

# Construction of Transjugular Intrahepatic Portosystemic Shunt: Bare Metal Stent/Stent-graft Combination versus Single Stent-graft, a Prospective Randomized Controlled Study with Long-term Patency and Clinical Analysis

Chang-Ming Wang, Xuan Li, Jun Fu, Jing-Yuan Luan, Tian-Run Li, Jun Zhao, Guo-Xiang Dong

Department of Interventional Radiology and Vascular Surgery, Peking University Third Hospital, Beijing 100191, China

## Abstract

**Background:** Balanced adjustment of the portal vein shunt volume during a transjugular intrahepatic portosystemic shunt (TIPS) is critical for maintaining liver perfusion and decreasing the incidence of liver insufficiency. A stent-graft is proved to be superior to a bare metal stent (BMS) for the construction of a TIPS. However, the clinical results of the combination application of stents and stent-grafts have not been determined. This study aimed to compare the technique of using a combination of stents and stent-grafts with using a single stent-graft to construct a TIPS.

**Methods:** From April 2011 to November 2014, a total of fifty patients were randomly assigned to a stents-combination group (Group I,  $n = 28$ ) or a stent-graft group (Group II,  $n = 22$ ). Primary patency rates were calculated. Clinical data, including the technical success rate, bleeding control results, incidence of encephalopathy, liver function preservation, and survival rate, were assessed.

**Results:** Technically, the success rate was 100% for both groups. The primary patency rates at 1, 2, and 3 years for Group I were 96%, 84%, and 77%, respectively; for Group II, they were 90%, 90%, and 78%, respectively. The survival rates at 1, 2, and 3 years for Group I were 79%, 74%, and 68%, respectively; for Group II, they were 82%, 82%, and 74%, respectively. The incidence of hepatic encephalopathy was 14.3% for Group I and 13.6% for Group II. The Child-Pugh score in Group I was stable at the end of the follow-up but had significantly increased in Group II ( $t = -2.474$ ,  $P = 0.022$ ).

**Conclusions:** The construction of a TIPS with either the single stent-graft or BMS/stent-graft combination is effective for controlling variceal bleeding. The BMS/stent-graft combination technique is superior to the stent-graft technique in terms of hepatic function preservation indicated by the Child-Pugh score. However, considering the clinical results of the TIPS, the two techniques are comparable in their primary shunt patency, incidence of encephalopathy and patient survival during the long-term follow-up.

**Key words:** Esophageal and Gastric Varices; Hypertension, Portal; Radiology, Interventional; Stent

## INTRODUCTION

Transjugular intrahepatic portosystemic shunts (TIPSS) are currently used for the treatment of portal hypertension complications, especially variceal bleeding refractory to medical or endoscopic treatment. However, shunt dysfunction, hepatic encephalopathy (HE), liver insufficiency, and even liver failure remain frequent complications of the procedure.

Stent-grafts have been proved to be superior to bare metal stents (BMSs) in terms of shunt patency.<sup>[1]</sup> Thus, the

specialized stent-graft Viatorr® (W. L. Gore & Associates, Inc., AZ, USA) TIPS endoprosthesis has been widely adopted to create a TIPS.<sup>[2]</sup>

**Address for correspondence:** Prof. Xuan Li,

Department of Interventional Radiology and Vascular Surgery, Peking University Third Hospital, No. 49, Huayuanbeilu Road, Haidian District, Beijing 100191, China  
E-Mail: lixuanbysy@163.com

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A balanced adjustment of the portal vein shunt volume during the operation is critical for maintaining liver perfusion and decreasing the incidence of liver insufficiency.<sup>[3]</sup> In most guidelines, the emphasis of TIPS is on reducing the portosystemic gradient (PSG), not on PSG adjustment. An excess shunt flow volume depends on the revision procedures thereafter. In fact, some of the shunt flow volumes were never revised due to deteriorated liver function.

Inspired by the shunt flow reduction procedures used in the treatment of HE,<sup>[4,5]</sup> we tried using a BMS/stent-graft combination to create a TIPS. During a step-by-step employment of the stents, we tried to precisely cover the parenchymal segment of the shunt with a stent-graft while maintaining nutrient portal perfusion and to actively adjust the PSG by implementing various combinations of percutaneous transluminal angioplasty (PTA) balloons and stents.

Thus, the aims of the present prospective randomized control study were to investigate the probability of PSG adjustment in the step-by-step shunt creation procedures and to compare the clinical results of the stent combination technique for the creation of a TIPS with a routine stent-graft technique in the treatment of variceal bleeding due to portal hypertension.

## METHODS

### Study design

This study was designed as a prospective, randomized, single-center, open-label, active control trial to investigate the efficacy of a stents-combination technique for the creation of a TIPS, and a classical single stent-graft (Fluency<sup>®</sup>, Bard International, Inc., USA because Viatorr<sup>®</sup> is not available here) technique was the control arm. The trial was performed in our department.

Between April 2011 and November 2014, fifty consecutive cases of variceal bleeding due to portal hypertension were enrolled in the study. The ethics committee of our hospital approved the study protocol. The inclusion criteria were (1) a definite diagnosis of variceal bleeding due to portal hypertension by endoscopy, (2) medical and endoscopic treatment failure, (3) age between 18 and 75 years with written informed consent, and (4) absence of early-stage cancer or malignancy. The major exclusion criteria were (1) previous interventional or surgical shunt treatment, (2) thrombosis or cavernous transformation of the portal vein, (3) Child-Pugh's score >10, and (4) poor operation tolerance because of comorbidities such as heart failure.

Patients enrolled were randomized into two treatment arms, a stents-combination arm (Group I) and a stent-graft arm (Group II), according to a computer-generated randomization list made by an independent biostatistics unit before the study. The purpose of the study, enrollment and randomization procedures, and details of the TIPS operation were clearly explained to all patients before obtaining their written informed consent. The same interventional radiology team carried out all of the TIPS procedures.

### Diagnosis and definitions

In our study, a gastroscopy was used as both a first-line diagnosis measure and a temporary hemostasis measure of variceal bleeding. If a patient's condition was adequately stable, computed tomography (CT) was undertaken to clarify the status of the liver and the portal vein system to determine any possible malignancies and to exclude portal vein occlusion, cavernous transformation, extensive thrombosis, and other adverse conditions. If the condition of a patient was unstable, they were transferred directly from the emergency room to the interventional catheterization room for an emergency operation.

A confirmation diagnosis of liver cirrhosis was established by the history of liver disease, signs of portal hypertension, ultrasonography or CT exam of the liver, and deteriorated liver function.

Technical success of the shunt was defined as (1) a shunt created between the portal vein branches and inferior vena cava (IVC) with the stents in the right position and (2) PSG decreased to <50% of its original value.<sup>[6]</sup>

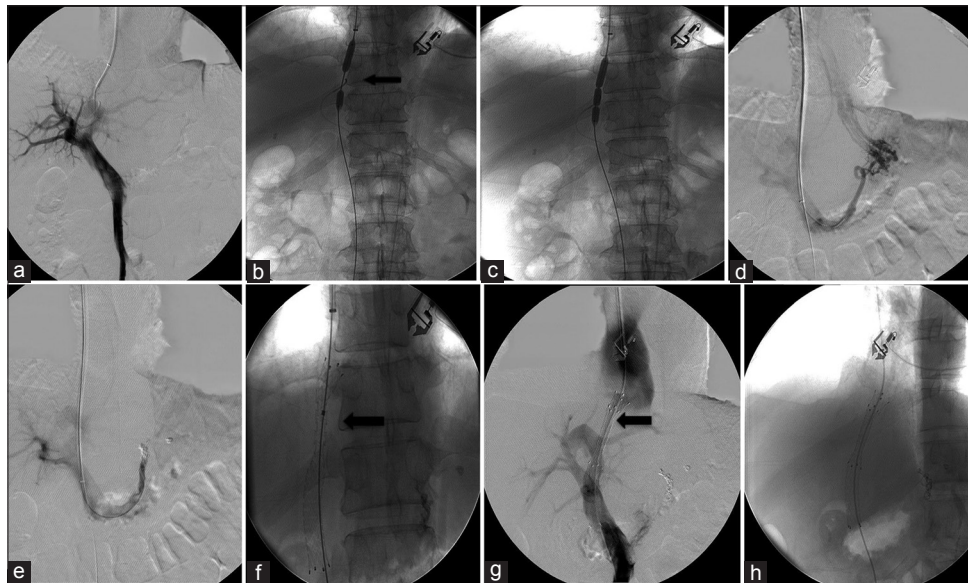
Shunt dysfunction was suspected when the following conditions arose: (1) variceal bleeding recurrence, (2) increasing ascites, or (3) a shunt maximum flow velocity <50 cm/s or an absence of flow by Doppler ultrasound. A CT scan was then used to show details of the liver, portal vein, and stents. However, shunt dysfunction was finally confirmed by portography and portal venous pressure measurements that showed an obliterated shunt or shunt stenosis >50% and/or PSG >12 mmHg (1 mmHg = 0.133kPa).<sup>[6,7]</sup>

### Transjugular intrahepatic portosystemic shunt procedures for the stents-combination and stent-graft groups

All TIPS procedures were performed under local anesthesia and used a transjugular approach. An RUPS-100 puncture set (Cook, Bloomington, IN, USA) was used in all patients. Indirect portography was achieved by a superior mesenteric arteriography or splenography. An angiography catheter was then selectively inserted into the left hepatic artery and kept there for an indirect indication of the left portal vein, which was our preferable target vessel for puncture. Once a successful puncture of the portal vein was achieved, a pigtail angiographic catheter was introduced into the superior mesenteric vein (SMV) to obtain an outline of the portal venous anatomy [Figure 1a]. The pressure of the portal vein and IVC was then recorded.

A guide wire (0.035 in., Amplatz Super Stiff, Cordis Corporation, Fremont Campus, CA, USA) was introduced and kept in the SMV. A  $\Phi 6$  mm  $\times$  6 cm PTA-balloon was led into the shunt for dilation. The parenchymal segment of the shunt was clearly shown and its distance was recorded as shown in Figure 1b and 1c.

A 10-F sheath was advanced into the main stem of the portal vein. A 4-F Cobra catheter was introduced into the gastric coronary vein to identify the variceal veins and embolize them with coils [Figure 1d and 1e].



**Figure 1:** Procedures of TIPS in stents-combination Group. (a) The umbilical portion of left portal vein was punctured with RUPS-100 system under the guidance of deliberately placed catheter into the left hepatic artery beforehand. (b) The shunt was dilated with PTA balloon (the arrow indicated the liver parenchymal segment of the shunt). (c) The length of the parenchymal segment was measured. (d and e) Variceal veins were identified and embolized with coils. (f) BMS was placed, the narrowed area corresponding to the parenchymal segment (indicated by the arrow). (g) The parenchymal area was covered by the stent-graft (indicated by the arrow). (h) The final status of the stents-combination. TIPS: Transjugular intrahepatic portosystemic shunt; PTA: Percutaneous transluminal angioplasty; BMS: Bare metal stent.

For the stents-combination group, a BMS ( $\Phi = 10$  mm, E-Luminexx<sup>®</sup>, Bard International, Inc., NJ, USA) was positioned between the left portal vein and IVC. With the deployment of the BMS, the liver parenchymal segment of the shunt was clearly displayed [the narrow segment of the stent, Figure 1f] for stent-graft deployment. PSG was measured. If it was higher than required, the shunt was dilated with a larger diameter PTA balloon ( $\Phi > 6$  mm). The corresponding diameter stent-graft (Fluency<sup>®</sup>) was then deployed to exactly cover the parenchymal section of the shunt [Figure 1g and 1h]. If the PSG was lower than required, a smaller diameter stent-graft (Fluency<sup>®</sup>) was deployed with the corresponding length of the parenchymal section. A final PSG was then recorded.

For the stent-graft group, when the 10-F sheath was introduced into the main stem of the portal vein and the variceal veins were embolized, the portal pressure was recorded, and the PSG was calculated. A 8- or 10-mm-diameter stent-graft (Fluency<sup>®</sup>) (depending roughly on the PSG) was deployed to connect the left portal vein and IVC.

Intraoperatively, one dosage of intravenous heparin (80 IU/kg) was injected. Postoperatively, an intravenous heparin infusion was continued for 24 h to achieve an activated partial thromboplastin time of up to 2 times the upper limit of normal to prevent shunt thrombosis. No anticoagulation or antiplatelet therapy was scheduled thereafter.

Intravenous branched chain amino acids and antibiotics were administered as prophylactics for encephalopathy and infection, respectively, for 3–5 days before discharge. A low-protein diet was suggested. A TIPS revision was planned if any evidence of shunt dysfunction was seen.

### Follow-up

A clinical follow-up was performed at 1, 3, 6, and 12 months postoperatively. Thereafter, the visits were semiannual until the end of the study, including a scheduled clinical examination with an assessment of variceal bleeding, HE, routine blood tests (e.g., hepatic function, coagulation status, and ammonia) and Doppler sonography (direction and velocity of blood flow in the portal vein and the shunt).

Clinical success was defined as a resolution of symptoms (stopping variceal bleeding for our study groups). Recurrent variceal hemorrhage was defined as re-bleeding and not responding to pharmacological and endoscopic therapies. A diagnosis of HE was confirmed if the concentration of blood ammonia was over twice the upper limit of normal and the value of a Karnofsky performance status scale was  $< 60$ . Follow-up endpoints were liver transplantation, end of the observation period (July 2015), loss to follow-up, and death.

### Statistical analysis

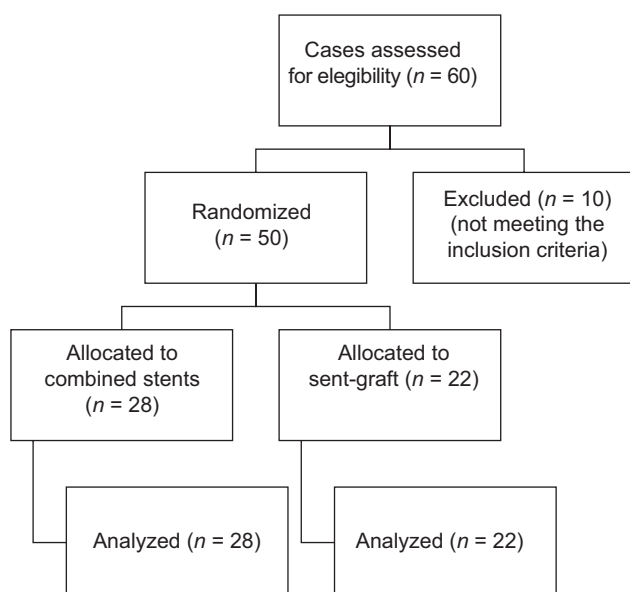
Continuous variables were presented as the mean  $\pm$  standard deviation (SD) and ranges. Categorical data were expressed as absolute and percentage values. For comparative statistics, continuous and categorical variables were analyzed using a *t*-test or Mann–Whitney *U*-test. A Chi-square test was used when appropriate. Patient survival was estimated by performing a Kaplan–Meier technique and comparing the data between the study groups using the log-rank-test. A value of  $P < 0.05$  was considered statistically significant. Statistics were performed using a commercially available software package (SPSS, version 20.0; SPSS Inc., Chicago, IL, USA).

## RESULTS

In total, sixty patients with variceal bleeding were consecutively admitted to our department from April 2011 to November 2014. Of these patients, we excluded ten with advanced malignancies, portal vein thrombosis, or other interventions prior to starting the study. Thus, fifty patients were prospectively analyzed in this study. These patients were indicated for therapy for emergent active variceal bleeding uncontrolled by a medical or endoscopic therapy ( $n = 10$ ) or elective management for variceal re-bleeding unresponsive to a medical or endoscopic therapy ( $n = 40$ ). They were randomized either into a stents-combination arm ( $n = 28$ ) or a stent-graft arm ( $n = 22$ ), as indicated in Figure 2. Detailed patient characteristics before the TIPS are presented in Table 1.

### Tips procedures

The primary technique success rate was 100% for both groups. An effective portal decompression and free antegrade shunt flow were achieved in all patients. The PSG before and after the TIPS was ( $37.0 \pm 9.2$ ) mmHg versus ( $15.2 \pm 4.0$ ) mmHg for Group I and was ( $34.4 \pm 7.7$ ) mmHg versus ( $15.5 \pm 5.2$ ) mmHg for Group II. Accordingly, the final PSG was ( $41.8 \pm 8.0$ ) % that of the original for the Group I and ( $45.5 \pm 10.9$ ) % for Group II. The reduction of PSG was significant ( $P = 0.000$  for both groups, paired  $t$ -test) for both groups. In both groups, the portal venous entry sites were the left portal veins in all patients. The average parenchymal length of the shunt (anterior-posterior position), as shown in Figure 1, was ( $25.2 \pm 7.8$ ) mm for all cases. Accordingly, the actual stent combination of Group I was largely accomplished with the BMS ( $\Phi = 10$  mm, length: 80–100 mm) and Fluency<sup>®</sup> stent-grafts ( $\Phi = 8$  mm), whose lengths were shorter than 4 cm.



**Figure 2:** Flow diagram of the participants of the randomized control study. The consecutive sixty patients, in which fifty were randomized either into the stents-combination arm (Group I,  $n = 28$ ) or the stent-graft arm (Group II,  $n = 22$ ), while the other ten were excluded because of not meeting the inclusion criteria.

In all fifty cases, the procedures were completed without any serious periprocedural complications. Only minor complications were noted, including a few cases of small local hematomas and one case of transient intraperitoneal hemorrhage that was managed successfully with conservative measures except for blood transfusion.

### Clinical follow-up

All patients were available for the follow-up. The median follow-up interval was 726 days (range: 6–1439 days).

There was one death in Group I within 30 days (6<sup>th</sup> day) post-TIPS because of renal failure, hepatic failure, and sepsis. The patient had Child C cirrhosis because of alcohol abuse and complicated refractory ascites before the operation. The renal failure was initiated with ascites tapping (approximately 1000 ml at a time and repeated 6 h later) to relieve his continual complaint of abdominal distention and dyspnea. He refused dialysis treatment and died on the 6<sup>th</sup> day.

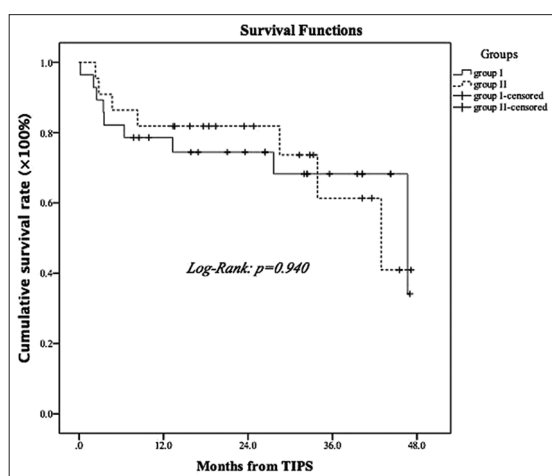
During the follow-up, 30 days after the TIPS, there were another eight deaths in Group I. Four of them died from hepatic failure, two died from hepatocellular carcinoma (HCC)-related hepatic failure, one died from encephalopathy, and one died from digestive re-bleeding. In Group II, there were six deaths. Three died from hepatic failure and three died from HCC, hepatopulmonary syndrome, and digestive re-bleeding, respectively.

The Kaplan–Meier survival analysis of the two groups is shown in Figure 3. The 1-, 2-, and 3-year survival rate for Group I was ( $78.6 \pm 7.8$ )%, ( $74.4 \pm 8.4$ )%, and ( $68.2 \pm 9.7$ )%,

**Table 1: Patient demographic and clinical characteristics undergoing a TIPS**

| Characteristics                 | Stents-combination group | Stent-graft group | Statistical      | <i>P</i> |
|---------------------------------|--------------------------|-------------------|------------------|----------|
| Number of patients, <i>n</i>    | 28                       | 22                | –                | –        |
| Male/female, <i>n</i>           | 19:9                     | 13:9              | $\chi^2 = 0.411$ | 0.565    |
| Age (years), mean $\pm$ SD      | $55.8 \pm 8.4$           | $62.0 \pm 10.5$   | $t = -2.131$     | 0.065    |
| Liver disease, <i>n</i>         |                          |                   |                  |          |
| Viral hepatitis                 | 15                       | 11                | –                | –        |
| Alcoholic cirrhosis             | 4                        | 1                 | –                | –        |
| Autoimmune hepatitis            | 4                        | 4                 | –                | –        |
| Others                          | 5                        | 6                 | –                | –        |
| Child-Pugh score, mean $\pm$ SD | $7.5 \pm 1.8$            | $6.6 \pm 1.9$     | $t = 1.905$      | 0.063    |
| Child-Pugh class, <i>n</i>      |                          |                   |                  |          |
| A                               | 10                       | 13                | –                | –        |
| B                               | 14                       | 6                 | –                | –        |
| C                               | 4                        | 3                 | –                | –        |
| Indications for TIPS, <i>n</i>  |                          |                   |                  |          |
| Acute hemorrhage                | 5                        | 7                 | –                | –        |
| Recurrent hemorrhage            | 23                       | 15                | –                | –        |

Values are presented as mean  $\pm$  SD or *n*. TIPS: Transjugular intrahepatic portosystemic shunt; –: Not applicable; A: Child-Pugh score 5–6; B: Child-Pugh score 7–9; C: Child-Pugh score 10–15; SD: Standard deviation.



**Figure 3:** Kaplan–Meier survival analyses for the combined-stent group and stent-graft group. The Kaplan–Meier survival analysis for the combined-stent group and the stent-graft group indicated that no significant difference was found between these two groups (log-rank [Mantel–Cox],  $\chi^2 = 0.006$ ,  $P = 0.940$ ). TIPS: Transjugular intrahepatic portosystemic shunt.

respectively. The 1-, 2-, and 3-year survival rate for Group II was  $(81.8 \pm 8.2)\%$ ,  $(81.8 \pm 8.2)\%$ , and  $(73.6 \pm 10.7)\%$ , respectively. There was no significant difference between the groups (log-rank [Mantel–Cox],  $\chi^2 = 0.006$ ,  $P = 0.940$ ).

### Hepatic encephalopathy

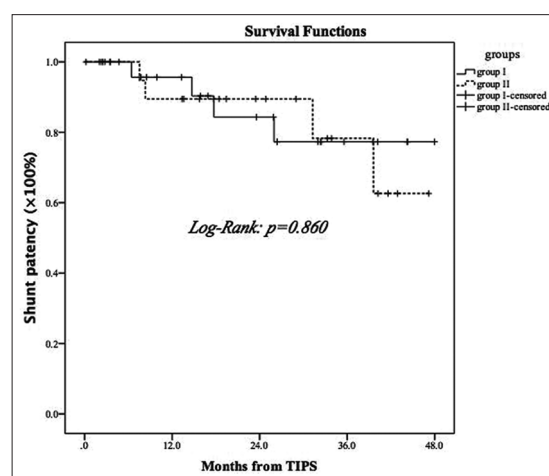
In addition to the previously mentioned one death from encephalopathy in Group I, *de novo* HE was observed in six patients during the follow-up period, three in each group. The incidence of HE was 14.3% and 13.6% for Groups I and II, respectively. Examined by a Chi-square test, the difference of HE incidence between the groups was not statistically significant (Pearson  $\chi^2 = 0.004$ ,  $P = 0.948$ ).

### Shunt patency rate and bleeding recurrence

During the follow-up period, four relapses of digestive tract bleeding were observed, with three in Group I and 1 in Group II. Accordingly, the incidence of re-bleeding was 10.7% for Group I and 4.5% for Group II. Examined by a Chi-square test, the difference of re-bleeding incidence between the groups was not statistically significant (Pearson  $\chi^2 = 0.637$ ,  $P = 0.425$ ).

The primary shunt patency rate is shown in Figure 4. By the Kaplan–Meier survival analysis, the 1-, 2-, and 3-year patency rate for Group I was  $(95.7 \pm 4.3)\%$ ,  $(84.3 \pm 8.4)\%$ , and  $(77.3 \pm 10.2)\%$ , respectively; for Group II, it was  $(89.5 \pm 7.0)\%$ ,  $(89.5 \pm 7.0)\%$ , and  $(78.3 \pm 12.1)\%$ , respectively. There were no significant differences between the two groups (log-rank [Mantel–Cox],  $\chi^2 = 0.031$ ,  $P = 0.860$ ).

For the Child-Pugh classification, before the TIPS and at the end of the follow-up, the scores were  $7.5 \pm 1.9$  and  $7.3 \pm 2.1$ , respectively, for Group I and  $6.6 \pm 1.9$  and  $7.6 \pm 2.0$ , respectively, for Group II. Using the paired *t*-test, the difference was not significant for Group I. However, it was significant for Group II (Group I:  $t = 0.626$ ,  $P = 0.507$ ; Group II:  $t = -2.474$ ,  $P = 0.022$ ).



**Figure 4:** Kaplan–Meier shunt patency analyses for combined-stent group and stent-graft group. There was no significant difference between the two groups (log-rank [Mantel–Cox],  $\chi^2 = 0.031$ ,  $P = 0.860$ ). TIPS: Transjugular intrahepatic portosystemic shunt.

## DISCUSSION

TIPS techniques have been under continual improvement since the procedure’s creation. Today, BMS and self-expanding stent-grafts are routinely used for TIPS.<sup>[8,9]</sup> The Viatorr® stent-graft significantly improved the shunt function with decreased numbers of revisions.<sup>[8–10]</sup> However, shunt dysfunction is still a major drawback of TIPSs.

The cause of shunt dysfunction varies. Pseudointima hyperplasia is one of the major causes of intrastent stenosis, especially at the hepatic vein end. Several studies<sup>[9,11–12]</sup> have identified the sites of stenosis after creating a TIPS with a Viatorr® stent-graft. Hepatic venous-end stenosis represents 43%–100% of the stenosis found. Extending the TIPS stents to the hepatic vein/IVC junction is essential for reducing hepatic venous end stenosis and thereby increasing TIPS patency.

The authors suggested two improvement points for this purpose. Typically, the right portal vein was the preferred entry site. However, we suggested the opposite side as the entry site [Figure 1], i.e., the sagittal segment of the left portal vein. Anatomically, the shunt at this direction had a more straight angle than that through the right portal vein [Figure 1]. The second improvement was the indirect marking of the target vein. Before puncturing the left portal vein, a catheter would be selectively inserted into the left hepatic artery. Thus, an operator obtained a visible “target” of the left portal vein. The success rate of the puncture procedure could be improved to as high as 100%, which was our result for fifty patients and was consistent with other studies,<sup>[1,13]</sup> in which the right portal vein was the preferred target vein. Therefore, technically, the left (portal vein) entry was as efficient as the right entry.

The PSG control was another key point during shunt construction. The degree of PSG reduction depended largely on the choice of the stents’ diameter. Most of the centers preferred 10-mm-diameter stents to 8-mm-diameter stents.<sup>[14]</sup> In the authors’ center, we took this as a step-by-step procedure to meet the technical requirements (PSG: 50%

of the original). Thus, the 8-mm-diameter stent-grafts were used most frequently.

### The patency rate and clinical efficacy of transjugular intrahepatic portosystemic shunt

Most studies assessing the patency of TIPS created with expanded polytetrafluoroethylene (ePTFE)-covered stent-grafts only evaluated the short- to intermediate-term follow-up results. The literature contains few data evaluating long-term patency beyond 2 years [Table 2]. The present study provided an opportunity to evaluate the long-term patency and clinical efficacy of a TIPS created with the combined use of an ePTFE-covered stent-graft and self-expanding metal stents. The series demonstrated acceptable primary patency rates at the 1- and 2-year follow-ups. Compared with the statistics [Table 2] from the TIPSs with a Viatorr® stent-graft, the primary 2-year patency rate for both groups (90% for Group I vs. 84% for Group II) were excellent and consistent with earlier studies. Three-year follow-up results of primary patency are rarely seen in the statistics. For this study, it was approximately 77% for both groups. From the perspective of shunt patency, the TIPS created with the Fluency® stent-graft either alone or combined with a BMS when located in the left portal vein had a comparable primary patency rate to that of the specialized stent-graft Viatorr®.

Previous studies on TIPS created with the ePTFE-covered stent-grafts demonstrated a 1-year mortality rate ranging between 11% and 35%,<sup>[2,11,17]</sup> which was comparable to the rate observed in the present study. One year later, the mortality rate continued to slightly increase. It then stabilized until the end of the second year. It was approximately 20% for both groups, however, the rate of Group II was lower than that of Group I. The difference might be the result of the patients' better liver function (as indicated by the Child-Pugh score) in Group II.

The clinical success rate for bleeding control ranges between 71% and 100%, with the majority of studies reporting a range of 90%–100%.<sup>[1,12,13]</sup> The present study had a comparable successful bleeding control rate during

the 4-year follow-up period. The higher re-bleeding rate in Group I (10.7%) compared to Group II (4.5%) might be the result of portal venous system thrombosis. Two of the three re-bleeding patients in Group I had a mural SMV or splenic vein thrombosis before the TIPS, and the shunts were found to be occluded by thrombi when the re-bleeding occurred. The re-bleeding was successfully controlled by revising the TIPS shunt with a BMS and long-term anticoagulation therapy with warfarin until the end of the study.

### Encephalopathy and liver function

Deterioration of the liver function after TIPS has always been a major concern. Portal blood bypassing the liver is considered a trigger factor. However, some studies have reported an improvement of liver function. Bureau *et al.* reported a significant reduction of the Child-Pugh score 2 years after a TIPS with a Viatorr® stent-graft.<sup>[8]</sup>

We analyzed the patients' Child-Pugh scores to determine the changing profile of the liver function for both groups. For Group I, the Child-Pugh score decreased slightly from  $7.5 \pm 1.9$  to  $7.3 \pm 2.1$ . For Group II, it increased from  $6.6 \pm 1.9$  to  $7.6 \pm 2.0$ . Based on the results of the paired *t*-test, the change was significant for Group II but not for Group I. When the Fluency® stent-graft alone was positioned between the left portal vein and IVC, as done in Group II, almost all of the flushing portal blood for the left hepatic lobe was diverted to the IVC compared with Group I, in which only a short-length Fluency® was adopted to cover the parenchymal section of the shunt to maintain the patency of the portal vein branches. This difference might account for the liver function deterioration observed in Group II.

HE is another major concern for complications after a TIPS. The incidence of *de novo* or worsening of existing HE can occur in approximately 30% of patients, regardless of whether the Viatorr® stent-graft or BMS is used.<sup>[22]</sup> In contrast, we found a relatively low incidence in this series: 14.3% for Group I and 13.6% for Group II. All of the HE patients were controlled by conservative measures, except for necessary revisions of the shunts. We attributed this to several factors. First, the quality control idea for the PSG adjustment during the construction of

**Table 2: Primary patency rates for ePTFE-covered TIPS\***

| Study  | Number of TIPS, <i>n</i> | Follow-up (years) | Primary patency (%) |         |         | Study design          |
|--|--------------------------|-------------------|---------------------|---------|---------|-----------------------|
|  |                          |                   | 1 year              | 2 years | 3 years |                       |
| Rössle <i>et al.</i> , 2006 <sup>[12]</sup>  | 100                      | 3                 | 90                  | 84      | 74      | ePTFE only            |
| Tripathi <i>et al.</i> , 2006 <sup>[9]</sup> | 157                      | 2                 | 92                  | 89      | –       | ePTFE versus BMS      |
| Jung <i>et al.</i> , 2009 <sup>[15]</sup>    | 40                       | 1                 | 38                  | –       | –       | ePTFE versus BMS      |
| Saad <i>et al.</i> , 2010 <sup>[16]</sup>    | 126                      | 2                 | 87                  | 62      | –       | ePTFE only            |
| Luca <i>et al.</i> , 2011 <sup>[17]</sup>    | 57                       | 2                 | 79                  | 71      | –       | ePTFE versus BMS      |
| Gaba <i>et al.</i> , 2012 <sup>[13]</sup>    | 70                       | 2                 | 90                  | 78      | –       | ePTFE versus BMS      |
| Sommer <i>et al.</i> , 2012 <sup>[1]</sup>   | 58                       | 1                 | 62                  | –       | –       | ePTFE versus BMS      |
| Chen <i>et al.</i> , 2014 <sup>[18]</sup>    | 103                      | 3                 | 81                  | 76      | 76      | ePTFE only            |
| Luo <i>et al.</i> , 2013 <sup>[19]</sup>     | 33                       | 2                 | 91                  | 85      | –       | ePTFE versus BMS      |
| Sajja <i>et al.</i> , 2013 <sup>[20]</sup>   | 59                       | 2                 | –                   | 80      | –       | ePTFE only            |
| Wu <i>et al.</i> , 2013 <sup>[21]</sup>      | 114                      | 2                 | 87                  | 75      | –       | ePTFE only (Fluency®) |

\*Created with the Viatorr® stent-graft or as specified. –: No data; ePTFE: Expanded polytetrafluoroethylene; TIPS: Transjugular intrahepatic portosystemic shunt; BMS: Bare metal stent.

the TIPS. Second, we employed stent-grafts of 8 mm in diameter for most of the patients. The limited but required (PSG: 50% of original) fulfilled portal blood bypassing contributed to decreasing the incidence of encephalopathy. Finally, all of our patients were asked to keep a strict, low-protein diet after the operation for as long as 3 months.

The principal weakness of this study was the limited number of cases enrolled and the limited indications (only bleeding patients were indicated) of TIPS. Therefore, the results of the study were only applicable for patients with upper digestive bleeding and not for all TIPS patients, especially not those with refractory ascites. The 4-year follow-up period was longer than that used in most previous studies [Table 2], however, it should be extended to observe longer-term results. Fortunately, the study was prospective and further results could be reported later following ongoing observation. Another obvious weakness was the absence of a control group in which TIPS was constructed with the specialized Viatorr® stent-graft, which is currently widely used. This weakness was difficult to overcome because the Viatorr® stent-graft is not commercially available in China.

In conclusion, this prospective controlled study suggested the following: (1) constructing the TIPS through the left entry into the portal vein with either single stent-graft or stents-combination technique was effective for the control of variceal bleeding; (2) the stents-combination technique was comparable to a single Fluency® stent-graft technique in terms of the shunt patency, incidence of HE, and patient survival rate; (3) the stents-combination technique was superior to the Fluency® alone in liver function preservation, as indicated by the Child-Pugh score; and (4) the 50% reduction of the PSG as the technical requirement was effective for bleeding control and with an acceptable lower HE incidence.

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### Conflicts of interest

There are no conflicts of interest.

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