

## Retrospective Study

# Transjugular intrahepatic portosystemic shunt for severe jaundice in patients with acute Budd-Chiari syndrome

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**Data sharing:** Technical appendix, statistical code and dataset are available from the corresponding author at [liufq\\_sjt@163.com](mailto:liufq_sjt@163.com).

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## Abstract

**AIM:** To evaluate the feasibility of transjugular intrahepatic portosystemic shunt (TIPS) for severe jaundice secondary to acute Budd-Chiari syndrome (BCS).

**METHODS:** From February 2009 to March 2013, 37 patients with severe jaundice secondary to acute BCS were treated. Sixteen patients without hepatic venule, hepatic veins (HV) obstruction underwent percutaneous angioplasty of the inferior vena cava (IVC) and/or HVs. Twenty-one patients with HV occlusion underwent TIPS. Serum bilirubin, liver function, demographic data and operative data of the two groups of patients were analyzed.

**RESULTS:** Twenty-one patients underwent TIPS and the technical success rate was 100%, with no technical complications. Sixteen patients underwent recanalization of the IVC and/or HVs and the technical success rate was 100%. The mean procedure time for TIPS was  $84.0 \pm 12.11$  min and angioplasty was  $44.11 \pm 5.12$  min ( $P < 0.01$ ). The mean portosystemic pressure in the TIPS group decreased significantly from  $40.50 \pm 4.32$  to  $16.05 \pm 3.50$  mmHg ( $P < 0.01$ ). The mean portosystemic pressure gradient decreased significantly from  $33.60 \pm 2.62$  to  $7.30 \pm 2.21$  mmHg ( $P < 0.01$ ). At 8 wk after the procedures, in the TIPS group, total bilirubin (TBIL) decreased significantly from  $266.24 \pm 122.03$  before surgery to  $40.11 \pm 3.52$   $\mu\text{mol/L}$  ( $P < 0.01$ ) and direct bilirubin (DBIL) decreased significantly from  $194.22 \pm 69.82$   $\mu\text{mol/L}$  to  $29.82 \pm 3.10$   $\mu\text{mol/L}$  ( $P < 0.01$ ). In the angioplasty group, bilirubin returned to the normal range, with TBIL decreased significantly from  $258.22 \pm 72.71$   $\mu\text{mol/L}$  to  $13.33 \pm 3.54$   $\mu\text{mol/L}$  ( $P < 0.01$ ) and DBIL from  $175.08 \pm 39.27$  to  $4.03 \pm 1.74$   $\mu\text{mol/L}$  ( $P < 0.01$ ). Liver function improved faster than TBIL. After 2 wk, in the TIPS group, alanine aminotransferase (ALT) decreased significantly from  $50.33 \pm 40.61$  U/L to  $28.67 \pm 7.02$

U/L ( $P < 0.01$ ) and aspartate aminotransferase (AST) from  $49.46 \pm 34.33$  U/L to  $26.89 \pm 8.68$  U/L ( $P < 0.01$ ). In the angioplasty group, ALT decreased significantly from  $51.56 \pm 27.90$  to  $14.22 \pm 2.59$   $\mu\text{mol/L}$  ( $P < 0.01$ ) and AST from  $60.66 \pm 39.89$   $\mu\text{mol/L}$  to  $8.18 \pm 1.89$   $\mu\text{mol/L}$  ( $P < 0.01$ ). After mean follow-up of 12.6 mo, there was no recurrence of jaundice in either group.

**CONCLUSION:** Severe jaundice is not a contraindication for TIPS in patients with acute BCS and TIPS is appropriate for severe jaundice due to BCS.

**Key words:** Budd-Chiari syndrome; Jaundice; Transjugular intrahepatic portosystemic shunt; Interventional therapy; Percutaneous angioplasty

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**Core tip:** Jaundice with bilirubin  $> 51.3$   $\mu\text{mol/L}$  (3 mg/dL) is a contraindication for transjugular intrahepatic portosystemic shunt (TIPS) in patients with liver cirrhosis or end-stage liver disease. However, 21 patients in our single center underwent TIPS due to severe jaundice secondary to acute Budd-Chiari syndrome (BCS) and good clinical outcomes were achieved. We present a single center clinical experience and discuss the feasibility and effectiveness of treating severe jaundice secondary to acute BCS with TIPS.

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## INTRODUCTION

Budd-Chiari syndrome (BCS) is a group of disorders resulting from hepatic venous obstruction at the level of the hepatic vein (HV), the inferior vena cava (IVC) or the hepatic venules. The clinical features include jaundice, digestive discomfort, abdominal distention, abdominal pain, refractory ascites, hepatosplenomegaly, portal hypertension, gastrointestinal bleeding, liver cirrhosis and even liver failure. Patients with acute BCS rarely benefit from conservative treatment. The major interventional treatment for BCS is percutaneous angioplasty of outflow vessels, including the IVC and HV; however, when all the hepatic venules are occluded, recanalization of the IVC and HVs did not relieve the symptoms. Transjugular intrahepatic portosystemic shunt (TIPS) has been performed since 1992 and good outcomes have been achieved. Jaundice of acute BCS is caused by HV occlusion. In the past, jaundice with total bilirubin (TBIL)  $> 51.3$   $\mu\text{mol/L}$  (3 mg/dL) was a

contraindication for TIPS in patients with liver cirrhosis or end-stage liver diseases<sup>[1]</sup>. However, from February 2009 to March 2013, 21 patients in our single center underwent TIPS for severe jaundice secondary to acute BCS and good clinical outcomes were achieved.

Here, we retrospectively review these patients and compare them with patients with jaundice secondary to acute BCS that was relieved by percutaneous angioplasty of the HV and/or IVC during the same period. We present a single center clinical experience and discuss the feasibility and effectiveness of treating severe jaundice secondary to acute BCS with TIPS.

## MATERIALS AND METHODS

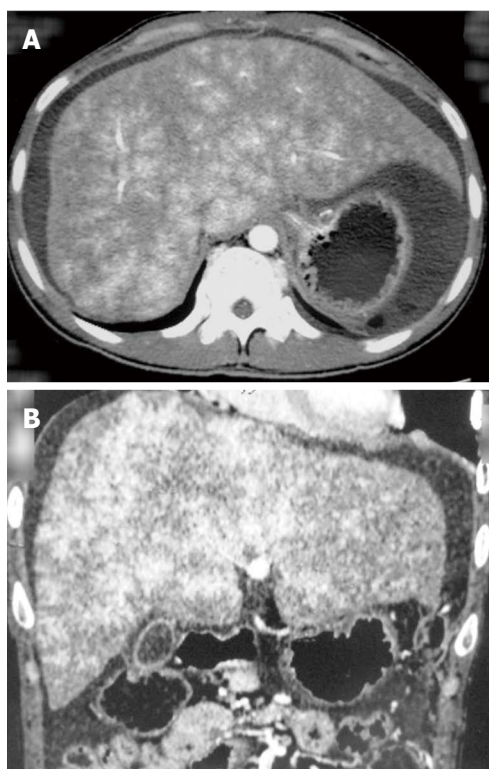
### Patient data

Between February 2009 and March 2013, 37 patients (22 female, 15 male; all from China) were referred to the Department of Interventional Therapy of Beijing Shijitan Hospital due to jaundice symptoms, including severe yellow sclera and film, pruritus, abdominal discomfort and other features. Three patients also had massive ascites. All the patients were diagnosed with acute BCS in the local hospital. The mean age was  $39.67 \pm 2.74$  years. Duration of symptoms ranged from 5 to 42 d (mean  $14.5 \pm 7.89$  d).

After administration, abdominal computed tomography (CT), a magnetic resonance imaging of the portal vein (Figure 1) and vena cava angiography were performed on each patient. Occlusion of the IVC or HVs was confirmed for each patient. Percutaneous angioplasty of the IVC and/or HVs was performed on 16 (10 female, 6 male) patients without hepatic venule obstruction. TIPS was performed on the other 21 (12 female, 9 male) patients (2 also had massive ascites) with occluded hepatic venules (Figure 2). Laboratory tests, including TBIL, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and blood ammonia, were recorded for each patient before the procedures. The two groups of patients were compared with regard to operative and postoperative data. Anti-coagulation treatment with warfarin was administered to both groups of patients after the procedures and low-molecular-weight heparin was given before the international normalized ratio reached 2-3.

### TIPS placement technique

The TIPS procedures were performed under local anesthesia in the Interventional Radiology Suite of Shijitan Hospital of Capital Medical University. The Rösch-Uchida Transjugular Liver Access Set (Cook) was used for each patient. After right jugular venous access was gained with a 10 F sheath, a 5 F multipurpose catheter was inserted into the hepatic vein and angiography was performed. As already stated, 21 patients had occlusion of the hepatic venules. TIPS was then performed. A TIPS needle was advanced into the portal vein through the liver parenchyma from



**Figure 1** Abdominal computed tomography. A and B: Enlargement, congestion and geographic change of the liver were noted.

the vena cava and the guide wire was placed into the portal vein through the sheath. Subsequently, the shunt was dilated with an angioplasty balloon of 8 mm diameter and a covered stent with a diameter of 8 mm was deployed. If the stent was not long enough, one or two additional stents were utilized to extend the length. Portal vein angiography and pressure measurements were repeated.

### Clinical observations

All the patients were under close monitoring during the perioperative period. Reduction of jaundice was recorded and laboratory tests were repeated. Complications, including abdominal cavity hemorrhage, acute hepatic failure and hepatic encephalopathy (HE), were observed during the perioperative period.

### Follow-up

Monthly follow-up was planned during the first 6 mo after the procedure and then at 6 mo intervals thereafter. Clinical observations included reduction of jaundice, hepatic failure and HE. Abdominal CT was repeated at each point. Laboratory investigations, including TBIL, ALT, AST and ammonia, were also checked at each follow-up point.

### Statistical analysis

SPSS for Windows version 17.0 was utilized for data processing. Statistical analysis with paired sample *t* test was used for measurement data. Numerical data

were summarized as frequencies and continuous variables as  $\pm$  standard deviation.  $P < 0.05$  was considered to be statistically significant.

## RESULTS

### Technique success and hemodynamic changes

In the TIPS group, the procedures were successful in all 21 patients, with no technical complications. In the percutaneous angioplasty group, recanalization of the IVC and/or HVs was successful in all 16 patients. In the TIPS group, 42 covered stents were deployed in the patients and four bare stents were used in four patients to extend the shunt in the portal vein. The mean operation time of the TIPS group was  $84.0 \pm 12.11$  min and the mean procedure time of the angioplasty group was  $44.11 \pm 5.12$  min ( $P < 0.01$ ). Portal vein hypertension was found in all patients and was improved after TIPS. The mean portosystemic pressure prior to TIPS placement was  $40.50 \pm 4.32$  mmHg, which decreased significantly to  $16.05 \pm 3.50$  mmHg after the shunt was established ( $P < 0.01$ ). The mean PSG prior to TIPS was  $33.60 \pm 2.62$  mmHg and decreased significantly to  $7.30 \pm 2.21$  mmHg after the procedure ( $P < 0.01$ ). Mild-to-moderate gastroesophageal varices were found in two patients in TIPS group and were embolized with coils after the TIPS shunt was formed.

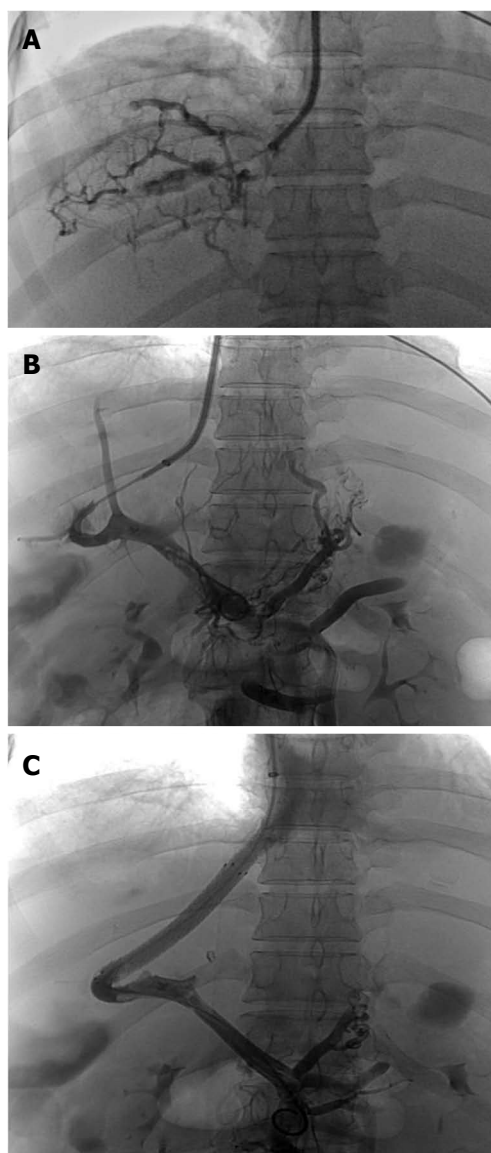
### Clinical effects

Clinical improvement was seen in both groups of patients. In the TIPS group, jaundice symptoms were relieved within 2-8 wk and in the angioplasty group, the symptoms were relieved within 1-4 wk. Ascites decreased obviously in both groups of patients within 1-2 wk after the procedure (Figure 3).

At 8 wk after TIPS, TBIL decreased significantly from  $266.24 \pm 122.03$   $\mu\text{mol/L}$  before surgery to  $40.11 \pm 3.52$   $\mu\text{mol/L}$  ( $P < 0.01$ ) and direct bilirubin (DBIL) dropped significantly from  $194.22 \pm 69.82$   $\mu\text{mol/L}$  to  $29.82 \pm 3.10$   $\mu\text{mol/L}$  ( $P < 0.01$ ). At 8 wk after angioplasty, bilirubin level returned to normal, with TBIL decreasing significantly from  $258.22 \pm 72.71$   $\mu\text{mol/L}$  to  $13.33 \pm 3.54$   $\mu\text{mol/L}$  ( $P < 0.01$ ) and DBIL from  $175.08 \pm 39.27$   $\mu\text{mol/L}$  to  $4.03 \pm 1.74$   $\mu\text{mol/L}$  ( $P < 0.01$ ) (Table 1).

Before the procedures, liver function was abnormal in 28 patients (18 in the TIPS group and 10 in the angioplasty group). After the procedures, liver function improved faster than TBIL. ALT and AST improved significantly within 1 wk after the procedures and returned to normal within 2 wk in both groups. At 2 wk after TIPS, ALT decreased significantly from  $50.33 \pm 40.61$  U/L to  $28.67 \pm 7.02$  U/L ( $P < 0.01$ ) and AST from  $49.46 \pm 34.33$  U/L to  $26.89 \pm 8.68$  U/L ( $P < 0.01$ ). Two weeks after angioplasty, ALT decreased significantly from  $51.56 \pm 27.90$   $\mu\text{mol/L}$  to  $14.22 \pm 2.59$   $\mu\text{mol/L}$  ( $P < 0.01$ ) and AST from  $60.66 \pm 39.89$





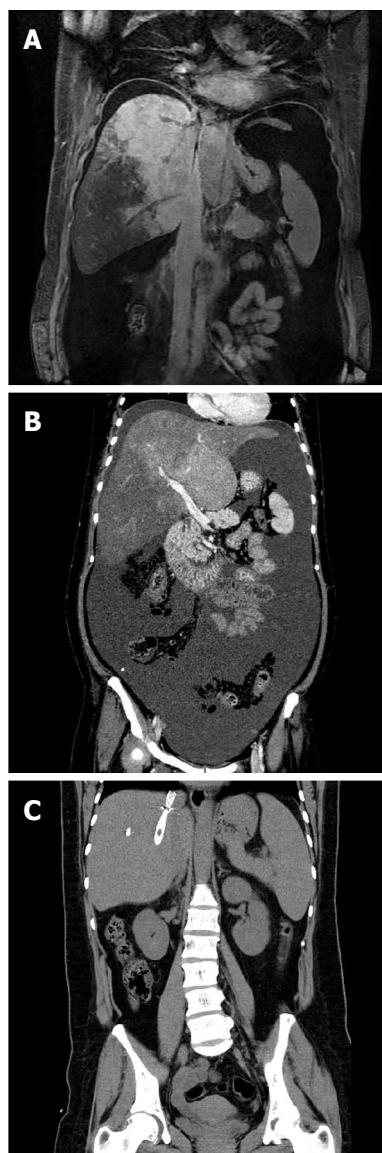
**Figure 2** Transjugular intrahepatic portosystemic shunt. A: Angiography revealed occluded hepatic venules; B: A guide wire was placed into the portal vein from the inferior vena cava and the varicose gastric coronary vein was noted by angiography of the portal vein; C: Transjugular intrahepatic portosystemic shunt was formed and the gastric coronary vein was embolized.

to  $8.18 \pm 1.89 \mu\text{mol/L}$  ( $P < 0.01$ ).

Although ammonia level was abnormal in 17 patients (10 in the TIPS group and 7 in the angioplasty group), no patient had HE after TIPS or percutaneous angioplasty of the IVC and/or HV. Mean ammonia level decreased significantly from  $50.21 \pm 21.17 \mu\text{mol/L}$  before the procedures to  $39.09 \pm 9.90 \mu\text{mol/L}$  2 wk after TIPS ( $P < 0.01$ ) and from  $56.78 \pm 18.90 \mu\text{mol/L}$  to  $26.38 \pm 5.19 \mu\text{mol/L}$  in the angioplasty group ( $P < 0.01$ ).

#### Follow-up

The patients underwent a mean follow-up of 12.6 mo without loss. No recurrence of jaundice was observed during follow-up and no stenosis of the recanalization or TIPS shunt was found. No patients had HE during



**Figure 3** Coronal scans of magnetic resonance imaging of the portal vein and abdominal computed tomography of the same patient. A and B: Magnetic resonance imaging of the portal vein and abdominal computed tomography revealed liver congestion and massive ascites before transjugular intrahepatic portosystemic shunt; C: Liver congestion and ascites disappeared 4 wk after the procedure.

follow-up. In the TIPS group, TBIL, ALT, AST and ammonia were  $37.23 \pm 3.24 \mu\text{mol/L}$ ,  $25.66 \pm 4.51 \text{ U/L}$ ,  $22.87 \pm 5.15 \text{ U/L}$  and  $41.56 \pm 2.42 \mu\text{mol/L}$  at 6 mo follow-up, respectively. In the angioplasty group, TBIL, ALT, AST and ammonia were  $14.55 \pm 3.21 \mu\text{mol/L}$ ,  $12.64 \pm 1.12 \text{ U/L}$ ,  $6.62 \pm 2.73 \text{ U/L}$  and  $18.52 \pm 4.91 \mu\text{mol/L}$  at 6 mo follow-up, respectively. Before surgery, abdominal CT showed hepatomegaly but the liver returned to its normal size at 6 mo follow-up.

#### DISCUSSION

BCS is a group of disorders caused by occlusion of hepatic venules, HVs and/or conterminous IVC affecting younger to middle-aged patients (median

**Table 1 Comparison of transjugular intrahepatic portosystemic shunt and angioplasty groups**

	TIPS group			Angioplasty group			
	Before (mean $\pm$ SD)	After (mean $\pm$ SD)	<i>P</i> value	Before (mean $\pm$ SD)	After (mean $\pm$ SD)	<i>P</i> value	<i>P</i> value <sup>1</sup>
TBIL ( $\mu$ mol/L)	266.24 $\pm$ 122.03	40.11 $\pm$ 3.52	< 0.01	258.22 $\pm$ 72.71	13.33 $\pm$ 3.54	< 0.01	< 0.01
DBIL ( $\mu$ mol/L)	194.22 $\pm$ 69.82	29.82 $\pm$ 3.10	< 0.01	175.08 $\pm$ 39.27	4.03 $\pm$ 1.74	< 0.01	< 0.01
ALT (U/L)	50.33 $\pm$ 40.61	28.67 $\pm$ 7.02	< 0.01	51.56 $\pm$ 27.90	14.22 $\pm$ 2.59	< 0.01	< 0.01
AST (U/L)	49.46 $\pm$ 34.33	26.89 $\pm$ 8.68	< 0.01	60.66 $\pm$ 39.89	8.18 $\pm$ 1.89	< 0.01	< 0.01
Ammonia ( $\mu$ mol/L)	50.21 $\pm$ 21.17	39.09 $\pm$ 9.90	< 0.01	56.78 $\pm$ 18.90	26.38 $\pm$ 5.19	< 0.01	< 0.01

<sup>1</sup>Comparison of data after the procedures. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; DBIL: Direct bilirubin; TBIL: Total bilirubin; TIPS: Transjugular intrahepatic portosystemic shunt.

age 40 years). The average age of the 21 patients in our study was  $42.64 \pm 2.13$  years, which was similar to a previously reported series. The symptoms of BCS include abdominal pain, jaundice, hepatosplenomegaly, HE and ascites or gastrointestinal bleeding caused by portal hypertension, and hepatic failure and cirrhosis are often also observed. The natural course of BCS with symptoms is progressive, while congestion caused by total occlusion of HVs leads to fulminant jaundice, ascites, hepatic failure and cirrhosis without proper treatment. In our study, the symptoms of jaundice progressed rapidly within a few weeks.

Randomized clinical trials of treatment for BCS are still lacking. Anti-coagulation therapy has been proved to be sufficient in controlling the liver disease in cases of mild BCS and is recommended by British and American guidelines at diagnosis<sup>[2,3]</sup>. In the present study, both groups of patients received anti-coagulation therapy after the procedures and no internal bleeding was seen in the perioperative or follow-up periods. Acute BCS treated with catheter-directed thrombolysis might be effective for hyperacute thrombosis within 3 d. Once thrombolytic therapy is given, no interventional measures should be performed until the drug is metabolized completely.

Interventional management of patients with BCS focuses on the relief of hepatic venous outflow tract obstruction. About 30% of BCS patients present with stenosis or occlusion of IVC and/or HVs. The efficacy of percutaneous angioplasty for these patients has been confirmed. In a retrospective study of one single center in China that involved 177 patients<sup>[4]</sup>, the survival rates at 1, 5 and 10 years after the procedures were 96%, 83% and 73%, respectively. Active searching for such stenosis or occlusion following angioplasty is recommended in patients with symptomatic BCS. Patients with occlusion of both IVC and HVs require recanalization of both segments. Stents may be placed when necessary. Transjugular and transfemoral routes are used in these patients and in some cases a combined jugular and femoral approach is utilized. Percutaneous angioplasty of IVC and/or HVs is frequently practiced in our institute and the prognosis is favorable. In the present study, the jaundice decreased significantly in the angioplasty group and liver function recovered to normal within

a few weeks after the procedures. Good clinical outcomes have also been achieved in patients with other symptoms, including abdominal pain, ascites and hepatosplenomegaly, after percutaneous angioplasty of IVC and/or HVs. In patients with asymptomatic BCS, aggressive management of IVC and/or HVs is still debated<sup>[1]</sup>.

When BCS symptoms cannot be controlled by angioplasty of the IVC and/or HVs, the next step should be TIPS. With a relatively good midterm prognosis, TIPS is now the preferred treatment for BCS. A 90% of 5-year and 80% of 10-year survival can now be achieved after TIPS<sup>[5]</sup>. The transcaval approach performed by an experienced doctor is technically and clinically successful in most patients. In our single center, > 200 TIPS procedures have been performed annually since 2009 and the success rate is > 95%. Meanwhile, with covered stent grafts routinely applied in TIPS procedures, the patency rates have clearly increased and in the present study, no stenosis of the TIPS shunt was found during follow-up.

When dealing with patients with end-stage liver disease or advanced cirrhosis, severe jaundice with bilirubin > 3 mg/dL is a contraindication for TIPS. Furthermore, pre-TIPS bilirubin level is an independent predictor of 30-d mortality of TIPS and a 1-mg/dL increase above 3.0 mg/dL leads to a 40% increased risk of death<sup>[6]</sup>. Patients with MELD (Model for End-Stage Liver Disease) score > 18 have a significantly higher mortality than patients with scores of  $\leq 18$ <sup>[7,8]</sup> and MELD score is better in predicting 3-mo survival of patients undergoing TIPS than Child-Pugh score.

However, patients in the present study had acute or sub-acute BCS, with mildly abnormal liver function. Portal hypertension was observed in all patients, with mild-to-moderate gastroesophageal varices in two patients, and no advanced cirrhosis was observed. Although the mean bilirubin of the TIPS group was > 3 mg/dL, a good clinical outcome was achieved. In other words, severe jaundice with bilirubin > 3 mg/dL is not a contraindication for TIPS in patients with acute or sub-acute BCS. In the present study, there was a significant difference in postprocedural data between the TIPS and angioplasty groups. However, the data were close to normal and improved greatly compared

with before TIPS. Thus, we suggest that severe jaundice due to BCS is an indication for TIPS after unsuccessful angioplasty of IVC and/or HVs.

The utilization of covered stent grafts has greatly increased the patency rates after TIPS in patients with cirrhosis, yet the risk of HE has increased. The incidence of HE is between 33% and 48% in patients with liver cirrhosis at 6 mo after TIPS<sup>[9]</sup>. Some risk factors for HE after TIPS have already been mentioned: age > 60 years, female sex, previous history of HE, hypoproteinemia, final pressure gradient, basal disease severity and shunt diameter<sup>[10]</sup>. In our previous study on parallel TIPS shunting in patients with hepatitis B virus cirrhosis, HE was the major complication after the second shunt was established<sup>[11]</sup>. However, according to the literature, the risk of HE is relatively low after TIPS for BCS, with an incidence of 0-25%<sup>[12]</sup>. In the present study, no patient had HE after TIPS. Nevertheless, we still suggest that treatment for HE should be given before and after TIPS.

In conclusion, severe jaundice due to acute BCS can be relieved by TIPS when hepatic venules are occluded, leading to a satisfactory clinical outcome. Severe jaundice with bilirubin > 3 mg/dL is not a contraindication for TIPS in patients with acute BCS. On the contrary, TIPS is an appropriate option for severe jaundice due to BCS.

## COMMENTS

### Background

In the past, jaundice with total bilirubin of over 51.3  $\mu\text{mol/L}$  (3 mg/dL) was a contraindication for transjugular intrahepatic portosystemic shunt (TIPS) in patients with liver cirrhosis or end-stage liver diseases and pre-TIPS bilirubin level was an independent predictor of 30-d mortality of TIPS.

### Research frontiers

TIPS has been applied for patients with Budd-Chiari syndrome (BCS) since 1992 and good outcomes have been achieved.

### Innovations and breakthroughs

With a relatively good mid-term prognosis, TIPS is now the preferred treatment for BCS. A 90% of 5-year and 80% of 10-year survival can now be achieved after TIPS. There has been no research about treatment of severe jaundice due to acute BCS.

### Applications

The authors present a single center clinical experience in treating severe jaundice secondary to acute BCS with TIPS and believe that TIPS is an appropriate option for severe jaundice due to BCS.

### Terminology

TIPS is a shunt (tube) placed between the portal vein which carries blood from the intestines and intraabdominal organs to the liver and the hepatic vein which carries blood from the liver back to the vena cava and the heart.

### Peer-review

This is a study about TIPS for severe jaundice in patients with acute BCS. The authors believe that severe jaundice with bilirubin above 3 mg/dL is not a

contraindication for TIPS in patients with acute BCS and TIPS is an appropriate option for severe jaundice due to BCS. The idea is very interesting and the article is of great value.

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