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Accessory hepatic vein recanalization for treatment of Budd-Chiari syndrome due to long-segment obstruction of the hepatic vein: initial clinical experience

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PURPOSE
We aimed to investigate the feasibility and effectiveness of accessory hepatic vein recanalization (balloon dilatation/stent insertion) for patients with Budd-Chiari syndrome (BCS) due to long-segment obstruction of the hepatic vein.

METHODS
From March 2010 to December 2013, 20 consecutive patients with BCS, due to long-segment obstruction of three hepatic veins, treated with accessory hepatic vein recanalization (11 males, 9 females; mean age, 33.4±10.9 years; range, 22–56 years) were included in this retrospective study. Data on technical success, clinical success, and follow-up were collected and analyzed.

RESULTS
Technical and clinical success was achieved in all patients. Each patient was managed with a single accessory hepatic vein recanalization procedure. No procedure-related complications occurred. The diameter of the accessory hepatic vein was 8.45±1.47 mm (6–11 mm) at the stem, and there were many collateral circulations between the hepatic vein and the accessory hepatic vein. The mean pressure of accessory hepatic vein decreased from 47.50±5.59 cm H_2O before treatment to 28.80±3.47 cm H_2O after treatment ($P < 0.001$). Abnormal levels of total bilirubin, albumin, aspartate aminotransferase, and alanine transaminase improved after the treatment. During the follow-up, three patients experienced restenosis or stenting of the accessory hepatic vein.

CONCLUSIONS
In BCS due to long-segment obstruction of the hepatic veins, it is important to confirm whether there is a compensatory accessory hepatic vein. For patients with a compensatory but obstructed accessory hepatic vein, recanalization is a simple, safe, and effective treatment option.

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Budd-Chiari syndrome (BCS) is a rare disease characterized by hepatic venous outflow obstruction at the level of the hepatic vein (HV) or inferior vena cava (IVC) resulting in portal hypertension (1, 2). Thrombus is the most frequent cause in Western countries, whereas membranous webs are more common in Asia (2). HV recanalization has been reported as a simple, effective, and safe method for patients with BCS due to hepatic venous obstruction (1, 2). However, if the patients display long-segment obstruction of the HV, recanalization is always difficult with a high failure rate of 31%–100% (1, 2). Even when successfully managed, there is a risk of HV reobstruction after treatment (2).

Various treatments, including transjugular intrahepatic portosystemic shunt (TIPS), surgical shunts, and liver transplantation have been described as potential treatment options for BCS (3–6). However, there are only a few studies on accessory hepatic vein (AHV) recanalization for treatment of BCS. In this study, we present our initial clinical results of AHV recanalization in 20 patients with BCS due to long-segment obstruction of HV.

Methods

Study design and patients selection

Our Institutional Review Board approved this study. Before treatment, all patients received detailed information about AHV recanalization and provided written informed consent for the procedure. From March 2010 to December 2013, consecutive patients with BCS due to long-segment obstruction of three HVs treated by AHV recanalization (balloon dilatation/stent insertion) were included in this retrospective study. The inclusion criteria were as follows: a definite diagnosis of BCS due to long-segment obstruction of three HVs; presence of a compensatory but obstructed AHV; and short-segment or membranous obstruction of the AHV. The exclusion criteria were as follows: hepatic venous outflow obstructed by malignancy, dysfunction of blood coagulation, active bleeding, active infection, significant cardiac or pulmonary disease, or significant psychological or psychosocial dysfunction.

Diagnosis and definitions

Diagnosis of BCS was established by reviewing the patients' history as well as the results of abdominal Doppler ultrasonography (US) and magnetic resonance angiography (MRA) (Fig. 1). Computed tomography angiography (CTA) was performed in patients with metallic implants.

Long-segment obstruction was defined as an obstruction length ≥3 cm, short-segment obstruction was defined as an obstruction length >1 cm and <3 cm, and membranous obstruction was defined as an obstruction length ≤1 cm (1).

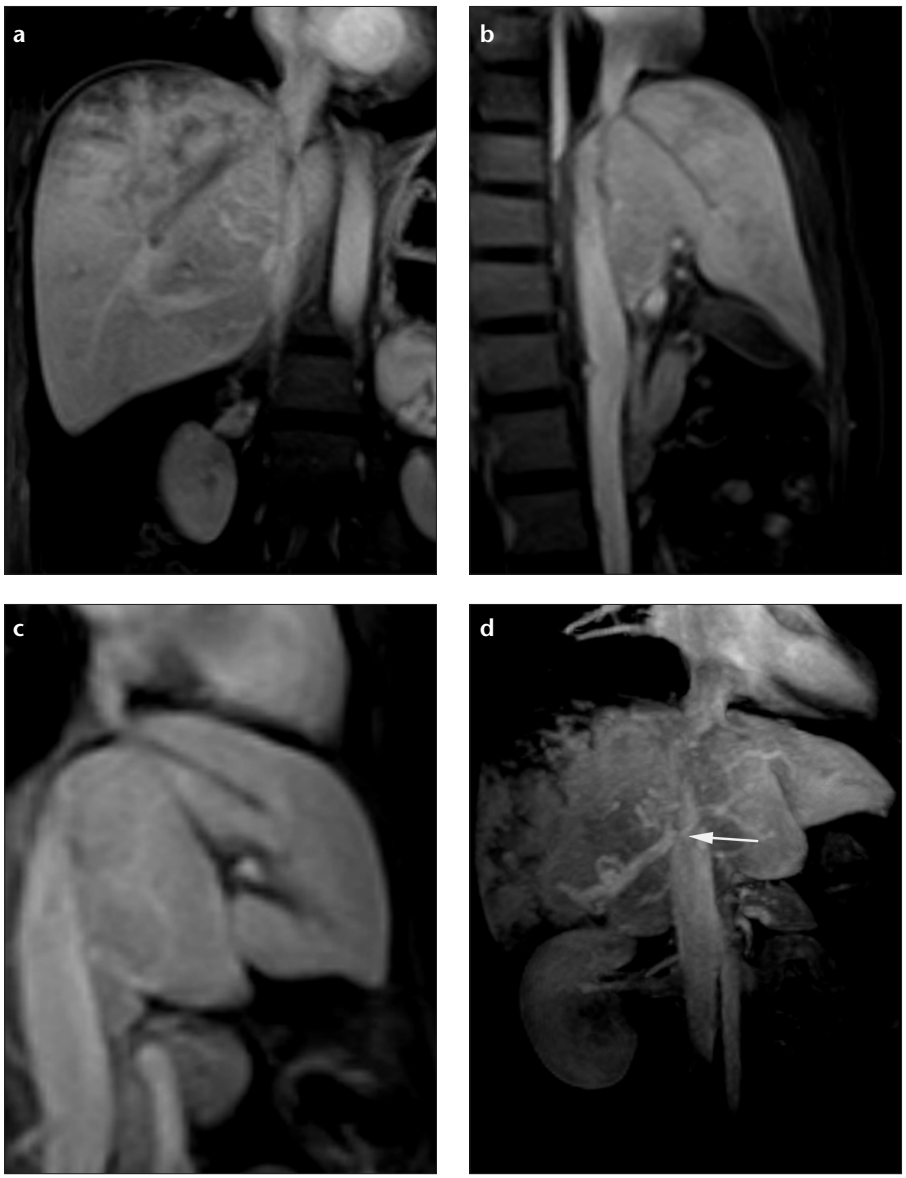

Figure 1. a–d. A 24-year-old female with Budd-Chiari syndrome due to long-segment obstruction of three hepatic veins. Magnetic resonance angiography images show obstruction of right **(a)**, middle **(b)**, and left **(c)** hepatic veins. The accessory hepatic vein displays ostial membranous obstruction (**d,** *arrow*).

Assessment of AHV

The AHV was detected using both US and MRA/CTA, and the angle between the ostium of AHV and the distal side of IVC was evaluated before treatment. The diameter of the AHV was measured at the stem, from the results of AHV venography performed after recanalization.

Treatment procedure

All patients enrolled in this study underwent AHV recanalization for two reasons: first, AHV recanalization was simpler because the obstruction of the AHV was shorter than those of the three HVs. Second, compared with TIPS placement, AHV recanalization was performed in reference to the patient's physiological anatomy, and there was no portacaval shunt placement after treatment.

Blood pressure, heart rate, arterial oxygen saturation, and respiratory rate were monitored throughout the treatment. Patients were placed in the supine position. All procedures were performed by three interventional radiologists under fluoroscopic guidance and local anesthesia with 5 mL of 2% lidocaine (Hualu Pharmacy, Shipping, China) administered at the right femoral or right jugular puncture site. Treatment approach depended on the angle between the ostium of AHV and the distal side of IVC: right femoral vein puncture was performed if the angle was obtuse or right; otherwise, jugular puncture was performed.

A 0.035-inch guidewire (Terumo Corp) and a 4 F angled tip angiographic catheter (Cordis) were used to detect the obstruction of the AHV. If the guidewire could be inserted directly into the AHV, then the catheter was sent into the AHV via the guidewire. If the guidewire could not pass the obstruction of the AHV, a Brockenbrough needle (J-type needle, Cook Medical) was used to break through the obstruction, after which the guidewire and 4 F angled tip catheter were inserted into the AHV. Finally, AHV recanalization was performed using a balloon catheter of 10–15 mm in diameter (Venous balloon, Cook Medical) or a stent of 10–12 mm (Venous stent, Bard Medical).

The balloon was dilated twice, and each procedure lasted approximately 40 s. The pressure of the balloon dilatation was 5–6 atm. Stent insertion was required if more than 30% residual stenosis was present after balloon dilatation (7). Balloon and stent dimensions were chosen individually. Pressure of the AHV was measured using a piezometric tube before and after recanalization (Fig. 2).

All patients were prescribed oral warfarin (Xinyi Pharmaceutical Co.) for anticoagulation from the second day following treatment for 24 months, and the dose of warfarin was adjusted to maintain an international normalized ratio of 2–3.

Clinical assessment

Clinical examination and liver function tests were performed seven days after the recanalization treatment to evaluate its effectiveness. Technical success was defined as elimination of AHV obstruction as determined by venography, along with a decrease in AHV pressure. Clinical success was defined as stabilization or improvement of patient's symptoms and liver function test results within seven days of technically successful AHV recanalization (8).

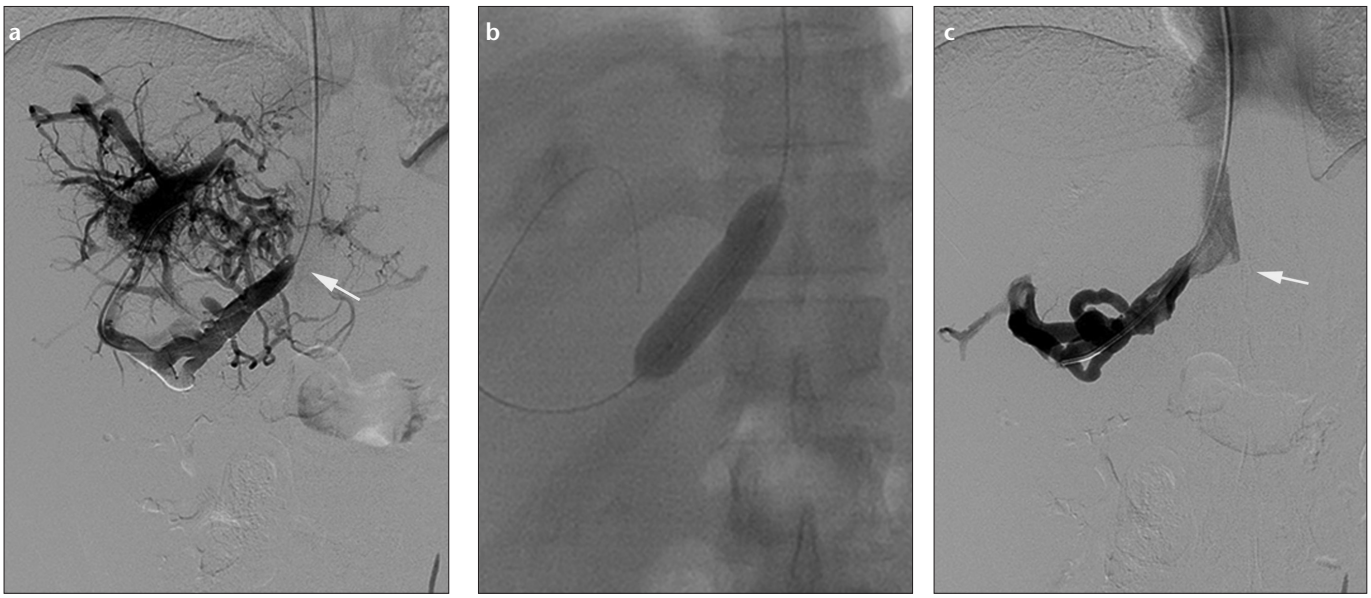

Figure 2. a–c. The procedure of accessory hepatic vein (AHV) recanalization. Venography **(a)** reveals the ostial membranous obstruction of the AHV *(arrow)*. The AHV and the obstructed right HV are connected by collateral circulations. The ostial obstruction of the AHV is treated by balloon dilatation **(b)**. The AHV is widely patent after treatment (**c,** *arrow*).

Table 1. Patient characteristics

	n=20
Age (years), mean±SD (range)	33.40±10.86 (22–56)
Male/female	11/9 (55/45)
Duration of portal hypertension (months), mean±SD (range)	5.10±1.89 (1–7)
Risk factors	
JAK2 mutation	0 (0)
Protein C deficiency	0 (0)
Protein S deficiency	0 (0)
Factor V Leiden mutation	0 (0)
Liver function before treatment	
Child Pugh A	11 (55)
Child Pugh B	7 (35)
Child Pugh C	2 (10)

Unless otherwise noted, data are presented as n (%).
SD, standard deviation.

All patients were followed by abdominal Doppler US at seven days, and every 1–2 months to confirm the long-term patency of the AHV (Fig. 3). Each patient's condition was ascertained by contacting the patient or his/her family every month after treatment.

Statistical analysis

Continuous variables were summarized using mean±standard deviation (SD) or median. The paired samples t test or Wilcoxon test (SPSS version 16.0, SPSS Inc.) was performed to compare variables before and after treatment. A *P* value of less than 0.05 was considered statistically significant.

Results

A total of 88 patients with BCS due to obstruction of three HVs, with (n=37) or without (n=51) IVC obstruction were admitted to our hospital. We first excluded 35 patients, because they had both IVC and three HVs obstruction with a dilated and patent AHV, and only underwent IVC recanalization. We further excluded 30 patients, because they had at least one HV presenting with short-segment or ostial membranous obstruction and underwent recanalization of HV (n=28) or IVC and HV (n=2). Finally, three patients were excluded, because the AHV could not be detected, and they underwent TIPS placement. Thus, data from a total of 20 patients who were treated with AHV recanalization were included in this study (Table 1).

Of these 20 patients, one patient had a previous IVC stent insertion. Risk factors for BCS, including JAK2 mutation, factor V Leiden mutation, protein C deficiency, and protein S deficiency, were not found in any of these patients. All 20 patients presented with secondary portal hypertension for 1–7 months (mean, 5.10±1.89 months). Dominant clinical presentations were abdominal distension, abdominal pain, ascites, hepatomegaly, and splenomegaly. Liver function was evaluated using the Child-Pugh classification. Eleven patients were classified as Child-Pugh A, seven patients as Child-Pugh B, and two patients as Child-Pugh C.

The presence of the AHV was detected by US (n=3), MRA/CTA (n=2), or both (n=15). The AHV exhibited ostial membranous obstruction in all patients. The angle between the ostium of AHV and the distal side of IVC was acute in 15 patients, and obtuse in five

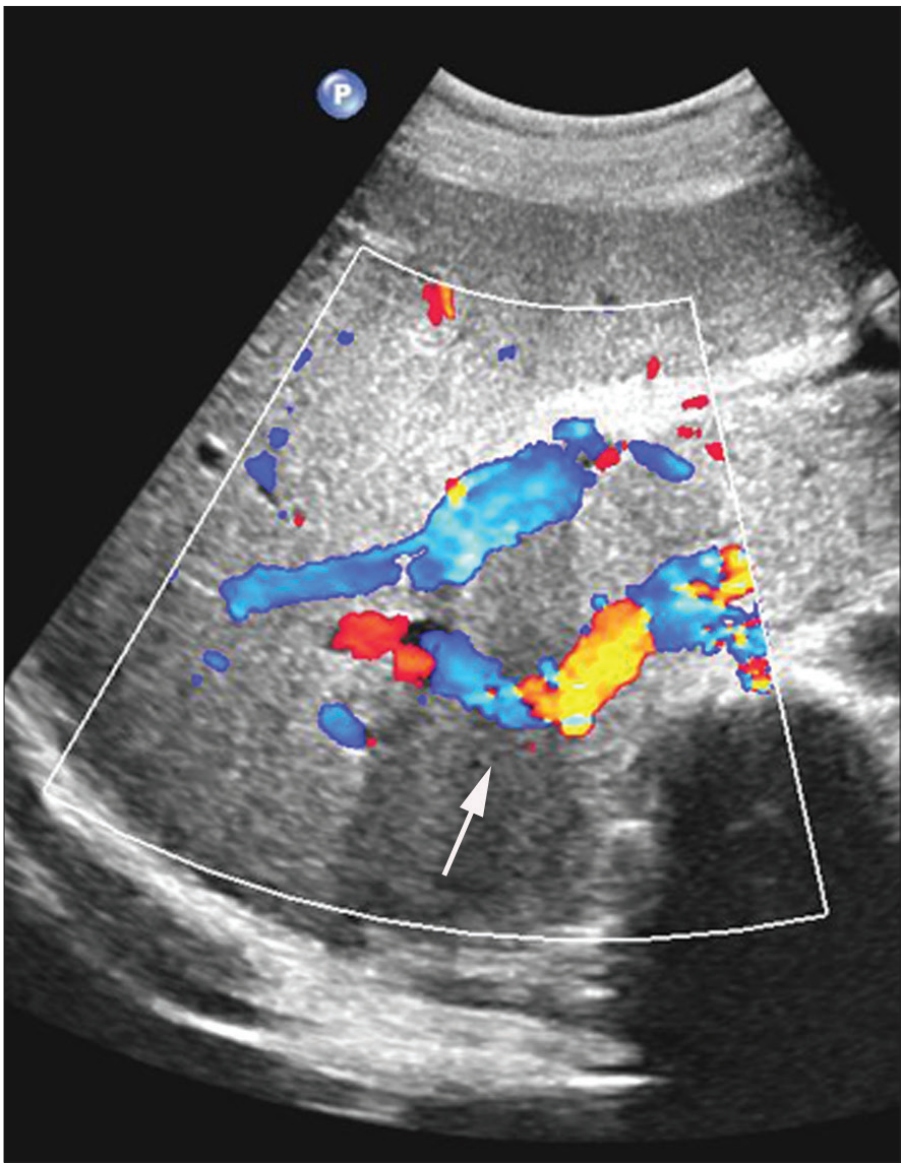

Figure 3. Ultrasonography confirms the patency of AHV *(arrow)* seven days after treatment.

Table 2. Baseline of accessory hepatic vein and the results of treatment

	n=20
Angle between the ostium of AHV and distal side of IVC	
Acute	15 (75)
Obtuse	5 (25)
Diameter at the stem of AHV (mm)	8.45±1.47 (6–11)
AHV recanalization	
Balloon dilatation	18 (90)
Stent insertion	2 (10)
AHV pressure (cm H_2O)	
Before, mean±SD (range)	47.50±5.59 (38–55)
After, mean±SD (range)	28.80±3.47 (22–36)

Unless otherwise noted, data are presented as n (%).
AHV, accessory hepatic vein; IVC, inferior vena cava; SD, standard deviation.

patients. The diameter of the AHV was 6–11 mm (mean, 8.45±1.47 mm) at the stem, and there were many collateral circulations between the obstructed HV and the AHV.

Technical success was achieved in all patients. A total of 20 AHVs were managed in 20 patients. Eighteen patients underwent AHV balloon dilation, and two patients underwent AHV stent insertion. No procedure-related complication occurred in any of these patients. The average pressure of the AHV decreased from 47.50±5.59 cm H_2O before treatment to 28.80±3.47 cm H_2O (1 cm H_2O=0.098 kPa) after treatment (paired t test, $P < 0.001$). Clinical success was observed in all patients (Table 2), with the symptoms beginning to improve on the next day following the treatment. According to liver function tests performed seven days after treatment, 14 patients were classified as Child-Pugh A, five patients as Child-Pugh B, and one patient as Child-Pugh C.

Serum total bilirubin (normal range, 1.7–20 µmol/L) levels were abnormal in all patients before treatment; levels improved from 30.43±9.26 µmol/L before treatment to 25.04±8.67 µmol/L after treatment (paired t test, $P < 0.001$). Serum albumin (normal range, 35–55 g/L) levels were abnormal in seven patients before treatment; the median albumin level of these seven patients improved from 31 g/L (23.5–33.5 g/L) before treatment to 33.5 g/L (29.6–35.5 g/L) after treatment (Wilcoxon test, $P = 0.017$). Before treatment, two patients had abnormal aspartate aminotransferase (AST; normal range, 0–40 U/L) levels and two patients had abnormal alanine transaminase (ALT; normal range, 0–40 U/L) levels. All abnormal preoperative AST and ALT values decreased after treatment. Normal preoperative albumin, AST, and ALT values remained within their normal ranges after treatment.

Patients were followed up for 3–47 months (mean, 15.75±10.47 months). All patients were alive with improvement of their symptoms at the time of this report. The details of their improvements are shown in Table 3. Three patients experienced restenosis of the AHV (n=2) or AHV stent (n=1) 4–9 months (mean, 6.33±2.52 months) after treatment. These patients were suc-

cessfully treated with repeat AHV balloon dilation. There was no evidence of AHV reobstruction in the remaining 17 patients at the time of this report.

Table 3. Improvement in patients' clinical presentations

	Before	After	
	n	Disappearance n	Relief n
Abdominal distension	20	18	2
Abdominal pain	18	18	0
Ascites	20	16	4
Hepatomegaly	16	12	4
Splenomegaly	13	8	5

Discussion

This study evaluated the feasibility and effectiveness of AHV recanalization in the management of patients with BCS due to long-segment obstruction of three HVs, presenting with intrahepatic collateral circulations and a compensatory AHV. The initial results were positive, demonstrating technical and clinical success in all patients. During the follow-up, the patency of the AHV or AHV stent was confirmed in 17 of 20 patients (85%).

Recanalization of the HV has been increasingly used in the treatment of BCS in recent years, with the purpose of relieving hepatic congestion and resolving the symptoms of BCS (1, 2, 8, 9). A retrospective study of HV recanalization in 101 BCS patients demonstrated that clinical improvement was achieved in all patients (92/92) who successfully underwent the procedure (2). However, the study also demonstrated that nine patients experienced technical failure due to long-segment obstruction or diffused stenosis of the HV (2). The difficulty and challenge of HV recanalization in patients with long-segment obstruction of the HV may be attributed to the following factors: first, it is extremely difficult to cut through the long-segment of obstruction (1, 2). Second, long-segment obstruction of the HV occasionally results in narrowing of the HV stem, which will impede its drainage function (2).

Currently, TIPS has been used as the first treatment choice for BCS due to long-segment obstruction of the HV, in most institutions (4, 10). Although TIPS can effectively decrease the portal vein pressure and significantly improve patient symptoms, hepatic encephalopathy occurs in 17%–35% of patients undergoing TIPS (10, 11). In addition, shunt dysfunction is another problem, occurring in up to 13%–50% of patients when metal stents are used for TIPS (5).

In addition to three main HVs (left, middle, and right HV), there are some small dispersive HVs that connect to the IVC and function as drainage vessels. These small veins are called AHV (12–14). For patients with BCS due to hepatic venous obstruction, vascular endothelial cells express cytokines and growth factors such as vascular endothelial cell growth factor and fibroblast growth factor that promote angiogenesis, resulting in the formation of intrahepatic collateral circulations (15). Blood flows from the obstructed HV to AHV through the intrahepatic collateral vessels, and the AHV dilates to compensate (16). However, some patients display the ostial obstruction because the ostium of the AHV is restricted by the IVC wall, and it does not dilate along with the dilatation of the AHV stem (16).

In this study, we used the AHV as the hepatic drainage vein instead of the HV. The high success rate (100%) of AHV recanalization was primarily attributable to the fact that patients only displayed ostial membranous obstruction of the AHV, and therefore, it was simple and safe to use a guidewire or Brockenbrough needle to pass over the obstruction and establish a pathway of AHV recanalization. The high clinical success rate (100%) of AHV recanalization may be attributable to the following factors: first, to be a significant hepatic drainage vein, the diameter of the HV/AHV must be at least 5 mm at the stem (12–14). The diameter of the AHV in our patients was 6–11 mm, ensuring a sufficient drainage volume. Second, well-developed collateral circulation between the HV and the AHV ensured smooth blood flow from the obstructed HV to IVC through the AHV (13). Additionally, the improvements in liver function seven days after treatment also indicated that AHV recanalization is an effective method in the management of BCS.

There are some limitations in this study: First, the present report was a retrospective case analysis, and the sample size was small. Second, it is not a comparative study. However, our purpose in this study was to provide an additional treatment option for patients with BCS due to long-segment obstruction of HV. Third, our proposed treatment cannot be performed if patients display long-segment obstruction of the HV without a compensatory AHV.

In conclusion, we suggest that it is important to confirm the presence of a compensatory AHV in patients with BCS presenting with long-segment obstruction of the HV. In patients with a compensatory but obstructed AHV, recanalization of the AHV is a simple, safe, and effective treatment option.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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