Original Article

Transjugular intrahepatic porto-systemic shunt in bleeding esophageal varices and refractory ascites. The first 4 years experience in Assiut University Hospital

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Abstract

Aim: To evaluate our first four years experience with 71 cases of TIPSS procedures performed in Assiut University Hospital. Patients and methods: Between February 2011 and April 2015, seventy-one patients who underwent TIPSS procedure in Assiut University Hospital were included in this study. The patients were selected among those suffering from refractory hepatic ascites and/or recurrent hematemesis due to variceal bleeding. Follow-up duration of our patients ranged from 3 to 34 months (mean 15.8). Results: The mean age of the patients was 47 ± 10.7 years. The technical success rate was 83%. Seventy-five percent of patients with refractory ascites improved after TIPSS. Reduction of variceal size occurred in 84.6% of patients. The 3 months mortality rate was 8%. Conclusion: Proper pre-procedural investigations and patients selection are mandatory for practicing TIPSS. BCS is a common cause of technical and clinical failure of TIPSS, so practicing TIPSS in BCS should be reserved for experts.

Keywords
TIPSS; Esophageal varices; Refractory ascites

1. Introduction

Transjugular intrahepatic porto-systemic shunt (TIPSS) was described by Josef Rosch in 1969 as a “radiologic portocaval shunt” in the frame of research on transjugular cholangiography which had already shifted to research in transjugular portography (1). This type of shunt was introduced into clinical practice by Rossle et al., in 1988 (2). Nowadays, TIPSS is an established treatment for the complications of portal hypertension. It is a creation of an intrahepatic tract between hepatic and portal veins, shunting the blood away from hepatic sinusoids to reduce the portal venous pressure. The use of TIPSS for the treatment of variceal hemorrhage refractory to...
endoscopic and medical therapy, and the treatment of refractory ascites represent 99% of all TIPSS procedures (3). The indications of TIPSS continuously expanded over the past years, to include a broader spectrum of clinical situations such as hepatorenal syndrome, cirrhotic hydrothorax, Budd–Chiari syndrome, extrahepatic portal vein thrombosis, venoocclusive disease, and hepatopulmonary syndrome (4). In this study we try to evaluate our first four years experience with 71 cases of TIPS procedures performed in Assiut University Hospital.

2. Patients and methods

Between February 2011 and April 2015, seventy-one patients who underwent TIPSS procedure in Assiut University Hospital were included in this study. The patients were selected among those suffering from refractory hepatic ascites and/or recurrent hematemesis due to variceal bleeding. All patients with hematemesis failed to respond to medical and endoscopic treatment, and all of them had at least two bleeding episodes after endoscopic treatment. The presence of esophageo-gastric varices was confirmed endoscopically. Also, we included patients with refractory ascites, lacking response to salt restriction and diuretic therapy, and needed 3 or more therapeutic paracentesis per month. We excluded patients with the following criteria: clinically significant hepatic encephalopathy grade 2 or more, portal vein thrombosis, uncorrectable coagulopathy (platelets < 40,000, prothrombin concentration < 45%, or INR > 2), moderate and severe pulmonary hypertension, serum bilirubin > 3.0 mg/dl, large or central hepatoma, congestive heart failure, multiple hepatic cysts, or uncontrolled systemic infection.

2.1. Pre-procedural evaluation

All cases were subjected to: (a) History taking which included personal history, detailed medical therapeutic history, and history of previous interventions such as endoscopic management of hematemesis, and therapeutic paracentesis (number, volume, and frequency), (b) general and abdominal examinations, (c) imaging studies included abdominal ultrasonography, color doppler evaluation of the portal and hepatic veins, echocardiography (stressed on evaluation of the ejection fraction and pulmonary arterial pressure), chest X-ray, tri-phasic CT or MRI of the liver, (d) upper GIT endoscopy and (e) laboratory investigations included Liver biochemical, and serological profile and coagulation parameters, renal functions, blood counts, serum electrolytes, and thrombophilia studies for pre-procedural diagnosed Budd–Chiari syndrome (BCS). Panel of investigations; including hepatitis markers, alpha one antitrypsin, ceruloplasmin, serum ferritin, ANA, rectal snip and liver biopsy were performed to rule out any etiology for cirrhosis before diagnosis of cryptogenic cirrhosis.

A multidisciplinary team evaluated all the patients and a written consent was taken from all patients before the procedure. Large-volume paracentesis was done regularly in patients with massive ascites a day or two before TIPSS procedure.

2.2. The procedure

All procedures were performed under general anesthesia. The right internal jugular vein was accessed using ultrasonographic guidance. A 5 F multipurpose catheter was placed into the right hepatic vein for both free and wedged hepatic venography (Fig. 1a). Thereafter, a long 10 F sheath was introduced through the jugular down the right hepatic vein (or IVC in BCS).

The portal vein was accessed using a TIPSS needle. If the needle tip was centrally placed in right (Fig. 1), or left (Fig. 2) main portal branch, we introduced an angled super stiff wire immediately down the splenic or superior mesenteric vein. If the needle tip was eccentric in the vein lumen or laterally placed needing special negotiation, we tried a 0.035-in. standard, angled tip hydrophilic wire. Then we exchanged it with the super stiff wire using a 4 F or 5 F diagnostic catheter. Thereafter, a pigtail or multi-side-hole straight catheter was used both for measurement of the portal and systemic pressures, and for doing subtraction portography. If the hepatic artery or the liver capsule was punctured during trial of portal vein accessing, we used to do tract embolization with metallic coils (if available) to avoid internal hemorrhage (Fig. 3).

Tract dilation was performed to the intended diameter of the shunt. Our standard balloon diameter was 8 mm. In few cases with highly fibrotic liver, it required initial dilation with a smaller (4–5 mm) balloon (Fig. 1b) before the introduction of the 8 mm balloon. The TIPS sheath then was advanced into the main portal vein several centimeters beyond the site of portal access for proper placement of the stent device (Fig. 1c).

We used self expandable bare metal stent (Wall-stent, Boston Scientific). The device was deployed with its upper end within 1 cm of the hepatic vein-IVC junction and lower end in the main PV. We used either fluoroscopic landmarks or angiographic image (during injection of the both the pigtail catheter and the 10 F sheath simultaneously) for mapping of the needed stent covering area. Then, we used either a graded pigtail catheter or special software of the angiography equipment for calculation of the stent length. Either digital roadmaping or fluoroscopy overlay technique was used to enable precise positioning of the stent. We post-dilated the stent using the same balloon that was used for initial tract dilation (Fig. 1d).

The multi-holes catheter was then reinserted for measurement of the portosystemic gradient (Fig. 1e). We used a target portal pressure gradient (PPG) ≤12 mmHg for patients with variceal bleeding and a gradient ≤8 mmHg for patients with ascites. If a 10-mm-diameter stent had been placed and the target portosystemic gradient had not been reached, we used to re-dilate the stent with a 9- or 10-mm balloon (except patients with previous encephalopathy).

In cases with BCS (Fig. 4) who had occlusion of all hepatic veins, we resorted to direct puncture (n = 6) of the IVC down the right portal vein or portal bifurcation (if intrahepatic). The needle was passed through the hepatic parenchyma to access the portal vein under either fluoroscopic or ultrasound guidance. The TIPSS needle was introduced through the IVC 0–2 cm below the proposed hepatic vein insertion. In cases with IVC web (Fig. 5), we did not try to recanalize the IVC and the procedure was stopped (n = 3).

Technical success was defined as successful implantation of a TIPSS stent connecting the portal venous system to the hepatic veins or IVC with significant reduction of the portal pressure gradient. Clinical success meant disappearance of patients’ clinical problems i.e. no recurrence of hematemesis and reduction of the amount of ascites.
Fig. 1 Classic TIPS procedure. Right hepatic venography (a); dilatation of the portal entry using a small balloon (b); introduction of the long sheath in the PV and doing portogram (c); postdilatation of the stent (d); and post-stenting portogram (e).

Fig. 2 Trans-left portal TIPSS. Puncture of the left PV (a); portogram with the catheter in the main PV (b); and post-stenting portogram (c).

Fig. 3 TIPSS with coiling of capsular puncture tract. Portogram showing filling of the left gastric varices (a); post-dilatation of the stent and a metallic coil in the false tract (b), and post-stenting portogram showing poor filling of the left gastric varices (c).
2.3. Early post-procedural workup

Bolus intravenous heparin of 3000 units was given to patients who have no suspicion of liver capsular puncture or lacerations. All patients were referred to a specialized liver intensive care unit. After occurrence of two stent thromboses, we began giving fractionated heparin subcutaneously for 3 days, and antiplatelet for 3 months to all patients with good bleeding indices and without capsular puncture. Intravenous proton pump inhibitor was given for 2 days. Intravenous broad spectrum antibiotic was given (cefotaxime sodium or intravenous ciprofloxacin) for one day before and 3 days after the procedure. All patients were given a full protection against hepatic encephalopathy including intravenous l-ornithine N-aspartate, oral lactulose, and rifaximin or metronidazole. Diuretics were stopped during the early post-procedural period. We performed therapeutic paracentesis for patients with marked ascites once or twice before discharge. Intravenous fluids, plasma or blood were given according to fluid charts. Early post procedural ultrasound was routinely performed to detect intraperitoneal bleeding, and Doppler Ultrasonography was used to evaluate shunt patency.

2.4. Later post-procedural visits

All patients were seen after 1–2 weeks then every 3 months after the procedure. The work-up included the following: (a) history taking with stress on any disturbance of the conscious level, number of therapeutic paracentesis needed, development of hematemesis, and diuretic dose; (b) clinical examination; (c) imaging studies (ultrasonography, color doppler, and multidetector CT in cases with suspected stent dysfunction); (d) laboratory tests (liver functions, renal functions, ascetic fluid study and full blood picture); and (e) endoscopic evaluation of variceal grade.

Follow-up duration of our patients ranged from 3 to 34 months (mean duration was 15.8 months). We excluded the failed cases and early post-procedure deaths from follow-up. Follow-up was done by out-patient clinical visits, personal communications and periodic examination of patients’ medical

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**Fig. 4**  Budd–Chiari syndrome. Coronal CT image (a); and post-TIPSS portogram (b) showing the stent connecting the portal vein to the IVC.

**Fig. 5**  Failed TIPSS of Budd–Chiari syndrome with IVC web. Transjugular (a), and transfemoral (b) inferior vena cavography showing occlusion of the suprahepatic IVC, non-filling of the hepatic veins, and dilated collaterals.
files. This was done until patient’s death, lost follow-up or the end of our study in April 2015.

3. Results

The ages of the patients ranged from 15 to 70 years. The mean age was 47 ± 10.7 years. Sixty-two percent of the patients were males and thirty-eight percent were females. The most common etiology of cirrhosis in our patients was chronic hepatitis C infection (76%), followed by chronic BCS (12.6%) (Table 1). The third cause was cryptogenic cirrhosis occurred in 10% of the patients. Only one patient had Schistosoma mansoni chronic infestation that was diagnosed by history, rectal snap, and biopsy.

The main indication for TIPSS among the patients of this study was refractory ascites that was found in 42 patients (59%). The second indication was recurrent variceal bleeding in 29 patients (41%).

The technical success rate of the procedure was 83% (59/71). Failure of the procedure occurred in 17% (12/71). Six out of the first 20 patients had failed trial (50% success rate). The other 6 failed cases occurred in the next 51 patients (88.2% success rate). Failure of PV access was encountered in 9 patients. Three of them had BCS disease. Hard track was a problem that we faced in 2 patients. In these cases we accessed the portal vein using TIPSS needle and we passed a wire into the portal vein, but we couldn’t pass a catheter or balloon due to tough liver tissue and stiff portal vein wall. Massive hematemesis occurred during the procedure in one patient, which forced us to terminate the procedure and applied a Sengstaken–Blakemore tube to stop bleeding. We stopped the procedure in 3 cases after diagnosis of IVC web, because we have not enough experience to recanalize the IVC.

The porto-systemic gradient ≤8 mmHg was achieved in only 23 (54.8%) patients with refractory ascites. The presence of mild encephalopathy in many cases prevented us from over-dilatation of the stent to avoid worsening of encephalopathy. Seventy-five percent (75%) of patients with refractory ascites had lesser sonographic grade of ascites, improved quality of life and needed lower doses of diuretic during the follow-up (Fig. 6). Ten patients (27.8%) had no ascites at the last follow-up visit. Nine patients (25%) still had refractory ascites after stenting. Seven of them (77.7%) had stent dysfunction (thrombosis or stenosis).

Esophageal varices were detected in 39 patients. Twenty-nine of them developed repeated hematemesis, and the other 10 patients were detected during routine preprocedural evaluation for TIPSS that was indicated for treatment of refractory ascites. Reduction of variceal size occurred in 84.6% of patients on follow-up endoscopy (Table 2). Complete disappearance of varices occurred in 12.8% of patients. Four patients (10.3%) suffered from hematemesis within the first month after TIPSS. Two of them were found to have gastric ulcers. The other 2 patients had shunt thrombosis and were managed by endoscopic band ligation.

Intraprocedural complications included (Table 3) puncture of the liver capsule in 4 patients and puncture of hepatic artery in 2 patients. We deployed coils to ensure occlusion of the parenchymal tract in 4 patients who passed with uneventful recovery. One of the two patients for whom we did not embolize the tract after capsular puncture developed significant (about 400 cc) hemoperitonium. He was managed conservatively and the hemoperitoneum resolved within few days. One patient with refractory ascites suffered from respiratory embarrassment during recovery from anesthesia. He was treated successfully with paracentesis of 3 l of ascetic fluid and endotracheal re-intubation for oxygen administration. Also, puncture of the biliary tree occurred in 5 patients with no special measures taken. The overall rate of TIPSS failure was 30.5% (18/59) of our patients after successful procedure. Two patients developed stent thrombosis 24 h, and 7 days after the procedure consequently. The first patient had BCS with hypercoagulability, and the stent was just flushed with the wall of the IVC (inadequate stent covering). Most of the stent stenoses (56%) occurred during the first 6 months, 33% occurred after 6–12 months, and only 11% occurred after 1 year. Hepatic encephalopathy was encountered in 16 of successful cases (27.6%). It was more frequent during the first 3 months after the procedure (50%) and less frequent during the next three months (35.6%).

In this study, 2 patients died during the first week after the procedure. One of them died of acute right sided heart failure 3 days after the procedure, and the other of massive unexplained hematemesis a day after the procedure. The 3 months mortality rate was 8% (6/71).

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Table 1 Causes of liver cirrhosis in the study group.

<table>
<thead>
<tr>
<th>Cause of cirrhosis</th>
<th>(n = 71)</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>54</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td>Budd-Chiari</td>
<td>9</td>
<td>12.6</td>
<td></td>
</tr>
<tr>
<td>Cryptogenic</td>
<td>7</td>
<td>10</td>
<td></td>
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<tr>
<td>Bilharzial</td>
<td>1</td>
<td>1.4</td>
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</table>

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Table 2 Response of esophageal varices (OV) to TIPSS.

<table>
<thead>
<tr>
<th>OV changes</th>
<th>(n = 39)</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Disappeared</td>
<td>5</td>
<td>12.8</td>
</tr>
<tr>
<td>Decreased</td>
<td>28</td>
<td>71.8</td>
</tr>
<tr>
<td>No improvement</td>
<td>6</td>
<td>15.4</td>
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</table>

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Fig. 6 Grades of ascites after TIPSS.
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4. Discussion

TIPSS creation could be technically difficult and so should only be performed by a suitably experienced interventional radiologist (5). The success rate with TIPSS for the decompression of the portal vein is as high as 90% in most series (6–8). In this study, the technical success rate was 83.1%. The success rate increased with time; it was 50% success in the first 20 cases, and reached 88.2% in the next 51 cases. We improved our skills by: better pre-procedural interpretation of the radiological images, proper selection of the patients, and improvement of our practice with more cautious PV targeting, and good preparation of the material and equipments of various sizes, types and different manufacturers.

Therapeutic approaches for patients with the BCS include medical management, percutaneous or transhepatic angioplasty of the narrowed hepatic vein or IVC web (9,10), TIPSS (11,12), surgical shunts (portal or mesenteric–systemic shunts) (13,14), and liver transplantation in selected patients. TIPSS provides instant decompression of both sinusoidal and splanchnic beds and facilitates arterial perfusion. In these cases, TIPSS could be performed either by transjugular cavo-portal shunt, or by transhepatic retrograde approach. In this study, we did not try IVC web dilatation in three patients, and we failed to construct TIPSS in another three patients. Hence, BCS was the most common cause of technical failure.

Many challenges faced us and technical tricks helped us to overcome these situations. The first trick is the manipulation of TIPS needle to gain more or less angulations to overcome spatial PV and HV relative orientation. The second is the use of hydrophilic wire to negotiate the PV after its puncture in more lateral position. The third is the use of hydrophilic Cobra catheter instead of MP catheter for catheterization of hard tract or stiff portal vein wall.

Development of ascites is associated with a poor quality of life, increased risk of infections and renal failure, and a poor long-term outcome (15). Cirrhotic patients who develop ascites have a probability of survival of 85% at 1 year and 56% at 5 years without liver transplantation (16). In patients who become resistant to diuretic therapy, the prognosis decreases to 50% survival at 2 years (17). A meta-analysis study was published in 2005 (18) comparing TIPSS to large volume paracentesis (LVP) in the treatment of patients with refractory cirrhotic ascites. In the TIPSS groups the percentage (mean ± SD) of patients who showed improvement in their ascites was 62.0 ± 19.2% while in the LVP groups improvement was seen in 23.6 ± 18.5% of patients. In another meta-analysis study published in 2007 (19), TIPSS was more effective than paracentesis and its use was associated with a significantly better transplant free survival (TIPS year-1, 63.1%; year-2, 49.0%; versus LVP year-1, 52.5%; year-2, 35.2%). Encephalopathy occurred somewhat more frequently in the TIPSS groups as compared to the LVP groups (39.4 ± 20.9% and 22.6 ± 13.9% of patients, respectively).

Many authors (20–22) found that the 1-year survival for TIPSS patients when the indication was bleeding varices (48–90%), is similar to those for ascites (48–76%). In one study, the survival rate was significantly worse when the indication was refractory ascites compared with variceal bleeding (23). These differences likely reflect variations in the severity of liver disease between the different studies. It may be difficult to establish an absolute value of decompression in patients with refractory ascites and pre-existing encephalopathy. We achieved the 8 mmHg PSG in only 54.8% (23/42) of our patients, treated for refractory ascites. However, 75% improved after TIPS with lesser sonographic grade of ascites, and lower doses of diuretics. These data suggest that higher gradient may be appropriate in such patients to avoid worsening of encephalopathy.

Two meta-analysis studies were reported in 1999 (24), and 2008 (25) comparing TIPSS to endoscopic therapy. The results of both studies showed that TIPSS mirrors the results with surgical shunts, i.e. there is less rebleeding compared to endoscopic therapy but at the price of more encephalopathy without an improvement in overall survival. In this study, the reduction of variceal size (endoscopically) occurred in 84.6%, and complete disappearance of varices occurred in 12.8% of patients. Rebleeding after TIPSS occurred in 13.7% of successful cases which is similar to the majority of the previously published data with rebleeding rates ranged from 9% to 23% (26).

In a retrospective series (27) of 1750 patients the incidence of fatal complications (intra-abdominal hemorrhage, laceration of the hepatic artery or portal vein, and right heart failure) was 1.7%. In a study included 119 TIPSS procedures, Baldini et al. (28) stated that the survival rate was 87% at three months, 74% at one year, and 57% at three years. In this study we achieved 89.8% survival rate at the first 3 months, and 84.7% at one year which is comparable to that of the literature. We have only one periprocedural death mostly due to acute right sided heart failure. All patients with puncture of the liver capsule or hepatic artery were managed conservatively. We did not embolize the tract with coils in two patients, and one of them developed hemoperitoneum, reflecting the importance of tract occlusion with hemostatic device after capsular puncture.

Porto-systemic encephalopathy (PSE) is a very frequent complication, and certainly constitutes one major drawback of TIPS, probably the most limiting one in terms of the indication of TIPS insertion (4). The overall incidence of HE (27.6%) among our patients was lower than that published (35–55%) in the previous studies (29,30). It could be due to cautious selection of patients and avoiding overdilatation of the stent even if the targeted pressure gradient was not achieved in patient with previous mild encephalopathy. Fifty percent of PSE occurred in the first 3 months after TIPSS procedure, and 35.6% during

<table>
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<th>Table 3 Complications of TIPSS procedures.</th>
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<tr>
<td>TIPSS complications</td>
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</tr>
<tr>
<td>Procedural complications</td>
</tr>
<tr>
<td>• Liver Capsule puncture</td>
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<td>• Bile duct puncture</td>
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<td>• Hepatic artery puncture</td>
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<tr>
<td>• Accidental massive hematemesis</td>
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<tr>
<td>Post procedural complications</td>
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<tr>
<td>• Encephalopathy (new or worse)</td>
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<tr>
<td>o Mild</td>
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<tr>
<td>o Severe</td>
</tr>
<tr>
<td>• Stent stenosis</td>
</tr>
<tr>
<td>• Congestive heart failure</td>
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<tr>
<td>3-months mortality</td>
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</tbody>
</table>

| Stent stenosis | 18 | 30.5 |
| Accidental massive hematemesis | 1 | 1.4 |
| Hepatic artery puncture | 2 | 2.8 |
| Bile duct puncture | 5 | 7 |
|  MILD | 4 | 7 |
|  SEVERE | 12 | 20 |
| Stent stenosis | 18 | 30.5 |
| Congestive heart failure | 1 | 1.7 |
| 3-months mortality | 6 | 8 |
the next three months. This is the time at which the stent is fully patent, and portal pressure is lower than 12 mm Hg (4). In this study, hepatic encephalopathy was significantly higher in patients with refractory ascites than patients with rebleeding varices (37% versus 13% respectively), because the former were cirrhotic patients already in the decompensated phase of the disease. Most of the episodes of hepatic encephalopathy were of mild degree (grade I–II), and the most common precipitants were diet rich in animal protein and diuretic over-dose. Thus, dietary restriction of animal proteins, and avoidance of diuretic overdose are of paramount importance in avoiding hepatic encephalopathy.

It was reported that up to 70% of patients experience some degree of TIPS stenosis within the first year (4). In our study, the incidence of stent stenosis or thrombosis was 31% within 36 months of follow-up. Fifty-five percent were due to shunt thrombosis during the first 3 months after stenting. Some authors (30,31) reported that the causes of stent thrombosis include leakage of bile into the shunt, hypercoagulable syndromes, or inadequate coverage of the TIPS tract with sufficient stents. Inadequate stent coverage of the tract with subsequent stent thrombosis was reported in one of our patients with BCS. However, we didn’t find any relation between bile duct injury and stent stenosis, as only two of five patients underwent bile duct puncture, developed late stent stenosis.

5. Conclusion

TIPS is an effective procedure to prevent rebleeding from varices and decrease the need paracentesis and diuretics in patients with refractory ascites. Creation of TIPSS ranks among the more complex interventional techniques; hence, proper selection of the patients and proper pre-procedural investigations are mandatory for practicing TIPSS. BCS is a common cause of technical and clinical failure of TIPSS, so practicing TIPSS in BCS should be reserved for experts.

Conflict of interest

The authors declare that there are no conflict of interests.

References