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TOPIC HIGHLIGHT

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Selection of a TIPS stent for management of portal hypertension in liver cirrhosis: An evidence-based review

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Abstract

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. Herein, we attempt to review the current evidence regarding the diameter, type, brand, and position of TIPS stents. Several following recommendations may be considered in the clinical practice: (1) a 10-mm stent may be more effective than an 8-mm stent for the management of portal hypertension, and may be superior to a 12-mm stent for the improvement of survival and shunt patency; (2) covered stents are superior to bare stents for reducing the development of shunt dysfunction; (3) if available, Viatorr stent-grafts may be recommended due to a higher rate of shunt patency; and (4) the placement of a TIPS stent in the left portal vein branch may be more reasonable for decreasing

the development of hepatic encephalopathy. However, given relatively low quality of evidence, prospective well-designed studies should be warranted to further confirm these recommendations.

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

Core tip: This review suggests the following: first, a 10-mm stent may be more effective than an 8-mm or 12-mm stent for the management of portal hypertension in liver cirrhosis; second, Viatorr covered stents may be recommended for maintaining the shunt patency; finally, the placement of a transjugular intrahepatic portosystemic shunt stent in the left portal vein branch may be more reasonable for decreasing the development of hepatic encephalopathy.

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INTRODUCTION

Transjugular intrahepatic portosystemic shunt (TIPS) refers to an interventional creation of a shunt between the portal vein and the hepatic vein or inferior vena cava by deploying an expandable stent, thereby reducing the portosystemic pressure gradient^[1,2]. Compared with the traditional surgical portosystemic shunt, the major advantages of TIPS include local anaesthesia and less invasive-



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Table 1 Transjugular intrahepatic portosystemic shunt for the prevention of variceal rebleeding: An overview of meta-analyses

Ref.	Design	No. trials	Comparative arms	Target population	Efficacy of TIPS	Encephalopathy	Survival or death
Zheng et al ^[6]	Meta-analysis	12	TIPS vs endoscopic	Variceal	Variceal rebleeding:	The frequency	Death due to all
	of RCTs		treatment	rebleeding in	TIPS was lower	of HE: TIPS was	causes: NS
				cirrhosis	(P < 0.00001)	higher (<i>P</i> < 0.00001)	
Khan et al ^[7]	Meta-analysis	22	Portosystemic	Variceal	Rebleeding: shunt	Acute or chronic	Mortality: NS
	of RCTs		shunts (surgical or	rebleeding in	was lower	HE: shunt was	
			TIPS) vs endoscopic	cirrhosis		higher	
			therapy				
Burroughs et al ^[8]	Meta-analysis	13	TIPS vs endoscopic	Variceal	Recurrent bleeding:	Encephalopathy:	Survival: NS
	of RCTs		treatment	rebleeding in	TIPS was lower	TIPS was higher	
				cirrhosis			
Papatheodoridis et al ^[9]	Meta-analysis	11	TIPS vs endoscopic	Variceal	Variceal rebleeding:	Encephalopathy:	Overall mortality:
	of RCTs		treatment	rebleeding	TIPS was lower	TIPS was higher	NS; sensitivity
					(P < 0.001)	(P < 0.001)	analyses: NS
Luca et al ^[10]	Meta-analysis	11	TIPS vs endoscopic	Recurrent	Recurrent bleeding:	Encephalopathy:	Death due to all
	of RCTs		treatment with or	bleeding in	TIPS was lower	TIPS was higher	causes: NS; death
			without propranolol	cirrhosis			due to bleeding: NS

HE: Hepatic encephalopathy; NS: Not significant; RCT: Randomized controlled trial; TIPS: Transjugular intrahepatic portosystemic shunt.

Table 2 Transjugular intrahepatic portosystemic shunt for the treatment of refractory ascites: An overview of meta-analyses

Ref.	Design	No. trials	Comparative arms	Target population	Efficacy of TIPS	Encephalopathy	Survival or death
Chen <i>et al</i> ^[25]	Meta-regression and Trial Sequential Meta- analysis	6	TIPS <i>vs</i> large- volume paracentesis	Refractory ascites in liver cirrhosis	Ameliorate refractory ascites: TIPS was better (P < 0.05)	Frequency of HE: TIPS was higher (<i>P</i> < 0.01)	Overall mortality: NS; subgroup mortality (patients with better hepatic and renal function): TIPS was lower (<i>P</i> < 0.05)
Salerno <i>et al</i> ^[26]	Meta-analysis of individual patient data	4	TIPS <i>vs</i> large- volume paracentesis	Refractory ascites in liver cirrhosis	Tense ascites recurrence: TIPS was lower (<i>P</i> < 0.0001)	Average number of HE episodes: TIPS was higher (<i>P</i> = 0.006)	Transplant-free survival: TIPS was better (P = 0.035)
Saab et al ^[27]	Meta-analysis of RCTs	5	TIPS vs paracentesis	Refractory ascites in liver cirrhosis	Re-accumulation of ascites: TIPS was lower (<i>P</i> < 0.01)	Frequency of HE: TIPS was higher (P < 0.01)	30-d mortality: NS; 24-mo mortality: NS
D'Amico et al ^[28]	Meta-analysis of RCTs	5	TIPS vs paracentesis	Refractory ascites in liver cirrhosis	Recurrence of ascites: TIPS was lower ($P < 0.05$)	Frequency of HE: TIPS was higher (P < 0.05)	Mortality: NS
Albillos et al ^[29]	Meta-analysis of RCTs	5	TIPS vs paracente- sis	Refractory ascites in liver cirrhosis	Ascites recurrence: TIPS was lower (P < 0.05)	Risk of HE: TIPS was greater	Overall mortality: NS; sub- group mortality (patients with recidivant ascites): TIPS was lower ($P < 0.05$)
Deltenre <i>et al</i> ^[30]	Meta-analysis of RCTs	5	TIPS vs large-vol- ume paracentesis	Refractory ascites in liver cirrhosis	Control of ascites: TIPS was better (P < 0.001)	HE: TIPS was higher (<i>P</i> < 0.001)	Survival: NS

HE: Hepatic encephalopathy; NS: Not significant; RCT: Randomized controlled trial; TIPS: Transjugular intrahepatic portosystemic shunt.

ness. Since its first clinical application, TIPS has been widely used for the treatment of portal hypertension-related complications in liver cirrhosis for nearly 25 years^[3]. Existing and well-established evidence supports the following indications for TIPS^[4,5]. First, TIPS should be recommended as the second-line treatment option for the prevention of variceal rebleeding in liver cirrhosis^[4]. This recommendation is mainly based on the results of 5 meta-analyses^[6-10] and 12 randomized controlled trials^[11-22] (Table 1). Although TIPS significantly reduces the incidence of variceal rebleeding in liver cirrhosis, it cannot improve the survival with a significantly higher rate of hepatic encephalopathy and shunt dysfunction. Second,

TIPS should be used as the rescue treatment for acute varcieal bleeding that is not responsive to medical and/or endoscopic therapy in liver cirrhosis^[4]. However, a recent multi-center randomized trial has shown a significant survival benefit of early TIPS with covered stents for the treatment of acute variceal bleeding in high-risk cirrhotic patients^[23], which potentially challenges the current recommendation^[24]. Third, TIPS should be used for the treatment of refractory ascites that is not responsive to large volume paracentesis^[4]. This recommendation primarily originates from the results of 6 meta-analyses^[25-30] and 6 randomized controlled trials^[31-35] (Table 2). Notably, the subgroup meta-analyses have shown that TIPS

can significantly reduce the mortality in patients with recidivant ascites^[29] and those with better hepatic and renal function^[25]. More importantly, a meta-analysis of individual data has revealed that TIPS can significantly improve the transplant-free survival^[26]. This positive conclusion is also confirmed by our recent meta-analysis using hazard ratios (our unpublished data). However, due to a high incidence of post-TIPS hepatic encephalopathy, it is still regarded as the second-line therapy of choice. Apart from these classical indications, emerging evidence has attempted to establish the novel indications for TIPS, such as the management of gastric variceal bleeding^[36,37], ectopic variceal bleeding^[37,39], hepatic hydrothorax^[40-42], hepatorenal syndrome^[42-44], portal vein thrombosis^[45-49], and Budd-Chiari syndrome (BCS)^[50-52].

Generally, accumulated evidence has witnessed the essential role of TIPS for the management of portal hypertension in liver cirrhosis. Notwithstanding, the technical details remain controversial, such as the selection of stents and puncture position, necessity of adjunctive variceal embolization (see a recent meta-analysis^[53]), and benefit of postoperative anticoagulation or anti-platelets (see previous randomized controlled trials^[54,55]). In this paper, we focus on reviewing the current evidence regarding the diameter, type, brand, and position of TIPS stents. Other issues are beyond the scope of this review.

DIAMETER OF TIPS STENTS: 8-MM, 10-MM *VS* 12-MM

Theoretically, a larger diameter of TIPS stent can reach the target portosystemic pressure gradient more effectively and rapidly. However, the excessive shunting of portal blood flow can induce the development of hepatic dysfunction and encephalopathy. Therefore, it is important to choose an appropriate diameter of stent to balance between the efficacy and complications of TIPS.

An early retrospective study compared the outcomes of TIPS between cirrhotic patients receiving 10-mm (n = 23) and 12-mm (n = 23) Wallstents^[56]. The 1-d occlusion rate was significantly higher in the 12-mm stent group than in the 10-mm stent group (17% vs 0%). But the long-term primary and secondary patency rates were similar between the two groups. Additionally, the 1-mo mortality rate was higher in the 12-mm stent group than in the 10-mm stent group (26% vs 4%). 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, an Italian, single-center, randomized controlled trial compared the outcomes of TIPS between cirrhotic patients with variceal bleeding or refractory ascites receiving 8-mm (n = 22) and 10-mm (n = 23) PTFEcovered stents^[57]. The 10-mm stents were more effective than the 8-mm stents for reducing the portosystemic pressure gradient after TIPS ($6.5 \pm 2.7 \text{ mmHg} vs 8.9 \pm 2.7 \text{ mmHg}$, 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% vs 41.9%, P = 0.002, by Log-Rank test). In details, the difference was statistically significant in patients treated for refractory ascites, but was slight in those treated for variceal bleeding. In spite of its advantages in the improvement of portal hypertension, the 10-mm stent group was similar to the 8-mm stent group for the 1-year rate of remaining free of post-TIPS hepatic encephalopathy (46.7% vs 42.6%, P = 0.48, by Log-Rank test) and 1-year cumulative survival rate (79.6% vs 79.1%, P = 0.20, 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^[57]. The behavior might influence the weight of these conclusions. 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^[57]. Due to the potential limitations, a randomized controlled trial (ClinicalTrials. gov: NCT01410591) is ongoing to primarily compare the incidence of shunt dysfunction as the primary endpoint in cirrhotic patients with at least one episode of variceal bleeding receiving 10-mm and 8-mm covered stents.

TYPE OF STENTS: COVERED VS BARE

In the era of bare stents, a high incidence of shunt dysfunction is one of the most severe complications of TIPS. Since the introduction of covered stents, numerous comparative studies^[45,58-69] (Table 3) and case series^[70-77] (Table 4) have shown their remarkable benefit in the improvement of shunt patency. However, only one of these studies was randomized controlled trial^[68]. In this European, multi-national, randomized controlled trial, 80 cirrhotic patients were assigned to the covered (n = 39)and bare (n = 41) stent groups^[68]. The preliminary analysis confirmed a lower incidence of shunt dysfunction (5/39 vs 18/41, P < 0.001) and clinical relapse (3/39 vs 18/41, P < 0.001)12/41, P < 0.05) in the covered stent group. Subsequently, an extended follow-up analysis further demonstrated a higher actuarial rate of remaining free of hepatic encephalopathy (67% vs 51%, P < 0.05) in the covered stent group^[69]. But no survival benefit from the covered stents was found^[68,69]. Thus, the wide application of covered stents during a TIPS procedure was greatly prompted by these promising findings. But the potentially lethal complication associated with covered stents should not be neglected, such as segmental liver ischemia due to the obstruction of hepatic venous outflow caused by covered stents^[78-80].

Recently, a meta-analysis of 6 studies, including 346 and 929 patients receiving covered and bare stents, re-

Table 3 Comparison of outcome after transjugular intrahepatic portosystemic shunt between covered and bare stents: An overview of comparative studies

Ref.	Period	Target population	No. patients (covered/ bare)	Efficacy of TIPS (covered/bare)	Shunt dysfunction or patency (covered/bare)	Post-TIPS encephalopathy (covered/bare)	Survival or death (covered/bare)
Luca <i>et al</i> ^[45]	2003.1-2010.2	Cirrhotic patients with non-tumoural PVT	70 (57/13)	NA	12-mo shunt dysfunction rate: 21%/38%; 24-mo shunt dysfunction rate: 29%/85%	NA	NA
Sommer <i>et al</i> ^[58]	2001.2-2011.1	Patients with elective TIPS procedures	174 (58/116)	Clinical success rate: ascites: 90.5%/81.3%; ascites + bleeding: 85.7%/73.7%; bleeding: 90.0%/86.2% (NS)	12-mo primary shunt patency rate: 62.4%/43.9% (<i>P</i> < 0.05)	Overall rate: 36.5%/37.5% (NS)	12-mo survival rate: 79.1%/75.6%; overall survival time: 835.25 ± 823.0 (9-3200)/805.6 ± 868.4 (6-3290) d (NS)
Clark <i>et al</i> ^[59]	2001-2010	Patients with PH	246 (176/70)	NA	Overall shunt dysfunction rate: 22% / 57% (P = 0.05)	NA	Survival time: 33/31 mo (P = 0.5)
Maleux et al ^[60]	1992-2006	Cirrhotic patients with refractory ascites	222 (126/96)	Rate of clinically significant residual ascites 1 mo after TIPS: $35.5\%/55.6\%$ (P = 0.003)	1-yr shunt dysfunction rate: 19%/49% (P < 0.0001)	1-yr rate: 22%/56% (<i>P</i> < 0.0001)	6-mo survival rate: 73.2%/62.8%; 1-yr survival rate: 65.5%/55.0% (P = 0.0071)
Wu et al ^[61]	2007.4-2009.4	Patients with PH	60 (30/30)	Number of rebleeding: $1/6$ ($P = 0.04$)	Number of shunt dysfunction: $0/9$ (P = 0.002)	Number: 5/6 (<i>P</i> = 0.74)	Number of death: 0/4 (<i>P</i> = 0.038)
Bandi <i>et al</i> ^[62]	2006.3-2009.3	Patients with PH	66 (33/33)	Clinical relapse number (rate): 8 (26%)/15 (45%) (P < 0.05)	Number of shunt dysfunction: $5/15$ (P < 0.05)	Overall rate: 22%/33% (NS)	Overall survival rate: 66%/37% (P < 0.05)
Jung et al ^[63]	1996.6-2006.2	Patients who received de novo TIPS	81 (51/30)	Bleeding group: 3-mo clinical success rate: 100%/58% ($P = 0.03$); 12-mo clinical success rate: 67%/18% ($P = 0.046$). Ascites group: 3-mo clinical success rate: 77%/70% ($P = 0.2$); 12-mo clinical success rate: 64%/33% ($P = 0.18$)	rate: 38%/24% (P = 0.65)	Overall rate: 15%/14% (<i>P</i> = 0.7)	Bleeding group: 30-d mortality rate: 40%/33% (P = 0.69); overall mortality rate: 40%/50% (P = 0.57). Ascites group: 30-d mortality rate: 6%/27% (P = 0.13); overall mortality rate: 13%/55% (P = 0.02)
Pan <i>et al</i> ^[64]	2001.1- 2005.12	Patients with variceal bleeding and refractory ascites	128 (57/71)	NĂ	30-d shunt dysfunction rate: 1.8%/4.2% ($P = 0.4$); 6-mo shunt dysfunction rate: $5.2/25.3\%$ ($P = 0.003$); 1-yr shunt dysfunction rate: $5.2\%/30.9\%$ ($P = 0.004$); overall shunt dysfunction rate: $8.7\%/40.8\%$ ($P = 0.004$)	NA	6-mo mortality rate: 10.5%/16.9% (P = 0.3); 1-yr mortality rate: 14%/23.9% (P = 0.2); overall mortality rate: 21.1%/35.2% (P = 0.08)
Tripathi <i>et al</i> ⁽⁶⁵⁾	1991.7- 2004.12	Patients with variceal bleeding, ascites, portal hypertensive gastropathy, hepatic hydrothorax	473 (157/316)	2-yr cumulative rebleeding rate: 6%/17% (<i>P</i> < 0.05)	2-yr cumulative	2-yr cumulative rate: 23%/38% (P < 0.05)	2-yr cumulative mortality rate: 49%/50%



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Gandini <i>et al</i> ^[66]	1994.1- 2003.11	Patients with BCS	13 (7/6)	Clinical relapse rate: 100%/0%	6-mo primary patency rate: 100%/16.7%; 12-mo primary patency rate: 85.7%/0% (<i>P</i> < 0.001, Log- Rank)	Overall rate: 0%/0%	NA
Barrio <i>et al^[67]</i>	1998.9-2002.5	Cirrhotic patients with PH related complications	70 (20/50)	Rate of clinical recurrence of portal hypertension related complications: 0%/22% (<i>P</i> = 0.085)	6-mo shunt dysfunction rate: 0%/32%; 12-mo shunt dysfunction rate: 0%/82% (P = 0.03, Log- Rank)	1-mo rate: 41%/20%; 3-mo rate: 44%/34%; 9-mo rate: 44%/40% (P = 0.5, Log-Rank)	6-mo survival rate: 67%/88%; 12-mo survival rate: 67%/81% (<i>P</i> = 0.11, Log-Rank)
Bureau <i>et al^[68,69]</i>	2000.2-2002.4	Patients with cirrhosis and uncontrolled bleeding, recurrent bleeding, or refractory ascites	80 (39/41)	Clinical relapse rate: 7.7%/29.3%	1-yr primary patency rate: 85.6%/46.6%; 2-yr primary patency rate: 80.2%/18.6% (<i>P</i> = 0.0005, Log- Rank)	1-yr rate: 22%/41% (<i>P</i> = 0.0586)	1-yr survival rate: 70.9%/59.5%; 2-yr survival rate: 64.5%/40.5%

BCS: Budd-Chiari syndrome; NA: Not available; NS: Not significant; PH: Portal hypertension; PVT: Portal vein thrombosis; TIPS: Transjugular intrahepatic portosystemic shunt.

spectively, showed not only a significant improvement of primary patency (HR = 0.28) and a significant reduction of risk of hepatic encephalopathy (HR = 0.65) but also a significant decrease of mortality in the covered stent group (HR = 0.76)^[81]. In addition, the heterogeneity among studies was not significant in all analyses. But it should be noted that the indication for TIPS was heterogeneous among these included studies.

Taken together, covered stents should be recommended for the TIPS procedure. More importantly, because bare stents were employed in all previous randomized controlled trials comparing the outcome between cirrhotic patients with portal hypertension receiving TIPS and those receiving other treatments, the role of TIPS with covered stents in the management of portal hypertension should be reconsidered in future trials^[82]. Until now, one completed trial (Current Controlled Trials number: ISRCTN58150114) has shown positive results that the early use of TIPS with covered stents can significantly reduce the treatment failure and mortality of acute variceal bleeding in high-risk cirrhotic patients^[23]. Additionally, several ongoing trials have attempted to further update the indications of TIPS, as follows: (1) whether TIPS with coated stents or paracentesis plus albumin administration is better for the treatment of refractory ascites in patients with cirrhosis (ClinicalTrials.gov: NCT00222014); (2) whether TIPS with covered stents or endoscopic band ligation is better in cirrhosis with recurrent variceal bleeding non-responding to medical therapy (ClinicalTrials.gov: NCT00570973); (3) whether TIPS endoprosthesis or large volume paracentesis is better for the treatment of ascites in patients with portal hypertension (ClinicalTrials.gov: NCT01236339); (4) whether early TIPS with covered stents or non-selective beta blocker plus endoscopic treatment is better for acute variceal bleeding in high-risk cirrhotic patients (ClinicalTrials. gov: NCT01370161); and (5) whether TIPS with covered

stents or conventional treatment is better for the prevention of variceal rebleeding in cirrhotic patients with portal vein thrombosis (Clinical Trials.gov: NCT01326949).

As for BCS patients, the benefit of covered stents appears to be controversial. In 17 retrospective case series focusing on the outcome of BCS treated with TIPS alone^[52], the rate of shunt dysfunction is 18%-100%, which is higher in patients with BCS than in those with cirrhotic portal hypertension. This phenomenon may be attributed to the hypercoagulability and more complex anatomy in BCS patients. Although most of studies support the use of covered stents for improving the shunt patency^[50,66,83-88], a large study reports a similar shunt patency rate (bare stents: 81% vs covered stents: 85%)^[89]. More recently, our retrospective study of 51 BCS patients treated with TIPS, by using Cox regression, demonstrated no significant association between the type of stents (bare vs covered) and the development of shunt dysfunction (HR = 1.14, 95%CI: 0.46-2.82, P = 0.775^[51]. Certainly, the results should be cautiously interpreted, due to a relatively small number of patients, a short follow-up time, the retrospective nature of this study, and the use of Fluency stents.

BRAND OF COVERED STENTS: FLUENCY VS VIATORR

Currently, the Viatorr stent-graft (Gore WL and Associates, Flagstaff, AZ, United States), which is produced as the specialized TIPS endoprosthesis, is commercially available in the United States and Europe. Alternatively, Fluency covered stent (Angiomed GmbH Co. subsidiary of C.R. Bard, Inc.), which is mainly employed for the treatment of iliac artery diseases, can be purchased in some other countries, such as China mainland. They have different designs. The former mainly includes a 4 to 8-cm-long intra-hepatic region covered by PTFE inside a

Ref.	Period	n	Indication for TIPS	Liver function	Follow-up time ¹	Patients with shunt dysfunction (n)	Cumulative shunt dysfunction or patency rate	HE (<i>n</i>)	No. Pts death (<i>n</i>)
Sajja <i>et al</i> ^[70]	2001.1-2011.12	59	Ascites (16), variceal bleeding (31), both (12)	MELD score: 12.5	654 ± 341 (253-1584) d	6-mo: 8; overall: 14	NA	15	7
Wu et al ^[71]	NA	114	Pure esophageal variceal disruption hemorrhage (92), pure refractory cirrhotic ascites (8), esophageal variceal disruption hemorrhage with refractory ascites (14)	CPC A/B/C: 29/68/34	NA	16	1-yr dysfunction rate: 13.3%; 2-yr dysfunction rate: 24.8%	23	NA
Wu et al ^[72]	2008.1-2011.12	150	Gastroesophageal variceal bleeding (134), refractory ascites (16)	CPC A/B/C: 30/81/39	24.1 ± 8.8 mo	17	NA	23	18
Rössle et al ^[73]	2000.4-2004.10	100	Variceal bleeding (41); refractory ascites, hydrothorax, or hepatorenal syndrome (59)	CPC A/B/C: 21/58/21	22 ± 15 (0.8-47) mo	6-mo: 6; 1-yr: 7; 2-yr: 11; overall: 16	NA	NA	22
Vignali <i>et al</i> ^[74]	2001.2-2003.12	114	Variceal bleeding (49), refractory ascites (52), hypertensive gastropathy (10), BCS (1), hepatorenal syndrome (2)	CPC A/B/C: 8/60/46	11.9 ± 10.2 (0-38) mo	15	6-mo dysfunction rate: 8.1%; 1-yr dysfunction rate: 20.1%; 2-yr dysfunction rate: 24.1%	27	35
Maleux <i>et al</i> ^[75]	2000.8-2003.5	56	Upper variceal bleeding (18), refractory ascites (23), variceal bleeding with refractory ascites (10), refractory ascites with hydrothorax (4), hydrothorax (1)	CPC A/B/C: 8/13/35	337 (4-962) d	1	NA	10	30-d: 3; overall: 16
Charon <i>et al</i> ^[76]	2000.7-2003.1	100	Variceal bleeding (81), refractory ascites (19)	CPC A/B/C: 20/46/34	261 (45-837) d	11	1-yr patency rate: 84%	Acute: 13	45
Hausegger et al ^[77]	1999.9-2002.3	71	Refractory ascites (44), recurrent esophageal bleeding (27)	CPC A/B/C: 10/43/18	NA	9	6-mo patency rate: 87.4%; 1-yr patency rate: 80.8%	18	30-d: 7; overall: 20

Table 4 Outcome of transjugular intrahepatic portosystemic shunt with covered stents: An overview of case series

¹Data are expressed as absolute mean ± SD (range) or mean (range). BCS: Budd-Chiari syndrome; CPC: Child-Pugh class; HE: Hepatic encephalopathy; MELD: Model for end-stage liver disease; NA: Not available.

stent and a 2-cm-long portal-vein region uncovered. The latter is fully covered by PTFE inside and outside a bare stent without a bare segment at the portal vein end of the stent. Thus, the placement of a Fluency stent should not be extended into the main portal vein trunk. Otherwise, the hepatic perfusion from the portal vein blood flow would be affected.

In a retrospective study, the investigators compared the outcome of TIPS between patients receiving Viatorr stents only (n = 28) and those receiving Fluency stents only (n = 93)^[90]. Although the major encephalopathy rate was not significantly different between the two groups (3.6% vs 4.3%, P = 1.0), the Viatorr stent group showed a higher hemodynamic success rate (98% vs 90%) and primary unassisted patency rate (6-mo: 95% vs 87%; 12-mo: 89% vs 81%, P = 0.03) than the Fluency stent group. No-

tably, the development of shunt dysfunction was primarily attributed to the stenosis of the portal and hepatic vein end in the Fluency and Viatorr stent groups, respectively. The difference in the causes of shunt dysfunction might be explained by the different design of the two stents.

In a retrospective case series regarding the outcome of TIPS for the treatment of BCS, Fluency covered stents elevated the incidence of post-TIPS hepatic encephalopathy than bare stents^[51]. This might be explained by the possibility that fully covered stents decreased hepatic perfusion, thereby preventing the liver from removing toxic substances from the body. However, the retrospective nature and a small sample size of this study might limit the generalization of this finding.

Collectively, the Viatorr stent may be superior to the Fluency stent in reducing the incidence of shunt dysfunction. Certainly, the Fluency stent should be an alternative choice due to the limited availability of Viatorr stent in some regions. In addition, a combined Wallstent/Fluency stent may be considered to further improve the shunt patency^[90].

POSITION OF STENT PLACEMENT: LEFT VS RIGHT PORTAL VEIN BRANCH

As for the proximal (i.e., hepatic vein) end of the stent placement, the optimal position is the confluence of the hepatic vein and the inferior vena cava^[91]. This is primarily because venous intimal hyperplasia would develop due to the increased high-velocity blood flow after TIPS insertion and thereby lead to hepatic vein stenosis^[92], if a stent did not cover the proximal end of the hepatic vein. As for the distant (i.e., portal vein) end, the stent placement into the right portal vein branch is preferred during a TIPS procedure. This is mainly because it is relatively easier to puncture from the hepatic vein to the right portal vein branch in routine clinical practice. However, whether the placement of TIPS stents into the left or right portal vein branch is more beneficial has been rarely recognized. In a recent randomized controlled trial, 72 advanced cirrhotic patients undergoing TIPS were assigned to the left and right portal vein branch groups^[93]. The findings of this trial were impressive that the placement of stents into the left portal vein branch led to a significantly lower incidence of overall hepatic encephalopathy (7/36 vs 14/32, P = 0.036) and de novo encephalopathy (4/36 vs 12/32, P = 0.012) after TIPS insertion. Accordingly, the proportion of patients re-admitted to the hospital at least once was significantly lower in the left portal vein branch group than in the right portal vein branch group (16/36 vs 24/32, P = 0.015). Also, the total cost per patient within the first 2 years was significantly lower in the left portal vein branch group than in the right portal vein branch group. But the position of stent placement did not significantly impact the reduction of portosystemic pressure gradient after TIPS (10.2 \pm 1.6 vs 10.4 ± 1.4 , P = 0.889), the prevention of variceal rebleeding (6/36 vs 5/32, P = 0.907), and the control of ascites persistence or recurrence (11/36 vs 15/32, P = 0.167).

This randomized study suggests the rationality of placing a stent into the left portal vein branch during a TIPS procedure. This may be explained by the anatomy of the portal venous system. In the normal circumstance, 30% and 70% of the blood from the main portal vein is drained into the left and right portal vein branch, respectively. Thus, as the stent is placed in the right portal vein branch, a larger amount of blood will be bypassed from the right liver lobe that is nearly 6 times larger than the left liver lobe, thereby greatly decreasing the hepatic perfusion and inducing the development of liver dysfunction and hepatic encephalopathy. By comparison, the stent placement into the left portal vein branch may produce a lower risk of hepatic encephalopathy.

Notably, this conclusion needs to be balanced in the

real-world clinical situations. An occlusive intrahepatic portal vein branch is considered an important factor for TIPS failure in patients with portal vein thrombosis^[46]. Thus, to increase the rate of TIPS success, the stent should be placed in a patent vessel, regardless of left or right portal vein branch. In addition, an ideal position of stent placement is often difficult to be achieved in BCS patients with hepatic vein thrombosis and hepatic enlargement and congestion, because the stent is often placed through a long distance between the IVC and portal vein.

CONCLUSION

Selection of an appropriate stent during a TIPS procedure is very important for the shunt function and treatment efficacy. By reviewing the current evidence, several following recommendations may be considered in the clinical practice: (1) a 10-mm stent may be superior to an 8-mm or 12-mm stent for the management of portal hypertension and the improvement of shunt patency; (2) covered stents are better than bare stents for decreasing the shunt dysfunction; (3) if available, Viatorr stent-grafts may be superior to Fluency stent-grafts for the improvement of shunt patency; and (4) the placement of a stent in the left portal vein branch may improve the hepatic perfusion and decrease the incidence of hepatic encephalopathy. However, we have to acknowledge that these recommendations are based on a majority of retrospective studies. Therefore, prospective well-designed studies should be warranted to confirm them.

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