

Relations between spontaneous portosystemic shunts and outcomes in hepatitis B virus-related cirrhotic patients with esophagogastric variceal bleeding after repeated endotherapy

Jia-li Ma

Capital Medical University

Yu Jiang

Capital Medical University

Ju-long Hu

Capital Medical University

Yu-ling Zhou

Capital Medical University

Zheng-lin Ai

Capital Medical University

Xiu-xia Liang

Capital Medical University

Ru-ming Xie

Capital Medical University

Hong-shan Wei

Capital Medical University

ping Li (✉ endolp@126.com)

Capital Medical University

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Abstract

Aims: Investigating the prevalence and characteristics of spontaneous portosystemic shunts (SPSS) in hepatitis B-related cirrhotic patients with acute variceal bleeding (AVB) after repeated endotherapy.

Methods: 442 hepatitis B-related cirrhotic patients with AVB, who were treated with repeated endotherapy were included in the final analysis. We collected data on demographic features, laboratory and clinical variables, complications, treatment options and Child/MELD scores. The contrast-enhanced abdominal computed tomography (CT) were reviewed to search for the presence and classification of SPSS. SPSS were divided into large or small size according to its maximum diameter. The primary outcome was 3 and 5-years survival.

Results: SPSS were identified in 174 patients (39.37%), including 97 large-SPSS (21.95%) and 77 small-SPSS (17.42%). The median survival time was significantly longer in SPSS patients (99.4 months, [95% CI: 94.7-104.1]) compared with non-SPSS patients (83.5 months, [95% CI: 78.1-88.8]) ($P=0.001$). The 3-years, and 5-years survival rates were significantly higher in SPSS group (87.4% vs 70.9%, $P=0.001$; 65.5% vs 37.0%, $P=0.001$). Age, antiviral therapy, variceal rebleeding, Child/MELD-score and the presence of SPSS were independent predictors of survival.

Conclusions: SPSS is not rare in cirrhotic patients, for patients with AVB who underwent repeated endotherapy, and received fine aetiological treatment, SPSS was likely to be a protective factor for survival.

Introduction

Spontaneous portosystemic shunts (SPSS) is one of the upshot of portal hypertension, as the formation of portosystemic collateral vessels. SPSS is a try to decompress the portal venous system. Cirrhotic patients frequently develop a massive variety of SPSS as a complication of long-standing portal hypertension. SPSS are communications between portal vein and systemic circulations, which opens when portal pressure increases in cirrhotic patients. SPSS are "release vents" to reduce the portal pressure, but also are "by-passes" to normal liver flow. Of note, SPSS represent an insufficient compensatory mechanism, not allowing for a sufficient compensatory mechanism, or an adequate reduction of portal pressure, but lessening hepatic portal-venous perfusion.

SPSS can be visualized and characterized by imagine examinations. Different SPSS have been identified. It seems that gastric variceal bleeding is the most important complication of gastro-renal shunt (GRS); and hepatic encephalopathy (HE) and portal vein thrombosis (PVT), are usually related to spleno-renal shunt. Portal hypertensive bleeding, particularly acute variceal bleeding (AVB) is a lethal complication in cirrhotic patients, vaso-active drugs, prophylactic antibiotics, a restrictive blood transfusion policy, as well as early endoscopy are the mainstays of treatment for AVB. Most cirrhotic patients cannot receive liver transplantation after repeated AVB and other severe cirrhotic complications in China, since donated livers are not available and the price is unaffordable. Interventional therapies such as TIPS, BRTO might best serve as a bridge to liver transplantation for patients with refractory AVB and SPSS, but, the technique is difficult, the cost is high, can be carried out in only a few hospitals. Consequently, endoscopic therapy is one of most common techniques to control AVB in such patients in China. Identification of SPSS have been assessed as a therapeutic target by embolization in patients with good preserved liver function. Outcomes in patients with AVB after endoscopic therapy may be affected by the presence of SPSS in opposing ways. On one hand, SPSS might have a portal flow "stealing" effect, decreasing the portal inflow, and sometimes worsening liver function. On the other hand, SPSS might have a protective effect by shunting the blood away and reducing the transient portal hypertension after endoscopic therapy. While the position of SPSS in the cirrhotic patients after repeated endoscopic therapy for AVB is rarely discussed.

The aim of current study is to evaluate the prevalence and characteristics of SPSS in cirrhotic patients after repeated endoscopic therapy for AVB, and to assess the impact on clinical outcomes and mortality.

Patients And Methods

Study population

This is a single-center retrospective study, completed at the Beijing Ditan Hospital of Capital Medical University. Patients were collected from October 2010 and December 2019. Since etiological factors may influence the prognosis of cirrhosis, the inclusion criteria were the following: hepatitis B virus-related cirrhosis patients with variceal bleeding, who were treated with endoscopic therapy, and finally 442 out of 1074 patients were included in the analysis. Liver cirrhosis was defined according to previous consensus recommendation. The exclusion criteria were as follows: non-hepatitis B cirrhosis, multiple possible etiologies of liver cirrhosis, or non-cirrhotic portal hypertensive bleeding; regional portal hypertension; patients who received liver transplantation, TIPS, BRTO, splenic embolization, pericardial devascularization

with splenectomy or other interventions for varices/portal hypertension; patients with hepatocellular carcinoma (HCC) or any serious concurrent medical condition with expected survival of fewer than 12 months; patients who were lost to follow-up or had no abdominal imaging. Endoscopy is the gold-standard to assess AVB, the following can be used to define AVB: acute variceal bleeding episode were seen; "white nipple sign" or adherent clot; or showed varices without another potential source of bleeding.

The study protocol conformed to the Declaration of Helsinki and was approved by the Ethics Committee of Beijing Ditan Hospital, Capital Medical University [JDLKZ (2018-021-01)].

Data collection

All enrolled cirrhotic patients were suffered with AVB, all of them were underwent a contrast-enhanced abdominal computed tomography(CT) before or after endoscopic therapy within two weeks. All CT scans were reviewed by a radiologist with expertise in liver diseases. SPSS were divided into large or small size according to its maximum diameter, with the cut-off value of 8 mm, according to the report of previous literature. Demographic characteristics, etiology of liver disease, comorbidities, previous complications of cirrhosis were recorded. Laboratory and clinical variables, trans-abdominal ultrasonography values were also collected, Child-Pugh score and MELD score were recorded. All information was gathered from medical records of the first endoscopic therapy for AVB. Severe complications after the first endoscopic therapy were also recorded. Follow-up was performed.

Treatments and endoscopic therapy

All patients with AVB were started on vasoactive drugs as initial treatment before endoscopic therapy. Antibiotics and restrictive blood transfusion were also administered. Endoscopic therapy was performed when the patients achieved hemodynamic stability, 6–24 hours after hospital admission.

The endoscopic therapy was performed using the following methods: i) endoscopic variceal ligation (EVL) was applied for patients with first esophageal variceal bleeding; ii) cyanoacrylate injection was used for patients with gastric variceal hemorrhage; iii) the "sandwich therapy" (polidocanol + n-butyl-2 cyanoacrylate + polidocanol) was performed in patients with esophageal gastric variceal hemorrhage, injections were repeated, if necessary. ⓧ) for some patients with gastric variceal hemorrhage, accompanied by SPSS, metal clip-assisted "sandwich therapy" was performed, especially for GRS and SRS(Fig. 1). Endoscopic injection sclerotherapy (EIS) was also performed for some patients with esophageal variceal rebleeding based on the clinical guidelines; clinical setting, the specialists' preference and experience for formulating the best treatment plan. Non-selective beta blockers (*NSBBs*) were also administered for secondary prevention of rebleeding, usually 5 to 7 days after the bleeding episode stopped.

Follow-up

Patients who underwent endoscopic therapy were investigated and received endoscopic therapy repeatedly every 4–12 weeks according to the variceal size and severity; the interval extended to 1 year after the eradication of varices. Follow-up was performed by recording the decompensating events including variceal rebleeding, HE, ascites, spontaneous bacterial peritonitis, and severe complications including PVT. The follow-up ended on December 2020 or death. The primary outcome was 3 and 5-years survival. The secondary outcome was variceal rebleeding.

Statistical analysis

Statistical analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY, United States). Quantitative data was detected for normal distribution. Student's t-test was used if the data accorded with normal distribution and Mann-Whitney *U* test was used if the data did not accord with normal distribution. χ^2 test was used for analyzing qualitative data. Results are presented in percentage, as mean and SD or as median and interquartile range(IQR). All reported *p* values are 2-tailed. *P* values ≤ 0.05 were considered as statistically significant.

To examine the survival differences among the groups, Kaplan-Meier method was used to generate the survival curves. Log-rank method was used to compare the differences between the groups. Univariate and multivariate Cox analyses were conducted to identify the impact factors that influenced the long-term survival. Two-sided *P*-values < 0.05 were considered statistically significant. Well-known confounding factors (age, sex, and comprehensive liver function) were also included in the models regardless of *P* value at univariate analysis.

Results

From a total of 1074 patients who were assessed for eligibility, 442 patients were included in present study(Fig. 2). SPSS were identified in 174 patients(39.37%), including 97 large-SPSS (21.95%) and 77 small-SPSS (17.42%). The median follow-up duration was 57 months(IQR 36.25 months, minimum 5 days, maximum 111 months); Non-SPSS, 49 months(IQR 37.5 months, minimum 5 days, maximum 110

months); SPSS, 65 months(IQR 37.5 months, minimum 17 days, maximum 111 months).(Z=-5.382, $P<0.001$). Distribution of SPSS is shown in detail in Table 1.

Table 1
Baseline characteristics of the patients.

Characteristics	total	SPSS			Non-SPSS	#P
		Small-SPSS	Large-SPSS	*P		
Age(Year)	49.47 ± 10.29	49.10 ± 10.17			49.71 ± 10.38	0.545
		49.83 ± 10.01	48.52 ± 10.31	0.398		
Sex(male)	325(73.53)	126/174			199/268	0.741
		60/77	66/97	0.173		
Current drinking	141(31.90%)	28/77	32/97	0.748	81/268	0.350
Ascites	74.9%	18/77	29/97	0.392	204/268	0.501
Hepatic encephalopathy	9%	5/77	5/97	0.752	30/268	0.062
Portal vein thrombosis	24.89%	28/77	35/97	0.969	47/268	<0.001
Tissue glue(ml)	2.5(1–5)	2.5(1–5.5)			2.5(1–5)	0.732
		2(1–5)	2.5(1–6)	0.644		
Lauromacrogol(ml)	70(30–140)	80(40–150)			70(22.5–120)	0.023
		80(40–145)	80(40–155)	0.740		
Antiviral therapy	79.9%	63/77	82/97	0.685	208/268	0.148
WBC(×10 ⁹ /L)	3.64(2.40–6.00)	3.62(2.33–5.45)			3.69(2.46–6.21)	0.314
		3.68(2.52–6.11)	3.42(2.31–4.93)	0.288		
NEU(×10 ⁹ /L)	2.59(1.52–4.47)	2.41(1.47–4.12)			2.69(1.56–4.65)	0.218
		2.65(1.54–4.45)	2.22(1.38–3.44)	0.206		
HGB(g/L)	92.55 ± 27.64	97.6(77.2–119.43)			87.1(69.05–109.9)	0.001
		97.2(82.5–118)	100(76.55–124.75)	0.786		
PLT(×10 ⁹ /L)	58(42.4–81.0)	55.6(41.93–78.10)			60.70(43.10–83.00)	0.153
		56(44.55–84.50)	54(40.40–75.65)	0.120		
ALT(U/L)	27.95(20.05–41.60)	27.7(19.80–41.13)			27.95(20.20–44.15)	0.414
		30.20(19.40–40.50)	27.40(20.30–41.15)	0.832		
AST(U/L)	35.45(25.28–49.53)	35.55(26.38–49.53)			35.40(24.20–49.53)	0.516
		36.20(25.45–50.15)	35.40(26.55–49.00)	0.910		
TBIL(μmol/L)	20.10(13.80–30.8)	21.85(15.30–33.35)			18.40(13.05–28.18)	0.003

Note:

*For comparison between small-SPSS and large-SPSS.

#For comparison between SPSS and non-SPSS.

WBC, white blood cell; NEU, neutrophilic granulocyte; HGB, hemoglobin;

PLT, platelet; ALT, glutamic-pyruvic transaminase; AST, glutamic oxalacetic transaminase;

TBIL, total bilirubin; ALB, albumin; GGT, gamma-glutamyl transpeptidase;

CHE, cholinesterase; Cr, creatinine; INR, International standard ratio; AFP, alpha fetal protein;

Characteristics	total	SPSS			Non-SPSS	#P
		Small-SPSS	Large-SPSS	*P		
		21.90(14.75–30.25)	21.80(15.65–36.85)	0.406		
ALB(g/L)	31.86 ± 5.90	32.29 ± 6.20			31.59 ± 5.70	0.224
		32.14 ± 6.22	32.40 ± 6.21	0.780		
GGT(U/L)	28.10(16.50–44.30)	25.75(15.78–37.83)			30.00(17.00–48.20)	0.028
		30.40(18.40–43.50)	21.60(14.25–35.80)	0.025		
CHE(U/L)	3334.21 ± 1497.22	3047(2245–4060)			3076(2332–4114)	0.733
		3023.50(2279.75–4004.25)	3047(2219.5–4136)	0.895		
Cr(μmol/L)	64.35(53.93–75.02)	64.00(51.88–74.90)			65.15(54.90–75.10)	0.324
		65(55.3–76.8)	62.2(49.25–72.85)	0.131		
INR	1.33 ± 0.24	1.30(1.20–1.41)			1.27(1.16–1.41)	0.365
		1.28(1.20–1.38)	1.31(1.20–1.48)	0.225		
AFP(ng/ml)	4.70(2.53–8.98)	4.80(2.70–9.0)			4.50(2.45–8.85)	0.445
		4.7(2.7–9.28)	4.8(2.7–9.0)	0.795		
Gastric varices	30.54%	39/77	47/97	0.879	49/268	<0.001
Median grade of varices(G1,G2,G3)	2.4	2.4		0.649	2.4	0.768
		2.5	2.3			
Child-Pugh class(A/B/C)	110/220/112	17/40/20	28/44/25	0.562	65/136/67	0.874
MELD score	6.78(4.24–9.62)	6.98(4.27–9.82)			6.45(4.21–9.51)	0.464
		6.99(4.39–9.57)	6.98(4.02–9.99)	0.608		
Note:						
*For comparison between small-SPSS and large-SPSS.						
#For comparison between SPSS and non-SPSS.						
WBC, white blood cell; NEU, neutrophilic granulocyte; HGB, hemoglobin;						
PLT, platelet;ALT, glutamic-pyruvic transaminase; AST,glutamic oxalacetic transaminase;						
TBIL, total bilirubin; ALB, albumin; GGT, gamma-glutamyl transpeptidase;						
CHE, cholinesterase; Cr, creatinine; INR,International standard ratio; AFP,alpha fetal protein;						

Effect of SPSS

The included with large-SPSS were 97 out of 442 patients, including 40 gastro-renal shunts(GRS), 12 spleno-renal shunts (SRS), 24 multiple shunts,8 oeso-gastric shunts (OGS), 7 umbilical shunts (UmS) and 6 other shunts. A comparison of demographics and baseline parameters between each group are shown in Table 1.

To evaluate the outcomes of the patients, the survival rates between the SPSS and non-SPSS groups were analyzed. The result showed that the median survival time was significantly longer in SPSS patients (99.4 months, [95% CI: 94.7-104.1]) compared with non-SPSS cirrhosis patients (83.5months, [95% CI: 78.1–88.8]) ($P<0.001$). The 3-years survival rate of the SPSS group was 87.4%, which was higher than the non-SPSS group (70.9%) ($P<0.001$). The 5-years survival rate of the SPSS group was 65.5%, which was significantly higher than the non-

SPSS group (37.0%) ($P < 0.001$) (Fig. 3). The survival time between the small-SPSS (95.3 months, [95% CI: 87.7-102.8]) and large-SPSS groups (101.2 months, [95% CI: 95.5–107.0]) were similar ($P = 0.405$) (Fig. 4). The cumulative survival rate in large-SPSS group was significantly higher than no-SPSS group ($P = 0.001$).

The rebleeding rate was also evaluated between each pair of groups. There was no significant difference in rebleeding rate between SPSS group and no-SPSS group ($\chi^2 = 0.792$, $P = 0.374$) (Fig. 5A). The cumulative rebleeding rate was higher in small-SPSS group than large-SPSS group ($\chi^2 = 4.268$, $P = 0.039$) (Fig. 5B).

The Cox regression analysis was used to identify independent factors for mortality. Variables significantly associated with the death and entered into the multivariate model. Age, antiviral therapy, the presence of variceal rebleeding, Child-score, MELD-score and the presence of SPSS were independent predictors of survival. The details are shown in Table 2.

Table 2
Cox analysis of factors at baseline related to death.

Variable	Univariate analysis HR (95% CI)	<i>P</i>	Multivariate analysis HR (95% CI)	<i>P</i>
Age(year)	1.034(1.013–1.055)	0.001	1.037(1.015–1.059)	0.001
Sex	0.958(0.601–1.525)	0.856	0.895(0.526–1.524)	0.683
Antiviral therapy	0.562(0.359–0.881)	0.012	0.565(0.354–0.901)	0.017
HE	2.406(1.403–4.127)	0.001	0.962(0.492–1.883)	0.911
Ascites	2.160(1.201–3.883)	0.010	1.166(0.577–2.357)	0.669
Rebleeding	0.579(0.377–0.889)	0.013	0.561(0.361–0.871)	0.010
Child-score	1.309(1.195–1.435)	<0.001	1.173(1.006–1.366)	0.041
MELD-score	1.116(1.082–1.151)	<0.001	1.035(1.083–1.035)	0.001
SPSS	0.414(0.254–0.674)	<0.001	0.399(0.243–0.657)	<0.001

Risk factors for complications after endoscopic therapy

Since repeated endoscopic therapy were applied, the first treatment is the most important, most prone to complications. For SPSS patients, endoscopic clipping prior n-butyl-2 cyanoacrylate injection were applied to reduce the risk of ectopic embolization. Severe complications occurred in 62 patients in the endoscopic group (14.03%); 12 experienced sepsis, 3 in small-SPSS group, 4 in large-SPSS group ($P = 0.626$, comparison between group small-SPSS and group large-SPSS), and 5 in non-SPSS group ($P = 0.144$, comparison between group SPSS and group non-SPSS); and 50 developed PVT, 14 in small-SPSS group, 17 in large-SPSS group ($P = 0.911$, comparison between group small-SPSS and group large-SPSS), and 19 in non-SPSS group ($P = 0.001$, comparison between group SPSS and group non-SPSS). No patient died of complications. Patients with SPSS may be more predisposed to suffering PVT.

Discussion

Here, we presented our experiences of endoscopic therapy for varices with reference to SPSS. The results show that: firstly, SPSS are very frequent in cirrhotic patients, around 40% patients had some type of SPSS detected by CT scan. Secondly, endoscopic therapy is a feasible option for treatment of variceal rebleeding in patients with hepatitis B–related cirrhosis and SPSS, when endoscopic clipping prior to injection is applied. The interesting finding is that the existence of SPSS do not increase the rebleeding rate, but improve the long-term survival.

From a security perspective, no procedure-related mortality was reported. SPSS connecting the portal system to the caval system to alleviate portal hypertension, which placing patients at high risk for ectopic embolism after endoscopic therapy¹⁷. However, no symptomatic ectopic embolization occurred. PVT is a heterogeneous condition with respect to etiology, manifestations, natural history, and therapeutic options. As PVT location and extent with long-term outcome in patients with cirrhosis lacks clinical correlation, in this study, no intestinal ischemic necrosis, septic shock, or short-term death due to severe acute PVT were occurred, PVT was not further classified. We identified patients with SPSS suffered with increased risk of PVT after endoscopic therapy, for SPSS shunted the portal blood flow to the caval system when the varices were blocked, and decreased velocity of portal vein flow has been recognized as a risk factor for PVT in cirrhotic patients²¹. While, the increased PVT didn't transfer to higher rebleeding rate ($P = 0.374$), PVT was opposed to being an etiologic

factor and was not independently associated with disease progression. Whether PVT is a manifestation of disease or an cause of disease progression is uncertain.

Another aspect to highlight is that the presence of SPSS increases the long-term survival rate of cirrhotic patients after repeated endoscopic therapy. It is quite clear that the liver function, the comprehensive scores of the liver determined the long-term prognosis¹. At baseline, the Child class and MELD score was similar among each group, suggesting the liver function was at the same level. Moreover, treatment for the root cause of the underlying disease reduces portal hypertension and prevents complications in patients with liver cirrhosis². It is reported that antiviral therapy significantly improved the Child score, reduced the rebleeding rate, the incidence of HCC and improved patient's overall clinical course³. In the present study, the two groups of antiviral therapy was basically balanced at baseline for prognosis factors. Our interpretation of this result is that, on the basis of aetiological treatment and repeated endoscopic therapy for varices, the portal pressure was shunted by SPSS, the recurrence and aggravation of varices was alleviated, the portal flow "stealing" effect was compensated by the increasing portal hypertension after endoscopic therapy. The same founding was reported by Riggio et al, they performed a case-control study and the result showed that patients with chronic HE and large-SPSS had less ascites, esophageal varices and portal-hypertensive gastropathy than patients without SPSS, suggesting a protective profile of SPSS.

The study has some limitations. First, the study was retrospective designed, only the patients with endoscopic treatment were enrolled, the possibility of selection bias cannot be excluded, even patients were screened by the inclusion and exclusion criteria. Second, we were unable to demonstrate the association between HE and SPSS, for on the long-run of follow-up time, only the worst episode of HE could be recorded, too much information was lost.

In conclusion, the present study suggested that SPSS was likely to be a protective factor for patients with varices and variceal bleeding, who chooses repeated endoscopic therapy, on the basis of fine aetiological treatment.

List Of Abbreviations

SPSS, Spontaneous portosystemic shunts

HE, hepatic encephalopathy

AVB, acute variceal bleeding

HCC, hepatocellular carcinoma

CT, computed tomography

EVL, endoscopic variceal ligation

EIS, endoscopic injection sclerotherapy

NSBBs, Non-selective beta blockers

GRS, gastro-renal shunts

SRS, spleno-renal shunts

OGS, oeso-gastric shunts

UmS, umbilical shunts

PVT, portal vein thrombosis

Declarations

Ethics approval and consent to participate

Our retrospective study was approved by the Clinical Ethics Committees of Beijing Ditan Hospital, Capital Medical University (JDLKZ2018-021-01). All Patients provided written informed consents in accordance with the Declaration of Helsinki. We confirm that all methods were carried out in accordance with relevant guidelines and regulations.

Competing interests

The authors declare that they have no competing interests. Copyright transfer, authorship responsibility and Conflict of Interest were signed by all authors

All authors had access to the study data and had reviewed and approved the final manuscript.

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Authors' contributions

LP and WH designed the present study; MJ wrote the main manuscript, MJ ,JY and HJ collected the clinical data; MJ, ZY, AZ and LX performed statistical analysis; XR reviewed the CT scan; All authors read and approved the final manuscript.

Consent for publication

Not applicable.

Availability of data and materials

We are willing to share our raw data, you can request it by email the corresponding author.

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Each author's affiliation

Ping Li, Bachelor's degree, Department of Gastroenterology, Beijing Ditan Hospital, Capital Medical University, Beijing, China. endlp@126.com

Hong-shan Wei, PhD, Department of Gastroenterology, Beijing Ditan Hospital, Capital Medical University, Beijing, China. drwei@ccmu.edu.cn

Jia-li Ma, MD, Department of Gastroenterology, Beijing Ditan Hospital, Capital Medical University, Beijing, China. Jalin421@126.com

Yu Jiang, Bachelor's degree, Department of Gastroenterology, Beijing Ditan Hospital, Capital Medical University, Beijing, China. jarod352@gmail.com

Ju-long Hu, Master's degree, Department of Gastroenterology, Beijing Ditan Hospital, Capital Medical University, Beijing, China. drhujulong@163.com

Yu-ling Zhou, Master's degree, Department of Gastroenterology, Beijing Ditan Hospital, Capital Medical University, Beijing, China. zhouditan@163.com

Zheng-lin Ai, MD, Department of Gastroenterology, Beijing Ditan Hospital, Capital Medical University, Beijing, China. aizhenglin@126.com

Xiu-xia Liang, Master's degree, Department of Gastroenterology, Beijing Ditan Hospital, Capital Medical University, Beijing, China. yliangxiuxia@163.com

Ru-ming xie, Master's degree,, Department of radiology, Beijing Ditan Hospital, Capital Medical University, Beijing, China. mingrux@126.com

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Figures

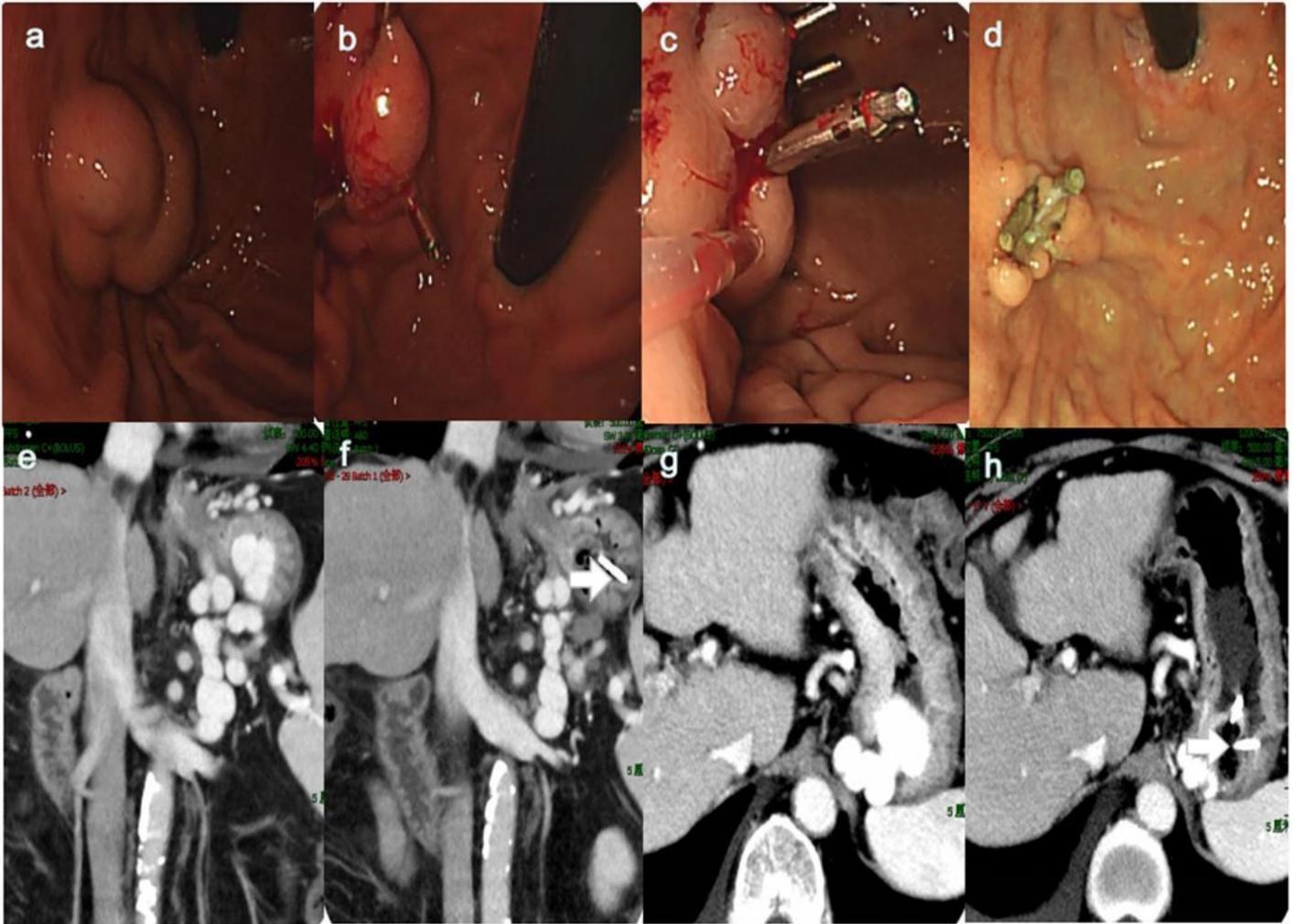


Figure 1

A patient with isolated gastric varices (IGV1) accompanied with gastro-renal shunts received metal clip–assisted “sandwich therapy”therapy.

a, endoscopic examination found isolated gastric varices; b,metal-clips were deployed on the inflow and outflow veins to restrict the blood flow; c, “sandwich therapy” was applied; d,gastric varices were collapsed and shrunk after 3 months of the therapy; e and g,Contrast-enhanced CT scan showed gastro-renal shunts(before therapy); f and h, 1 week after the therapy,contrast-enhanced CT scan found gastric varices were disappeared, metal-clip can be seen(white arrow).

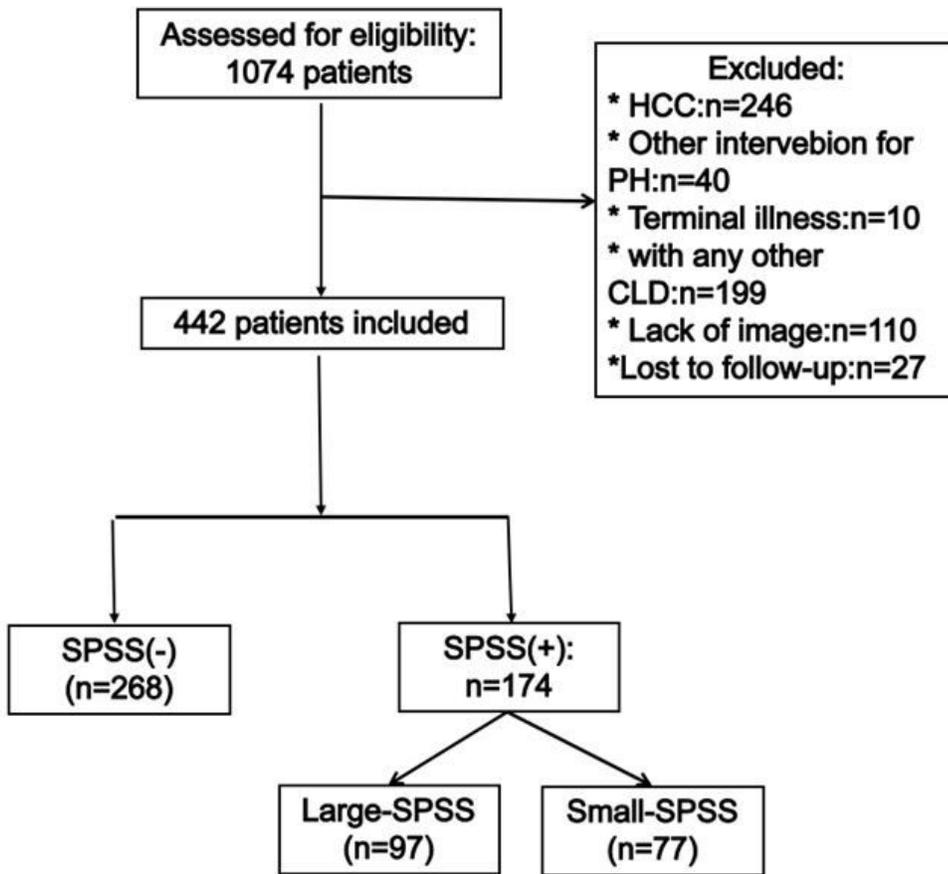


Figure 2

Flow chart of the study

A total of 1074 patients who were assessed for eligibility, 442 patients were included in present study. SPSS were identified in 174 patients(39.37%), including 97 large-SPSS (21.95%) and 77 small-SPSS (17.42%).

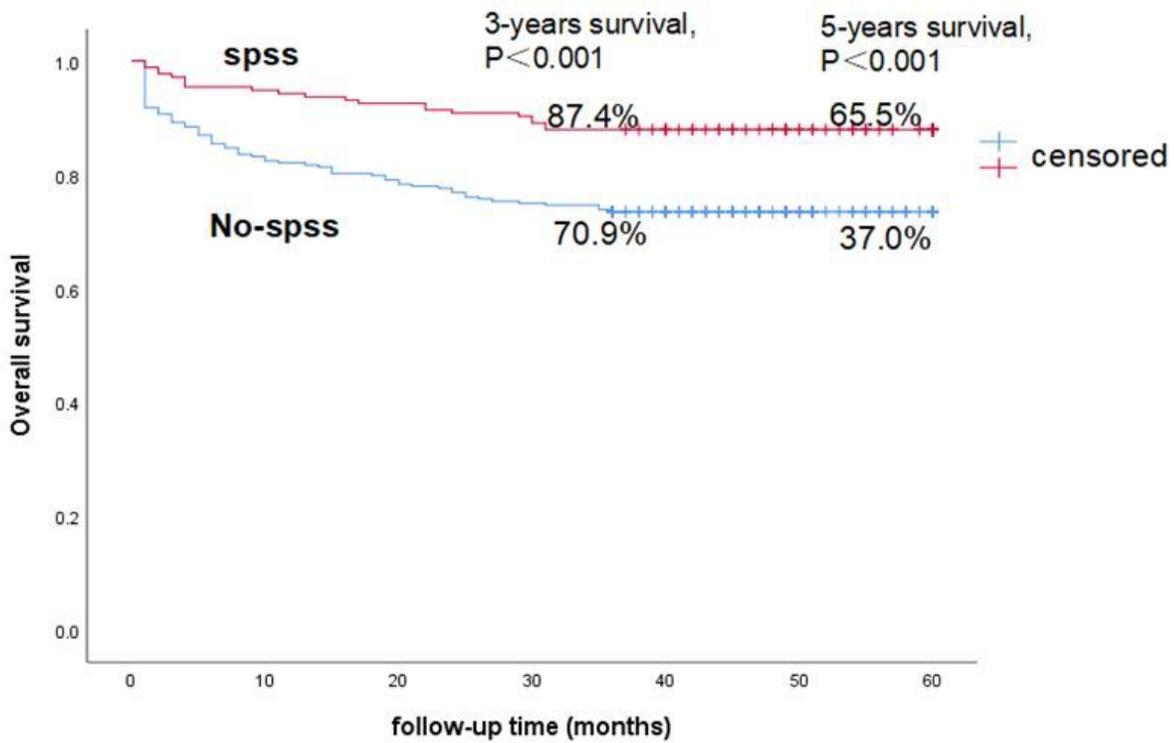


Figure 3

Overall survival for the HBV-related cirrhotic patients with varices who performed with repeated endoscopic therapy

The 3-years survival rate of the SPSS group was 87.4%, which was higher than the non-SPSS group (70.9%) ($P=0.001$). The 5-years survival rate of the SPSS group was 65.5%, which was significantly higher than the non-SPSS group (37.0%) ($P=0.001$).

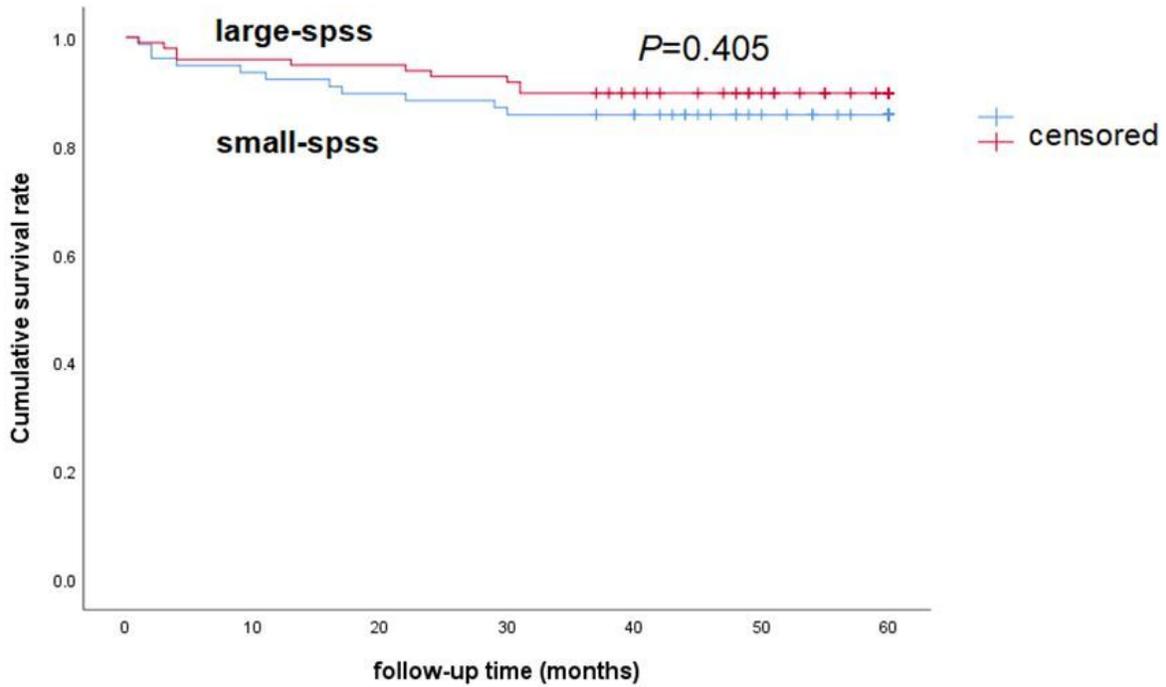


Figure 4

Cumulative survival for the HBV-related cirrhotic patients with varices who performed with repeated endoscopic therapy between large and small-SPSS groups.

The survival time between the small-SPSS (95.3 months, [95% CI: 87.7-102.8]) and large-SPSS groups(101.2 months, [95% CI: 95.5-107.0]) were similar($P=0.405$).

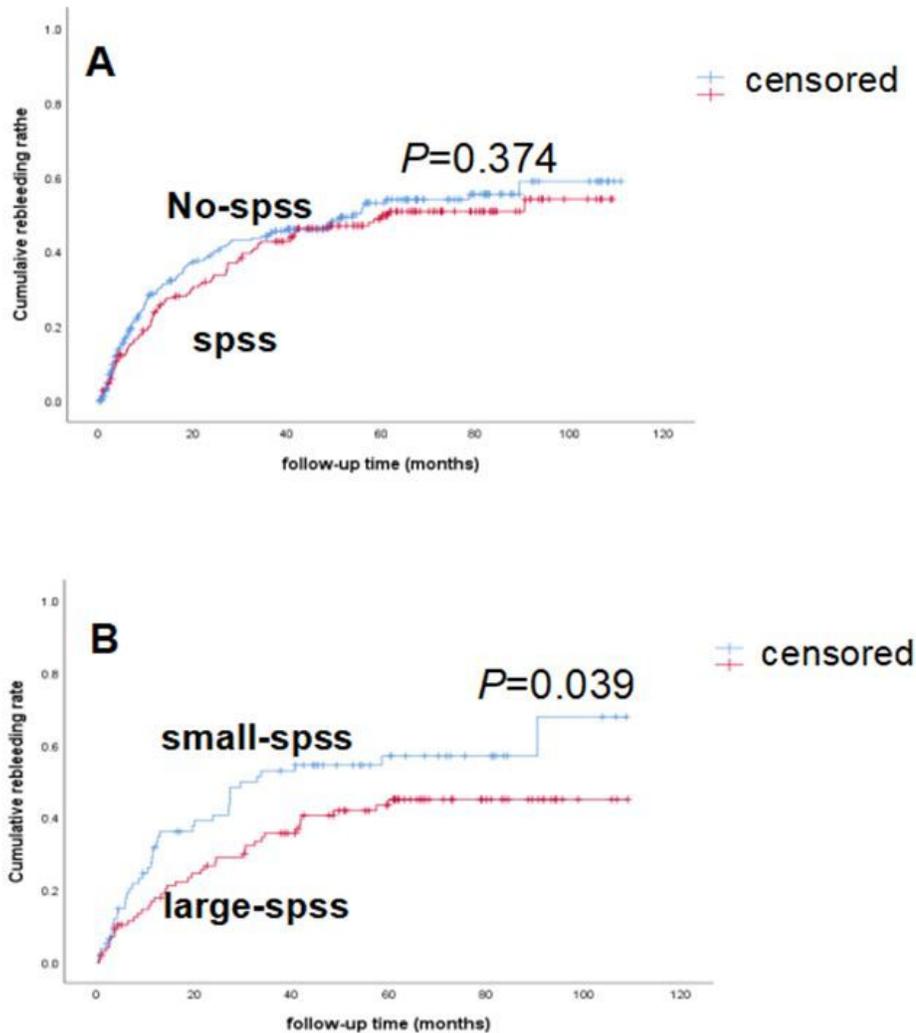


Figure 5

A: Cumulative rebleeding rate for the HBV-related cirrhotic patients with varices who performed with repeated endoscopic therapy between SPSS and no-SPSS groups. There was no significant difference in rebleeding rate between SPSS group and no-SPSS group ($\chi^2 = 0.792$, $P = 0.374$).

B: Cumulative rebleeding rate for the HBV-related cirrhotic patients with varices who performed with repeated endoscopic therapy between small-SPSS and large-SPSS groups. The cumulative rebleeding rate was higher in small-SPSS group than large-SPSS group ($\chi^2 = 4.268$, $P = 0.039$).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [rawdata.xls](#)