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# Interventional Treatment Strategy for Primary Budd–Chiari Syndrome with Both Inferior Vena Cava and Hepatic Vein Involvement: Patients from Two Centers in China

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## Abstract

*Objective* This retrospective study evaluated interventional treatments (recanalization, balloon dilation, and/or stent placement) for Budd–Chiari syndrome (BCS), caused by combined obstruction of the inferior vena cava (IVC) and hepatic veins (HVs).

*Methods* Before and after interventional therapy, patients with BCS ($n = 162$; asymptomatic $105.2 \pm 103.3$ mo; follow-up 15 [6–24] mo) underwent imaging studies (color Doppler ultrasound, CT, or MRI), and inferior vena cavography and manometry. Venous lesions were characterized by occlusion features, and presence of thrombosis and peripheral collateral vessels.

*Results* One, 2, and 3 main HV occlusions were observed, respectively, in 25 (15.4%), 61 (37.7%), and 76 (46.9%) patients. Eighty-three (51.2%), 98 (60.5%), and 104 (64.2%) patients had, respectively, large accessory HVs, venous collaterals formed between the HVs, or venous communicating branches between the HV and the peritoneal veins. The middle, left, and right HV was patent in 32 (19.8%), 35 (21.6%), and 44 (27.2%) patients. Recanalization of both hepatic and caval occlusions was successful in 96% (51/53) of those attempted; recanalization of IVC occlusion was successful in 97% (106/109). Among 157 patients successfully treated, 146 were cured and 11 showed clinical improvement. Clinical symptoms were relieved in 82.4% after the initial intervention, and 94.2% after the second intervention.

*Conclusion* Recanalization and balloon angioplasty was effective for the management of BCS with concurrent HV and IVC occlusions. The majority of patients required only IVC recanalization. The outcome of patients treated only by IVC intervention was similar to that of patients given combined HV and IVC intervention.

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**Keywords** Budd–Chiari syndrome · Interventional treatment · Hepatic veins · Survival rate

**Abbreviations**

| | |
|---|---|
| BCS | Budd–Chiari syndrome |
| CI | Confidence interval |
| HV | Hepatic vein |
| IVC | Inferior vena cava |
| MRI | Magnetic resonance imaging |

## Introduction

Budd–Chiari syndrome (BCS) is caused by an obstruction of hepatic vein (HV) outflow, which may occur anywhere from the small HVs to the suprahepatic inferior vena cava (IVC) [1, 2]. The obstructions in BCS may be classified as primary or secondary, depending on whether the source is inside the vein (membranous or thrombosis) or outside (compression or invasion by tumors or abscesses) [2]. In Western countries, the most common cause is thrombotic obstruction of the HVs. HV thrombosis may result from hypercoagulable states, such as occur in polycythemia vera, paroxysmal nocturnal hemoglobinuria, and sickle cell anemia, or secondary to the use of oral contraceptives. However, BCS is more prevalent in developing countries, such as China, India, Nepal, and South Africa, where the most common etiological factor is membranous obstruction, an underlying thrombotic disorder that has been characterized in only a few patients [3].

Hepatic outflow obstruction at the level of the main HVs, suprahepatic IVC, or both, is managed with endovascular techniques including balloon angioplasty and stent placement. In Western countries, the mainstay treatment of BCS is anticoagulation and transjugular intrahepatic portosystemic shunt [1, 2]. Most patients in China with BCS have both IVC and HV occlusions, based on venography and imaging studies by Doppler ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). The predominant cause is membranous obstruction, while relatively few have a predisposing thrombophilic factor [3, 4]. Due to these distinctive features, most patients with BCS in China undergo percutaneous recanalization and anticoagulation therapy, with excellent long-term patency and survival [3–5].

Several case reports and series from China have evaluated the short- and long-term outcomes of percutaneous recanalization for patients with BCS [6–10]. Most have focused on endovascular intervention for management of IVC obstruction. However, there is relatively less knowledge regarding interventional treatment for occlusion or thrombosis of both the IVC and HVs, which is the most typical scenario in China.

The present retrospective study in two interventional centers in China reviewed the strategy, successful treatment, technical success, and efficacy of interventional treatments for occlusion of the IVC and HVs in patients with primary BCS.

## Methods

The Ethics Committee of Anhui Provincial Hospital and Affiliated Hospital of Xuzhou Medical University approved this retrospective cohort study. All patients received detailed information about the endovascular procedures. The patients provided written informed consent before treatment.

### Patients

A series of 227 patients (with first-time diagnosis of primary BCS) were treated from June 2014 to March 2016 at Anhui Provincial Hospital and Affiliated Hospital of Xuzhou Medical University. All the enrolled patients underwent interventional treatment as inpatients. Obstruction of hepatic venous outflow was confirmed by Doppler ultrasound imaging, CT, MRI, and venography. If the diagnosis could not be confirmed by ultrasonography, CT or MRI then confirmed diagnosis by venography.

Based on the imaging results, there were 45 patients with isolated HV obstructive lesions, 8 patients with isolated IVC obstructive lesions, and 12 patients were lost to follow-up. Therefore, there were 162 eligible patients (94 men and 68 women), with a median age of 46 years (range, 18–78 years). The median follow-up was 15 months (range, 6–24 months).

### Evaluation

All the 162 patients in this case series were examined using Doppler ultrasound and venography (Innova 3100, GE Medical Systems, USA). The patients underwent Doppler ultrasonography before admission to assess the location, extent, morphology, collateral vessel formation, blood flow direction of HVs, and IVC lesions.

In addition, 141 underwent MRI (3.0 T whole-body MR hybrid system, Signa, GE Medical Systems, USA), and the remaining 21 were given CT examination (Discovery HD750, GE Medical Systems, USA). CT and MRI were conducted for evaluation of vascular lesions after admission.

A 3-stage enhanced CT scanning technique was performed. Arterial-phase imaging was performed with bolus

tracking. The data acquisition was initiated 10 s after reaching 80 HU in the region of interest, which was positioned in the aorta at the level of the celiac artery. The portal and HV phase acquisition times were 30 and 60 s, respectively, after the arterial phase. If the IVC and HV were unclear, CT scan was performed to collect images delayed 30 s again. MR scans were performed using conventional T1WI, T2WI, and fast imaging employing steady-state acquisition (FIESTA) sequences. Enhanced MR was applied via axial, coronal, and sagittal scans and original image reconstruction to evaluate the HV and IVC vascular lesions.

All the patients were examined with IVC angiography through the femoral vein during interventional therapy to assess the extent of the IVC and HV lesions and collateral vessel formation. After the IVC angiography, a catheter was inserted into each HV via the internal jugular vein or femoral vein. The venous angiography was performed to evaluate the lesion range and collateral vessel formation. The HV free and wedge pressures were measured. For patients with complete HV occlusion, puncture of the HV was percutaneous or retrograde via the IVC, and venography was performed to evaluate the hepatic venous lesions and collateral vessel formation.

### Strategy for Selecting Target Veins for Treatment

In our experience, when the hepatic segment of the IVC was occluded, caval–caval collateral pathways develop through accessory (inferior) hepatic-right or middle hepatic venous connections. In HV occlusion, hepatic venous outflow usually develops through dilated accessory (caudate) HVs, accounting for an enlarged caudate lobe in BCS.

In this study, for patients with at least one main HV, or with more than 2 accessory HVs, IVC recanalization was performed. Most of the IVC obstructions were located in the suprahepatic segment, but some patients had both suprahepatic and hepatic IVC obstructions. Patients who simultaneously had occlusions of 3 main HVs (i.e., no open HV could be observed) and fewer than 2 large ($\geq$ 10 mm diameter) accessory HVs were subjected to recanalization of both the IVC and HV (IVC + HV). In most cases, only one main HV was recanalized. Recanalization of more than one HV was only performed if technically straightforward. Main HVs with a larger drainage scope (i.e., responsible for blood circulation of a large area of the liver), and caudally directed between the HVs and the IVC, were considered more suitable for recanalization.

A 5F VER catheter (100-cm, Cordis, Miami, USA) was introduced into the distal end of small HV branches to measure the wedged HV pressure. A second HV was targeted if no improvement in flow or pressure was recorded after recanalization. Recanalization for more than one HV was also considered if the portal hypertension could not be relieved by recanalization of a single main HV then recanalization of accessory HVs was performed when recanalization of the main HVs was technically not possible.

### IVC Recanalization

All procedures were performed by 2 interventional radiologists with at least 5 years of experience. Under local anesthesia, 6 Fr introducer sheaths (Cordis, Miami, FL, USA) were inserted into the right femoral vein and right jugular vein. The extent of IVC occlusion was identified through inferior vena venography, with injections of contrast medium above and below the occlusion. A guidewire in combination with a 5F VER catheter was then used to access the IVC obstructive lesions. If this was achieved, IVC recanalization was performed via the transfemoral approach. Otherwise, a Rosch-Uchida Transjugular Liver Access Set (Cook Med, IN, USA) was used to puncture and traverse the obstruction from the jugular side.

### HV Recanalization

The location, extent, and type of obstruction (e.g., ostial stenosis, membranous occlusion, and long segment obliterans), and the angle between the HVs and the IVC, were identified based on the imaging studies and venography. Then, the HVs were explored via the jugular vein, femoral vein, or both. For patients with HV ostial stenotic lesions, a 5F VER catheter and guidewires were used to detect the openings of the HVs.

In patients with HV occlusion, the trunk or branches of the HVs were punctured using a direct trans-caval puncture (Rösch-Uchida Transjugular Liver Access Set) via the IVC. In these cases, recanalization via the IVC was similar to that of puncture of the portal vein through the IVC in transjugular intrahepatic portosystemic shunt (TIPS). A preoperative imaging examination was performed to determine the relative position between the occluded HV and the IVC, and then, the HV was punctured through the IVC under the guidance of digital subtraction angiography.

For patients with failed recanalization from the jugular vein or femoral vein, HVs were punctured using a percutaneous transhepatic approach under ultrasound guidance (Neff Percutaneous Access Set, ANPAS-100-RH-NT, Cook Medical, US). After successful percutaneous puncture of one of the HV branches, the guidewire was passed through the obstructed segment and then drawn out from the internal jugular or femoral vein. HV recanalization was then performed in the opposite direction through the IVC using an internal jugular or femoral vein approach.

When the target HV or IVC lesions were crossed, venography was performed to assess the venous lesion and the pressures were recorded. Venous pressure was measured and digitally displayed with a multifunction monitor (Datex Instrumentarium, USA) connected to a pressure transducer (Edward Life sciences, USA). After completion of the assessment, the HV stenosis or occlusion was dilated with a balloon catheter, after which the patency of the vessels was evaluated by repeated venography and venous pressure measurement. Recanalization was considered successful when the target vein showed residual stenosis of $< 25\%$, and the pressure difference across the lesions was $< 3$ mmHg; otherwise, stent implantation was performed.

### IVC and HV Stenting

First, the occluded IVC was cleared and a self-expanding Z type stent (diameter 28–30 mm; length 70 mm; Yongtong, Shenyang, China) was implanted. Pressure and venography data were collected from the HVs and IVC. A self-expanding bare vascular stent (diameter 10–14 mm, length 40–60 mm, Bard, Germany) was implanted (deployed through the mesh of the IVC stents) if venous drainage of HVs was blocked.

### Thrombolysis and Anticoagulation

If occlusion of the HVs/IVC was associated with thrombosis, then a 5F Muti-Sideport Catheter Infusion Set (MCIS-5.0-35-130-20.0, Cook Medical, US) was inserted for local thrombolysis (urokinase: 4–6 ×/days, 100,000 U in 100 mL saline, each time).

Radiography was performed every 3 days, and the catheter was adjusted accordingly (to make sure the catheter's lateral orifice was within the thrombus). Recanalization of the HVs/IVC was performed when the thrombosis was completely dissolved, or when no thrombosis progression was observed after 6 days (upon 2 consecutive radiography reviews, venography for HVs and IVC).

Anticoagulant therapy was given by subcutaneous injection of 5000 U of molecular heparin during the thrombolytic treatment, and within 3–5 days after the interventional therapy. Warfarin (5 mg/days, orally) was administered from the second day to maintain an international normalized ratio of 2-to-3.

The international normalized ratio was monitored every week until stable and in the therapeutic range. Further monitoring was performed monthly. After recanalization of the HVs or IVC, the patients received warfarin (orally) for 6–12 months.

### Follow-Up and Data Collection

Patients were followed up or called on the telephone at weeks 1 to 4, and months 2, 3, 6, 9, 12, 15, and 18, or until death. Significant clinical events were recorded, including clinical deterioration, new radiographic liver findings, and new BCS-related interventions. Clinical deterioration was considered any new hospital admission, recurrence of massive ascites, venous dilatation over the trunk, leg edema, variceal bleeding, or hepatic encephalopathy. Radiographic liver findings of concern included hepatic neoplasm and IVC/HV re-obstruction.

Ascites volume was recorded as small, moderate, or large [11]. Small volume was defined as limited to the subdiaphragmatic regions or spaces between the liver, spleen, kidney, or rectum and bladder. A moderate volume of ascites was considered diffused within the middle and lower abdomen plus flanks, surrounding or between the intestine and solid organs. A large volume of ascites filled the entire abdominal cavity with floating or fixed intestine.

The last follow-up visit took place in May 2017. The median follow-up was 15 months (range, 6–24 months). One specific doctor was responsible for collecting the data of every participating patient, including socio-demographic features, risk factors, clinical manifestations, radiology findings, interventional treatments, and outcomes. Another doctor checked and assessed the data monthly.

### Statistical Analysis

Results are expressed as percentage for qualitative data, and mean ± standard deviation for quantitative data. If normality was confirmed by Kolmogorov–Smirnov test, the paired sample $t$ test was used for measuring the venous pressure before and after treatment. Otherwise, the Wilcoxon rank test was used for comparison. The difference in ascites volume [11] before and after treatment was analyzed using Pearson's chi-squared test ($\chi^2$). The survival rate of patients was calculated by the Kaplan–Meier method, and confidence interval (CI) was determined by exact probability computation and normal approximation. The survival rate between the 2 groups was compared using the log-rank $\chi^2$ test. $< 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS software for Windows version 16.0 (SPSS, Chicago, IL, USA).

**Table 1** Characteristics of venous lesion in 162 patients with primary Budd–Chiari syndrome with both IVC and HV involvement at diagnosis

| | | *n* | (%) |
|---|---|---|---|
| Total subjects, *n* | | 162 | 100 |
| Venous lesions, *n* | IVC +1 HV | 25 | 15.4 |
| | IVC +2 HVs | 61 | 37.7 |
| | IVC +3 HVs | 76 | 46.9 |
| Accessory HV ≥ 10 mm* | | 83 | 51.2 |
| Intrahepatic collateral circulation | | 98 | 60.5 |
| Collateral circulation in the body | | 104 | 64.2 |
| Site of thrombosis | IVC | 28 | 17.3 |
| | HV | 12 | 7.4 |
| | IVC + HV | 5 | 3.1 |
| IVC | Stenosis | 55 | 34.0 |
| | Occlusion | 107 | 66.0 |
| Right HV | Patency | 44 | 27.2 |
| | By collateral circulation drainage | 23 | 14.2 |
| | Stenosis | 18 | 11.1 |
| | Occlusion | 77 | 47.5 |
| Middle HV | Patency | 32 | 19.8 |
| | By collateral circulation drainage | 50 | 30.9 |
| | Stenosis | 11 | 6.8 |
| | Occlusion | 69 | 42.6 |
| Left HV | Patency | 35 | 21.6 |
| | By collateral circulation drainage | 49 | 30.2 |
| | Stenosis | 15 | 9.3 |
| | Occlusion | 63 | 38.9 |

*An accessory HV with an internal diameter > 1 cm

## Results

### Vascular Lesion Characteristics

The study population comprised of 162 patients with BCS with both IVC and HV obstruction. The duration of BCS in these patients was 105.2 ± 103.3 months. Among them, 25 (15.4%), 61 (37.7%), and 76 (46.9%) had obstruction of 1, 2, and 3 main HVs, respectively.

Among the 162 patients, 98 (60.5%) had venous collaterals formed between the HVs (Fig. 1A, arrow c). In 104 (64.2%) patients, an extrahepatic venous system of branched vessels, which had formed during the occlusion, communicated with the HV (Fig. 1A, arrows d); examples include vessels between the HV and the right atrium, abdominal wall vein, or diaphragm vein. In addition, 83 (51.2%) patients had large accessory HVs. An HV was considered patent if it appeared clear and the blood flowed smoothly. Therefore, among the 162 patients, the right, middle, and left HV were patent in 44 (27.2%), 32 (19.8%), and 35 (21.6%) patients, respectively and were presented in Table 1.

### Therapeutic Methods

There were 162 patients, among which 53 (32.7%) underwent treatment for occlusions of both HVs and the IVC (IVC + HV), and 109 (67.3%) received only IVC recanalization (IVC-only). Of the former 53, the recanalization of 51 (96.3%) was successful, and unsuccessful in 2 patients due to extensive occlusion of the HVs and IVC. The other 109 patients (109/162, 67.3%) received only IVC recanalization (Fig. 1). Of these, 106 patients were treated successfully, and the other 3 patients failed because of complete occlusion of the IVC. Thus, overall, 157/162 patients (96.9%) were treated successfully, and 5/162 patients, for whom recanalization therapy failed (2 and 3 in the IVC + HV and IVC-only groups, respectively) were treated with TIPS.

In the IVC + HV group, of the 51 patients treated successfully, the routes for recanalization of the HVs were via the jugular vein, femoral vein, and percutaneous transhepatic venous approach in 39 (76.5%), 8 (15.7%), and 4 (7.8%) patients, respectively. The recanalization of the target HV included 1 main HV-only in 28 (54.9%) patients; accessory HV-only in 6 (11.8%) patients; ≥ 2 main HVs-only in 11

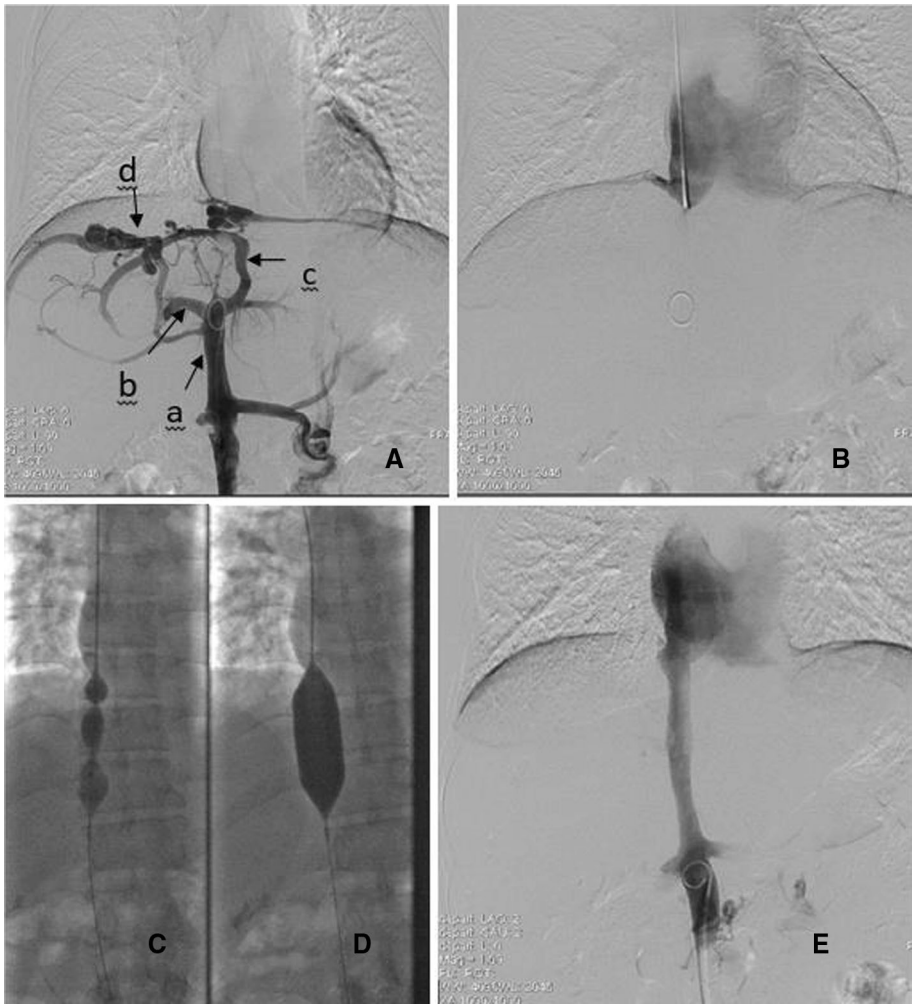


**Fig. 1** Angioplasty of occluded hepatic segment of the IVC in 46-year-old man with BCS. **A** Digital subtraction with the injection of contrast medium in the infrarenal IVC. In angiography of the IVC, the contrast agent flow countercurrent into the IVC and the HV collateral vessels, resulting in visualization of the traffic branch vessels. After recanalization of the occluded IVC, the IVC pressure lessens, and the flow in collateral blood vessels is smooth. When the IVC angiography was reviewed, no collateral vessels were seen. Occlusion of the hepatic segment of the IVC with collateral circulation can be seen from the infrahepatic IVC (arrow a) through the accessory HVs (arrows b and c) to the right HV (arrow d). **B** Contrast injection in the suprahepatic IVC from the right internal jugular vein revealed occlusion of the suprahepatic IVC. **C** After crossing the occluded IVC from the jugular access, an angioplasty balloon was positioned in the occluded portion of the IVC and the injected contrast medium showed the waist at the proximal and distal ends of the occlusion. **D** The balloon was fully inflated. **E** The IVC after balloon angioplasty showed a widely patent angioplasty site with brisk blood flow into the right atrium. Collateral veins were no longer filled. The cavoatrial pressure gradients before and after the angioplasty was 19 mmHg and 4 mmHg, respectively. The right main HV was occluded. The accessory HV pressure fell from 31 mmHg (pre-angioplasty) to 13 mmHg (post-angioplasty). Right HV recanalization was not conducted since the blood flow from the accessory to the right main HVs was reversed after angioplasty of the IVC. Portal hypertensive gastric disease symptoms (e.g., abdominal distention and poor appetite) were relieved post-angioplasty

(21.6%) patients, and 1 main HV plus accessory HVs in 6 (11.8%) patients. If recanalization of a single main HV failed to relieve portal hypertension (assessed by measuring wedged HV pressure), and the other main HVs were difficult to recanalize, an accessory HV was used. Regarding the methods for HV recanalization, 32 (62.7%), 14 (27.5%), 3 (5.9%), and 2 (3.9%) patients were treated with, respectively, balloon catheter, balloon catheter + thrombolytic therapy, balloon catheter + thrombolysis + stenting, and balloon catheter + stenting (Fig. 2).

Among the 157 patients successfully treated with recanalization of the IVC, 112 (71.3%) and 45 (28.7%) were approached through the jugular vein and femoral vein, respectively. In 113 (72%), 19 (12.1%), 14 (8.9%), and 11 (7%) patients, the methods of IVC recanalization were balloon catheter only, balloon catheter + thrombolysis + stenting, balloon catheter + thrombolytic therapy,

and balloon catheter + stenting. The average thrombolytic treatment duration was 5.1 days (range, 2.8–7.4 days) for patients with thrombolysis.

### Instant Recanalization Effect

Among the 157 patients successfully treated, before recanalization the pressures in the HV and IVC were 29.6 ± 6.7 mmHg and 20.7 ± 5.2 mmHg, respectively, and the postoperative pressures in these were 12.4 ± 4.2 mmHg and 11.0 ± 3.3 mmHg ($P < 0.01$, both). The HV and IVC pressures of patients in the IVC + HV and IVC-only groups were statistically analyzed, and in each group, the difference between the venous pressure before and after treatment was statistically significant ($P < 0.01$, both; Table 2). In the 157 patients successfully treated, the atrial pressures before and after the intervention were 6.0 ± 1.2 mmHg and 7.7 ± 1.9 mmHg ($P < 0.001$), respectively.

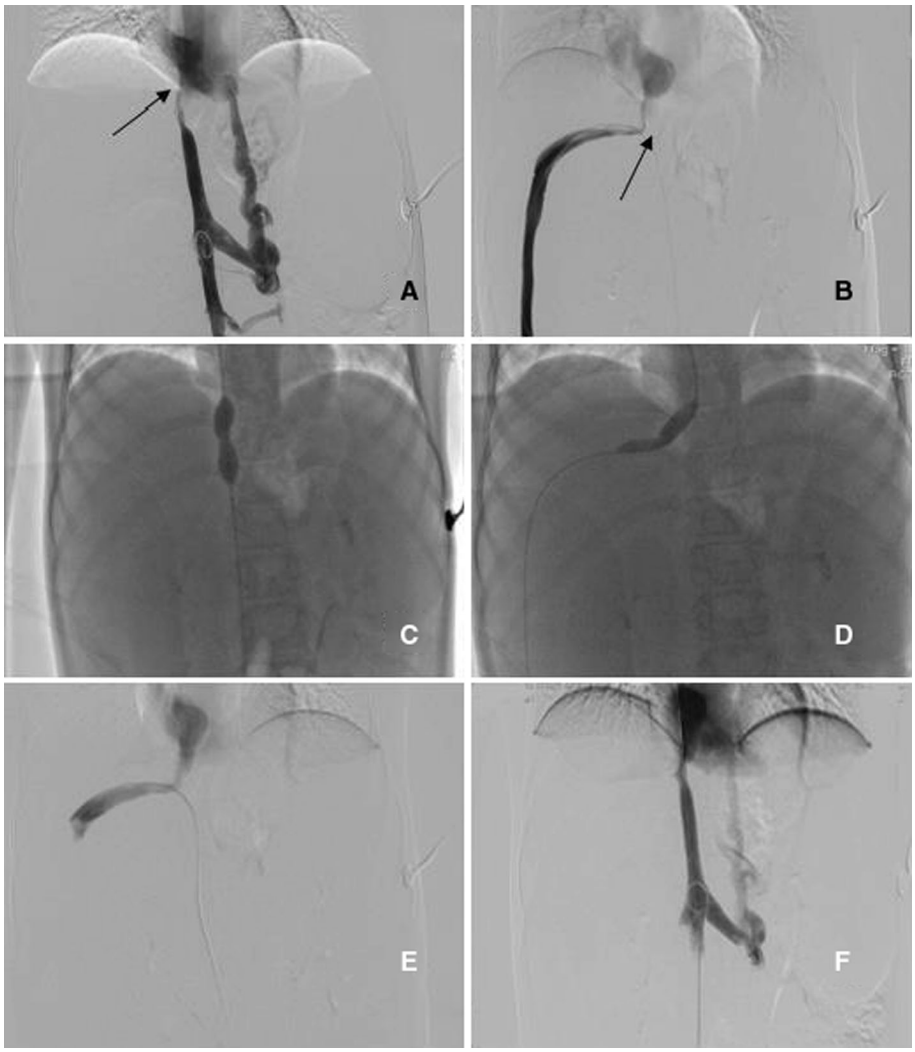


**Fig. 2** Kissing angioplasty of hepatic and caval stenosis in a 23-year-old woman with BCS. **A** Digital subtraction inferior vena cavogram revealed suprahepatic caval stenosis (arrow). The contrast medium entering the left renal vein drained through the dilated ascending lumbar vein to the azygos vein. The cavoatrial pressure gradient was 19 mmHg. **B** A 5F VER catheter (100 cm, Cordis, Miami, USA) was used to explore the obstructed HVs via the femoral vein. The corrected hepatic venous pressure is the difference between the portal venous and infrarenal IVC pressures. The corrected hepatic venous pressure of 8 mmHg represents a pressure gradient between the HV and IVC. The gradient between the HV and right atrium was 27 mmHg. **C–D** Kissing balloon angioplasty was performed of the HV (with 14 × 60 mm balloon) and the IVC (with 20 × 60 mm balloon). After balloon dilation the gradient between the HV and IVC was 3 mmHg. **E**, **F** Completion hepatic venogram and inferior vena cavogram show patent HV and IVC. The patient's interventional treatment HV and IVC pressure gradient was 3.3 mmHg, while the IVC-ventricular pressure gradient was 3.8 mmHg. The postoperative pressure gradient had returned to the normal range. Follow-up angiography after interventional therapy showed that a small amount of collateral vessels may be related to the opening of the collateral vessels (left renal vein level) and the amount of contrast agent per unit time

### Short-Term Efficacy

Among the 157 patients treated successfully, prior to recanalization, 87 (55.4%) patients had some amount of ascites. Specifically, 44 (28.9%), 19 (12.1%), and 24 (15.2%) patients, respectively, had a small, moderate, or large amounts of ascites. Upon hospital discharge, the ascites had disappeared in all but 37 (23.6%) patients. The differences in the amount of ascites of the patients between admission and discharge were significant. Upon discharge, 146 patients (93%) had complete symptom relief, and 11 patients (7%) had improved symptoms.

### Mid-Term and Long-Term Efficacy

Asymptomatic survival rate was defined as time until recurrence of symptoms. Among the 157 patients treated successfully, the asymptomatic survival rates at 2 years after the initial treatment and after repeat intervention were 82.4% (95% CI 72.8–92.0%) and 94.2% (95% CI 88.9–99.5%), respectively. For the 51 patients in the IVC + HV group, the asymptomatic survival rates after the initial and the repeat interventions were 77.3% (95% CI 62.6–92.0%) and 91.6% (95% CI 82.4–100.0%). For the 106 patients in the IVC-only group, the asymptomatic survival rates after the initial and repeat treatments were 84.6% (95% CI 71.7–97.5%) and 95.5% (95% CI 89.2–100.0%). The asymptomatic survival rates of the IVC + HV group after the initial and the revised treatments were lower than that of the IVC-only group ($\chi^2$ = 2.916 and 1.606, $P$ = 0.088 and 0.205). The differences between the 2 groups were not statistically significant (Fig. 3).

During the follow-up, symptoms of BCS recurred in 13 patients (7.3%). Specifically, HV and IVC obstructions occurred in 8 (4.5%) and 5 (2.8%) patients, respectively. The 13 patients with recurrence were again treated with venous recanalization. Among the 8 recurrent patients with HV obstruction, 5 (62.5%) underwent successful repeat treatment, while the repeat treatment failed for the remaining 3 patients (1 patient died due to upper gastrointestinal hemorrhage). All 5 patients with recurrent IVC obstruction experienced successful repeat treatment. Two patients died during the follow-up period, including 1 death due to brain metastases associated with liver cancer and 1 death due to hypertension that resulted in intracerebral hemorrhage.

## Discussion

In China, most patients with BCS are treated by angioplasty and recanalization of obstructed HVs and IVC. Procedures include balloon angioplasty, stent implantation, and local thrombolysis. Several studies have focused on the technical essentials of these interventional therapies [6, 8–10, 12, 13]. The concern of the present study was the choice of interventional therapy and recanalization strategy in patients with BCS that involves both HVs and the IVC. The endovascular intervention given to patients with BCS in this retrospective study was based on the characteristics of the vascular lesions, as determined by imaging studies and venography. Specifically, 32.7% of patients underwent treatment for HV + IVC obstruction, and the remaining for IVC obstruction alone. Good efficacy was demonstrated, with a low recurrence rate and high asymptomatic rate at 2 years.

Although most patients with BCS in China have obstruction of both the HVs and IVC [4, 5], only a small minority require recanalization of both. Similarly, in the present study, only a small percentage (32.7%) of patients underwent recanalization of both the IVC and HVs, and most (67.3%) received IVC recanalization alone. Even for patients who received HV recanalization, most (54.9%) required recanalization of only one HV. This was mainly due to the long duration of BCS in the patients with both HV and IVC obstructions (105.2 ± 103.3 mo), which meant that the majority of these patients had many large drainage branches in the main HVs (i.e., collateral veins from the occluded HVs), or between the HVs and other veins. These collateral vessels have a compensatory effect on HV occlusion, resulting in hepatic and portal

**Table 2** IVC and HV pressures before and after successful treatment in the HV + IVC and IVC-only groups

| | HV + IVC[a] | | | IVC-only[b] | | |
|---|---|---|---|---|---|---|
| | HV | IVC | RA | HV[c] | IVC | RA |
| Before treatment (mmHg) | 30.9 ± 6.3 | 20.9 ± 4.2 | 6.1 ± 1.3 | 28.4 ± 6.5 | 20.1 ± 4.7 | 5.9 ± 1.3 |
| After treatment (mmHg) | 13.5 ± 4.1 | 11.8 ± 3.0 | 7.5 ± 2.4 | 12.0 + 3.8 | 10.7 ± 3.1 | 7.7 ± 2.1 |
| $t$ value | 8.42 | 6.75 | −5.26 | 9.73 | 8.74 | −9.80 |
| $P$ value | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |

*RA* right atrial

[a] $n$ = 51; [b] $n$ = 106; [c] Free HV pressure was measured before treatment

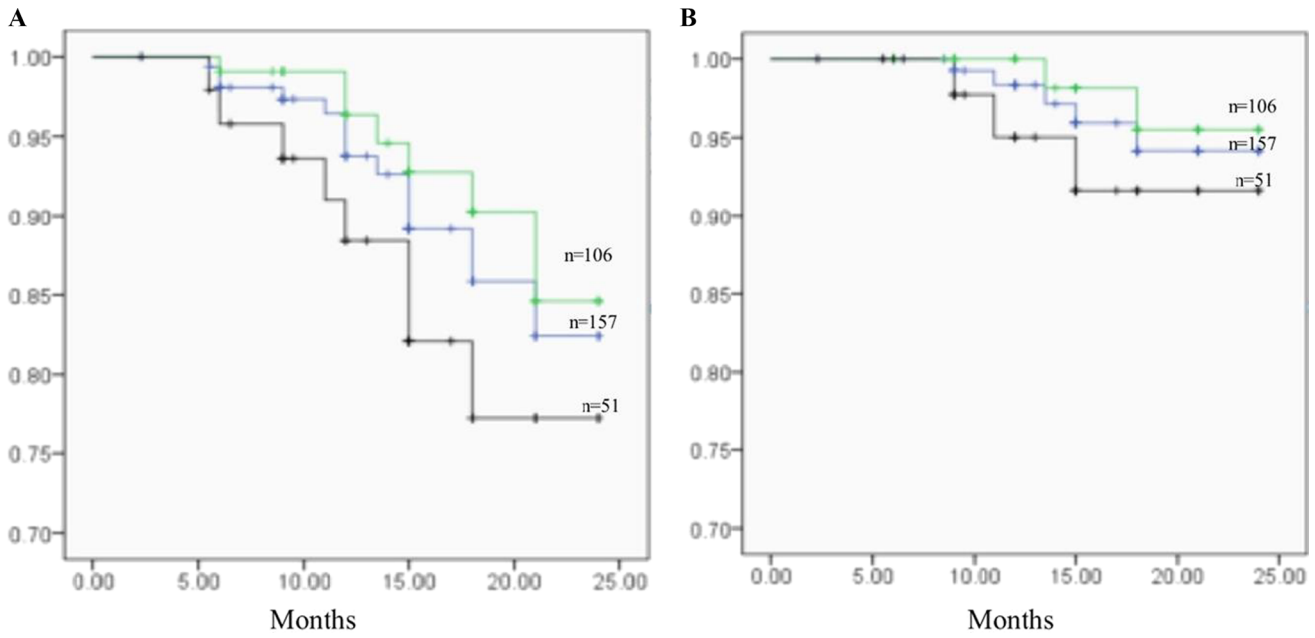


**Fig. 3** Asymptomatic survival rates at 2 years of the 157 patients after interventional treatment of BCS caused by both IVC and HV obstruction. **A** After the initial treatment. **B** After the revised treatment. Key: Overall patients ($n$ = 157). IVC-only group ($n$ = 106). IVC + HV group ($n$ = 51). Censored values of the overall patients. Censored values of the IVC-only group. Censored values of the IVC + HV group

decompression. Thus, the symptoms of portal hypertension and IVC hypertension can be relieved by IVC recanalization in patients with BCS in whom there is patency of more than one HV or more than 2 large accessory HVs.

In this study, patients with BCS were treated with recanalization of both the HV and IVC, or the IVC alone, based on the characteristics of the HV lesions. The postoperative HV and IVC pressures were significantly lower than that of the preoperative pressures and BCS-related symptoms were significantly alleviated. The 2-year rate of asymptomatic survival was 94.2%.

Currently, there are 3 methods of HV recanalization: via the jugular vein, femoral vein, or percutaneous transhepatic HV catheterization [13–17]. The majority of patients with BCS in China with HV obstruction have stenosis or membrane occlusion of the HV [3, 4, 13, 15, 17]. The cause of HV membrane occlusion is controversial and requires investigation. Some have proposed that it is caused by innate factors, but others think it is related to thrombus and inflammation.

In the present study, 113/162 patients (69.8%) were identified as having HV membrane occlusion, which is similar to our previous findings [3]. In our opinion, environmental and dietary factors may be of significant influence, since the incidence of HV membrane occlusion is high in the Yellow River basin in China, with high iodine content in the drinking water. Regions with higher iodine content have been associated with a higher rate of BCS incidence [3]. However, confirming a correlation between excessive consumption of iodine and HV membrane requires further study.

For patients with HV occlusion, the jugular vein approach for recanalization is preferred. This may be because the operation is relatively simple and has a high success rate, and percutaneous liver puncture is avoided with its risk of abdominal bleeding. Patients for whom the jugular vein approach fails may be treated via the femoral vein, although the greater distance makes recanalization of the HV occlusion more difficult. For accessory HVs and IVC at an obtuse angle, the occlusion is relatively easy to recanalize via the femoral vein. For patients who fail after both jugular vein and the femoral vein approaches, recanalization of HVs can be tried via percutaneous transhepatic HV catheterization (for recanalization of the middle, left, and accessory HVs).

In the present study, patients with involvement of both the HVs and IVC were considered first for recanalization of the main IVC. HV recanalization was considered if hepatic and portal hypertension persisted after IVC recanalization. The right HV is more suitable for recanalization, because of its greater diameter and drainage when compared with the other HVs. When the 3 main HVs are obstructed, recanalization of the right HV should be tried. If recanalization of the main HVs fails, then the accessory HVs should be tried, to alleviate the patient's portal hypertension-related symptoms. If the diameter and the drainage of the HVs are large, then recanalization of one HV can effectively relieve the symptoms of portal hypertension.

Simultaneous recanalization of multiple HVs should be considered when HVs are small in diameter and drainage.

The method used for recanalization of the HVs and IVC should be based on the nature of the vascular obstruction. For obstructive lesions of the HV without thrombosis, balloon angioplasty should be considered. Expansion of the balloon diameter should be based on the vessel diameter, with the HV balloon diameter ranging from 12 to 20 mm, and the IVC balloon diameter from 20 to 30 mm. If a fresh thrombus forms in the HVs and IVC, balloon angioplasty and stenting should be performed after the completion of thrombolytic therapy.

In the present study, 13 (7.3%) patients underwent additional treatment due to recurrence of HV or IVC obstruction. The recurrence of HV and IVC obstruction is an important cause of BCS recurrence and an important challenge in BCS interventional treatment. While some scholars [6] believe that stenting can reduce the incidence of IVC and HV re-occlusion, the vein stent is a permanent implant. Intravenous stent implantations not only increase the incidence of complications, but also the difficulty of an intervention when restenosis of the IVC or HVs occurs.

In our experience and opinion, the patency of the treated target vein after the balloon angioplasty does not require stent placement when the residual stenosis is $< 25\%$, and the pressure difference across the lesions is less than 3 mmHg. Studies have shown that covered stent placement in the transjugular intrahepatic portosystemic shunt can reduce the rate of stent restenosis caused by cell regeneration [18–21]. A case was reported of restenosis after HV and IVC stent implantation in a patient with BCS caused by fibrous hyperplasia at the end of the stent [22]. The use of covered stents is of little help to maintain long-term patency of the HV and IVC, and covered stent implantation can impede the formation of collateral vessels. Therefore, a bare stent should be used for recanalization of HVs and the IVC.

In the present study, among patients with obstructions of both HVs and the IVC, only 7.3% of patients showed a recurrence during the follow-up. Most of the relapsed patients underwent successful venous recanalization. Overall, the 2-year asymptomatic survival rate in this population was 94.2%. The asymptomatic survival rates of the HV + IVC group after the initial and revised treatments were 77.3% and 91.6%, respectively. The asymptomatic survival rates of the IVC-only group after initial and revised treatments were 84.6% and 95.5%. Thus, the asymptomatic survival rates of the HV + IVC group after the initial and the revised treatments were lower than that of the IVC group, although the differences were not statistically different. However, the sample size of this study is limited in statistical power.

## Conclusions

Recanalization and balloon angioplasty was found safe and effective for the management of patients with BCS that is due to concurrent hepatic and IVC occlusion. The majority of patients required IVC recanalization only. Clinical symptoms were relieved in 82.4% of patients after the initial intervention and in 94.2% after the second intervention. The 2-year outcomes of patients requiring IVC recanalization only were comparable to that of patients who underwent recanalization of both HVs and IVC. These results warrant further study with a larger sample size to confirm the efficacy of endovascular therapy for patients with BCS and occlusive disease of both HVs and the IVC.

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**Compliance with Ethical Standards**

**Conflict of interest** All authors declare that they have no conflict of interest.

**Ethical Approval** All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

**Informed Consent** Informed consent was obtained from all individual participants included in the study.

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