Ultrasound-guided direct intrahepatic portosystemic shunt in patients with Budd–Chiari syndrome: Short- and long-term results

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Abstract: *Background and aims:* Budd–Chiari syndrome (BCS) is treated with anticoagulation therapy, transjugular intrahepatic portosystemic shunt (TIPS), angioplasty, and liver transplantation. TIPS is not always technically feasible, due to the complete hepatic venous thrombosis. Direct intrahepatic portosystemic shunt (DIPS) is an alternative method for decompression of portal hypertension. This is a retrospective, single-center study aiming to evaluate the outcome of ultrasound (US)-guided DIPS in patients with BCS. *Materials and methods:* Between 2003 and 2016, six patients with BCS were treated with US-guided DIPS. Polytetrafluoroethylene (PTFE)-covered stents were used in two patients and bare-metal stents in four patients. Mean follow-up time was 71.4 months (range: 21–164). Technical/clinical success, technical difficulties, and complications of DIPS were analyzed. *Results:* Technical success without complications was achieved in all patients (100%). In one patient, DIPS was performed through the right femoral vein, without significant amelioration of portal hypertension (clinical success 83.3%). In four out of five patients, ascites and variceal bleeding resolved completely and in the other one ascites was relieved. Six- and 12-month primary patency rates were 100% in PTFE-covered stent group when compared with bare-metal stent group, the rates were 33% and 0%, respectively. *Conclusion:* US-guided DIPS is a safe and effective alternative technique for patients with BCS, with significant clinical improvement.

Keywords: portal hypertension, Budd–Chiari syndrome, TIPS, DIPS, PTFE-covered stents

Introduction

Budd–Chiari syndrome (BCS) is defined as a spectrum of clinical presentations characterized by narrowing and/or obstruction of hepatic venous outflow at any level among the small hepatic venules, the junction of the inferior vena cava (IVC), and the right atrium [1]. The clinical presentation of BCS depends on the extent and rapidity of obstruction of the hepatic vein and the presence of collateral veins that decompress the liver sinusoids. According to the clinical presentation, BCS can be classified as fulminant, acute, subacute, or chronic [2]. The most common underlying disorders in patients with BCS are hematologic abnormalities, such as polycythemia vera and essential thrombocytosis [3]. In Western countries, factor V Leiden and factor II gene mutations are also common etiologies [4]. Other causes include antiphospholipid syndrome, protein C or S deficiency, paroxysmal nocturnal hemoglobinuria, pregnancy, cancer, trauma, and oral contraceptive use [3]. Management includes anticoagulation therapy, radiological interventions [transjugular intrahepatic portosystemic shunt (TIPS) and angioplasty], very rarely used surgical portocaval shunt, and finally liver transplantation [5]. The most common treatment for BCS non-responsive

to medical therapy is TIPS. Nevertheless, this is not always technically successful, due to complete hepatic venous thrombosis [6]. Direct intrahepatic portosystemic shunt (DIPS) is an alternative interventional method for decompression of portal hypertension, which involves intravascular ultrasound (US)-guided puncture from the IVC to the portal vein [7]. The aim of this study is to evaluate the outcome of US-guided DIPS in patients with BCS and completely occluded hepatic veins.

Materials and Methods

Study design and patient selection

This is an observational, retrospective, single-center, case series study aiming to examine the efficacy of DIPS in patients with BCS. All patients gave their written informed consent before DIPS procedure.

All patients underwent evaluation for prothrombotic disorders. The diagnosis of BCS was based on clinical presentation, radiological findings [computed tomography (CT), US, and magnetic resonance imaging], and liver biopsy results in accordance with the criteria defined by the European Network for Vascular Disorders of the Liver [8].

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Patient data – Clinical information

Between 2003 and 2016, six patients (three men and three women) with a mean age of 36.2 years (range: 30–47 years) were referred to our hospital with BCS and portal hypertension. The diagnosis of BCS was based on clinical presentation, radiological findings, and liver biopsy results. All six patients presented with refractory ascites, five with concomitant variceal bleeding and four with splenomegaly. BCS causes were polycythemia vera ($n = 2$), antiphospholipid syndrome ($n = 1$), and factor V Leiden thrombophilia ($n = 1$). In two patients, no predisposing factor was recognized. Prior to the procedure, all patients were evaluated by both CT and color Doppler US (CDUS) for possible anatomical variations, patency of hepatic and portal veins, extension of disease, and finally planning of possible access route for intervention.

Procedural details

All procedures were performed under conscious sedation. Sterilization of the neck and anterior/lateral abdomen using an iodine solution was performed in a standard way. Right internal jugular access was used in five patients and right common femoral vein access in one patient. Having placed a vascular access sheath, a catheter was inserted in the right atrium and IVC and pressure measurement was performed to rule out the presence of right heart failure despite previous negative cardiac-echo-examination. Catheterization of the hepatic veins was not feasible, thus the decision in all six cases was to proceed to DIPS. Therefore, under fluoroscopic and transabdominal US guidance, TIPS-cannula/needle system (TIPS Set, Cook Medical, Bloomington, IN, USA) was intrahepatically directed from IVC to a portal vein main branch *(Fig. 1)*. After portal vein catheterization, pressure gradient was measured. Clinically significant portal hypertension was confirmed in all patients [hepatic venous pressure gradient (HVPG) > 12 mmHg]. In the sequel, same maneuvers used for conventional TIPS were utilized to place the appropriate stent or stent graft. Balloon angioplasty was performed before and after stent placement. All shunts created were 10 mm in diameter in accordance with the body weights of the patients. Polytetrafluoroethylene (PTFE)-covered stent grafts (Viatorr Endoprosthesis, W.L. Gore & Associates, Flagstaff, AZ, USA) were used in two patients and bare-metal stents (Luminexx, Bard, Billerica, MA, USA; Protege Everflex, Covidien, Mansfield, MA, USA) in four patients in accordance with the availability at certain time points. Additional uncovered stents were also used with covered stents for DIPS extension into IVC. We preferred PTFE-covered stent grafts, which are associated with improved primary patency, but the final selection of the stent was based on the availability of the desired stent (diameter and length) in our department at the time of insertion. Finally, venogram and pressure measurements were performed to check shunt patency and decompression of portal hypertension. All patients were placed on lifelong anticoagulation therapy in addition to the medical treatment of their underlying disease.

Endpoints – Statistical analysis

Patients were followed up by CDUS examination at 1 and 7 days after the procedure, then at 1, 3, 6, and 12 months and combined with other biochemical and hematological studies on an annual basis afterward. Mean follow-up time was 71.4 months (range: 21–164).

Demographic data, technical/clinical success, and procedure-related complications were analyzed. Technical success was defined as creation of shunt between the IVC and the portal vein with successful deployment of the stent/stent graft. Clinical success was defined as complete relief of symptoms. Primary patency was defined as exempt from re-stenosis without re-intervention and secondary patency was defined as sufficient patency of the shunt after re-intervention.

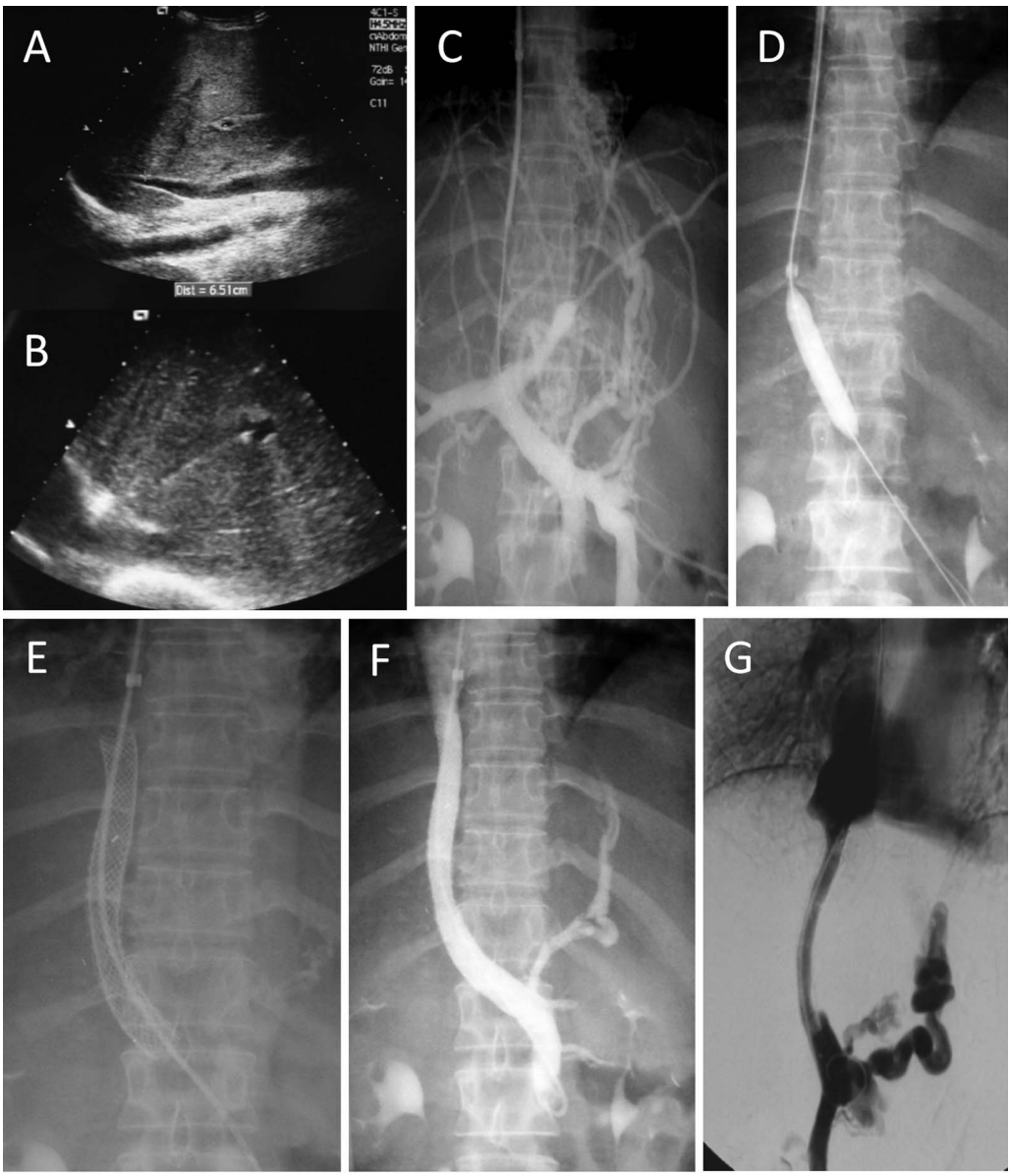

Fig. 1. A 30-year-old thrombophylic female patient with BCS and refractory ascites developed after pregnancy. (A) Abdominal US image shows right portal vein branch (transverse) and IVC (longitudinal) in same plane. (B) The transhepatic needle puncture from the IVC directly to a portal vein branch is ultrasonographically followed. (C) Portal venogram after TIPS catheter is advanced into the main portal vein. (D) Fluoroscopic image shows hepatic tract pre-dilatation with a 10×40 mm angioplasty balloon. (E) Fluoroscopic image demonstrates full deployment of the stent graft with additional bare-metal stent extension in the intrahepatic part of the IVC. (F) Portal venogram after DIPS placement shows excellent shunt patency. (G) Eleven years after DIPS placement, portal venogram shows nice shunt patency and variceal decompression

Statistical analysis was performed using GraphPad Prism 5.0 (GraphPad Software, Inc., San Diego, CA, USA). Overall survival, primary and secondary patency rates were evaluated using Kaplan–Meier statistics.

Results

DIPS placement was technically successful in all patients (technical success 100%) with significant decrease in HVPG (<12 mmHg). In one patient because of impaired hepatic venous anatomy, DIPS was performed through the right femoral vein, without significant amelioration of portal hypertension (clinical success 83.3%). This patient was lost to follow-up shortly after the procedure. In four out of five patients (who were followed up), ascites and variceal bleeding resolved completely whereas in the other patient ascites was slightly relieved. No minor or major complications occurred during or after the procedures and no patient developed hepatic encephalopathy. Peri-procedural mortality was 0% and all five follow-up patients are still alive (survival rate 100%).

Revisions were performed in all five patients. Two patients, to whom bare-metal stents were placed, developed thrombosis, after 3 and 4 days, respectively. In the first patient, after initial attempt to traverse the occlusion with a hydrophilic guide-wire through the IVC, the occluded stent was transhepatically punctured under US guidance using an 18-gauge, 20-cm Chiba needle *(Fig. 2)*. A 0.035-in. curved hydrophilic guide-wire was passed through the stent to the IVC and the right atrium. The transhepatic wire was snared using a guide-wire trapped in the lumen of the sheath, so providing through-and-through access. A straight 5-Fr catheter was then advanced from internal jugular venous (IJV) through the occluded stent to the portal vein and angioplasty was performed using PTA balloon catheter 10 × 40 mm (JUTURNA-vq PTA Balloon Catheter, TsunaMED, Winsen, Germany) with significant flow restoration in the occluded stent. The second patient who developed stent thrombosis 4 days after DIPS placement, as seen in CDUS was treated with a combination of

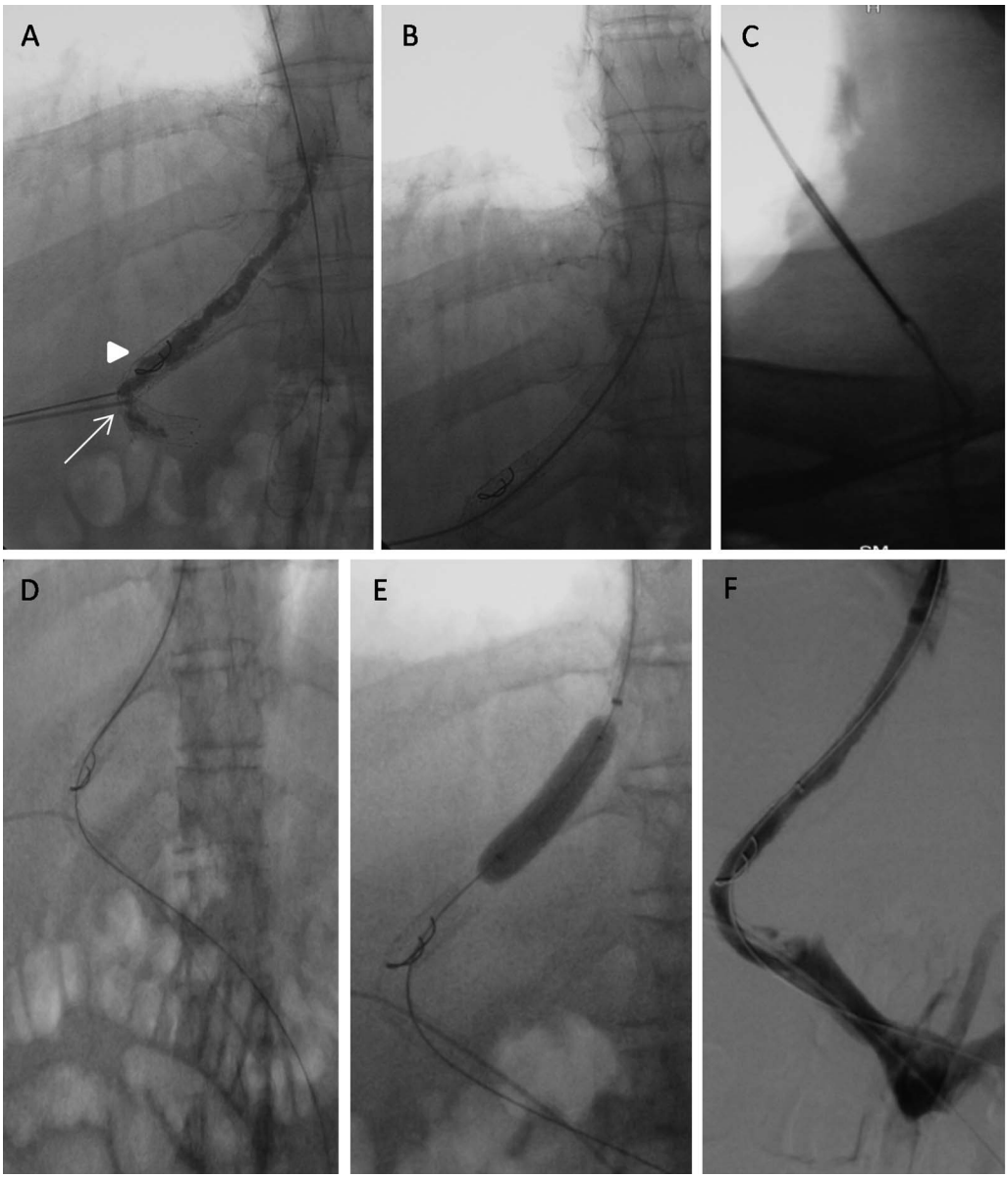

Fig. 2. A 47-year-old male patient with refractory ascites and bleeding esophageal varices caused by BCS. The patient did not improve after DIPS creation and 3 days later, color Duplex US revealed shunt occlusion. (A) After failed attempt to traverse occluded stent through IVC, the occluded stent was transhepatically punctured under fluoroscopic guidance (arrow). Contrast slowly filled the thrombosed stent [notice regarding the projection of previous inserted metallic coil due to inadvertent arterial puncture during DIPS (arrowhead)]. (B) A hydrophilic guide-wire was passed through the stent to the IVC. (C) Transhepatic guide-wire was snared using a guide-wire trapped in the lumen of a 6-Fr transjugular sheath placed in IVC, so providing through-and-through access. (D) A guide-wire was advanced from IJV through the occluded stent to the portal vein. (E) The occluded portovenous tract was dilated with a PTA balloon catheter 10 × 40 mm. (F) Final venogram shows significant flow restoration in the occluded tract

mechanical thrombectomy (AngioJet rheolytic thrombectomy catheter, DVX type, Possis Medical, Minneapolis, MN, USA), aspiration thrombectomy with a standard 8-Fr guiding catheter and PTA balloon angioplasty, resulting excellent stent patency. Both patients are now, 2 and 3 years respectively after DIPS, without ascites and with stable liver function showing no signs of DIPS dysfunction. There were also two cases of stent thrombosis 9 months *(Fig. 3)* and 11 years after DIPS procedure respectively who were treated by mechanical thrombectomy with AngioJet catheter and dilatation with a PTA balloon catheter 6 × 40 mm (Cronus Advanced Balloon Catheter, Rontis Medical, Zug, Switzerland). The other patient, where a Viatorr stent graft was used, presented DIPS dysfunction 5 years after DIPS placement due to shunt re-stenosis and was treated using a PTA balloon catheter 12 × 40 mm (JUTURNA-vq PTA Balloon Catheter, TsunaMED, Winsen, Germany).

Mean primary patency duration was 1,300 days. Six- and 12-month primary patency rate was 100% (2/2) in PTFE-covered stent group, which was significantly higher than those in bare-metal stent group 33% (1/3) and 0% (0/3), respectively. Secondary patency rate was 100% (5/5) in each stent group during follow-up *(Fig. 4)*.

Discussion

The therapeutic approach to BCS includes medical management and relief of hepatic venous outflow obstruction. Nevertheless, conservative treatment with anticoagulation drugs and correction of underlying disease is not always effective [9]. When conservative treatment alone is insufficient, a TIPS procedure or surgical portocaval shunt might be indicated. Surgical shunts in patients with BCS include side-to-side portocaval, central splenorenal, or mesocaval anastomosis [2]. Surgical shunts have been successful in managing BCS, but hemodynamic and anatomic factors as well as technical expertise can limit this option [10]. Moreover, they are associated with high dysfunction rates (up to 32%) [11] and high peri-operative mortality rates up to 50% [12].

In patients with patent hepatic vein segments, short hepatic vein stenoses can be managed by balloon angioplasty with or without stent deployment [13]. A Chinese study reported a case series of 115 patients with BCS, who underwent stenting in the IVC and hepatic veins with significant success rates of 94% and 87%, respectively [14]. Most patients present weeks to months after formation of thrombus with total occlusion of hepatic veins and treatment options such as angioplasty, stenting, or thrombolysis are usually ineffective. In these patients, TIPS is an attractive option for decompression of portal hypertension [15].

The first TIPS procedure on a patient with BCS was performed in 1993 [16]. Since then, multiple studies reported about the benefits of decompressing portal system with a less invasive procedure in comparison to surgical shunting [17–21]. Hepatic encephalopathy is a relatively common TIPS complication being refractory to medical therapy in 5% of the cases [22]. Nevertheless, TIPS can be used as a bridge to liver transplantation and offers excellent short- and long-term outcomes [23, 24]. The most critical and relative difficult aspect of TIPS procedure is accessing the portal vein. Moreover, TIPS is technically challenging in patients with BCS because of normal hepatic veins absence, so they cannot be used as a starting point for intrahepatic puncture. Fitsiori et al. [21] report that in 12 out of 14 cases hepatic vein catheterization was able through a small intrahepatic branch and that only in two cases an alternative access route was chosen. In our series, in all six cases intrahepatic access was not available. Therefore, the procedure requires technical modifications to overcome this anatomic problem. The gun-sight technique first described in 1996 as an alternative method for the creation of transcaval portosystemic shunt [25]. Boyvat et al. [26] used a modification of this method to insert percutaneously under US guidance a needle into a portal venous branch and then to IVC, where it could be snared after an IJV puncture. They used this technique in 11 patients with significant technical and clinical success. Intravascular US-guided placement of a DIPS, described by Petersen and Binkert [27], is another technical modification of TIPS procedure to create a portocaval shunt but requires special equipment. There are also several small series in which US guidance has been used to locate the portal vein and facilitate the procedure [28–30].

In this study, we used transabdominal US and fluoroscopic guidance for intrahepatic puncture of a portal vein main branch through the intrahepatic segment of IVC. The technical (100%) and clinical success (83.3%) compares well with the other reported studies. All five patients who were followed up showed a remarkable improvement of symptoms associated with portal hypertension. There was also no complication during or after the procedures. For DIPS, we preferred a straight angle and a minimal distance between the IVC entrance point and the portal vein to prevent stent thrombosis and shunt dysfunction, but this was not always achievable. US guidance was critical to accomplish this goal but was not sufficient in all cases. Another technical problem which we encountered in several cases was the fact of a long distance between IVC and the portal branch. This distance was longer than the needle length available for intrahepatic puncture (usually 4.5 cm). We overcame this hazard by advancing the whole needle–trocar system inside the liver parenchyma, before reaching the portal branch. In this way, we had also a more "stable" situation for exchanging trocar and catheters.

Despite the anticoagulation treatment, all patients presented DIPS dysfunction which subsequently required multiple re-interventions. Our stent patency rate is

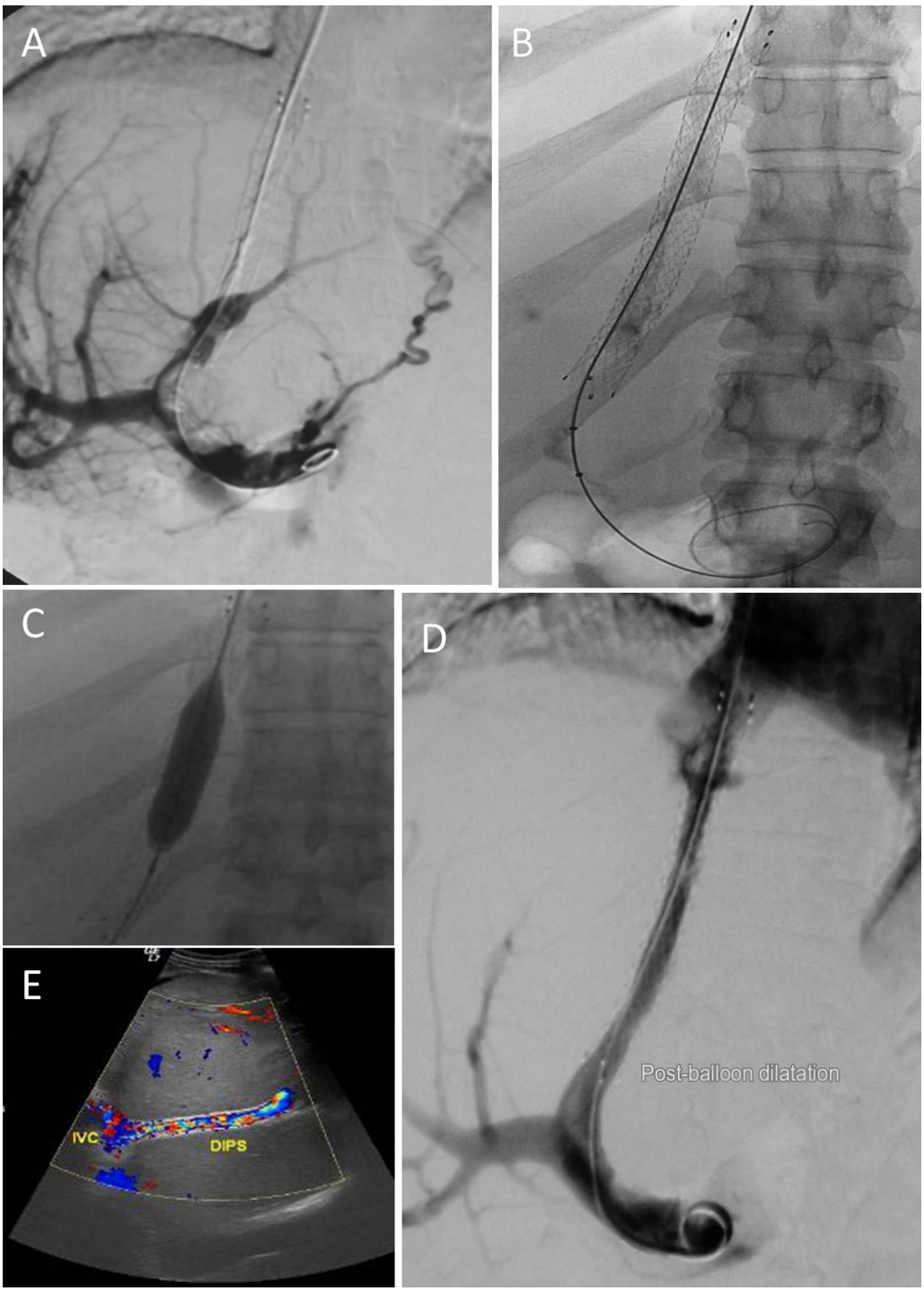

Fig. 3. A 30-year-old female patient with BCS presented with DIPS dysfunction due to shunt thrombosis as it was confirmed in the CDUS. (A) Portal venography through catheterized stent shows complete shunt thrombosis, probably due to distal endoluminal portal thrombus. (B) AngioJet rheolytic thrombectomy catheter was advanced over the wire and multiple passes were performed into the thrombus. (C) Additional dilatation with a PTA balloon catheter was performed. (D, E) Final venogram and CDUS show significant restoration of flow and complete stent patency

relatively poor. The small patient number is an understandable limitation of this study, not allowing safe conclusions about stent patency and patient clinical outcome.

AngioJet mechanical thrombectomy in combination with manual catheter aspiration and balloon disruption of the residual clot can be used for recanalization of occluded TIPS [31]. We used this technique in three patients with successful restoration of flow. In this study, PTFE-covered stent grafts increased primary patency significantly in comparison to bare-metal stents, showing a lower

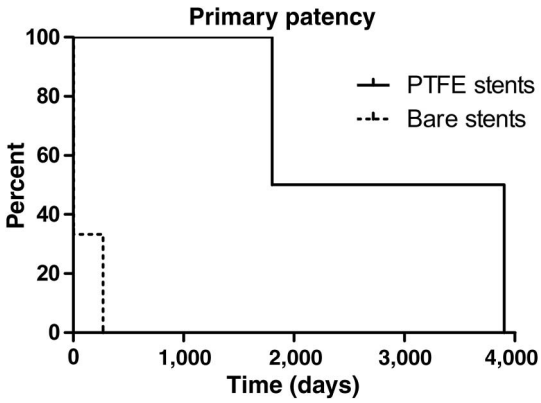

Fig. 4. Kaplan–Meier curve shows primary patency rates in relation to stent type

dysfunction rate and necessitated fewer re-interventions [32]. The use of stent grafts has been proposed for TIPS procedure in patients with BCS by different studies because it is associated with higher patency rates and lower risk of re-intervention [33–35]. Two of our patients are still in the waiting list for liver transplantation. This fact highlights the importance of DIPS maintenance during a longtime period.

Conclusion

US-guided DIPS is a safe and effective alternative technique for patients with BCS, with significant clinical improvement and low risk of complications. DIPS can be used as a bridge to liver transplantation for patients with BCS, who are not suitable for standard TIPS procedure.

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Conflict of interest: The authors declare no conflict of interest.

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