 ⁹ /L)	445	70.99 ± 13.86 70.00 (50.00–99.00)	156	222.06 ± 91.67 193.00 (150.00–836.00)	155	71.82 ± 14.02 72.00 (50.00–99.00)	< 0.001	155	71.82 ± 14.02 72.00 (50.00–99.00)	155	221.41 ± 90.61 192.00 (150.00–836.00)	< 0.001

(Continued)

Table 3. (Continued)

Variables	Overall analysis		PSM analysis			p Value				
	With moderate thrombocytopenia		With moderate thrombocytopenia		With normal PLT					
	No. Pts	Mean ± SD, median (range) or frequency (percentage)	No. Pts	Mean ± SD, median (range) or frequency (percentage)						
TBIL (μmol/L)	445	35.53 ± 43.44 23.95 [2.30–408.00]	156	29.72 ± 35.75 19.90 [5.30–295.83]	< 0.001	155	40.05 ± 55.69 24.50 [5.30–383.90]	155	29.87 ± 35.81 19.90 [5.30–295.83]	0.004
ALB (g/L)	445	31.26 ± 5.48 31.00 [15.00–55.00]	156	30.82 ± 5.78 30.65 [16.60–47.20]	0.403	155	31.19 ± 5.15 31.00 [19.00–55.00]	155	30.81 ± 5.79 30.60 [16.60–47.20]	0.505
Scr (μmol/L)	445	74.67 ± 57.36 64.00 [9.10–859.25]	156	82.17 ± 50.07 67.50 [30.30–433.16]	0.043	155	82.57 ± 80.27 66.80 [27.70–859.25]	155	81.00 ± 48.05 67.30 [30.30–433.16]	0.576
PT (s)	443	15.98 ± 3.53 15.11 [10.30–39.90]	156	15.39 ± 3.36 14.90 [10.80–36.80]	0.023	154	15.99 ± 3.46 15.20 [10.30–35.00]	155	15.40 ± 3.37 14.90 [10.80–36.80]	0.052
INR	445	1.39 ± 0.34 1.32 [0.93–4.13]	156	1.34 ± 0.32 1.27 [0.99–3.39]	0.011	155	1.39 ± 0.33 1.30 [0.93–3.30]	155	1.34 ± 0.32 1.27 [0.99–3.39]	0.089
INR ≥ 1.5 (%)	445	102 [22.9%]	156	28 [17.9%]	0.194	155	36 [23.2%]	155	28 [18.1%]	0.262
Child–Pugh score	445	7.61 ± 1.81 7.00 [5.00–15.00]	156	7.59 ± 1.85 7.00 [5.00–12.00]	0.942	155	7.72 ± 1.91 7.00 [5.00–15.00]	155	7.60 ± 1.85 7.00 [5.00–12.00]	0.706
MELD score	445	13.43 ± 5.12 11.89 [6.43–40.00]	156	13.60 ± 5.45 12.41 [6.43–32.27]	0.856	155	13.89 ± 5.61 12.09 [6.43–40.00]	155	13.56 ± 5.45 12.38 [6.43–32.27]	0.478
Endoscopy										
EV (%)	445	436 [98.0%]	156	148 [94.9%]	0.044	155	152 [98.1%]	155	147 [94.8%]	0.125
GV (%)	445	329 [73.9%]	156	92 [59.0%]	< 0.001	155	109 [70.3%]	155	92 [59.4%]	0.043
Medical therapy										
Vasoconstrictors	445	428 [96.2%]	156	149 [95.5%]	0.714	155	149 [96.1%]	155	149 [96.1%]	1.000
PPIs	445	439 [98.7%]	156	149 [95.5%]	0.046	155	153 [98.7%]	155	148 [95.5%]	0.176
Antibiotics	445	368 [82.7%]	156	130 [83.3%]	0.856	155	131 [84.5%]	155	129 [83.2%]	0.757

(Continued)

Table 3. (Continued)

Variables	Overall analysis			PSM analysis				p Value
	With moderate thrombocytopenia		With normal PLT	p Value	With moderate thrombocytopenia		With normal PLT	
	No. Pts	Mean ± SD, median (range) or frequency (percentage)			No. Pts	Mean ± SD, median (range) or frequency (percentage)		
Blood transfusions								
PLT	445	6 (1.3%)	156	1 (0.6%)	0.783	155	1 (0.6%)	1.000
RBC	445	189 (42.5%)	156	81 (51.9%)	0.041	155	75 (48.4%)	0.570
FFP	445	88 (19.8%)	156	28 (17.9%)	0.619	155	30 (19.4%)	0.771
Endoscopic variceal therapy								
EVL	445	177 (39.8%)	156	81 (51.9%)	0.008	155	65 (41.9%)	0.088
EIS	445	22 (4.9%)	156	6 (3.8%)	0.576	155	7 (4.5%)	0.777
ECGI	445	39 (8.8%)	156	20 (12.8%)	0.143	155	8 (5.2%)	0.017
EVL + EIS	445	8 (1.8%)	156	2 (1.3%)	0.945	155	1 (0.6%)	1.000
EVL + ECGI	445	74 (16.6%)	156	21 (13.5%)	0.351	155	23 (14.8%)	0.745
EIS + ECGI	445	84 (18.9%)	156	20 (12.8%)	0.085	155	34 (21.9%)	0.036
EVL + EIS + ECGI	445	33 (7.4%)	156	3 (1.9%)	0.013	155	14 (9.0%)	0.006
Others	445	8 (1.8%)	156	3 (1.9%)	1.000	155	3 (1.9%)	1.000
5-Day failure to control bleeding (%)	445	26 (5.8%)	156	7 (4.5%)	0.522	155	9 (5.8%)	0.608
The values in bold mean statistically significant. ACLF, acute-on-chronic liver failure; ALB, albumin; ECGI, endoscopic cyanoacrylate glue injection; EIS, endoscopic injection sclerotherapy; EV, esophageal varices; EVL, endoscopic variceal ligation; FFP, fresh frozen plasma; GV, gastric varices; HB, hemoglobin; HBV, Hepatitis B Virus; HCC, hepatocellular carcinoma; HCV, Hepatitis C Virus; HE, hepatic encephalopathy; INR, international normalized ratio; MELD, model for end-stage liver disease; No. Pts, number of patients; PLT, platelet; PPIs, proton pump inhibitors; PSM, propensity score matching; PT, prothrombin time; RBC, red blood cell; Scr, serum creatinine; SD, standard deviation; TBIL, total bilirubin; WBC, white blood cell.								

Table 4. Overall analysis and PSM analysis between patients with severe thrombocytopenia and normal PLT.

Variables	Overall analysis			PSM analysis			p Value	p Value		
	With severe thrombocytopenia		With normal PLT	With severe thrombocytopenia		With normal PLT				
	No. Pts	Mean ± SD, median (range) or frequency (percentage)		No. Pts	Mean ± SD, median (range) or frequency (percentage)					
Demographics										
Age (years)	237	54.15 ± 12.20 54.00 [26.00–85.00]	156	58.66 ± 13.40 58.00 [25.00–92.00]	< 0.001	132	56.35 ± 11.48 55.50 [28.00–85.00]	132	56.65 ± 12.54 57.50 [25.00–89.00]	0.838
Male (%)	237	169 [71.3%]	156	122 [78.2%]	0.127	132	103 [78.0%]	132	100 [75.8%]	0.661
Etiology of liver cirrhosis										
HBV (%)	237	151 [63.7%]	156	79 [50.6%]	0.010	132	87 [65.9%]	132	75 [56.8%]	0.129
HCV (%)	237	18 [7.6%]	156	6 [3.8%]	0.129	132	12 [9.1%]	132	5 [3.8%]	0.079
Alcohol (%)	237	31 [13.1%]	156	27 [17.3%]	0.248	132	18 [13.6%]	132	22 [16.7%]	0.492
Diabetes	237	44 [18.6%]	156	49 [31.4%]	0.003	132	29 [22.0%]	132	39 [29.5%]	0.159
Complications of liver cirrhosis (past and current)										
Ascites (%)	237	163 [68.8%]	156	94 [60.3%]	0.082	132	82 [62.1%]	132	81 [61.4%]	0.899
HE (%)	237	17 [7.2%]	156	25 [16.0%]	0.005	132	8 [6.1%]	132	20 [15.2%]	0.016
History of variceal bleeding (%)	237	158 [66.7%]	156	90 [57.7%]	0.071	132	88 [66.7%]	132	77 [58.3%]	0.162
ACLF (%)	237	12 [5.1%]	156	9 [5.8%]	0.761	132	4 [3.0%]	132	7 [5.3%]	0.355
HCC (%)	237	32 [13.5%]	156	32 [20.5%]	0.066	132	18 [13.6%]	132	27 [20.5%]	0.141
Laboratory tests										
WBC (10 ⁹ /L)	237	3.71 ± 2.70 2.87 [0.37–20.00]	156	9.44 ± 4.30 8.82 [1.47–22.20]	< 0.001	132	3.93 ± 2.86 2.92 [0.68–20.00]	132	9.56 ± 4.45 8.82 [1.47–22.20]	< 0.001
HB (g/L)	237	80.77 ± 22.89 79.00 [28.20–149.00]	156	81.80 ± 27.09 80.50 [16.00–151.00]	0.626	132	80.48 ± 24.25 77.50 [28.20–149.00]	132	83.49 ± 27.78 82.00 [16.00–151.00]	0.215

(Continued)

Table 4. (Continued)

Variables	Overall analysis		PSM analysis			
	With severe thrombocytopenia		With normal PLT		With severe thrombocytopenia	
	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)
PLT ($10^9/L$)	237	35.82 $\pm$ 9.74 38.00 (3.00–49.00)	156	222.06 $\pm$ 91.67 193.00 (150.00–836.00)	132	35.45 $\pm$ 9.52 37.00 (10.00–49.00)
					132	224.86 $\pm$ 96.40 195.00 (150.00–836.00)
TBIL ($\mu\text{mol/L}$)	237	35.83 $\pm$ 28.12 27.70 (6.84–240.90)	156	29.72 $\pm$ 35.75 19.90 (5.30–295.83)	132	33.64 $\pm$ 26.22 26.70 (6.84–240.90)
					132	27.60 $\pm$ 26.36 19.25 (5.30–200.00)
ALB (g/L)	237	31.21 $\pm$ 6.00 30.70 (12.40–49.20)	156	30.82 $\pm$ 5.78 30.65 (16.60–47.20)	132	31.39 $\pm$ 6.22 30.90 (12.40–49.20)
					132	30.93 $\pm$ 5.69 30.65 (16.60–47.20)
Scr ($\mu\text{mol/L}$)	237	71.80 $\pm$ 43.33 64.97 (7.00–491.50)	156	82.17 $\pm$ 50.07 67.50 (30.30–433.16)	132	70.21 $\pm$ 25.25 66.85 (7.00–150.00)
					132	79.99 $\pm$ 50.37 66.50 (30.30–433.16)
PT (s)	237	16.49 $\pm$ 3.35 15.70 (11.00–36.40)	156	15.39 $\pm$ 3.36 14.90 (10.80–36.80)	132	16.33 $\pm$ 3.43 15.70 (11.80–36.40)
					132	15.42 $\pm$ 3.58 14.70 (10.80–36.80)
INR	237	1.44 $\pm$ 0.29 1.37 (0.95–3.13)	156	1.34 $\pm$ 0.32 1.27 (0.99–3.39)	132	1.42 $\pm$ 0.28 1.36 (1.03–3.13)
					132	1.34 $\pm$ 0.33 1.25 (0.99–3.39)
INR $\geq$ 1.5 (%)	237	78 (32.9%)	156	28 (17.9%)	132	39 (29.5%)
					132	24 (18.2%)
Child-Pugh score	237	7.73 $\pm$ 1.72 8.00 (5.00–13.00)	156	7.59 $\pm$ 1.85 7.00 (5.00–12.00)	132	7.52 $\pm$ 1.68 7.00 (5.00–13.00)
					132	7.58 $\pm$ 1.83 7.00 (5.00–12.00)
MELD score	237	13.78 $\pm$ 4.25 13.07 (6.87–27.90)	156	13.60 $\pm$ 5.45 12.41 (6.43–32.27)	132	13.31 $\pm$ 3.98 12.52 (6.87–26.10)
					132	13.44 $\pm$ 5.49 11.95 (6.43–32.27)
Endoscopy						
EV (%)	237	234 (98.7%)	156	148 (94.9%)	132	130 (98.5%)
					132	125 (94.7%)
GV (%)	237	183 (77.2%)	156	92 (59.0%)	132	104 (78.8%)
					132	82 (62.1%)

(Continued)

Table 4. (Continued)

Variables	Overall analysis			PSM analysis		
	With severe thrombocytopenia			With severe thrombocytopenia		
	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)	No. Pts	Mean $\pm$ SD, median (range) or frequency (percentage)
Medical therapy						
Vasoconstrictors	237	226 [95.4%]	156	149 [95.5%]	132	126 [95.5%]
						0.776
PPIs	237	235 [99.2%]	156	149 [95.5%]	132	127 [96.2%]
						0.215
Antibiotics	237	197 [83.1%]	156	130 [83.3%]	132	107 [81.1%]
						0.874
Blood transfusions						
PLT	237	18 [7.6%]	156	1 [0.6%]	132	1 [0.8%]
						1.000
RBC	237	97 [40.9%]	156	81 [51.9%]	132	60 [45.5%]
						0.538
FFP	237	77 [32.5%]	156	28 [17.9%]	132	28 [21.2%]
						0.312
Endoscopic variceal therapy						
EVL	237	82 [34.6%]	156	81 [51.9%]	132	66 [50.0%]
						0.035
EIS	237	14 [5.9%]	156	6 [3.8%]	132	5 [3.8%]
						0.393
ECGI	237	29 [12.2%]	156	20 [12.8%]	132	16 [12.1%]
						0.713
EVL + EIS	237	6 [2.5%]	156	2 [1.3%]	132	2 [1.5%]
						1.000
EVL + ECGI	237	41 [17.3%]	156	21 [13.5%]	132	19 [14.4%]
						0.501
EIS + ECGI	237	36 [15.2%]	156	20 [12.8%]	132	19 [14.4%]
						0.462
EVL + EIS + ECGI	237	27 [11.4%]	156	3 [1.9%]	132	3 [2.3%]
						0.002
Others	237	2 [0.8%]	156	3 [1.9%]	132	2 [1.5%]
						1.000
5-Day failure to control bleeding (%)	237	10 [4.2%]	156	7 [4.5%]	132	7 [5.3%]
						0.555

The values in bold mean statistically significant.

ACLF, acute-on-chronic liver failure; ALB, albumin; ECGI, endoscopic cyanoacrylate glue injection; EIS, endoscopic injection sclerotherapy; EV, esophageal varices; EVL, endoscopic variceal ligation; FFP, fresh frozen plasma; GV, gastric varices; HB, hemoglobin; HBV, Hepatitis B Virus; HCC, hepatocellular carcinoma; HCV, Hepatitis C Virus; HE, hepatic encephalopathy; INR, international normalized ratio; MELD, model for end-stage liver disease; No. Pts, number of patients; PLT, platelet; PPIs, proton pump inhibitors; PSM, propensity score matching; PT, prothrombin time; RBC, red blood cell; Scr, serum creatinine; SD, standard deviation; TBIL, total bilirubin; WBC, white blood cell.

only available in specialized centers.^{17,18} By comparison, low PLT serves as a convenient noninvasive predictor for the presence of large gastroesophageal varices,^{19–21} which are a consequence of high portal pressure and more prone to cause variceal rupture.²² Our previous study found that PLT was significantly lower in cirrhotic patients with AVB than those without, indicating a close association of PLT with portal hypertension-related bleeding in cirrhosis.²³ Recent studies have further investigated the association of PLT with the outcomes of cirrhotic patients after EVT.^{24–26} Most of them focused on patients who underwent prophylactic EVT and found that the risk of bleeding after prophylactic EVT was not associated with PLT.^{24–26} But there are very limited data on the association between thrombocytopenia and failure to control bleeding within 5 days after EVT. A previous Italian study by Amitrano *et al.*¹¹ prospectively evaluated the risk factors of 5-day failure in 185 cirrhotic patients with AVB after EVT, and showed that Child-Pugh class C, WBC count over $10 \times 10^9/L$, and portal vein thrombosis were independent predictors of the 5-day failure, but not PLT ($89 \times 10^9/L$ vs $105 \times 10^9/L$, $p=0.184$). Besides, a Chinese nationwide study by Huang *et al.*¹³ retrospectively included 1399 cirrhotic patients with AVB to explore the risk factors of rebleeding within 5 days after emergency endoscopy, and showed that PLT was not significantly associated with the risk of rebleeding within 5 days after EVT. Another study conducted by Chau *et al.*¹² in the United Kingdom prospectively included 20 cirrhotic patients with AVB to explore the predictors of rebleeding within 1–7 days after EVT and found that PLT was not significantly different between patients who developed early rebleeding and those who did not after therapeutic endoscopy ($42 \times 10^9/L$ vs $71 \times 10^9/L$, $p=0.60$). Similarly, the main finding of our study was that thrombocytopenia may not be associated with failure to control bleeding within 5 days after EVT in cirrhotic patients with AVB. A major explanation for our finding should be that PLT function was often preserved in cirrhotic patients with thrombocytopenia, possibly due to elevated levels of von Willebrand factor.^{27–29} Another potential explanation could be that multiple risk factors for 5-day failure to control bleeding after EVT, such as hepatic encephalopathy, more severe cirrhosis, and presence of hepatocellular carcinoma,^{30,31} were not significantly different between cirrhotic patients with and without

thrombocytopenia in our patients. There is a seemingly counterintuitive phenomenon that the Child-Pugh score and MELD score were not significantly different between the patients with and without thrombocytopenia. Thus, thrombocytopenia may reflect an acute consumption of PLT in the setting of AGIB, but not sufficiently indicate the severity of liver cirrhosis.

As compared to previous studies, our study has several advantages in terms of study design. First, in our study, the data of cirrhotic patients with AGIB were prospectively and consecutively collected at 23 hospitals from 8 countries. Thus, such a large sample size in our study enhanced the credibility of our conclusions, and multiple sources of the included data allows for the generalizability of our conclusions. Second, the PSM analyses were performed to balance the severity of liver cirrhosis between the two groups. Notably, previous studies have demonstrated that the severity of liver cirrhosis evaluated by Child-Pugh class or MELD score was a strong predictor of 5-day failure in cirrhotic patients with AVB.^{7,31} Accordingly, our statistical results should be more reliable to reflect the impact of thrombocytopenia on the outcomes of cirrhotic patients with AVB. Third, we stratified the severity of thrombocytopenia and further explored the association between different grades of thrombocytopenia and the rate of failure to control bleeding within 5 days.

Our study also had several limitations. First, our study was retrospective with selection bias. Second, EVT was performed at different hospitals. The difference in the levels of endoscopists' skills could potentially influence the patients' outcomes. Third, the long-term outcomes of cirrhotic patients with AVB were not evaluated. Fourth, the data regarding liver stiffness value, HVPg, and portal vein thrombosis had not been collected in our multicenter study. Thus, their impact on the failure of treatment could not be further explored.

Conclusion

In conclusion, the short-term outcomes of cirrhotic patients with AVB after EVT might not be dependent upon the presence and grade of thrombocytopenia. Thus, it seems that the correction of thrombocytopenia by platelet infusion and use of thrombopoietin before EVT, an invasive procedure, is not warranted.

Declarations

Author's note

Number of patients enrolled from 23 participating centers for the present sub-study is listed as follows: (1) Bimin Li: The First Affiliated Hospital of Nanchang University, Nanchang, China ($N=212$); (2) Lei Liu: Tangdu Hospital, The Fourth Military Medical University, Xi'an, China ($N=193$); (3) Su Lin: The First Affiliated Hospital of Fujian Medical University, Fuzhou, China ($N=97$); (4) Fernando Gomes Romeiro: Botucatu Medical School, São Paulo State University, Botucatu, Brazil ($N=82$); (5) Xingshun Qi: General Hospital of Northern Theater Command, Shenyang, China ($N=82$); (6) Mingyu Sun: Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China ($N=70$); (7) Fanpu Ji: The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China ($N=53$); (8) Qiang Zhu: Shandong Provincial Hospital affiliated to Shandong First Medical University, Jinan, China ($N=51$); (9) Yingli He: The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China ($N=43$); (10) Dapeng Ma: The Sixth People's Hospital of Dalian, Dalian, China ($N=40$); (11) Shanshan Yuan: Xi'an Central Hospital, Xi'an, China ($N=40$); (12) Xiaofeng Liu: The 960th Hospital of Chinese PLA, Jinan, Shandong, China ($N=29$); (13) Cyriac Abby Philips: The Liver Institute, Center of Excellence in GI Sciences, Rajagiri Hospital, Kerala, India ($N=18$); (14) Metin Basaranoglu: Bezmialem Vakif University, Istanbul, Turkey ($N=15$); (15) Nahum Méndez-Sánchez: Medica Sur Clinic, National Autonomous University of Mexico, Mexico City, Mexico ($N=13$); (16) Kanokwan Pinyopornpanish: Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand ($N=12$); (17) Yiling Li: The First Affiliated Hospital of China Medical University, Shenyang, China ($N=11$); (18) Yunhai Wu: The Sixth People's Hospital of Shenyang, Shenyang, China ($N=6$); (19) Ling Yang: Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China ($N=4$); (20) Lichun Shao: Air Force Hospital of Northern Theater Command, Shenyang, China ($N=4$); (21) Andrea Mancuso: Azienda di Rilievo Nazionale ad Alta Specializzazione Civico-Di Cristina-Benfratelli, Palermo, Italy ($N=3$); (22) Yu Chen: Beijing You'an Hospital Affiliated to Capital Medical University, Beijing, China ($N=1$); (23)

Frank Tacke: Charité—Universitätsmedizin Berlin, Berlin, Germany ($N=0$).

Ethics approval and consent to participate

This study was approved by the Medical Ethical Committee of the General Hospital of Northern Theater Command with an ethical approval number (Y (2024) 139). Due to the retrospective nature of the study, the requirement for written informed consent was waived.

Consent for publication

Not applicable.

Author contributions

Yan He: Data curation; Formal analysis; Investigation; Methodology; Validation; Writing – original draft; Writing – review & editing.

Fernando Gomes Romeiro: Data curation; Investigation; Validation; Writing – review & editing.

Mingyu Sun: Data curation; Investigation; Validation; Writing – review & editing.

Fanpu Ji: Data curation; Investigation; Validation; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Appendix*Abbreviations*

AGIB	acute gastrointestinal bleeding	EVT	endoscopic variceal treatment
aORs	adjusted odd ratios	FFP	fresh frozen plasma
AVB	acute variceal bleeding	GV	gastric varices
CI	confidence intervals	HVPG	hepatic venous pressure gradient
cORs	crude odd ratios	INR	international normalized ratio
ECGI	endoscopic cyanoacrylate glue injection	MELD	model for end-stage liver disease
EIS	endoscopic injection sclerotherapy	PLT	platelet count
EV	esophageal varices	PSM	propensity score matching
EVL	endoscopic variceal ligation	PT	prothrombin time
		RBC	red blood cell
		TBIL	total bilirubin
		WBC	white blood cell

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