

Smaller-Diameter Covered Transjugular Intrahepatic Portosystemic Shunt Stents Are Associated With Increased Survival



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BACKGROUND & AIMS: We studied the effects of diameter of covered, self-expandable, nitinol stents on survival times of patients with a transjugular intrahepatic portosystemic shunt (TIPS).

METHODS: We collected data from 185 patients (median age, 55 y; 30% female) who received a covered nitinol stent, from February 2006 through September 2010, using the online multicenter German TIPS registry. TIPS were given to 107 patients for refractory ascites and to 78 patients for variceal bleeding. Patients at risk of hepatic encephalopathy (owing to advanced age, prior episodes) or liver failure (bilirubin level, >3 mg/dL), and bleeding patients receiving variceal embolization at TIPS, received 8-mm stents (n = 53). The remaining patients received 10-mm stents (n = 132). Eighty-one of the 10-mm stents were underdilated using 8-mm dilation balloons. Clinical and biochemical data were collected after TIPS placement at 1 month, 3 months, 6 months, 9 months, 1 year, and thereafter every 3 to 6 months. Groups were compared using propensity score analysis.

RESULTS: Patients who received 8-mm stents survived significantly longer (34 ± 26 mo) than patients who received 10-mm stents (18 ± 19 mo), regardless of whether they were fully dilated or underdilated. When we compared 10-mm stents with or without underdilation, we found that a significantly higher proportion of patients who received underdilated stents survived for 1 month after TIPS placement (95% vs 84%; *P* = .03), but not for 3 months (*P* = .10). In multivariate analysis, 1-year mortality correlated with full dilation of the stent to 10 mm (hazard ratio [HR], 2.0; 95% CI, 1.1–3.5) and with serum creatinine concentration at baseline (HR, 1.5; 95% CI, 1.0–1.7). Five-year mortality was associated with use of the 10-mm stents (HR, 1.8; 95% CI, 1.4–2.7) and baseline concentration of creatinine (HR, 1.3; 95% CI, 1.1–1.6).

CONCLUSIONS: A smaller stent (nominal diameter of 8 mm, but not underdilation of a 10-mm stent) is associated with a prolonged survival compared with 10-mm stents, independent of liver-specific prognostic criteria.

Keywords: Cirrhosis; Portal Hypertension; Covered; Comparison.

Portal hypertension is the pivotal vascular consequence of end-stage liver disease leading to severe complications, such as variceal bleeding and ascites. These complications can be treated successfully with a transjugular intrahepatic portosystemic shunt (TIPS).^{1,2} The use of a covered stent, available since 2000, has improved shunt patency^{3,4} as well as clinical outcomes, justifying its recommendation for the treatment of acute variceal bleeding and refractory ascites.^{1,2,5} Nevertheless,

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Abbreviations used in this paper: HE, hepatic encephalopathy; MELD, model for end-stage liver disease; PSPG, portal systemic pressure gradient; TIPS, transjugular intrahepatic portosystemic shunt.

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the stent diameter remains an open question. A previous randomized controlled study showed that small-diameter stents had more rebleedings and did not reduce the rate of hepatic encephalopathy, the reason for premature termination of the trial.⁶ In contrast, a recent randomized study found good prevention of rebleeding and lower rates of hepatic encephalopathy (HE) with small, 8-mm covered stents as compared with 10-mm stents.⁷

In the clinical routine, underdilation of 10-mm stents is a frequently applied approach, and also has been recommended by a recent Italian consensus conference.⁵ In case of insufficient clinical response, shunt revision with further dilation of the stent may be an option to improve its efficacy. This common practice does not take into account the physical characteristics of stents manufactured from nitinol, an alloy that always tends to reach its nominal diameter. Consequently, recent studies have shown that underdilation was of short duration and not effective in permanently reducing the shunt flow and thus improving the incidence of post-TIPS HE.^{8–11} This is the reason why investigators are about to abandon underdilation of 10-mm stents, using smaller stents with a nominal diameter of 8 mm instead.

Previous studies investigating the effects of stent diameter are contradictory and did not evaluate survival.^{6,7} This study adds additional information by comparing the survival of patients receiving covered nitinol stents with nominal diameters of 8 or 10 mm. All patients were included in the German TIPS registry and their data were prospectively assessed and documented.

Patients and Methods

The prospective, open-label, multicenter German TIPS registry (www.TIPS-Register.de) was started in February 2006 and closed in September 2010. The respective local ethical committees approved the study protocol and patients signed written informed consent (Freiburg, 136/05; Bonn, 257/14). The registry consisted of 4 computer-based data sheets: the first sheet contained the biomedical baseline characteristics of the patients; the second sheet contained the characteristics of the procedure, including pressures, stent characteristics, duration of the procedure, radiation time, medication at intervention (including anticoagulation), and technical complications; the third and fourth sheets were used to collect data from the index hospital stay and the follow-up evaluation, such as biochemical tests, clinical complications, including HE, response to treatment, duplex-examination results, and death, respectively. The follow-up intervals were as follows: 1 month, 3 months, 6 months, 9 months, 1 year, and thereafter every 3 to 6 months.

De novo TIPS implantation or TIPS revision was performed in 617 patients and documented electronically. In 115 patients the follow-up documentation was incomplete (patients referred only for the intervention from

What You Need to Know

Background

We collected data from the German transjugular intrahepatic portosystemic shunt registry to compare the effects of different stent diameters on survival times of 185 patients who received a transjugular intrahepatic portosystemic shunt for variceal bleeding or refractory ascites.

Findings

Patients who received the 8-mm stents survived significantly longer than patients who received 10-mm stents—regardless of whether stents were fully dilated or underdilated. Implantation of 10-mm stents increased the risk of death within 1 year by 90%, compared with 8-mm stents. In multivariate analysis, 10-mm stents increased the risk of death within 5 years by 80%; increased serum level of creatinine increased the risk of death within 5 years by 30%. All other conventional predictors showed no independent association with survival.

Implications for patient care

A smaller stent (nominal diameter, 8 mm) is associated with prolonged survival in patients with variceal bleeding and refractory ascites compared with patients receiving larger stents. Although underdilation of a 10-mm stent could provide a temporary benefit, it does not increase patient survival compared with an 8-mm stent.

other centers), only 502 patients could be evaluated. De novo TIPS implantation was performed in 351 patients: 31 of these patients had noncirrhotic portal hypertension owing to vascular liver disease and 135 patients received bare-metal stents, and 185 patients received covered stent grafts and participated in this study.

Procedure

TIPS placement was performed as previously described.^{1,11–14} Portal and central venous pressures were measured using a pressure transducer system and a multichannel monitor. The portosystemic pressure gradient (PSPG) was determined before and at the end of the stent implantation and defined as the difference between the pressure measured in the portal vein and the pressure measured in the right atrium, as previously described.¹⁴ Our primary aim was to reduce the pre-TIPS PSPG by 40% to 50% or to less than 12 mm Hg. Optimal TIPS function was assumed when remnant liver and lack of collateral perfusion were seen at final angiography after TIPS implantation.

All patients included in this analysis received a covered nitinol stent (Viatore; Gore, Phoenix, AZ). The dilation of the stent was performed using balloon

catheters according to the manufacturer's instructions for use. The use of smaller (nominal, 8 mm) or wider stents (nominal, 10 mm) was at the decision of the interventionalists. Smaller stents or underdilation of the stent was preferred when patients were at increased risk of HE (eg, advanced age, prior episodes) or liver failure (bilirubin level, >3 mg/dL). In addition, most patients receiving TIPS for variceal bleeding received covered 8-mm stents because graded reduction of the pressure gradient together with variceal embolization are believed to be sufficiently effective to prevent rebleeding. The physical data of the patient (eg, dimensions, body mass index) or the liver (eg, medioclavicular diameter, volume) did not influence the selection of the stent diameter or size of the dilation balloon.

Patients with a platelet count greater than 100,000/ μ L and an uneventful intervention received heparin during the procedure (1000–2000 IU) and low-molecular-weight heparin (prophylactic dosing) during the same hospital stay in which the TIPS was inserted. Long-term, low-dose acetylic-salicylic acid (100 mg/d) was given per the hepatologist's decision. The administration of heparin and/or acetylic-salicylic acid were center-based decisions and not evidence-based.

Follow-Up Evaluation

Outpatient visits were performed at regular intervals as outlined earlier. The visits included clinical examination and routine laboratory work-up including liver and kidney function tests and ultrasound investigation of the stent function. The need for TIPS revision was considered when patients showed clinical sign of TIPS dysfunction (progress of varices or bleeding, persistent need for paracentesis after 3 months) or in case duplex-sonography indicated shunt failure. The latter was defined as a very slow (<40 cm/s) or a rapid (>200 cm/s) flow velocity in the stent or a low-flow velocity in the portal vein (<20 cm/s). HE was defined and graded according to existing guidelines¹⁵ and was assessed in all patients according to the West Haven Criteria, in some patients with additional critical flicker frequency and number connection test.¹⁵ Acute-on-chronic liver failure was diagnosed according to the Chronic Liver Failure - Sequential Organ Failure Assessment score and the CLIF Acute-on-Chronic Liver Failure in Cirrhosis definition.¹⁶

For patients who did not show up for scheduled follow-up visits, patients or their physician were contacted by telephone and foreign hospital admissions were documented as well. Data collection, documentation, and screening for plausibility were terminated in August 2015.

Statistical Analysis

Data are presented as medians and ranges or as the number of patients and percentage. The Wilcoxon test

was used for comparison of paired data and the Mann-Whitney *U* test and the Kruskal-Wallis *H* test were used for unpaired comparisons of 2 or more groups. Univariate time-to-event analysis was performed to identify parameters that might significantly predict transplant-free survival. Cox regression analysis (forward step-wise likelihood quotient) using the significant predictors in the univariate analysis was performed to identify independent predictors of transplant-free survival at 1 and 5 years after TIPS. Kaplan-Meier curves were used to analyze the transplant-free survival rates of patients using the log-rank test, and *P* values less than .05 were considered statistically significant.

To account for the lack of randomization, a (1:1) propensity score matching of the entire cohort for nominal 10- and 8-mm diameter TIPS stents was performed adjusted for age, model of end-stage liver disease (MELD), and serum bilirubin level with a maximum propensity score distance (caliper) of 0.5. The assessment of the probabilities of different outcomes, which compete with each other to occur, first requires the use of competing-risks analysis. Liver transplantation is a competing event for survival. Accounting for competing risks also has implications for prognosis and treatment efficacy research. We therefore performed competing-risk analysis with the Fine and Gray method to rule out liver transplantation influencing survival data.

Statistical analyses were performed using SPSS 22 (SPSS, Inc, Chicago, IL) and R statistics version 2.14 (The R Foundation, Vienna, Austria).

Results

Patients and Procedures

The biomedical and procedural characteristics of all patients are shown in [Table 1](#). Briefly, the median age was 55 years and 30% of the patients were female. Fifty-eight percent of the patients had Child-Pugh class B cirrhosis and the median MELD score was 12. The majority of patients received TIPS for refractory ascites. HE was present in 64 patients, and most of them received TIPS for severe variceal bleeding. TIPS reduced the PSPG adequately in all patients. The nominal stent diameter was 10 mm in 132 patients and 8 mm in 53 patients. Eighty-one of the 132 patients with a 10-mm stent had underdilation to only 8 mm, while 51 patients received full dilation of the stent. During follow-up evaluation, 64 patients died and 10 patients were transplanted. Thirty-one patients died from their liver disease and 11 deaths were not related to liver disease. In 21 patients the cause of death could not be evaluated ([Supplementary Table 1](#)).

As shown in [Supplementary Table 2](#), the 3 subgroups with 8-mm stents, 10-mm underdilated stents, and 10-mm fully dilated stents differed in several respects. Most patients treated for variceal bleeding received

Table 1. Main Characteristics and Outcomes of Patients Receiving Covered TIPS (n = 185 Patients)

	Covered stent (n = 185)
Age, y	55 (29–81)
Sex, male/female	129/56
MELD score	12 (6–37)
MELD-Na score	15 (6–37)
ACLF at TIPS, no/yes	146/39
Child–Pugh class, A/B/C	34/107/44
Etiology of cirrhosis, viral/ alcoholic/other	31/128/26
Indication for TIPS, bleeding/ ascites	78/107
Varices, absent/esophageal/ ectopic	78/103/17
Ascites, absent/present	49/136
Hepatic encephalopathy, absent/ I–II°/III–IV°	121/54/10
Bilirubin level, mg/dL	1.3 (0.2–13.2)
Creatinine level, mg/dL	1.2 (0.5–14)
INR	1.1 (0.9–2.5)
Sodium level, mmol/L	136 (115–149)
PSPG before TIPS, mm Hg	19 (8–35)
PSPG after TIPS, mm Hg	7 (1–28)
Nominal stent diameter, 8/10 mm	53/132
Effective stent diameter, to 8 mm/ to 10 mm	134/51
Hospital stay after TIPS, d	7 (1–50)
TIPS revision, no/yes	138/47
Time to TIPS revision, d	350 (0–2144)
Dead/transplanted	63/10

NOTE. Values are reported as median and (ranges).

ACLF, acute-on-chronic liver failure; INR, international normalized ratio; MELD, model for end-stage liver disease; PSPG, portal systemic pressure gradient; TIPS, transjugular intrahepatic portosystemic shunt.

8-mm stents, while patients with refractory ascites predominantly received 10-mm stents with or without underdilation. This implies differences in MELD scores, Child–Pugh classes, creatinine level, and hospital stay. Compared with 10-mm stents, the 8-mm stents resulted in less reduction of the pressure gradient (–45% vs –65%). However, subgroups with 10-mm stents with or without underdilation showed a similar reduction of the PSPG. With respect to revisions needed during follow-up evaluation, patients with an 8-mm stent required significantly more revisions (40%) than patients with 10-mm stents (16% after full dilation, 22% after underdilation). Surprisingly, the smaller 8-mm stents were revised later than the 10-mm stents regardless of whether they were fully dilated or not.

Univariate and Multivariate Analyses of Survival

Univariate and multivariate analyses were performed including all 185 patients to detect confounding factors for 5-year survival. **Table 2** shows the univariate and multivariate analyses, which were performed with the end point of 5-year transplant-free survival. Several

Table 2. Univariate Time-to-Event Analysis and Multivariate Cox Regression Analysis (Forward Stepwise Likelihood Quotient) Using the Significant Predictors in the Univariate Analysis Predicting 5-Year Mortality of the Whole Cohort (n = 185)

Parameters	Univariate		Multivariate analysis	
	P value	Hazard ratio	P value	Hazard ratio (95% CI)
Age	.155			
Sex	.381			
Bleeding vs ascites as TIPS indication	.001	2.328		
PSPG after TIPS	.016	0.931		
Serum bilirubin	.003	1.334		
INR	.003	4.154		
Serum creatinine	<.001	1.316	<.001	1.342 (1.148–1.572)
Serum sodium	.023	0.943		
8-mm vs 10-mm nominal diameter	<.001	2.870	<.001	1.838 (1.392–2.704)
10-mm fully dilated ^a	<.001	1.930		

NOTE. Boldface indicates independent predictors.

INR, international normalized ratio; PSPG, portal systemic pressure gradient; TIPS, transjugular intrahepatic portosystemic shunt.

^aFor this variable, the categories were a fully dilated 10-mm stent vs an underdiluted 10-mm stents vs 8-mm stents.

factors influenced 5-year survival including indication for TIPS and biochemical variables of the severity of the disease such as bilirubin level, creatinine level, and international normalized ratio. Age and sex at the time of TIPS insertion showed no impact on transplant-free survival. With respect to stent diameters, smaller stents were associated with improved survival. In the multivariate analysis, higher serum creatinine concentration and the implantation of a 10-mm stent, regardless of whether the dilation was to 8 mm or 10 mm, remained the only significant parameters.

Propensity Score Matching

To address the differences between groups (**Supplementary Table 2**), a propensity analysis was performed. After propensity matching for age, MELD score, and bilirubin concentration, 41 patients with an 8-mm stent were matched to 41 patients with a 10-mm stent (**Table 3**). As shown, there were still some differences between the groups regarding indication for TIPS, Child score, and the presence of ascites (**Table 3**). Unfortunately, matching reduced the cohorts of 8- and 10-mm stents from 53 to 41 and 132 to 41, respectively. To facilitate matching and to avoid further reduction in the sample size, both subgroups with 10-mm stents were included in the propensity score analysis. This seems to

Table 3. Main Characteristics and Outcomes of Patients Receiving Covered TIPS Matched Cohort (n = 82 Patients)

	Covered stent (n = 82)	8 mm (n = 41)	10 mm (n = 41)	P value
Age, y	56 (33–81)	56 (33–81)	56 (41–71)	.921
Sex, male/female	58/24	29/12	29/12	1.000
MELD score	11 (6–29)	10 (6–20)	12 (7–29)	.065
MELD-Na score	13 (6–30)	12 (6–27)	14 (8–30)	.057
ACLF at TIPS, no/yes	67/15	36/5	31/10	.253
Child–Pugh class, A/B/C	22/45/15	19/18/4	3/27/11	<.001
Etiology of cirrhosis, viral/alcoholic/other	56/22/4	25/12/4	31/10/0	.185
Indication for TIPS, bleeding/ascites	35/47	29/12	6/35	<.001
Varices, absent/esophageal/ectopic	42/40	21/20	21/20	1.000
Ascites, absent/present	28/54	22/19	6/35	<.001
Hepatic encephalopathy, absent/I–II°/III–IV°	57/21/4	30/8/3	27/13/1	.309
Bilirubin, mg/dL	1.2 (0.3–2.8)	1.2 (0.3–2.6)	1.2 (0.3–2.8)	.929
Creatinine, mg/dL	1.2 (0.5–14.1)	1.0 (0.5–4.9)	1.4 (0.7–14.1)	.058
INR	1.1 (0.9–1.6)	1.1 (0.9–1.5)	1.1 (1.0–1.6)	.250
Sodium level, mmol/L	137 (115–144)	137 (115–144)	137 (121–143)	.294

NOTE. Values are reported as median and (ranges) or number of patients and (%).

ACLF, acute-on-chronic liver failure; INR, international normalized ratio; MELD, model for end-stage liver disease; TIPS, transjugular intrahepatic portosystemic shunt.

be justified by the fact that underdilation of a 10-mm stent had no effect on survival (Table 2).

Kaplan–Maier Analyses of Survival by Propensity Score Matching

Figure 1 shows the Kaplan–Maier analysis of transplant-free survival comparing groups with 8-mm and 10-mm stents in the matched cohort. Significantly better survival was seen in patients who had received a stent with a nominal diameter of 8 mm compared with patients who received a stent with a nominal diameter of 10 mm (Figure 1).

In addition, a competing event analysis with death and liver transplantation as competing risks was performed. The 1:1 propensity score–matched patients showed a tendency toward reduced mortality with 8-mm stents when compared with the 10-mm stents ($P < .126$), but no difference in receiving liver transplantation. Similarly, the dilation of the stent did not influence the probability of liver transplantation in these propensity score–matched patients.

Discussion

Our study investigated the effect of the stent diameter on survival of patients treated for variceal bleeding or refractory ascites. Only patients with a covered Viatorr stent were included. Because of its longer patency and better symptom control, these covered stents have become the standard of care.^{1–5,17,18} With respect to optimal stent diameter, previous findings have been controversial.^{6,7} The fact that 2 recently published randomized studies^{19,20} in patients with variceal bleeding

found HE rates of 18% and 35% with 8- and 10-mm stents, respectively, shows that smaller stents may be preferable.

This study shows a possible independent transplant-free survival benefit of the smaller 8-mm stents. The fact that smaller stents resulted in a lower reduction of the PSPG and a higher rate of revisions does not outbalance the improvement in survival. Our results, therefore, recommend the routine use of 8-mm stents.

As shown again, underdilation of a 10-mm nitinol stent is no solution. Compared with full dilation of a 10-mm stent, underdilation to 8 mm yielded similar results with respect to portal pressure reduction and survival. At the time of TIPS creation, the radial recoil of the stent exerted by the surrounding tissue lead to similar diameters of a 10-mm stent irrespective of whether 8- or 10-mm balloons were used.¹¹ With time, the persistent radial forces of the underdilated stent caused further expansion to reach the nominal diameter of 10 mm. This has been confirmed by previous studies^{8–11} showing rapid self-expansion of nitinol stents together with little or no clinical benefit of underdilation. These findings are in contrast to the recommendation of the Italian National Consensus Guideline⁵ and a recent study from Italy showing that underdilation persisted and resulted in less HE.²¹ Fortunately, an improved covered stent has been marketed recently (Viatorr CX) that allows stent adjustment to 8, 9, or 10 mm without spontaneous further self-expansion. In any case, our results encourage dilation to 8 mm as a routine, independent of the degree of reduction of the pressure gradient, and to revise and dilate further if necessary.

We focused on the analysis of the nominal stent diameter as a predictor of survival. The decrease in the PSPG, which should be correlated closely with stent

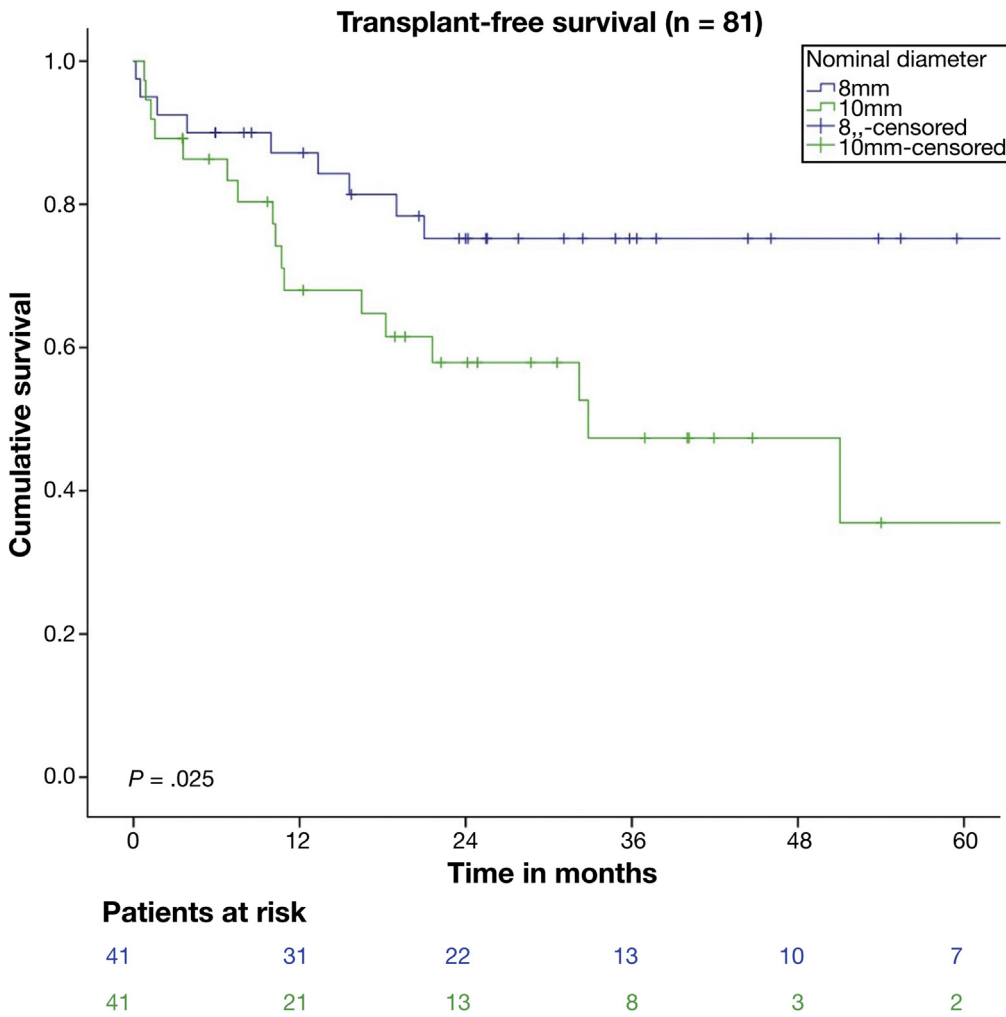


Figure 1. Kaplan-Meier analysis comparing 1:1 propensity-matched patients with 8-mm (n = 41) or 10-mm (n = 41) nominal stent diameters adjusted for age, model for end-stage liver disease, and serum bilirubin concentration.

diameter, has not been analyzed in detail. Because PSPG measurements were performed only at TIPS insertion they do not represent pressures during follow-up evaluation with sufficient accuracy.²² In particular, self-expansion during follow-up evaluation, which is seen with any nitinol stent irrespective of its partial or full dilatation, may be the reason for further reduction in the PSPG.¹¹ This explains our unexpected finding that a higher PSPG was not associated independently with survival, while the nominal diameter of the stent was. Of note, another reason for this negative finding might be that the measurement of PSPG in our study was performed using right atrial pressure,¹⁴ and not inferior vena cava or hepatic vein pressures. This should be taken into account when interpreting our data.

This study was limited by its observational character, which led to patient selection favoring the small-diameter stent group. The smaller or underdilated TIPS was used more frequently in patients with an increased risk of HE or with variceal bleeding showing lower Child-Pugh and MELD scores. Other confounding factors such as sarcopenia or malnutrition were not regarded because they were not recorded in the registry. Although data were obtained prospectively, the retrospective

design and the post hoc character of its analysis were further limitations of this study. To address the problem of selection bias, propensity analysis was performed. After propensity score matching for age, MELD score, and serum bilirubin concentration, only 82 patients were comparable. Matching reduced the sample size of the 10-mm stent group from 132 to 41 patients. Unfortunately, groups remained different with respect to indication (ascites vs bleeding) and creatinine concentration. Expanding matching by inclusion of the indication or creatinine concentration was not possible because of a further critical reduction in the sample size. Nevertheless, the better survival of the 8-mm stent group seen after matching underlines the finding of the multivariate analysis of the total cohort that small-diameter stents may be associated independently with prolonged survival. We focused our analysis only on survival and did not analyze other clinical end points such as rebleeding, recurrence of ascites, or HE. We believed that our sample size did not allow augmentation of end points.

In summary, covered stents with an 8-mm diameter may prolong survival in TIPS patients treated for variceal bleeding and refractory ascites when compared with 10-mm stents. Our results recommend the routine insertion

of small shunts irrespective of the TIPS indication. The availability of a novel covered stent with variable diameters (8, 9, or 10 mm) and without the disadvantage of self-expansion during follow-up evaluation may facilitate the decision to establish small shunts.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at <https://doi.org/10.1016/j.cgh.2019.03.042>.

References

- Rossle M. TIPS: 25 years later. *J Hepatol* 2013;59:1081–1093.
- Trebicka J. Emergency TIPS in a Child-Pugh B patient: when does the window of opportunity open and close? *J Hepatol* 2017;66:442–450.
- Bureau C, Garcia-Pagan JC, Otal P, et al. Improved clinical outcome using polytetrafluoroethylene-coated stents for TIPS: results of a randomized study. *Gastroenterology* 2004;126:469–475.
- Bureau C, Pagán JCG, Layrargues GP, et al. Patency of stents covered with polytetrafluoroethylene in patients treated by transjugular intrahepatic portosystemic shunts: long-term results of a randomized multicentre study. *Liver Int* 2007;27:742–747.
- Fagioli S, Bruno R, Debernardi Venon W, et al. Consensus conference on TIPS management: techniques, indications, contraindications. *Dig Liver Dis* 2017;49:121–137.
- Riggio O, Ridola L, Angeloni S, et al. Clinical efficacy of transjugular intrahepatic portosystemic shunt created with covered stents with different diameters: results of a randomized controlled trial. *J Hepatol* 2010;53:267–272.
- Wang Q, Lv Y, Bai M, et al. Eight millimeter covered TIPS does not compromise shunt function but reduces hepatic encephalopathy in preventing variceal rebleeding. *J Hepatol* 2017;67:508–516.
- Pieper CC, Sprinkart AM, Nadal J, et al. Postinterventional passive expansion of partially dilated transjugular intrahepatic portosystemic shunt stents. *J Vasc Interv Radiol* 2015;26:388–394.
- Hsu MC, Weber CN, Stavropoulos SW, et al. Passive expansion of sub-maximally dilated transjugular intrahepatic portosystemic shunts and assessment of clinical outcomes. *World J Hepatol* 2017;9:603–612.
- Pieper CC, Jansen C, Meyer C, et al. prospective evaluation of passive expansion of partially dilated transjugular intrahepatic portosystemic shunt stent grafts—a three-dimensional sonography study. *J Vasc Interv Radiol* 2017;28:117–125.
- Mollaiyan A, Bettinger D, Rossle M. The underdilation of nitinol stents at TIPS implantation: solution or illusion? *Eur J Radiol* 2017;89:123–128.
- Trebicka J, Krag A, Gansweid S, et al. Endotoxin and tumor necrosis factor-receptor levels in portal and hepatic vein of patients with alcoholic liver cirrhosis receiving elective transjugular intrahepatic portosystemic shunt. *Eur J Gastroenterol Hepatol* 2011;23:1218–1225.
- Trebicka J, Krag A, Gansweid S, et al. Soluble TNF-alpha-receptors I are prognostic markers in TIPS-treated patients with cirrhosis and portal hypertension. *PLoS One* 2013;8:e83341.
- Rossle M, Blanke P, Fritz B, et al. Free hepatic vein pressure is not useful to calculate the portal pressure gradient in cirrhosis: a morphologic and hemodynamic study. *J Vasc Interv Radiol* 2016;27:1130–1137.
- Vilstrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. *Hepatology* 2014;60:715–735.
- Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. *Gastroenterology* 2013;144:1426–1437, 1437 e1–9.
- Perarnau JM, Le Gouge A, Nicolas C, et al. Covered vs. uncovered stents for transjugular intrahepatic portosystemic shunt: a randomized controlled trial. *J Hepatol* 2014;60:962–968.
- de Franchis R, Faculty BV. Expanding consensus in portal hypertension: report of the Baveno VI Consensus Workshop: stratifying risk and individualizing care for portal hypertension. *J Hepatol* 2015;63:743–752.
- Sauerbruch T, Mengel M, Dollinger M, et al. Prevention of rebleeding from esophageal varices in patients with cirrhosis receiving small-diameter stents versus hemodynamically controlled medical therapy. *Gastroenterology* 2015;149:660–668.e1.
- Holster IL, Tjwa ETL, Moelker A, et al. Covered transjugular intrahepatic portosystemic shunt versus endoscopic therapy + β -blocker for prevention of variceal rebleeding. *Hepatology* 2016;63:581–589.
- Schepis F, Vizzutti F, Garcia-Tsao G, et al. Under-dilated TIPS associate with efficacy and reduced encephalopathy in a prospective, non-randomized study of patients with cirrhosis. *Clin Gastroenterol Hepatol* 2018;16:1153–1162 e7.
- Silva-Junior G, Turon F, Baiges A, et al. Timing affects measurement of portal pressure gradient after placement of transjugular intrahepatic portosystemic shunts in patients with portal hypertension. *Gastroenterology* 2017;152:1358–1365.

Reprint requests

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Conflicts of interest

The authors disclose no conflicts.

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Supplementary Table 1. Causes of Death

Cause of death	Patients, n
ACLF	15
Sepsis or infection	14
Bleeding	2
Non-liver-related	11
Unknown	21

ACLF, acute-on-chronic liver failure.

Supplementary Table 2. Main Characteristics and Outcomes of Patients Receiving Covered TIPS of 8- and 10-mm Nominal Diameter and Dilated to Either 8 or 10 mm

Parameters	8-mm stents (n = 53)	10-mm stents dilated to 8 mm (n = 81)	10-mm stents dilated to 10 mm (n = 51)
Age, y	53 (29–81)	57 (40–79)	54 (33–71)
Sex, male/female	36/17	54/27	39/12
MELD score ^a	9 (6–20)	12 (6–29)	14 (6–37)
Child–Pugh class, A/B/C ^a	26/23/4	4/56/21	4/28/19
Etiology of cirrhosis, viral/alcoholic/other	9/34/10	15/55/11	7/39/5
Indication for TIPS, bleeding/ascites ^a	40/13	23/58	15/36
Varices, absent/esophageal/ectopic	26/27/4	27/53/6	26/23/6
Ascites, absent/present ^a	31/22	12/69	6/46
Hepatic encephalopathy, absent/I–II°/III–IV°	38/11/4	47/31/3	36/12/3
Bilirubin level, mg/dL	0.9 (0.3–2.6)	1.2 (0.2–3.9)	1.3 (0.2–13.2)
Creatinine level, mg/dL ^a	0.8 (0.5–4.9)	1.6 (0.6–14.1)	1.4 (0.5–4.0)
INR ^b	1.1 (0.9–1.5)	1.2 (0.9–1.9)	1.2 (0.9–2.5)
Sodium level, mmol/L	137 (120–144)	137 (115–143)	136 (115–149)
PSPG before TIPS, mm Hg	20 (9–35)	19 (8–35)	20 (9–35)
PSPG after TIPS, mm Hg ^a	11 (2–28)	7 (1–20)	7 (1–17)
Hospital stay after TIPS, d ^b	7 (1–29)	9 (2–52)	8 (1–67)
TIPS revision, no/yes ^b	32/21	63/18	43/8
Time to TIPS revision, d ^b	400 (21–2144)	261 (0–963)	343 (0–1022)

NOTE. Values are reported as median and (ranges).

INR, international normalized ratio; MELD, model for end-stage liver disease; PSPG, portal systemic pressure gradient; TIPS, transjugular intrahepatic porto-systemic shunt.

^a*P* < .001 across the different groups tested using the Kruskal–Wallis H test.

^b*P* < .05 across the different groups tested using the Kruskal–Wallis H test.