Albumin-Bilirubin and Severity as Key Factors of Recovery in Patients With PA-HSOS Undergoing Transjugular Intrahepatic Portosystemic Shunt

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AIM: To evaluate the safety and efficacy of transjugular intrahepatic portosystemic shunt (TIPS) in the management of pyrrolizidine alkaloid-related hepatic sinusoidal obstruction syndrome (PA-HSOS) and to identify key factors influencing the recovery of liver imaging manifestation after TIPS procedure in PA-HSOS patients.

METHODS: A retrospective review was conducted of 30 PA-HSOS patients who received TIPS at Jinhua Municipal Central Hospital between 1 January 2018, and 30 September 2021, following failure of anticoagulation-based comprehensive treatments. Baseline characteristics and follow-up data were collected, including clinical manifestations, laboratory test results, computed tomography (CT) radiological manifestations of the liver, hepatic venous pressure gradient (HVPG), survival, and complications. Laboratory tests before and after TIPS were compared, and multiple linear regression was used to analyze factors associated with the recovery time of liver CT radiological manifestations.

RESULTS: TIPS was successfully performed in all 30 patients, with no procedure-related adverse events. All patients survived the follow-up period. The portal pressure gradient (PPG) significantly reduced from 22.65 $\pm$ 6.36 mmHg to 9.40 $\pm$ 3.38 mmHg ($p < 0.001$). The median time to complete ascites remission was 52 days (range: 29–161 days). The median recovery time for liver CT radiological manifestations was 196.5 days (range: 165–229 days). Disease severity and albumin-bilirubin (ALBI) grade were significant factors influencing the recovery time of liver CT radiological manifestations ($R^2 = 0.666$, $p = 0.007$). Patients with ALBI grade 2 had a significantly shorter recovery time of liver CT radiological manifestations compared to those with ALBI grade 3 (170.44 $\pm$ 50.56 days *vs* 224.83 $\pm$ 46.67 days, $p = 0.006$). Similarly, patients with severe or very severe disease had longer recovery times than those with mild or moderate diseases (218.25 $\pm$ 41.60 days *vs* 162.43 $\pm$ 55.11 days, $p = 0.004$).

CONCLUSIONS: TIPS is a safe and effective treatment for PA-HSOS. Disease severity and ALBI grade are key factors in estimating the recovery time of liver CT radiological manifestations in patients with PA-HSOS.

Keywords: HSOS; PA; TIPS; portal hypertension; ALBI grade

Introduction

Hepatic sinusoidal obstruction syndrome (HSOS), also known as a hepatic venous-occlusive disease (HVOD), is a vascular disease of the liver caused by a variety of factors [1,2]. The primary pathological features of HSOS include edema, necrosis, and shedding of endothelial cells within the hepatic sinusoids, venules, and interlobular veins. These changes result in microthrombi formation, which can cause intrahepatic congestion, portal hypertension, and liver dysfunction [3,4]. In Western countries, HSOS is usually associated with myeloablative conditioning regimens used prior to hematopoietic stem cell transplantation (HSCT)-related HSOS [5,6]. In China, however, the predominant cause is the ingestion of medicinal herbs containing pyrrolizidine alkaloids, such as *Gynura segetum*, leading to pyrrolizidine alkaloid-related HSOS [7]. Hepatomegaly and diffuse, heterogeneous density of the liver parenchyma with scattered hypodense areas are the main computed tomography (CT) radiological manifestations. Dynamic contrast-enhanced CT typically reveals map-like, non-homogeneous enhancement during the venous and equilibrium phases, as well as hypodense periportal edema [8].

The clinical manifestations of HSOS are non-specific, making early diagnosis relatively difficult. As a re-

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sult, most patients present at moderate to severe disease stages upon diagnosis, making HSOS a potentially life-threatening condition. Currently, anticoagulation therapy is the primary treatment for mild to moderate pyrrolizidine alkaloid-related hepatic sinusoidal obstruction syndrome (PA-HSOS) [9,10]. Transjugular intrahepatic portosystemic shunt (TIPS) placement may serve as an alternative therapy for severe PA-HSOS [11–13], as it can reduce portal hypertension and improve liver stasis. Several recent studies have shown promising results with TIPS [11,14,15]. However, TIPS is an invasive procedure associated with significant complications, including hepatic encephalopathy, bleeding, and sudden deterioration of liver function. While TIPS has been used in the management of PA-HSOS, its efficacy and safety remain controversial [11,15,16]. In contrast to cirrhosis, PA-HSOS exhibits different pathological and imaging features, as well as different prognosis. Moreover, there are relatively few studies focusing on postoperative liver imaging recovery, which is often indicative of remission.

Based on this background, this study aimed to evaluate the safety and efficacy of TIPS in the management of PA-HSOS and to investigate key factors associated with the recovery of liver imaging manifestations following TIPS in PA-HSOS patients.

Materials and Methods

Patients

This retrospective study included 30 patients diagnosed with PA-HSOS who received TIPS therapy at Jinhua Municipal Central Hospital between 1 January 2018 and 30 September 2021. The inclusion criteria were as follows: (1) patients with a clear history of *Gynura segetum* consumption and a subsequent diagnosis of HSOS confirmed by liver biopsy; (2) patients with failure of anticoagulation-based therapy (including anticoagulation, hepatoprotection, diuresis, ascites release, and supportive treatment) lasting at least two weeks; and (3) patients with a preoperative portal pressure gradient (PPG) exceeding 16 mmHg, as measured by hepatic venous pressure gradient (HVPG). The exclusion criteria were: (1) patients with a history of bone marrow transplantation and (2) patients with malignant tumors or other severe diseases. This study was approved by the institutional ethics committee (Approval No. 2025-65) and conducted in accordance with the Declaration of Helsinki. As this was a retrospective observational study, the requirement for informed consent was waived.

Measurement of Portal Pressure

Before measurement of portal pressure, all patients underwent CT hepatic angiography to assess the degree of liver perfusion in the portal phase, as well as the patency of the hepatic vein (HV), portal vein, inferior vena cava (IVC), and jugular vein, and to evaluate the degree of ascites. Portal pressure measurements were obtained in all patients before the TIPS procedure.

Hepatic Venous Pressure Gradient

The right atrial and IVC pressures were measured using a 4F pigtail catheter (18409398, Cook Medical, Bloomington, IN, USA) following jugular vein access under local anesthesia. Standard procedures were followed for measuring free hepatic vein pressure (FHVP) and wedged hepatic vein pressure (WHVP) using a Fogarty balloon catheter (65962363, Edwards Lifesciences, Irvine, CA, USA) [17]. At the end of the WHVP measurement, venography of the occluded hepatic vein was performed by injecting 5 mL of contrast medium (Ultravist 300, Bayer, Leverkusen, Germany) at a rate of 2 mL per second using a power injector. This was performed to verify complete balloon occlusion and assess for the presence of an intrahepatic venovenous shunt (IHVS). The persistence of hepatic vein communication with the wedged vein at the sinusoidal level, despite adjusting the balloon catheter or switching to another hepatic vein, is defined as IHVS. The HVPG was calculated as the difference between WHVP and FHVP. Both FHVP and WHVP were measured in triplicate, and the mean value was used.

TIPS Technique

Celiac arteriography was performed via radial access using a 4F MPA catheter to obtain an indirect portal venogram. Digital subtraction angiography (DSA) overlay software overlapped the hepatic artery and portal vein on the same image, creating a portal vein puncture navigation map. A 2.4-French microcatheter was then catheterized into the selected hepatic artery branch, with its tip serving as a marker. Following establishment and confirmation of Portal Vein (PV) access by contrast medium injection, a 0.035-inch, 260 cm guidewire (241225V, TERUMO, Fujinomiya, Japan) was then catheterized into the splenic vein by a 4F pigtail catheter to conduct direct portal venography and portal vein pressure measurement.

Depending on the patient's clinical status, the puncture route was dilated using a 6- or 8-millimeter balloon. Following that, an 8-millimeter VIATORR stent (29151568, GORE VIATORR, Gore, AZ, USA) was implanted, and a 6- or 8-millimeter balloon was used for re-dilation based on the extent of portal pressure decline. Post-TIPS portal venography was performed after TIPS creation, and portal pressure was measured (Fig. 1). Hepatic arteriography was also conducted to exclude hepatic artery injury, arterioportal fistula, and arteriovenous fistula. According to relevant guideline recommendations, a successful TIPS procedure was defined as achieving a post-procedure PPG of less than 12 mmHg or a reduction of more than 50% from the pre-procedure PPG [18,19].

Following TIPS procedures, all patients received symptomatic and supportive therapy until discharged. Warfarin

Fig. 1. Procedural digital subtraction angiography (DSA). Portal venography after transjugular intrahepatic portosystemic shunt (TIPS) placement.

anticoagulation therapy was continued for at least three months after TIPS procedures.

Data Collection and Follow-up

The Child-Pugh classification is a scoring system used to assess the severity of liver disease, particularly cirrhosis, based on five parameters: serum bilirubin, serum albumin, international normalized ratio (INR), ascites, and hepatic encephalopathy. It is divided into three grades: Class A (5–6 points) for mild liver damage with serum bilirubin $\leq$ 34 µmol/L, albumin $\geq$ 35 g/L, INR $\leq$ 1.7, no or controlled ascites, and no hepatic encephalopathy, offering a 1-year survival rate of 95–100%; Class B (7–9 points) for moderate damage with bilirubin 34–50 µmol/L, albumin 28–35 g/L, INR 1.7–2.3, moderate ascites, and mild or no encephalopathy, with a 1-year survival rate of 60–80%; and Class C (10–15 points) for severe damage with bilirubin $>$ 50 µmol/L, albumin $<$ 28 g/L, INR $>$ 2.3, refractory ascites, and moderate to severe encephalopathy, with a 1-year survival rate of 35–45%, often indicating the need for liver transplantation.

Demographic characteristics, clinical manifestations, laboratory tests, Child-Pugh scores, albumin-bilirubin (ALBI) grade, CT radiological manifestations of the liver, and PPG were recorded for all patients. The ALBI score was calculated using the following formula: ALBI score = [($\log_{10}$ bilirubin (in µmol/L) $\times$ 0.66) + (albumin (in g/L) $\times$ –0.085)], where ALBI score $\leq$–2.60 (ALBI grade 1), ALBI score –2.60 to –1.39 (ALBI grade 2), and ALBI score $>$–1.39 (ALBI grade 3) [20]. The severity of PA-HSOS was determined according to established criteria for grading HSCT-related HSOS in adults [21]. Based on clinical symptoms, bilirubin concentration, bilirubin kinetics, transaminase levels, weight increase, and renal function, this grading system classified disease severity as mild, moderate, severe, or very severe.

All patients underwent regular follow-up at 7 days, 1, 3, and 6 months, and 1 year after TIPS. Monthly ultrasound examinations were performed to monitor ascites, liver recovery, and stent patency. If ultrasound revealed disease progression, shunt obstruction, or inconclusive findings, a CT scan was performed to further assess the liver and shunt. Patients

Table 1. Baseline characteristics of 30 HSOS patients.

Characteristics	Total (n = 30)
Male, n (%)	24 (80.00%)
Age (years)	70.47 ± 9.81
Anticoagulant therapy, n (%)	30 (100%)
Clinical manifestations, n (%)	
The severity of ascites	
Moderate	2 (6.67%)
Severe	28 (93.33%)
Abdominal distention	30 (100%)
Poor appetite	28 (93.3%)
Right upper quadrant pain	8 (26.67%)
Lower limb oedema	10 (33.3%)
Hepatomegaly	28 (93.3%)
Splenomegaly	4 (13.3%)
Child-Pugh classification, n (%)	
A	2 (6.67%)
B	14 (46.67%)
C	14 (46.67%)
ALBI grade, n (%)	
2	18 (60%)
3	12 (40%)
Severity*, n (%)	
Mild	4 (13.33%)
Moderate	10 (33.33%)
Severe	14 (46.67%)
Very severe	2 (6.67%)
Hemoglobin (g/L)	139.53 ± 17.99
Platelets (10^9/L)	94.50 (55.50, 114.00)
White blood cell count (10^9/L)	6.17 ± 1.79
Total bilirubin (mmol/L)	33.40 (10.00, 88.70)
Albumin (g/L)	30.62 ± 2.28
Alanine transaminase (U/L)	33.00 (15.50,65.75)
Aspartate transaminase (U/L)	50.00 (14.25,57.50)
Serum creatinine (μmol/L)	102.70 ± 35.71
Prothrombin time (s)	15.94 ± 2.49
International normalized ratio	1.43 ± 0.22
Other liver diseases, n (%)	
Hepatitis	2 (6.67%)
Cirrhosis	6 (20%)
CT liver imaging	
Scattered hypodense area in the liver	30 (100%)
Inhomogeneous patchy enhancement	30 (100%)
Thinning or obscuration of the hepatic veins	16 (53.3%)
Inferior vena cava stenosis	16 (53.3%)
PPG (mmHg)	22.65 ± 6.36

PPG, portal pressure gradient; HSOS, hepatic sinusoidal obstruction syndrome; ALBI, albumin-bilirubin; CT, computed tomography.

Severity* refers to the criteria for severity grading of hematopoietic stem cell transplantation (HSCT)-related HSOS in adults.

whose CT radiological manifestations of the liver appeared normal were subsequently examined annually. Overall survival (OS) was the primary endpoint. The secondary endpoint was the time to normal CT radiological manifestations. The time to complete ascites remission was defined as the interval from the day of TIPS to the day when radi-

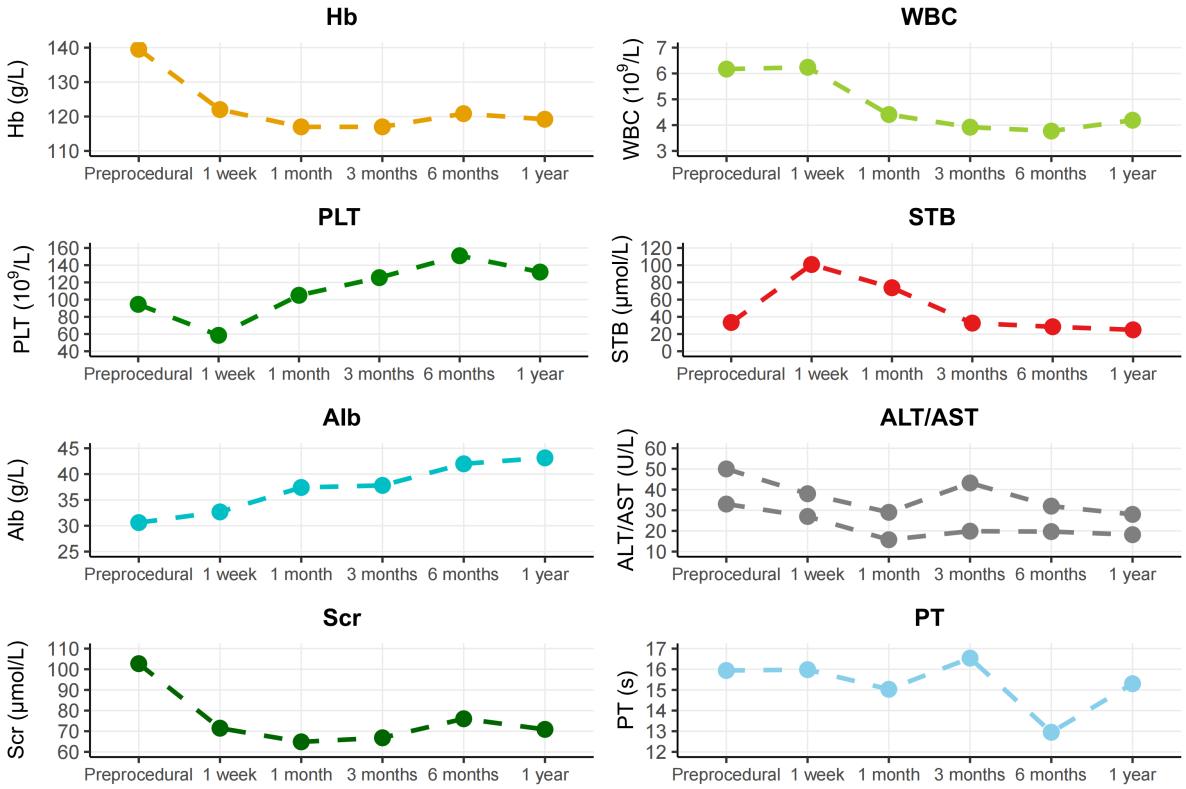

Fig. 2. Plot of the variations in laboratory results. Hb, Hemoglobin; WBC, white blood cell count; PLT, platelets; Alb, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; STB, serum total bilirubin; Scr, serum creatinine; PT, prothrombin time.

ological evaluation indicated no ascites. The recovery time of CT radiological manifestations of the liver was calculated from the day of TIPS to the day when CT radiological manifestations no longer demonstrated heterogeneous liver parenchyma density with scattered hypodense areas, patchy hepatic enhancement, or thinning or obscuration of the hepatic veins and inferior vena cava stenosis.

Statistical Analysis

The Shapiro-Wilk test was used to assess the normality of continuous variables. Continuous data with a normal distribution were expressed as the mean ± SD and compared using independent- or paired-sample *t*-tests. Non-normally distributed data were expressed as the median (25th–75th percentile) and compared using the Mann-Whitney U test or Kruskal-Wallis test. Spearman correlation analysis and multiple linear regression were used to determine the correlation of each factor with the recovery time of CT radiological manifestations. A p-value < 0.05 was considered statistically significant. SPSS (version 20.0, IBM Corp, Armonk, NY, USA) was used for statistical analyses.

Results

Patients' Characteristics

The present study included 30 patients, whose baseline characteristics are presented in Table 1. The most prominent clinical symptom observed was abdominal distension. The most frequent symptom was moderate to massive ascites (100% of patients), followed by hepatomegaly and poor appetite in 28 patients (93.3%). Before TIPS, the median HVPG was 24.5 mmHg (range: 18–31 mmHg). The median follow-up duration was 395 days (range: 35–427 days).

TIPS Procedures and Complications

TIPS procedures were successfully performed in all 30 patients, with no procedure-related adverse events observed. The PPG was significantly reduced from 22.65 ± 6.36 mmHg to 9.40 ± 3.38 mmHg ($p < 0.001$). During the follow-up period, no patient developed overt hepatic encephalopathy.

Laboratory Tests

Table 2 presents the changes in laboratory tests, and Fig. 2 illustrates their variation over time. All patients exhibited elevated total bilirubin levels 7 days after TIPS procedures. In the early postoperative period, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels showed transient increases, reaching 27.00 ± 7.56 U/L and 38.00 (24.75, 46.25) U/L, respectively, at 1 week, followed by a gradual recovery to normal (Table 2). One year after TIPS, total bilirubin levels decreased to 24.90

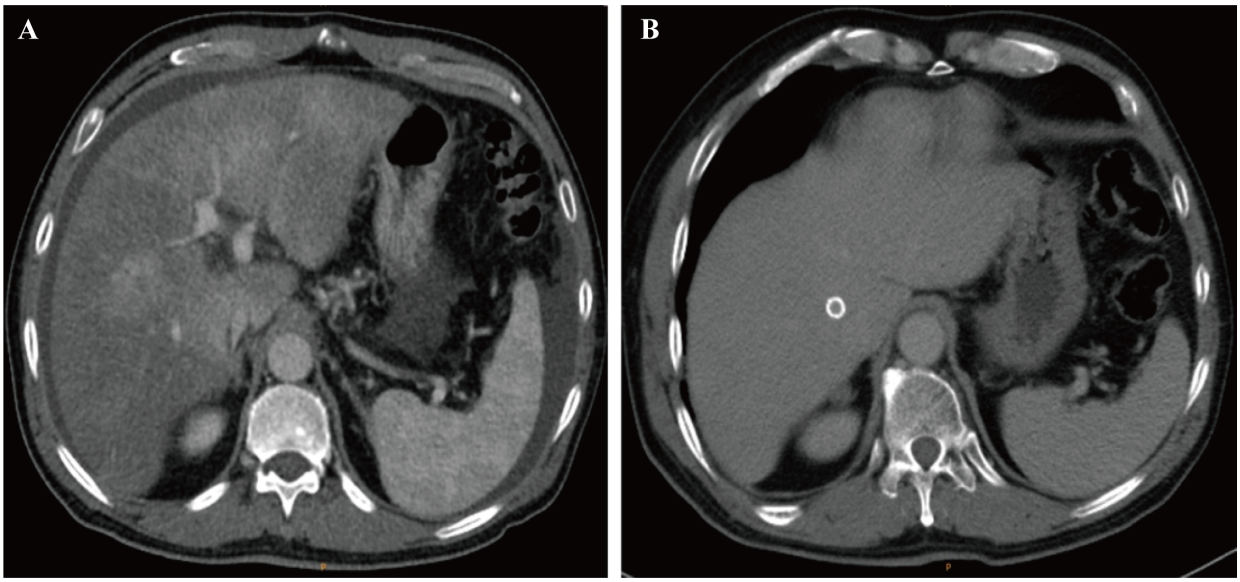

Fig. 3. Changes in computed tomography (CT) radiological manifestations of a pyrrolizidine alkaloid-related hepatic sinusoidal obstruction syndrome (PA-HSOS) patient. (A) Pre-procedural CT scan revealed ascites and a scattered hypodense area in the liver. (B) The patient's CT scan 6 months after the TIPS placement demonstrated a uniform liver density and no signs of ascites.

(21.23, 29.38) μmol/L, compared to the preoperative level of 33.40 (10.00, 88.70) μmol/L (p = 0.022), after an initial increase to 100.80 (22.25, 165.88) μmol/L at 1 week post-TIPS. Hemoglobin (Hb) decreased significantly from 139.5 ± 17.99 g/L preprocedurally to 119.20 ± 12.33 g/L at 1 year post-TIPS ($p < 0.001$). Similarly, white blood cell count (WBC) showed a significant reduction from 6.17 ± 1.79 (10^9/L) preprocedurally to 4.19 ± 0.64 (10^9/L) at 1 year post-TIPS ($p < 0.001$). ALT, AST, serum creatinine (Scr), and international normalized ratio (INR) all returned to the normal ranges.

Clinical Outcomes

All 30 patients survived during the follow-up period, with an overall survival rate of 100%. Clinical symptoms and signs were significantly improved in all patients after the TIPS procedures. Complete ascites remission was achieved in all 30 patients, with a median time to remission of 52 days (range: 29–161 days). In addition, all patients exhibited normal radiological manifestations during the follow-up period, with a median time of 196.5 days (165–229 days) (Fig. 3). No cases of hepatic encephalopathy were observed.

Prognostic Factors Analysis

Table 3 shows the correlation analysis between each factor and the recovery time of CT radiological manifestations of the liver. Both disease severity and ALBI grade were positively correlated with the time required for liver imaging to return to normal (r = 0.709, and 0.612, p = 0.010 and 0.034, respectively). Results from multiple linear regression analysis further identified severity and ALBI grade as independent prognostic factors for the recovery time of CT radiological manifestations of the liver (Table 4). Patients with ALBI grade 3 exhibited significantly longer recovery time compared to those with ALBI grade 2 (224.83 + 46.67 days *vs* 170.44 + 50.56 days, p = 0.006). Similarly, patients classified as severe or very severe had slower recovery time compared to those with mild or moderate disease (218.25 + 41.60 days *vs* 162.43 + 55.11 days, p = 0.004).

Discussion

Misuse of medicinal herbs containing pyrrolidine alkaloids is the primary cause of HSOS in China. PA-HSOS is often misdiagnosed due to its atypical manifestations [9,22]. Previously published research evaluating the therapeutic effects of TIPS in PA-HSOS enrolled patients primarily based on clinical manifestations and a history of PA-containing herbs use [22]. However, in our study, all enrolled patients had a confirmed history of using PA-containing herb consumption, elevated preoperative PPG (16 mmHg) measured by HVPG, and a definitive pathological diagnosis.

Peng *et al*. [23] demonstrated that anticoagulation combined with symptomatic treatment and supportive care was more effective than monotherapy in improving the prognosis of PA-HSOS patients. However, some patients did not respond to anticoagulation therapy and frequently exhibited severe symptoms of portal hypertension, resulting in a high mortality rate. Relevant studies have described that the mortality rate among PA-HSOS patients treated with anticoagulation-based comprehensive therapy is approximately 34–40% [23,24]. TIPS may serve as an alternative therapeutic option for patients who fail to respond to anticoagulation therapy, although its efficacy in PA-HSOS remains controversial.

Table 2. Changes of laboratory examinations of 30 HSOS patients.

Variable	Preprocedural	1 week after treatment	1 month after treatment	3 months after treatment	6 months after treatment	1 year after treatment	*t*/Z	*p**
Hb (g/L)	139.53 ± 17.99	122.01 ± 12.82	116.99 ± 16.82	117.00 ± 9.59	120.83 ± 14.65	119.20 ± 12.33	*t* = 5.356	<0.001
PLT (10^9/L)	94.50 (55.50, 114.00)	58.50 (20.00, 89.75)	105.00 (69.75, 169.75)	125.50 (86.00, 151.00)	151.00 (139.50, 170.50)	132.00 (122.00, 140.00)	Z = –3.364	0.001
WBC (10^9/L)	6.17 ± 1.79	6.24 ± 2.04	4.41 ± 0.92	3.92 ± 0.84	3.77 ± 1.03	4.19 ± 0.64	*t* = 5.420	<0.001
STB (μmol/L)	33.40 (10.00, 88.70)	100.80 (22.25, 165.88)	73.80 (23.88, 126.58)	32.70 (28.03, 39.15)	28.45 (24.88, 35.30)	24.90 (21.23, 29.38)	Z = –2.293	0.022
Alb (g/L)	30.61 ± 2.28	32.68 ± 5.57	37.41 ± 4.34	37.81 ± 5.82	41.99 ± 4.43	43.14 ± 2.53	*t* = –21.887	<0.001
ALT (U/L)	33.00 (15.50, 65.75)	27.00 ± 7.56	15.73 ± 4.34	19.87 ± 6.88	19.67 ± 8.87	18.17 ± 6.12	Z = –3.652	<0.001
AST (U/L)	50.00 (14.25, 57.50)	38.00 (24.75, 46.25)	29.00 (17.00, 39.75)	43.20 ± 16.86	32.00 ± 7.29	28 (27.5, 28.5)	Z = –2.850	0.004
Scr (μmol/L)	102.70 ± 35.71	71.47 ± 17.34	64.86 ± 12.53	66.82 ± 9.59	76.03 ± 6.16	70.89 ± 1.21	*t* = 4.829	<0.001
PT (s)	15.94 ± 2.49	15.98 ± 1.95	15.03 ± 2.31	16.54 ± 4.97	12.95 ± 3.26	15.30 ± 6.19	*t* = 0.483	0.633
INR	1.43 ± 0.22	1.44 ± 0.18	1.32 ± 0.18	1.49 ± 0.44	1.18 ± 0.30	1.22 ± 0.34	*t* = 2.682	0.012

Hb, Hemoglobin; WBC, white blood cell count; PLT, platelets; Alb, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; STB, serum total bilirubin; Scr, serum creatinine; PT, prothrombin time; INR, international normalized ratio.

*p**: Preoperative *vs* 1 year after treatment.

Table 3. Correlation of variables with the recovery time of radiological manifestation.

	The recovery time of radiological manifestation (days)	
Parameters	r	*p*
Age	0.115	0.721
Severity*	0.709	0.010
Child-Pugh grade**	0.169	0.600
ALBI	0.612	0.034
Hb (g/L)	–0.130	0.688
PLT (10^9/L)	–0.112	0.729
WBC (10^9/L)	–0.245	0.443
STB (μmol/L)	–0.168	0.602
Alb (g/L)	0.260	0.415
ALT (U/L)	–0.175	0.586
AST (U/L)	–0.350	0.265
Scr (μmol/L)	–0.133	0.681
PT (s)	–0.182	0.570
INR	–0.102	0.753
PPG (mmHg)	0.011	0.974

* Severe and very severe *vs* mild and moderate patients; ** Child-Pugh C *vs* Child-Pugh A and B.

Table 4. Multiple linear regression analysis of factors influencing the recovery time of CT radiological manifestations of liver.

Dependent variable	Independent variable	B	SE	Standardized coefficients	*t*	*p*	95% CI
The recovery time of radiological manifestations	ALBI grade	32.486	13.461	0.493	2.413	0.039	2.035–62.938
	Severity	21.610	8.689	0.508	2.487	0.035	1.954–41.267

F = 8.987, $p = 0.007$, $R^2 = 0.666$.

A previous study revealed that the cure rate of anticoagulation therapy alone was comparable to that of anticoagulation therapy combined with TIPS, with the mortality rate in the combination group being 35.7%, and no statistically significant difference between the two groups [24]. Nevertheless, some studies have reported that TIPS is safe and effective for treating PA-HSOS patients who have failed anticoagulation therapy, with survival rates from 64% to 95% [11,24–26].

In the present study, TIPS was performed in PA-HSOS patients who had failed anticoagulation therapy, and all patients survived throughout the follow-up period. In contrast, previous studies on HSCT-related HSOS have reported mortality rates ranging from 9% to 30% [27,28]. This higher mortality is likely attributable to the fact that most HSCT-related HSOS patients have severe hematological diseases and poor underlying conditions, which predispose them to multiorgan failure and may reduce the efficacy of TIPS, increasing the risk of hepatic encephalopathy and liver failure after TIPS. In contrast, PA-HSOS patients in China do not have other fatal comorbidities. Furthermore, the most prominent clinical manifestations in these patients, such as refractory ascites, are closely associated with significantly elevated portal pressure. The mechanisms by which TIPS benefits PA-HSOS may involve a substantial reduction in portal pressure, leading to a compensatory increase in hepatic arterial perfusion and thereby relieving hepatocyte hypoxia [11,13]. In the present study, a significant reduction in PPG was observed (from 22.65 ± 6.36 mmHg to 9.40 ± 3.38 mmHg, $p < 0.001$), which may help slow disease progression.

Transaminase levels increased within 3 days after procedures in our study, and serum total bilirubin (STB) levels were near or above baseline 1 month after surgery. This finding could be explained by transient liver damage caused by TIPS. Although portal blood flow decreases rapidly after treatment, hepatic recovery and arterial compensation require time. Over the 6-month and 1-year follow-up, total bilirubin levels gradually decreased, and transaminase levels returned to normal. Additionally, we found that the patients' ascites disappeared progressively over time during follow-up, and CT radiological manifestations demonstrated a gradual return to normal, indicating disease remission.

Johnson *et al*. [20] identified a novel ALBI grade tool for assessing liver function. In patients with PA-HSOS, refractory ascites was the prominent manifestation, which may compromise the accuracy of the Child-Pugh scoring system. In contrast, ALBI does not include subjective evaluation factors. Therefore, in PA-HSOS patients, the ALBI score may provide a more reliable assessment of liver function. Both ALBI grade and its severity reflect the extent of liver injury resulting from sinusoidal obstruction. In cases of severe liver damage, even if TIPS effectively relieves hepatic congestion, pre-existing sinusoidal injury may result in prolonged recovery time or even irreversible damage, potentially leading to poor outcomes. The present study demonstrated that the ALBI classification was closely associated with the time required for normal radiological manifestations of the liver. In multiple linear regression analysis, ALBI grade was a significant factor influencing the recovery time of CT radiological manifestations of the liver ($\beta = 0.493$, $p = 0.039$). Patients with ALBI grade 2 experienced a significantly shorter time to normal radiological manifestations of the liver compared to those with ALBI grade 3 ($p = 0.006$).

Xiao *et al*. [26] demonstrated that bilirubin was an independent and influential factor in the diagnosis of PA-HSOS. However, in the present study, no association was found between preoperative bilirubin levels and time to disease recovery, likely due to the small sample size. Studies with larger sample sizes are required to further investigate prognostic factors for survival in PA-HSOS patients.

The optimal timing of TIPS intervention for PA-HSOS remains a contentious issue. The present study recommends the use of HVPG to assess portal hypertension in patients who have failed anticoagulation therapy. TIPS may be most beneficial in patients with higher disease severity and ALBI grade. Our findings indicated that patients classified as severe or very severe patients had a longer recovery time for normal radiological manifestation of the liver compared to those with mild or moderate patients (218.25 ± 41.60 *vs* 162.43 ± 55.11 days, $p = 0.004$). Therefore, the timing of TIPS intervention should be individualized, considering both disease severity and ALBI grade.

This study has several limitations. First, it was a retrospective study with a small sample size, limiting the generalizability of the results. A large-scale prospective study is required to validate these findings. Second, the follow-up period was relatively short, which may be insufficient to assess long-term survival outcomes and thus requires further research. Third, the absence of a control group prevents direct comparison of treatment efficacy between patients receiving TIPS and those managed with non-TIPS

approaches. Additionally, although multivariate analyses were performed, the potential influence of unmeasured or uncontrolled confounding factors cannot be entirely excluded.

Conclusions

TIPS is a safe and effective treatment for patients with PA-HSOS who have not responded to anticoagulation therapy. The severity of disease and the ALBI grade appear to be important factors in estimating the recovery time of liver radiological manifestations on CT in patients with PA-HSOS.

Availability of Data and Materials

The data analyzed are available from the corresponding author upon reasonable request.

Author Contributions

JD, JH and XH contributed to the study conception and design. Material preparation and data collection were performed by YD, JL, JW and GL. Data analysis and interpretation were performed by JD and XY. The first draft of the manuscript was written by JD. All authors have been involved in revising it critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was approved by Jinhua Municipal Central Hospital (Approval No. 2025-65) and conducted in accordance with the Declaration of Helsinki. As this was a retrospective observational study, the requirement for informed consent was waived.

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Conflict of Interest

The authors declare no conflict of interest.

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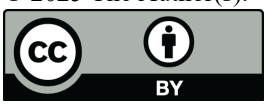
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