



Retrospective Cohort Study

Will partial splenic embolization followed by splenectomy increase intraoperative bleeding?

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Abstract

BACKGROUND

Partial splenic embolization (PSE) has been suggested as an alternative to splenectomy in the treatment of hypersplenism. However, some patients may experience recurrence of hypersplenism after PSE and require splenectomy. Currently, there is a lack of evidence-based medical support regarding whether preoperative PSE followed by splenectomy can reduce the incidence of complications.

AIM

To investigate the safety and therapeutic efficacy of preoperative PSE followed by splenectomy in patients with cirrhosis and hypersplenism.

METHODS

Between January 2010 and December 2021, 321 consecutive patients with cirrhosis and hypersplenism underwent splenectomy at our department. Based on whether PSE was performed prior to splenectomy, the patients were divided into two groups: PSE group ($n = 40$) and non-PSE group ($n = 281$). Patient characteristics, postoperative complications, and follow-up data were compared between groups. Propensity score matching (PSM) was conducted, and univariable and multivariable analyses were used to establish a nomogram predictive model for intraoperative bleeding (IB). The receiver operating characteristic curve, Hosmer-Lemeshow goodness-of-fit test, and decision curve analysis (DCA) were employed to evaluate the differentiation, calibration, and clinical performance of the

model.

RESULTS

After PSM, the non-PSE group showed significant reductions in hospital stay, intraoperative blood loss, and operation time (all $P = 0.00$). Multivariate analysis revealed that spleen length, portal vein diameter, splenic vein diameter, and history of PSE were independent predictive factors for IB. A nomogram predictive model of IB was constructed, and DCA demonstrated the clinical utility of this model. Both groups exhibited similar results in terms of overall survival during the follow-up period.

CONCLUSION

Preoperative PSE followed by splenectomy may increase the incidence of IB and a nomogram-based prediction model can predict the occurrence of IB.

Key Words: Partial splenic embolization; Splenectomy; Hypertension, Portal; Liver Cirrhosis; Intraoperative bleeding

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Core Tip: Partial splenic embolization (PSE) has been suggested as an alternative to splenectomy for treating hypersplenism, but some patients may experience recurrence of hypersplenism after PSE and still require splenectomy. Preoperative PSE followed by splenectomy may increase the incidence of intraoperative bleeding (IB), and a nomogram-based prediction model can predict the occurrence of IB.

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INTRODUCTION

Cirrhosis, an end-stage chronic liver injury, is frequently accompanied by severe complications such as portal hypertension (PH), esophageal and gastric variceal bleeding (EGVB), splenomegaly, and hypersplenism[1,2]. Previously, splenectomy has been used to treat patients with cirrhosis and hypersplenism[3]. Furthermore, a combined approach of splenectomy and peri esophagogastric devascularization has been shown to be an effective treatment option for cirrhotic patients with EGVB and PH. However, it is important to note that this procedure carries the risk of postoperative complications, including abdominal hemorrhage, pancreatic fistula, and portal vein thrombosis (PVT)[4]. Therefore, partial splenic embolization (PSE) has been proposed as an alternative to splenectomy for managing hypersplenism[5].

Currently, PSE has emerged as a crucial treatment modality for hypersplenism associated with PH. It effectively treats hypersplenism, lowers portal pressure, and improves liver function[6,7]. The occurrence of acute ischemia of the splenic segment tissue and subsequent splenic infarction were attributed to PSE. The subsequent absorption of necrotic tissue and the development of splenic tissue fibrosis results in spleen atrophy and a reduction in spleen volume. The reduction in spleen volume enhances the space within the splenic pedicle, leading to a more precise disconnection between the perisplenic ligament and the splenic pedicle vessels. Consequently, this reduces the occurrence of complications[8]. Despite the therapeutic effectiveness of PSE in treating hypersplenism and reducing PH, some patients may experience recurrence of hypersplenism following PSE treatment, leading to the need for splenectomy[9].

Previous research has indicated that PSE reduces surgical complexity and lowers the occurrence of postoperative complications[10]. However, some studies suggest that PSE increases perisplenic adhesions and intraoperative bleeding (IB) during splenectomy[11]. Despite these findings, there is insufficient evidence-based medical support to determine whether preoperative PSE followed by splenectomy reduces complications and the optimal timing for performing splenectomy after PSE remains uncertain. Furthermore, research on predictive factors for complications in patients undergoing preoperative PSE followed by splenectomy is limited.

This study aimed to assess the safety and therapeutic efficacy of preoperative PSE followed by splenectomy in patients with cirrhosis and hypersplenism. The aim of this study was to examine the occurrence of these complications. To achieve these objectives, we retrospectively analyzed the clinical data of patients who underwent preoperative PSE followed by splenectomy at our hospital over a period of 6 years. The ultimate goal was to develop a reliable risk model to identify the independent risk factors for IB in patients with cirrhosis.

MATERIALS AND METHODS

Prior to commencing this study, the objectives and specific details were comprehensively explained to the participants and informed consent was obtained from each participant or their respective representatives. This study was conducted in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki, revised in Fortaleza, Brazil, October 2013). The study protocol was approved by the Institutional Review Board of Anhui Provincial Traditional Chinese Hospital (ID: 2020AH-13).

Patient selection and study design

From January 2017 to June 2023, 344 consecutive patients underwent splenectomy at the First Hospital affiliated with Anhui University of Traditional Chinese Medicine. After careful application of the inclusion and exclusion criteria, 321 patients were enrolled in the study. This study employed a retrospective cohort design in which patients were divided into two groups based on whether they underwent preoperative PSE: The PSE group and the non-PSE group. Detailed assessments were conducted to evaluate the clinical characteristics of the patients, including age, sex, etiology of cirrhosis, spleen size, and portal vein system diameter. Additionally, intraoperative outcomes such as blood loss, operation time, and postoperative complications such as PVT and postoperative pancreatic fistula (PPF) were collected and analyzed. Furthermore, the study reviewed the follow-up data on the overall survival (OS) of patients.

We meticulously collected and analyzed clinical data from a standardized database of patients during the perioperative period. Color Doppler ultrasound was used to measure the diameters of the portal and splenic veins, assess the spleen size, and determine the presence of PVT.

All patients included in the study met the following inclusion criteria: (1) A diagnosis of cirrhosis and PH of any etiology; (2) display secondary splenomegaly and hypersplenism attributed to cirrhosis. Hypersplenism is defined as a leukocyte count less than $3.5 \times 10^9/L$ and a platelet count less than $7.5 \times 10^9/L$ [12]; and (3) have not previously undergone splenectomy.

The study excluded participants who had the following conditions: (1) Liver cirrhosis without hypersplenism or splenomegaly; (2) severe coagulation dysfunction; (3) liver or any other malignancy; (4) declined to participate; and (5) underwent early postoperative transfer. All surgical procedures were non-emergency procedures.

PSE and surgical technique

The puncture point for the right femoral artery, located under the inguinal ligament, was chosen as the most prominent point of femoral artery pulse. The right femoral artery was punctured using the modified Seldinger technique under digital subtraction angiography guidance. Imaging results were used to super selectively advance the microcatheter into the splenic artery. The extent of splenic artery embolism typically ranges from 50% to 70%.

All patients enrolled in the study underwent endotracheal intubation and received intravenous anesthesia for open splenectomy. The splenic artery was fully exposed for ligation, and the serosal tissue in front of the splenic pedicle space was separated and dissected after separating the perisplenic adhesions (Figure 1). To ensure safe dissection, dissection should be performed as close as possible to the splenic parenchyma to avoid the pancreatic tail and stomach. Each secondary splenic pedicle vessel was carefully dissected and ligated under direct visualization. Subsequently, splenic tissue was removed, ligated, and sutured. Finally, a drainage tube was placed in the splenic fossa.

Postoperative complications

This study collected and analyzed data on postoperative complications following splenectomy during hospitalization. These complications included PVT, postoperative abdominal hemorrhage, abdominal infection, PPF, liver failure, severe ascites, and encephalopathy. The criteria for diagnosing PPF were as follows: (1) Drainage duration exceeding 3 d; (2) amylase level in drainage fluid more than three times the upper limit of normal; and (3) no record of biochemical leakage [13]. PVT was defined as the presence of thrombosis in the portal vein (trunk and intrahepatic branches), mesenteric vein, or splenic vein confirmed by Doppler ultrasound displaying hyperechoic or isoechoic filling in the cavity. Postoperative abdominal hemorrhage was defined as abdominal bleeding exceeding 300 mL within 24 h after surgery. Additionally, clinical details of the surgery, such as operation time, intraoperative blood loss, and length of hospital stay, were recorded.

Follow-up

All patients who underwent splenectomy received routine follow-up assessments either *via* telephone or at the outpatient department. The follow-up assessment was completed on June 30, 2023. The primary endpoint was OS. OS was defined as the duration from surgery to death from any cause. Patients who survived until the last follow-up were excluded.

Statistical analysis

Statistical analyses and plotting were conducted using the SPSS Version 24.0 software (IBM Corp., Chicago, IL, United States) and R (Version 4.2.2). Continuous variables following a normal distribution were reported as mean \pm SD. Non-normally distributed variables were reported as medians with interquartile ranges (P25 and P75). Group comparisons of measurement data were performed using an independent t-test. Categorical variables were evaluated using the χ^2 test, with or without Fisher's exact test, as appropriate.

Propensity score matching (PSM) was performed to eliminate confounding variables associated with clinical characteristics between the two groups. PSM was performed using the 1:1 nearest-neighbor caliper matching method with the caliper value set at 0.2[14]. Factors influencing IB were assessed using univariate analysis. Variables that showed

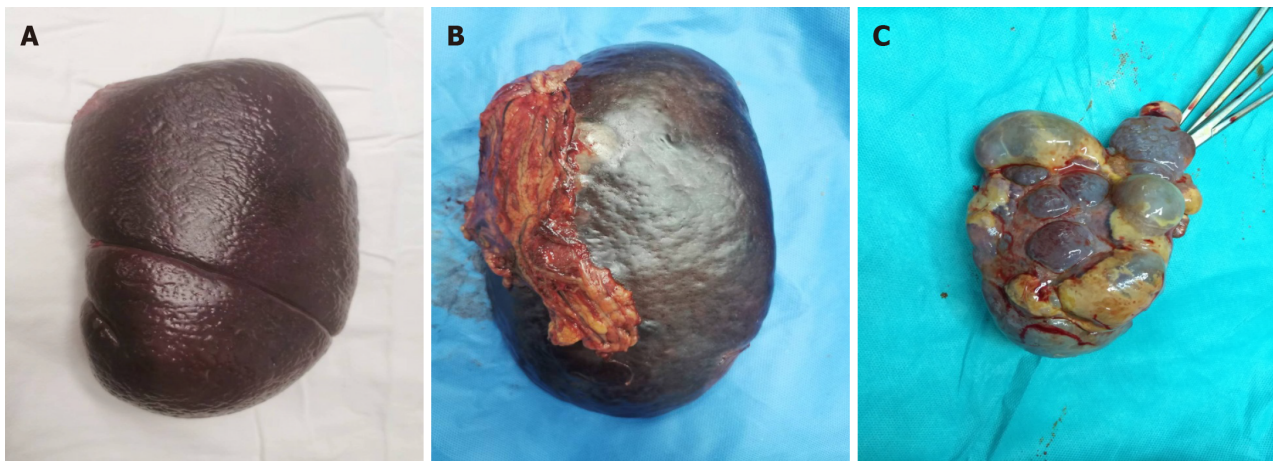


Figure 1 Situation of the spleen with/without partial splenic embolization. A: Splenomegaly without partial splenic embolization (PSE); B: Adhesion between spleen and omentum with preoperative PSE; C: Splenic infarction with preoperative PSE.

statistical significance ($P < 0.05$) were further evaluated using multivariable logistic analysis to identify the main independent risk factors. A nomogram was constructed using R software (version 4.2.2), and nomogram differentiation was assessed by calculating the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. To evaluate the clinical utility of the nomogram model, a decision curve analysis (DCA) was conducted using the R "rmda" package. Survival curves were plotted using the Kaplan-Meier method, and differences between the two groups were assessed using the log-rank test. Statistical significance was considered at the 5% level, and 2-tailed test were used for the analysis.

RESULTS

Comparison between the two groups by PSM analysis

Of the 344 patients who met the initial inclusion criteria, 23 were excluded from the study. Among them, eight patients had idiopathic thrombocytopenic purpura, four patients had hereditary spherocytosis and underwent splenectomy, showing no symptoms of hypersplenism or splenomegaly, four patients developed severe coagulopathy, three patients had liver malignancy, and four patients experienced early postoperative complications. Ultimately, 321 patients who met the inclusion criteria were enrolled in this study. Among the 321 patients, there were 173 men and 148 were female. The PSE group included 40 patients, while the non-PSE group included 281 patients (Figure 2).

When comparing the baseline clinical data between the PSE group and non-PSE group, no significant differences were observed in various indicators, including age, sex, etiology of cirrhosis, and portal and splenic vein diameters (SVDs) (all $P > 0.05$). Additionally, no significant differences were observed in parameters including white blood cell (WBC), red blood cell (RBC), hemoglobin (HGB), alanine aminotransferase (ALT), prothrombin time (PT), and operation between the two groups (all $P > 0.05$). In contrast to the PSE group, the non-PSE group demonstrated significantly reduced hospital stays (13.99 ± 3.57 d vs 17.10 ± 4.42 d), intraoperative blood loss (267.36 ± 161.07 mL vs 399.50 ± 240.76 mL), and operation time (181.64 ± 36.57 min vs 202.98 ± 36.38 min) (all $P = 0.00$).

Table 1 presents the results of PSM conducted at a 1:1 ratio, with 23 patients in each group. Following PSM, the clinical data of the matched PSE group were comparable to those of the matched non-PSE group, with all P values exceeding 0.05. Furthermore, the matched non-PSE group demonstrated significantly reduced hospital stays (13.52 ± 2.25 d compared to 16.70 ± 4.18 d), intraoperative blood loss (250.13 ± 129.02 mL compared to 450.00 ± 268.40 mL), and operation time (178.78 ± 37.42 min compared to 220.09 ± 35.41 min) when compared to the matched PSE group.

Comparison among pre- or post-PSE

Notable variations were observed in multiple indices between pre- and post-PSE, specifically in the diameters of the portal and splenic veins, along with changes in the HGB, platelet, total bilirubin, ALT, aspartate aminotransferase, albumin (ALB), and PT levels (all $P < 0.05$). No significant differences were observed in spleen length (LS) and thickness as well as WBC, RBC, and D-dimer levels (all $P > 0.05$) (Table 2).

Risk factors of IB using the uni- and multi-variable analyses

IB was defined as a volume exceeding 300 mL, determined by the median IB volume. A total of 26 patients (56.5%) experienced IB during splenectomy. Univariate analysis revealed significant differences in various indicators, including ALB, PT, LS, spleen thickness, portal vein diameter (PVD), SVD, and PSE history (all $P < 0.05$), when assessing the predictive factors of IB. Multivariable logistic analysis further confirmed that LS, PVD, SVD, and PSE history were independent risk factors for PVT (Table 3).

Table 1 Comparison of perioperative characteristics of included patients between the two groups by propensity score matching analysis

Variables	Unmatched		P value	Matched		P value
	PSE group, n = 40	Non-PSE group, n = 281		PSE group, n = 23	Non-PSE group, n = 23	
Age in yr	33.95 ± 12.21	35.07 ± 14.74	0.65	33.57 ± 13.56	34.04 ± 12.23	0.90
Sex, n (%)			0.12			0.57
Male	17	156		12	10	
Female	23	125		11	13	
Etiology of cirrhosis, n (%)			0.88			0.30
HLD cirrhosis	34	222		19	17	
HBV cirrhosis	4	48		3	4	
HCV cirrhosis	1	3		1	1	
Schistosomiasis cirrhosis	0	1		0	0	
Alcoholic cirrhosis	0	2		0	0	
Autoimmunity cirrhosis	1	3		0	1	
Unknown	0	1				
The size of spleen in mm						
Length of spleen	161.85 ± 21.26	171.21 ± 26.74	0.04	170.13 ± 15.64	163.00 ± 25.33	0.26
Thickness of spleen	66.45 ± 11.03	73.06 ± 16.91	0.02	69.74 ± 8.77	64.43 ± 15.88	0.17
The diameter of portal vein system in cm						
Portal vein	1.35 ± 0.16	1.41 ± 0.24	0.15	1.38 ± 0.19	1.28 ± 0.17	0.50
Splenic vein	1.24 ± 0.21	1.23 ± 0.24	0.71	1.23 ± 0.23	1.13 ± 0.17	0.10
Preoperative blood examination						
WBC as 10 ⁹ /L	2.69 ± 1.05	3.13 ± 2.08	0.19	2.51 ± 1.09	3.12 ± 2.44	0.28
RBC as 10 ¹² /L	3.76 ± 0.37	3.91 ± 0.65	0.16	3.77 ± 0.43	3.58 ± 0.54	0.18
HGB in g/L	106.40 ± 18.31	109.75 ± 18.71	0.29	103.61 ± 16.80	104.96 ± 15.08	0.75
PLT as 10 ⁹ /L	66.35 ± 30.04	50.03 ± 28.68	0	59.26 ± 29.86	59.04 ± 48.48	0.99
TBIL in μmol/L	34.54 ± 25.58	22.98 ± 15.61	0	30.09 ± 26.63	28.14 ± 22.13	0.79
ALT in U/L	30.20 ± 13.31	29.01 ± 17.01	0.67	28.74 ± 13.03	28.96 ± 21.20	0.97
AST in U/L	38.00 ± 16.13	30.00 ± 11.44	0	33.57 ± 11.18	35.48 ± 17.46	0.66
ALB in g/L	35.04 ± 3.42	37.60 ± 4.60	0	34.77 ± 3.07	34.98 ± 3.98	0.84
PT in s	14.95 ± 3.44	14.70 ± 2.43	0.57	15.08 ± 3.49	14.30 ± 2.26	0.37
D-dimer in mg/L	1.46 ± 4.28	0.67 ± 0.83	0.01	0.47 ± 0.26	0.56 ± 0.54	0.47
Operation, n (%)						
Splenectomy only	18	237	0	11	11	1
Concomitant pericardial devascularization	22	44		12	12	
Intraoperative outcomes						
Intraoperative blood loss in mL	399.50 ± 240.76	267.36 ± 161.07	0	450.00 ± 268.40	250.13 ± 129.02	0
Operation time in min	202.98 ± 36.38	181.64 ± 36.57	0.01	220.09 ± 35.41	189.78 ± 37.42	0.01
Postoperative complications, n (%)						
PVT	14	107	0.71	8	6	0.53
PPF	6	27	0.30	4	4	1

Abdominal hemorrhage	3	6	0.06	2	3	0.65
Hospital stay in d	17.10 ± 4.42	13.99 ± 3.57	0	16.70 ± 4.18	13.52 ± 2.25	0

ALB: Albumin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; HBV: Hepatitis B virus; HCV: Hepatitis C virus; HGB: Hemoglobin; HLD: Hepatolenticular degeneration; PLT: Platelet; PPF: Postoperative pancreatic fistula; PSE: Partial splenic embolization; PSM: Propensity score matching; PT: Prothrombin time; PVT: Portal vein thrombosis; RBC: Red blood cell; TBIL: Total bilirubin; WBC: White blood cell.

Table 2 Demographic and preoperative clinical characteristics between pre-/post-propensity score matching

Variables	Groups		t	P value
	Pre-PSE group, n = 40	Post-PSE group, n = 40		
Frequency	1.50 ± 0.82			
Time from last PSE to surgery in mo	5.03 ± 9.53			
The size of spleen in mm				
Length of spleen	171.70 ± 25.07	161.85 ± 21.26	18.28	0.06
Thickness of spleen	71.45 ± 14.07	66.45 ± 11.03	7.309	0.08
The diameter of portal vein system in cm				
Portal vein	1.57 ± 0.16	1.35 ± 0.16	8.953	0
Splenic vein	1.47 ± 0.19	1.24 ± 0.21	5.956	0
Preoperative blood examination				
WBC as 10 ⁹ /L	2.87 ± 0.93	2.69 ± 1.05	3.684	0.40
RBC as 10 ¹² /L	3.67 ± 0.23	3.76 ± 0.37	0.609	0.18
HGB in g/L	119.1 ± 6.30	106.40 ± 18.31	1.071	0
PLT as 10 ⁹ /L	28.55 ± 14.29	66.35 ± 30.04	4.15	0
TBIL in μmol/L	54.68 ± 16.26	34.54 ± 25.58	5.195	0
ALT in U/L	58.0 ± 17.32	30.20 ± 13.31	3.378	0
AST in U/L	77.15 ± 17.02	38.00 ± 16.13	8.136	0
ALB in g/L	29.90 ± 1.49	35.04 ± 3.42	1.844	0
PT in s	17.97 ± 1.09	14.95 ± 3.44	2.091	0
D-dimer in mg/L	0.33 ± 0.12	1.46 ± 4.28	3.756	0.10

ALB: Albumin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; HGB: Hemoglobin; PLT: Platelet; PSE: Partial splenic embolization; PT: Prothrombin time; RBC: Red blood cell; TBIL: Total bilirubin; WBC: White blood cell.

The construction of prediction model

Univariate and multivariate logistic regressions were employed to develop the clinical prediction model, with the occurrence of IB serving as the dependent variable, and incorporating the four selected variables derived from the Least Absolute Shrinkage and Selection Operator (LASSO) regression analysis. The findings revealed that the length of the spleen, PVD, SVD, and PSE history significantly influenced the occurrence of IB ($P < 0.05$). A nomogram constructed using the predicted variables is shown in [Figure 3](#).

The predictive performance of the differentiation model was assessed by generating a ROC curve and calculating the AUC to predict IB ([Figure 4](#)). The AUC value was 0.929 (95%CI: 0.950-0.846), indicating a strong discriminatory ability of the prediction model. Furthermore, the Hosmer-Lemeshow goodness-of-fit test ($P = 0.89$) demonstrated that the predicted probability of the model closely matched the actual probability, indicating a high degree of calibration. In summary, the nomogram models displayed superior predictive performance ([Figure 5](#)).

The DCA of the IB risk nomogram is shown in [Figure 6](#). The results demonstrate that the net benefits are greater for threshold probabilities within the range of 20%-99%, suggesting that intervention within this range is more favorable.

Follow-up

The follow-up rates in the non-PSE group were 92.2% (259/281) and 92.5% (37/40). The median follow-up time in the control group was 43 mo (range: 29-56 mo), while that in the study group was 34 months (range: 15-51 mo). The log-rank

Table 3 Risk factors of intraoperative bleeding using the uni- and multi-variate analyses

Characteristics	Univariate analysis			Multivariate analysis					
	Non-IB group, n = 20	IB group, n = 26	P value	β	S.E.	Wald	Odds ratio	95%CI	P value
ALB in g/L	36.34 ± 3.49	33.75 ± 3.15	0.01	-0.73	0.42	2.982	0.482	0.21-1.104	0.08
PT in s	13.70 ± 2.66	15.45 ± 2.95	0.04	0.336	0.34	3.724	1.94	0.99-3.802	0.05
LS in mm	152.25 ± 13.21	177.58 ± 19.51	0	0.123	0.06	5.003	1.131	1.015-1.259	0.03
Thickness of spleen in mm	62.10 ± 13.96	70.92 ± 10.92	0.02	0.095	0.05	3.216	1.1	0.991-1.221	0.07
PVD in cm	1.25 ± 0.15	1.40 ± 0.19	0.01	18.86	8.64	4.761	2E + 08	6.806-3.516E + 15	0.03
SVD in cm	1.11 ± 0.18	1.24 ± 0.22	0.04	-20	9.26	4.658	0	0-0.16	0.03
PSE history, n	0.8 ± 0.41	0.27 ± 0.45	0	-4.44	2.01	4.863	0.012	0-0.610	0.03

ALB: Albumin; IB: Intraoperative bleeding; LS: The length of the spleen; PSE: Partial splenic embolization; PT: Prothrombin time; PVD: Portal vein diameter; SVD: Splenic vein diameter.

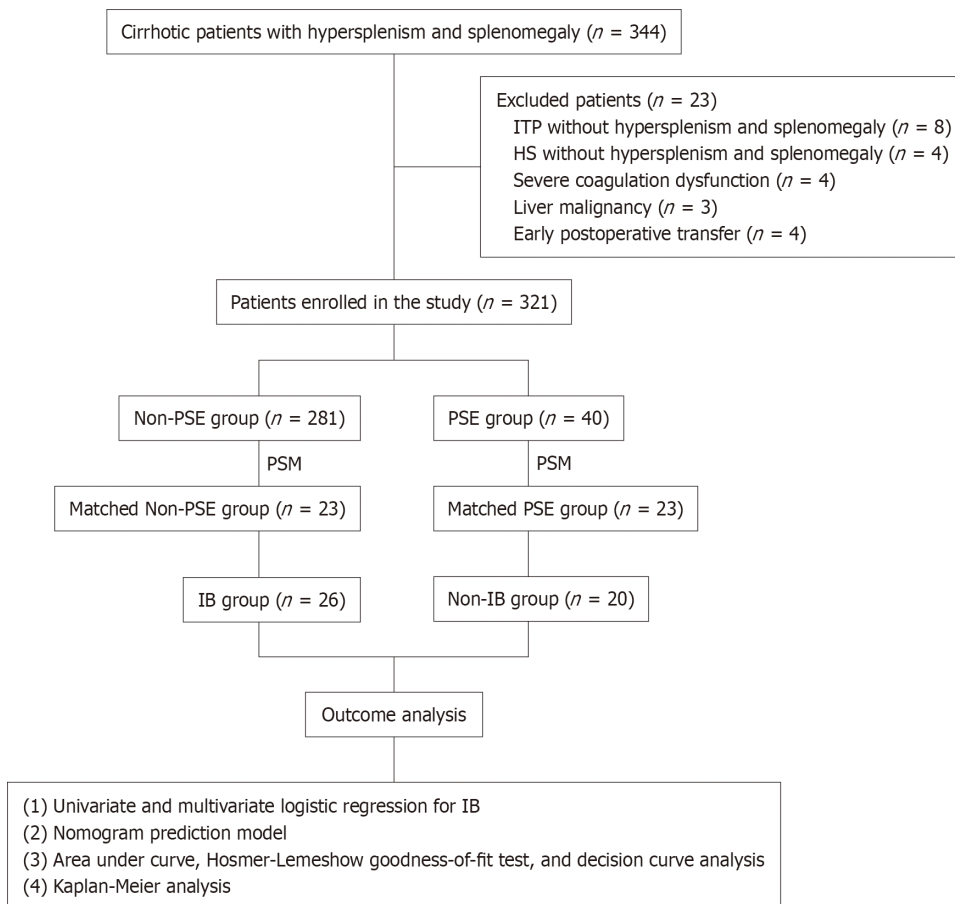


Figure 2 Classification and flow diagram of the study population. HS: Hereditary spherocytosis; IB: Intraoperative bleeding; ITP: Idiopathic thrombocytopenic purpura; PSE: Partial splenic embolization; PSM: Propensity score matching.

test ($P = 0.62$) indicated no significant differences in the follow-up data between the two groups (Figure 7).

In the non-PSE group, there were five deaths, whereas in the PSE group, there was one death. Three patients in the Non-PSE group died of liver failure during follow-up. One patient in the non-PSE group developed refractory ascites and subsequently died of a spontaneous ascitic fluid infection. In both groups, one patient died of pulmonary infection.

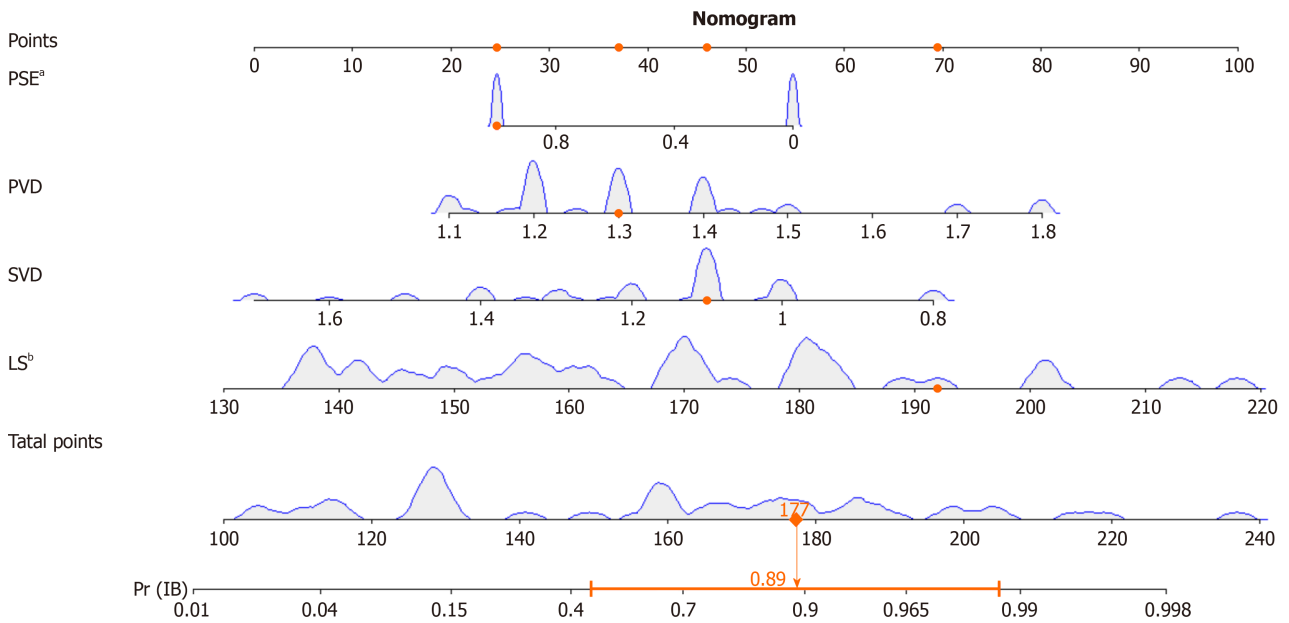


Figure 3 Nomogram predictive model for the risk of intraoperative bleeding in patients with cirrhosis and hypersplenism. The nomogram gives every predictive variable a score on the point scale. A total score was calculated by summing the points from each variable, marking the estimated probability of intraoperative bleeding occurrence in included patients. ^a*P* < 0.05. ^b*P* < 0.01. LS: Length of the spleen; PSE: Partial splenic embolization; PVD: Portal vein diameter; SVD: Splenic vein diameter.

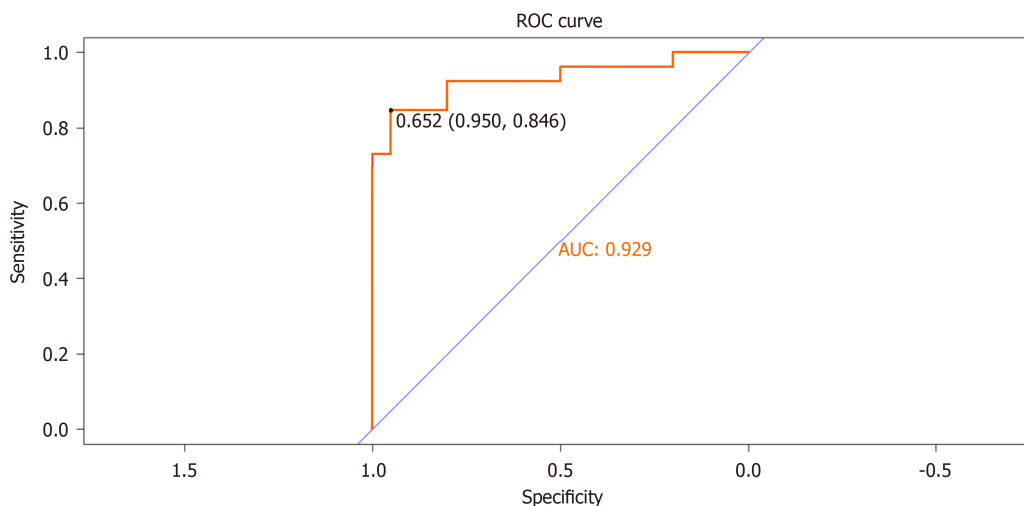


Figure 4 Discrimination of receiver operating characteristic curve curves of the nomogram model. AUC: Area under curve; ROC: Receiver operating characteristic curve.

DISCUSSION

With advancements in interventional radiology, PSE has gained widespread use in clinical practice for treating liver cirrhosis and hypersplenism. PSE is commonly used for patients with liver cirrhosis and hypersplenism who are in poor physical condition and are unable to undergo surgical treatment or preoperative treatment prior to splenectomy[15]. PSE has been demonstrated to reduce splenic volume, thereby improving surgical visibility and intraoperative exposure[16]. However, preoperative PSE prior to splenectomy reduces surgical risk. Some institutions have performed preoperative PSE followed by splenectomy and have arrived at conclusions that differ from ours[17-19].

PSE has the potential to reduce splenic venous blood flow, lower PH, and suppress splenic hyperfunction by impeding blood flow through the secondary splenic artery[20]. Furthermore, ischemic infarction may occur in the splenic region, and reducing splenic volume can be advantageous for splenectomy[21,22]. In contrast to previous studies, our study indicates that PSE followed by splenectomy may lead to increased perisplenic adhesions, prolonged surgical duration, and increased IB. We used PSM to control for confounding variables related to clinical characteristics between the two groups and performed logistic regression analysis to identify independent risk factors for IB. The results of our study suggest that parameters such as LS, PVD, SVD, and a history of PSE significantly affect the occurrence of IB. Additionally,

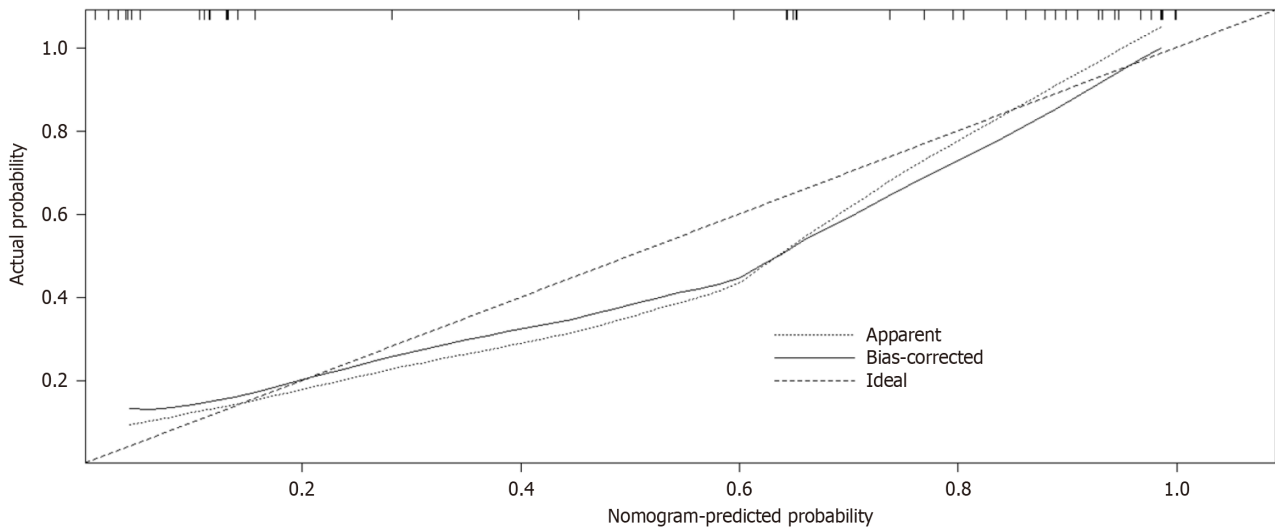


Figure 5 Nomogram calibration curve to predict the risk of intraoperative bleeding in in patients with cirrhosis and hypersplenism based on Hosmer-Lemeshow goodness-of-fit test. X-axis represents the probability of nomogram prediction of intraoperative bleeding (IB), and Y-axis represents the actual incidence of IB.

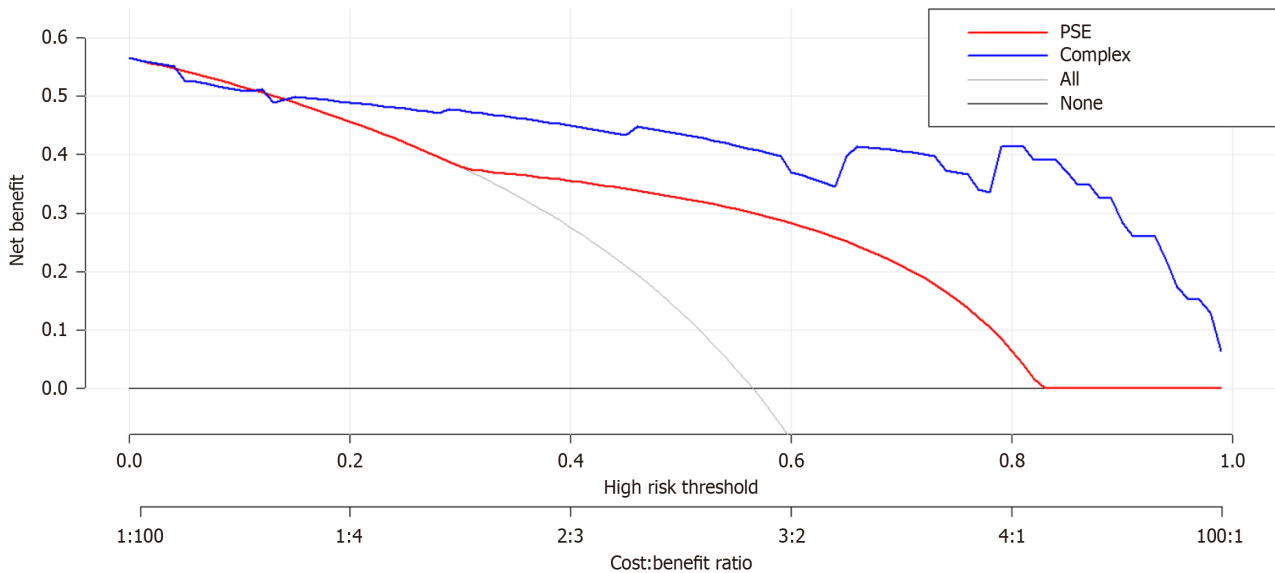


Figure 6 Nomogram decision curve analysis for intraoperative bleeding prediction in included patients. The Y-axis represents the net benefit, which was calculated as the true incidence of intraoperative bleeding minus the false-positive rate (true positive rate), the red and blue lines represent the nomogram prediction probability, and the gray line represents the extremes of intervention and non-intervention. PSE: Partial splenic embolization.

both AUC and DCA indicated the strong discriminative capabilities of the prediction model. The findings of this study suggest a potential increase in IB associated with preoperative PSE, followed by splenectomy.

A comprehensive analysis of the surgical procedures revealed that the disparity lies in the timing of the preoperative PSE. According to the literature[23], splenectomy within 24 h after PSE may reduce surgical risk. However, our findings indicate that performing splenectomy after a period exceeding 1 mo after PSE increases surgical complexity and the likelihood of IB.

Post-PSE complications can influence therapeutic outcomes. Complications include splenic infarction, splenic abscess, pleural effusion, spontaneous bacterial peritonitis, ectopic embolization, portal and splenic vein thrombosis, ascites, jaundice, and liver failure[24]. Splenic infarction is classified into four stages: Hyperacute, acute, subacute, and chronic [25]. The first stage lasts approximately 1 d, during which the spleen tissue exhibits congestion and edema. The second stage lasts around 1 wk and is characterized by inflammatory exudation in the spleen tissue and the formation of mild perisplenic adhesions. The third stage lasts from 1 wk to 1 mo and is characterized by a reduction in inflammation in the spleen tissue, leading to the development of dense adhesions with the surrounding tissues, such as the omentum. The fourth stage lasts for over a month and is characterized by fibrosis and scar formation in the spleen tissue[26]. Therefore, if splenectomy is performed more than a month after PSE, dense adhesions around the spleen can result in IB. However, only a small number of patients undergo splenectomy within a day after PSE, and the purpose of PSE sequential

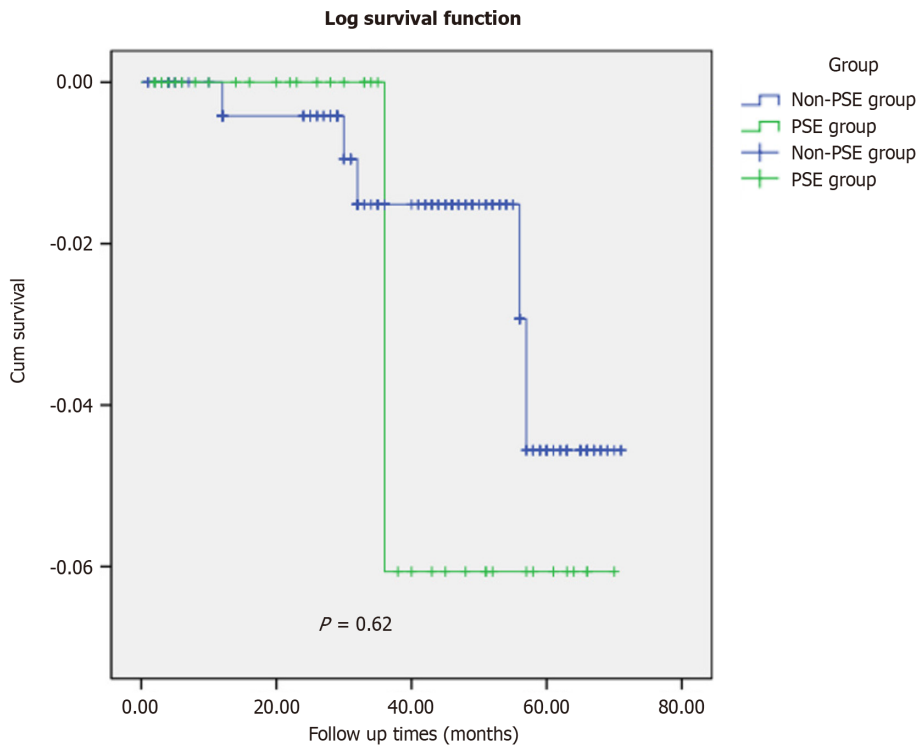


Figure 7 Overall survival data between the two groups in the follow-up. PSE: Partial splenic embolization.

splenectomy is to reduce the intraoperative splenic volume and facilitate surgery. Therefore, for most patients, splenectomy is performed more than a month after PSE[27].

Unlike previous studies[28], our splenectomy was typically performed 1 mo or more after PSE, which may have contributed to the increased IB. Enlarged spleens can limit surgical space and exposure, and increase surgical risk. PSE can reduce the size of the spleen, enhance operating space, and facilitate exposure. PSE can mitigate PH, improve liver function, and alleviate symptoms of hypersplenism, making it a potential alternative to splenectomy. Preoperative PSE before laparoscopic splenectomy can reduce surgical complexity and postoperative complication rates[29,30]. Some studies suggest that patients with PSE are at risk of massive IB due to splenic infarction, extensive adhesions, and thickened collateral circulation vessels. Patients with PSE who undergo splenectomy may experience prolonged operative times, substantial bleeding, and postoperative complications due to blood protein and coagulation factor loss. They also had longer hospital stays than those who did not undergo PSE. Currently, there is no consensus on the preferred embolization plan or optimal timing for splenectomy after embolization.

The optimal duration between embolization and splenectomy requires further investigation. It has been established that a PSE and splenectomy duration of less than 24 h effectively reduces splenic volume and enhances surgical visibility and exposure, thereby decreasing the risk of surgical complications. However, this study only considered cases with a duration exceeding 1mo. These results suggest that while a duration exceeding 1 mo may increase the risk of splenic adhesion-related complications, it can also improve liver function and facilitate surgical exposure by reducing the size of the spleen.

This study focused on PSE cases with embolization durations exceeding 1 mo. A significant reduction in spleen size was observed when comparing color Doppler ultrasound images before and after embolization. However, during intraoperative exploration, extensive inflammatory exudation and adhesions around the spleen were observed, resulting in a significant increase in IB and prolonged hospital stay. Therefore, based on the findings of this study, it is necessary to adopt precise intraoperative procedures and carefully separate adhesions in patients with embolization duration exceeding 1 mo to minimize IB.

Moreover, LS, PVD, and SVD were significant contributing factors for IB. The elongated shape of the spleen can result in adhesion between its upper end and the stomach, which can further complicate dissection of the short gastric artery and lead to increased surgical complexity and IB. Similarly, an increase in the diameter of the portal and splenic veins can lead to tortuous dilation of vessels within the splenic pedicle, making separation more challenging. Consequently, detaching the splenic pedicle can lead to an increase in IB. This finding suggests that further investigation is needed to evaluate the long-term efficacy of PSE as a treatment for patients with cirrhosis with PH and hypersplenism.

Nomograms, which are graphically intuitive representations of mathematical models, can be used to predict specific end points by integrating multiple influencing factors. This is because of their ability to provide personalized assessments, thereby facilitating disease management and clinical decision making[31]. Our study examined the clinical characteristics, hematology, and complications of patients diagnosed with cirrhosis and PH. Using LASSO and univariate and multivariate regression analyses, we identified several factors influencing IB, including history of LS, PVD, SVD, and PSE. To facilitate the visual analysis of complications, we developed a nomogram. In this study, we identified four factors that influence IB. Subsequently, the established model was validated, both internally and externally. The AUC was 0.929

(95%CI: 0.950-0.846), indicating the robustness of the model, as revealed by the Hosmer-Lemeshow goodness-of-fit test ($P = 0.89$). Furthermore, the DCA plot indicated a favorable net clinical benefit for the nomogram.

This study has several limitations. First, the retrospective nature of the study and its focus on a single institution limits the generalizability of the findings. Additionally, a small proportion of discharged patients were lost to follow-up and the sample size of patients with preoperative PSE was limited. A prospective, randomized, multicenter study is recommended to draw more comprehensive conclusions. Furthermore, it is crucial to investigate the molecular mechanisms of perisplenic adhesion after PSE using animal and cell experiments, as this remains an area of uncertainty.

CONCLUSION

In summary, preoperative PSE followed by splenectomy may increase the incidence of IB in patients with severe splenic adhesion. This results in significantly prolonged surgery duration and increased surgical risk. Additionally, the nomogram-based prediction model effectively predicted the occurrence of IB.

ARTICLE HIGHLIGHTS

Research background

Partial splenic embolization (PSE) has been suggested as an alternative to splenectomy for the treatment of hypersplenism; however, some patients may experience recurrence of hypersplenism after PSE and still require splenectomy. Studies have demonstrated that PSE can reduce surgical complexity and occurrence of postoperative complications. Currently, there is a lack of evidence-based medical support regarding whether preoperative PSE followed by splenectomy can reduce the incidence of complications.

Research motivation

There is a lack of clear evidence-based medical support regarding whether preoperative PSE followed by splenectomy can decrease complications and the optimal timing for performing splenectomy after PSE remains uncertain. Addressing these questions is crucial for providing evidence-based guidance for clinicians to decrease perioperative complications.

Research objectives

This study aimed to investigate the safety and therapeutic efficacy of preoperative PSE followed by splenectomy in patients with cirrhosis and hypersplenism.

Research methods

Between January 2010 and December 2021, 321 consecutive patients with cirrhosis and hypersplenism who underwent splenectomy were enrolled. Based on whether PSE was performed prior to splenectomy, the patients were divided into two groups: PSE group ($n = 40$) and non-PSE group ($n = 281$). Patient characteristics, postoperative complications, and follow-up data were compared between groups. Propensity score matching (PSM) was conducted, and univariable and multivariable analyses were used to establish a nomogram predictive model for intraoperative bleeding (IB). The receiver operating characteristic curve, Hosmer-Lemeshow goodness-of-fit test, and decision curve analysis (DCA) were employed to evaluate the differentiation, calibration, and clinical performance of the model.

Research results

After PSM, the non-PSE group showed significant reductions in hospital stay, intraoperative blood loss, and operation time (all $P = 0.00$). Multivariate analysis revealed that spleen length, portal vein diameter, splenic vein diameter, and history of PSE were independent predictive factors for IB. A nomogram predictive model of IB was constructed, and DCA demonstrated the clinical utility of this model. Both groups exhibited similar results in terms of overall survival during the follow-up period.

Research conclusions

Preoperative PSE followed by splenectomy may increase the incidence of IB and a nomogram-based prediction model can predict the occurrence of IB. Meticulous separation of splenic adhesions is imperative for achieving safe and efficacious surgical outcomes.

Research perspectives

Future research should focus on the duration between embolization and splenectomy to enhance the benefits of this approach and reduce the surgical risks. Additional prospective randomized controlled trials are necessary to expand the findings of this study.

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FOOTNOTES

Author contributions: Huang L wrote the paper; Huang L, Li QL and Yu QS designed the research; Shen Y and Zhang Q performed the research; Peng H and Zhen Z analyzed the data; All authors made substantial intellectual contributions to this paper.

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