ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 05, pp.30521-30524, May, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

SELECTION OF TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT STENTS FOR CONTROLLING PORTAL HYPERTENSION

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ARTICLE INFO

Article History:
Received 16th February, 2016
Received in revised form
27th March, 2016
Accepted 24th April, 2016
Published online 10th May, 2016

Key words:
Transjugular intrahepatic portosystemic Shunt; Liver cirrhosis;
Portal hypertension;
Hepatic encephalopathy;
Variceal bleeding;
Shunt dysfunction.

ABSTRACT

Background: Nowadays, transjugular intrahepatic portosystemic shunt (TIPS) has become a mainstay treatment option for the management of portal hypertension-related complications in liver cirrhosis. Accumulated evidence has shown that its indications are being gradually expanded. Notwithstanding, less attention has been paid for the selection of an appropriate stent during a TIPS procedure.
Aim: To evaluate efficacy of transjugular intrahepatic portosystemic shunt stent for decreasing portal pressure and estimate stent diameter according to the classification and patient condition.
Materials and Methods: We observed and surveyed 67 patients between 2002 and 2014, 67 patients with cirrhosis (60 males) with a mean age 51.08±12.574 years underwent TIPS in the Tashkent Medical Academy II clinic (18 patients) and Chonnam National University Hospital (49 patients) who underwent TIPS. 17 patients were infected with hepatitis B virus, 6 patients were with hepatitis C, 1 patient were diagnosed with both of HBV, HCV, and histiocytosis. In 2 patients developed cirrhosis cause of both alcohol and hepatitis B virus. The hepatic function status evaluated by Child-Pugh classification.
Results: We compared patients' condition and complications of the TIPS according to stent diameter. The first month mortality rate was higher in the 12-mm stent group than in the 10-mm stent group. The 10 mm stents were more effective than the 8 mm stents for reducing portosystemic pressure gradient after TIPS (6.5±2.7 mm Hg *and* 8.9±2.7 mm Hg, *P*=0.007). A 10-mm stent group was superior to the 8-mm stent group for decreasing the first year rate of remaining free of recurrence and/or persistence of complications due to portal hypertension (82.9% *and* 41.9%, *P* = 0.002, by Log-Rank test).
Conclusion: The study showed that a 10-mm stent might be effective and brought less complication than an 8-mm or 12-mm stent for the management of PH and the development of shunt patency. Covered stents are better than bare stents for decreasing the shunt dysfunction. The placement of a stent in the left portal vein branch may enhance the hepatic perfusion and decrease the incidence of hepatic encephalopathy.

Citation: Utkirbek Matkuliev, Kim Jae Kyu, and Bekhzod Abdullaev, 2016. "Selection of transjugular intrahepatic portosystemic shunt stents for controlling portal hypertension", *International Journal of Current Research*, 8, (05), 30521-30524.

INTRODUCTION

In Asia, portal hypertension develop after cirrhosis of the liver in over 95 % of cases. Cirrhosis of the liver is caused by chronic viral hepatitis B and C abuse in about 4/5 of the cases; 1/5 is due to alcohol and the remainder is the result of various metabolic or idiopathic disorders of the liver (Hoppe *et al*., 2008).

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Transjugular intrahepatic portosystemic shunt (TIPS) is effective method of creating a portosystemic shunt to decrease or treat portal hypertension. TIPS is a side-to side shunt of a determined diameter designed to function as a partial shunt that preserves a portion of portal flow to the liver. Flow through the completed shunt is assessed by comparing the degree of privileged filling of the shunt to that of the portal vein branches and portosystemic collaterals (mainly in the gastric veins). The identification of hepatofugal (reversed) blood circulation in portal vein branches (total shunting) is a sign of good flow through the shunt. Technical success is defined as a decrease of the portosystemic pressure incline to 12 mm Hg or less, or a

reduction of at least 25-30 % (Petersen *et al*., 2004). TIPS should be used as the rescue treatment for acute variceal bleeding that is not responsive to medical and/or endoscopic therapy in liver cirrhosis (Ro¨sch *et al*., 1969). However, after TIPS in patients who underwent TIPS that develop liver failure and encephalopathy. Thus, this cannot be the most effective method to manage portal hypertension in liver cirrhosis.

MATERIAL AND METHODS

Patient data

Between 2002 and 2014, 67 patients with cirrhosis (60 males) with a mean age 51.08±12.574 years underwent TIPS in the Tashkent Medical Academy II clinic (18 patients) and Chonnam National University Hospital (49 patients). 17 patients were infected with hepatitis B virus, 6 patients were with hepatitis C, 1 patient were diagnosed with both of HBV, HCV, and histiocytosis. In 2 patients developed cirrhosis cause of both alcohol and hepatitis B virus. The hepatic function status evaluated by Child-Pugh classification was group A in 24 patients, group B in 28 and group C in 15 patients (Table 1). All patients had complications from cirrhosis and portal hypertension. The indications for using TIPS were uncontrollable ascites (n=59) and gastrointestinal bleeding (n=8). In 5 patients were cannulation and all of them operations were failed. In 9 patients have developed thrombosis. After surgical treatment, 11 stents were blocked by a clot.

Table 1. Patient data

Clinical factor	No. of patients
Sex	
Male	60
Female	7
Age (year, mean ± SD)	51.08±12.574
Indication for TIPS	
Hemorrhage of upper digestive tract	28
Hepatorenal syndrome	12
Cause	
Cirrhosis after hepatitis B virus infection	27
Cirrhosis after hepatitis C virus infection	6
Hepatatis B virus infection complicated by hepatitis C and histiocytosis	1
Hepatitis B virus infection complicated by alcoholic cirrhosis	2
Alcoholic cirrhosis	14
Unexplained cirrhosis	17
Child-Pugh grading	
A	24
B	28
C	15

TIPS placement technique

TIPS procedure was performed in the Interventional Radiology Suite under local anesthesia. The Graft Transjugular Liver Access Set (Seoul, South Korea) was used for every patient. Right jugular venous access was established with a 10-F sheath. A 5-F multipurpose catheter was used to engage the right hepatic vein and perform angiography, and a curved cannula was then advanced with the guide wire into the right hepatic vein. A sheathed needle was advanced into the portal vein through the liver parenchyma and the guide wire was placed into the portal vein through the sheath. Portal vein angiography was performed with a 5-F pigtail catheter and portal vein pressure and right atrium pressure were measured. Subsequently, the shunt tract was dilated with an angioplasty balloon ranging from 6 to 12 mm, and a covered stent with a diameter of 6 or 12 mm was utilized. The varicose coronary gastric vein was embolized to prevent future gastrointestinal bleeding and the portal vein angiography and pressure measurements were performed again. The PSG was determined before and after the shunt creation. In ten patients, ascites was not released and periodic gastrointestinal bleeding occurred in the other patient, even though ultrasound proved the patency of all the first shunt tracts. Therefore, a second TIPS was established in 7 patients 3 month after the first procedure. Third TIPS was established in 5 patients. The right jugular venous access was used for the second shunt tract. Through the first shunt tract, portal vein angiography was carried out and pressure was measured.

Diameter of TIPS stents

Theoretically, a larger diameter of TIPS stent can reach the target portosystemic pressure gradient (PSG) more effectively and rapidly. However, the excessive shunting of portal blood flow can induce the development of hepatic dysfunction and encephalopathy. Thus, it is important to choose an appropriate diameter of stent to balance between the efficiency and complications of TIPS (Ro¨sch and Haskal, 2010). Stents were used according to Child-Pugh classification and degree of the liver failure. Retrospective study compared the outcomes of TIPS between cirrhotic patients receiving 6 mm (n=1), 7 mm (n=3), 8 mm (n=9), 9 mm (n=11), 10 mm (n=29), 12 mm (n=14) Wall stents. The first day occlusion rate was significantly higher in the 12-mm stent group than in the 10-mm stent group (21% *and* 0% *respectively*). However, the long-term primary and secondary patency rates were similar between the two groups.

Statistical analysis

Microsoft Office Excel 2013 in Windows 7 MS was used for data processing and statistical analysis, with paired sample *t* test for data measurement. Data are summarized and as frequencies and continuous variables as mean ± standard deviation (SD). $P < 0.05$ was considered statistically important.

RESULTS

Complication of TIPS

All the patients were under close monitoring during the perioperative period. Complications including abdominal cavity hemorrhage, hepatic failure and hepatic encephalopathy (HE) were observed. We compared patients' condition and complications of the TIPS according to stent diameter. Additionally, the first month mortality rate was higher in the 12-mm stent group than in the 10-mm stent group (25% *and* 6% *respectively*). More importantly, the survival time was significantly shorter in the 12-mm stent group than in the 10-mm stent group ($P < 0.03$) over the course of the study. Recently, in Uzbekistan, single-center, randomized controlled trial compared the outcomes of TIPS between cirrhotic patients

with variceal rebleeding or refractory ascites receiving 8 mm (*n*=7) and 10 mm (*n*=21) stents. The 10 mm stents were more effective than the 8 mm stents for reducing portosystemic pressure gradient after TIPS (6.5±2.7 mm Hg *and* 8.9±2.7 mm Hg, *P*=0.007). Accordingly, the 10-mm stent group was also superior to the 8-mm stent group for decreasing the 1-year rate of remaining free of recurrence and/or persistence of complications due to portal hypertension (82.9% *and* 41.9%, *P* = 0.002, by Log-Rank test). On the basis of these findings, it might be recommended that the 10 mm stent, rather than 12 mm or 8 mm stent, was more appropriate for TIPS procedure. Notably, the latter clinical trial was prematurely stopped due to the side effects of treatment failure from the 8-mm stent group. In this case, the statistical difference in the incidence of post-TIPS hepatic encephalopathy as the primary endpoint could not be reached. Additionally, the subgroup analysis of this trial did not show any significant improvement of variceal rebleeding in the 10-mm stent group.

Clinical effects of TIPS

The short-term hemostasis rate was 100% when TIPS was used in the treatment of emergency hemorrhage and recurrent hemorrhage unresponsive to medication, endoscopy or surgery. Ascites disappeared completely in 58% of patients, decreased obviously in 26% and remained in 16%. The total effective rate was 84%. Hydrothorax completely disappeared in 100% of patients. Ascites completely disappeared in 6 patients and was obviously reduced in 8 after 7-14 day of observation.

Hemodynamic changes

TIPS altered the portal pressure in all patients after the second operation. The mean portal system pressure prior to TIPS placement was 53.67 ± 4.21 mm Hg, which decreased to 25.10 ± 4.06 mmHg after the first shunt tract was established ($P < 0.001$). The mean portal system pressure prior to the second TIPS was 43.68 ± 3.98 mm Hg and decreased to 25.14 ± 4.67 mm Hg after the procedures ($P < 0.001$). The mean PSG prior to the TIPS placement was 43.80 ± 6.18 mmHg, which decreased to 15.27 ± 3.32 mm Hg after shunt tract was established ($P < 0.001$). The mean PSG prior to the next TIPS was 37.40 ± 2.76 mm Hg and decreased to 16.20 ± 3.17 mm Hg after the procedures ($P < 0.001$).

Follow-up

All the 67 patients who underwent TIPS were followed up. Stent function, hemorrhage, hepatic encephalopathy, hepatorenal syndrome and survival were observed during the follow-up. The incidence of recurring hemorrhage was 8% in 12 month, 18% in 24 month and 37% in 36 month. The incidence of stent stenosis was 24% in 12 month and 34% in 24 month postoperatively (Table 1). The incidence of hepatic encephalopathy was 14% in 3 month, 17% in 6 month and 19% in 12 month. The cumulative survival rate was 86% in 12 month, 81% in 24 month, 75% in 36 month, 57% in 48 month and 45% in 60 month. In our center, 3 patients died 1 month after TIPS, of whom 2 died of hepatic failure and 1 of septicemia.

DISCUSSION

TIPS is an effective method of treating complications of portal hypertension due to cirrhosis, and has been utilized extensively in clinical practice as a safe and minimally invasive procedure. Liver transplantation has not yet been popularized, therefore, TIPS is of major importance worldwide. TIPS has been proven to be effective in 62.4-92 % of cases for secondary prevention of variceal bleeding and in 36-83% of cases in controlling ascites. The symptoms improved after the TIPS procedure in our study. We believe that uncontrolled ascites and gastrointestinal bleeding after the TIPS procedure were due to high portal vein pressure and insufficient portosystemic pressure gradient (PSG) reduction. In our study, the mean portal vein pressure prior to TIPS was 53.67 ± 4.21 mm Hg, which was 10-15 mm Hg higher than that in patients who underwent TIPS reported before. The symptoms were controlled after the second procedure when the mean portal vein pressure decreased to 25.10 ± 4.06 mm Hg and the mean PSG decreased to 15.27 ± 3.32 mm Hg. When the first shunt was patient, which reduced the PSG to 9 mm Hg and relieve clinical symptoms. Parvinian reported two cases of parallel TIPS for treatment of complications of cirrhotic portal hypertension, with reduction of PSG to 12 and 10 mm Hg. The American Association for the Study of Liver Diseases (AASLD) recommends reducing PSG to < 8 mm Hg to improve quality of life. Reducing the portal vein pressure and PSG to an acceptable level is the key point of TIPS procedures. Covered stent implants have been regularly applied in TIPS procedures and have increased the patency rates. However, utilization of covered stent implants in TIPS procedures also increases the risk of hepatic encephalopathy (HE). In this study, 4 of 67 patients experienced transient grade HE, which may have resulted in a significant increase in outflow or large PSG reduction. In cases with TIPS, close attention should be paid to HE, and treatment against encephalopathy should be given before and after the procedure.

Conclusion

Selection of suitable stent during a TIPS procedure is very important for the shunt function and treatment efficacy. By studying the current indication, several following recommendations may be considered in the clinical practice:

- A 10-mm stent may be effective and brought fewer complication than an 8-mm or 12-mm stent for the management of PH and the development of shunt patency;
- Covered stents are better than bare stents for decreasing the shunt dysfunction;
- The placement of a stent in the left portal vein branch may enhance the hepatic perfusion and decrease the incidence of hepatic encephalopathy.

However, we have to accept that these recommendations are based on a majority of the studies. Therefore, potential well-designed studies should be warranted to confirm them.

Consent

It is not applicable.

Ethical Approval

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Acknowledgments

We thank Shavkat Ibragimovich Karimov for his help in initiating the study. The study was determined Tashkent Medical Academy II clinic and Chonnam National University Hospital.

Competing Interests

Authors have declared that no competing interests exist.

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