Under-dilated TIPS Associate With Efficacy and Reduced Encephalopathy in a Prospective, Non-randomized Study of Patients With Cirrhosis

Filippo Schepis,[*,a] Francesco Vizzutti,[‡,a] Guadalupe Garcia-Tsao,[*,§] Guido Marzocchi,[‖] Luigi Rega,[¶] Nicola De Maria,[*] Tommaso Di Maira,[*] Stefano Gitto,[*] Cristian Caporali,[‖] Stefano Colopi,[‖] Mario De Santis,[‖] Umberto Arena,[‡] Antonio Rampoldi,[#] Aldo Airoldi,[**] Alessandro Cannavale,[‡‡] Fabrizio Fanelli,[‡‡] Cristina Mosconi,[§§,‖‖] Matteo Renzulli,[§§,‖‖] Roberto Agazzi,[¶¶] Roberto Nani,[¶¶] Pietro Quaretti,[##] Ilaria Fiorina,[##] Lorenzo Moramarco,[##] Roberto Miraglia,[***] Angelo Luca,[***] Raffaele Bruno,[‡‡‡] Stefano Fagiuoli,[§§§] Rita Golfieri,[§§,‖‖] Pietro Torricelli,[‖] Fabrizio Di Benedetto,[‖‖‖] Luca Saverio Belli,[**] Federico Banchelli,[¶¶¶] Giacomo Laffi,[‡] Fabio Marra,[‡,###] and Erica Villa[*]

*Division of Gastroenterology, Modena Hospital, University of Modena and Reggio Emilia, Modena, Italy; [‡]Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy; [§]Section of Digestive Diseases, Department of Internal Medicine, Yale University School of Medicine and VA CT Healthcare System, New Haven, Connecticut; [‖]Department of Radiology, Modena Hospital, University of Modena and Reggio Emilia, Modena, Italy; [¶]Department of Radiology, Careggi Hospital, Florence, Italy; [#]Interventional Radiology Unit, Niguarda Ca' Granda Hospital, Milan, Italy; [**]Division of Hepatology and Gastroenterology, A.O. Niguarda Ca' Granda, Milan, Italy; [‡‡]Department of Radiology, "Sapienza" University, Rome, Italy; [§§]Radiology Unit, S. Orsola-Malpighi Hospital, Bologna, Italy; [‖‖]Department of Medical and Surgical Sciences, Alma Mater Studiorum, University of Bologna, Bologna, Italy; [¶¶]Interventional Radiology Unit, Papa Giovanni XXIII Hospital, Bergamo, Italy; [##]Unit of Interventional Radiology, Radiology Department, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; [***]Radiology Service, Department of Diagnostic and Therapeutic Services, Mediterranean Institute for Transplantation and Advanced Specialized Therapies, Palermo, Italy; [‡‡‡]Department of Infectious Diseases, University of Pavia, IRCCS Policlinico San Matteo, Pavia, Italy; [§§§]Division of Gastroenterology and Hepatology, Papa Giovanni XXIII Hospital, Bergamo, Italy; [‖‖‖]HPB Surgery and Liver Transplantation Unit, Modena Hospital, University of Modena and Reggio Emilia, Modena, Italy; [¶¶¶]Statistics Unit, Department of Clinical, Diagnostic and Public Health Medicine, University of Modena and Reggio Emilia, Modena, Italy; and the [###]Center for Research, High Education and Transfer DENOThe, University of Florence, Florence, Italy

BACKGROUND & AIMS: **Portosystemic encephalopathy (PSE) is a major complication of trans-jugular intrahepatic porto-systemic shunt (TIPS) placement. Most devices are self-expandable polytetrafluoroethylene-covered stent grafts (PTFE-SGs) that are dilated to their nominal diameter (8 or 10 mm). We investigated whether PTFE-SGs dilated to a smaller caliber (under-dilated TIPS) reduce PSE yet maintain clinical and hemodynamic efficacy. We also studied whether under-dilated TIPS self-expand to nominal diameter over time.**

METHODS: **We performed a prospective, non-randomized study of 42 unselected patients with cirrhosis who received under-dilated TIPS (7 and 6 mm) and 53 patients who received PTFE-SGs of 8 mm or more (controls) at referral centers in Italy. After completion of this study, dilation to 6 mm became the standard and 47 patients were included in a validation study. All patients were followed for 6 months; Doppler ultrasonography was performed 2 weeks and 3 months after TIPS placement and every 6 months thereafter. Stability of PTFE-SG diameter was evaluated by computed tomography analysis of 226 patients with cirrhosis whose stent grafts increased to 6, 7, 8, 9, or 10 mm. The primary outcomes were incidence of at least 1 episode of PSE grade 2 or higher during follow up, incidence of recurrent variceal hemorrhage or ascites, incidence of shunt dysfunction requiring TIPS recanalization, and reduction in porto-caval pressure gradient.**

[a]These authors contributed equally to the present study.

Abbreviations used in this paper: CG, control group; CI, confidence interval; CT, computed tomography; HVW, hepatic vein wall; LVP, large-volume paracentesis; MELD, model for end-stage liver disease; PCG, portocaval pressure gradient; PSE, portosystemic encephalopathy; PTFE-SG, polytetrafluoroethylene-covered stent graft; PVW, portal vein wall; RA, refractory ascites; TG, training group; TIPS, transjugular intrahepatic portosystemic shunt; VG, validation group; VH, variceal hemorrhage.

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RESULTS: **PSE developed in a significantly lower proportion of patients with under-dilated TIPS (27%) than controls (54%) during the first year after the procedure ($P = .015$), but the proportions of patients with recurrent variceal hemorrhage or ascites did not differ significantly between groups. No TIPS occlusions were observed. These results were confirmed in the validation cohort. In an analysis of self-expansion of stent grafts, during a mean follow-up period of 252 days after placement, none of the PTFE-SGs self-expanded to the nominal diameter in hemodynamically relevant sites (such as portal and hepatic vein vascular walls).**

CONCLUSIONS: **In prospective, non-randomized study of patients with cirrhosis, we found under-dilation of PTFE-SGs during TIPS placement to be feasible, associated with lower rates of PSE, and effective.**

Keywords: Portal Hypertensive Bleeding; Liver; Vascular Disease; Treatment.

The transjugular intrahepatic portosystemic shunt (TIPS) is an invasive treatment of portal hypertensive bleeding, refractory ascites (RA), and vascular diseases of the liver, which improves survival.[1–5] The availability of self-expandable polytetrafluoroethylene-covered stent grafts (PTFE-SGs) has dramatically improved the long-term patency of TIPS.[1,2] However, its major drawback is portosystemic encephalopathy (PSE), reported in 23%–55% within the first year.[3–11] Current guidelines recommend that post-TIPS portocaval pressure gradient (PCG) should be reduced below 12 mm Hg, particularly for rebleeding prevention.[1,2] A PCG reduction of more than 50% has been suggested as an alternative target.[1]

TIPS diameter influences PCG reduction and the eventual appearance of PSE because of a greater amount of portal blood diverted to the systemic circulation and a reduction in residual liver perfusion.[10–12] It is conceivable that balloon dilation of TIPS to diameters smaller than those currently indicated (ie, $\leq$7 mm) result in a lower risk of PSE.[12,13] However, this undersizing is not considered permanent because PTFE-SGs are expected to expand to their nominal diameter (ie, inner maximal diameter of a fully expanded PTFE-SG).[13,14]

We hypothesized that, within the cirrhotic parenchyma, underdilated PTFE-SGs would not self-expand to nominal diameter and could reduce post-TIPS encephalopathy. Thus, the aims of this study were to determine whether underdilated TIPS reduce the incidence of PSE while maintaining clinical efficacy, and to determine whether under-dilated TIPS maintain their size with time.

Materials and Methods

Study Design and Patients

Clinical study. This part of the study was a prospective, nonrandomized[15] analysis of clinical outcomes in consecutive patients with cirrhosis scheduled for TIPS placement at the referral centers of Modena and Florence, who agreed to participate in the study. In a first set of patients PTFE-SGs ballooned to 7 mm were studied to evaluate the feasibility and safety of under-dilation. Patients enrolled thereafter had PTFE-SGs underdilated to 6 mm. The latter (training group, TG) was compared with a control group (CG) including patients who had standard TIPS placed before the initiation of the study, patients who refused under-dilated TIPS, and those of the TG in whom TIPS was dilated to 8 mm for technical reasons (Figure 1*A*). After completion of this initial study, dilation to 6 mm became the standard and all patients were included in a validation group (VG) to confirm TG results (Figure 1*A*). Table 1 shows inclusion and exclusion criteria. All patients were followed in a dedicated outpatient clinic for 6 months, and then in a general hepatology clinic unless TIPS dysfunction or other complications, including PSE, were observed. Doppler ultrasonography of TIPS was performed 2 weeks and 3 months after TIPS placement and every 6 months thereafter.[2] No patients received pharmacologic prophylaxis for PSE after TIPS.

Outcomes evaluated were (1) incidence of at least 1 episode of PSE grade 2 or higher as evaluated by 2 observers at follow-up[8,9,16]; (2) incidence of recurrent variceal hemorrhage (VH) or ascites, defined as the need for at least 1 large-volume paracentesis (LVP) beyond 4 weeks after TIPS; (3) incidence of shunt dysfunction requiring TIPS recanalization; and (4) reduction in PCG. TIPS would be revised in case of recurrent VH, continued need for LVP, and/or if flow reversal in the intrahepatic portal branches was observed on Doppler ultrasonography.[2] PTFE-SGs (Viatorr, Gore, Flagstaff, AZ) were placed as previously described[4,5,7,8] using semicompliant balloon catheters (FoxCross, Abbott Park, IL).

In the CG, the intraparenchymal tract was initially dilated to 8 mm. Patients with post-TIPS PCG $\geq$12 mm Hg had further dilation to 9 or 10 mm, unless post-TIPS PCG was at or near the hemodynamic target and/or the patient was considered with limited functional reserve of the liver.[2,17]

In the TG and VG, the intraparenchymal tract was predilated to 6 mm, and the PTCE-SG was dilated to 7 or 6 mm unless the final TIPS path was angled. During dilation of the intraparenchymal tract, balloon pressure

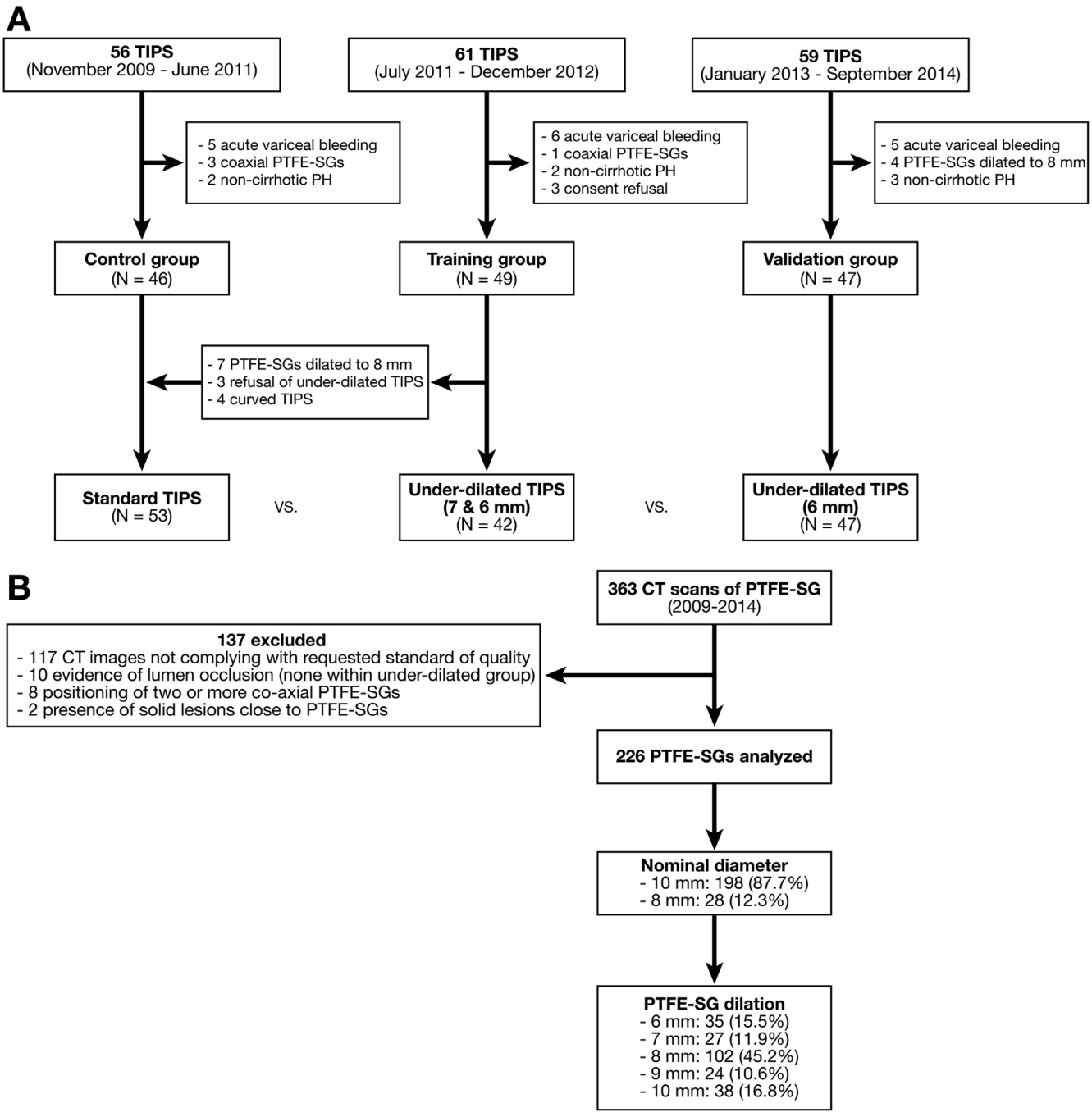

Figure 1. Study cohorts of the clinical (*A*) and imaging (*B*) studies. PH, portal hypertension.

was kept at the nominal value for 15–30 seconds, even in the lack of a complete flattening of notches at the level of portal (PVW) and hepatic vein (HVW) walls.

Immediately after TIPS placement, pressures in the portal vein, along the intraparenchymal tract of TIPS, and in the inferior vena cava were recorded until a stable tracing was obtained in each position (45–60 seconds). Permanent tracings were obtained with PowerLab (ADInstruments, Inc, Colorado Springs, CO). Post-TIPS PCG was calculated by subtracting the inferior vena cava pressure from the portal vein pressure. All procedures were performed by F.S., F.V., C.C., S.C., and M.D.S. under monitored anesthesia, without intubation and using midazolam and fentanyl as sedative and analgesic, respectively.[2,17]

Comparisons were made between patients who had the TIPS dilated to $\leq$7 mm (underdilated TIPS) versus those with diameters $\geq$8 mm (standard TIPS).

Imaging study

Patients with cirrhosis from 8 Italian referral centers (including those participating in the clinical study) who had TIPS placed using PTFE-SGs in the study period and who had an abdominal computed tomography (CT) scan

Table 1. Inclusion and Exclusion Criteria for Clinical and Imaging Studies

	Clinical study	Imaging study
Inclusion criteria	a) Diagnosis of cirrhosis determined on the basis of clinical history, histologic examination, morphologic characteristics of the liver at US, CT, and MRI; b) TIPS placed to prevent recurrent VH[1,2] or to control RA[21]; c) TIPS creation using PTFE-SG.	a) Diagnosis of cirrhosis determined on the basis of clinical history, histologic examination, morphologic characteristics of the liver at US, CT, and MRI; b) TIPS creation using PTFE-SG.
Exclusion criteria	a) Placement of 2 or more coaxial stent grafts; b) Refusal to consent to have PTFE-SG dilated to a small diameter and/or to attend follow-up visits; c) TIPS placed in the setting of acute variceal hemorrhage either as "early" TIPS or as salvage TIPS for continued bleeding or early rebleeding; d) Recurrent or persistent PSE; e) Common absolute contraindications to TIPS[1,2]	a) Placement of 2 or more coaxial stent grafts; b) Evidence of lumen occlusion on CT; c) Presence of solid or cystic lesions adjacent to the PTFE-SG; d) CT images that did not comply with the standards of quality detailed in Supplementary Materials and Methods.

CT, computed tomography; MRI, magnetic resonance imaging; PSE, portosystemic encephalopathy; PTFE-SG, polytetrafluoroethylene-covered stent graft; RA, refractory ascites; TIPS, transjugular intrahepatic portosystemic shunt; US, ultrasound; VH, variceal hemorrhage.

performed after TIPS placement were included (details on image analysis are reported in Supplementary Materials and Supplementary Figure 1). Table 1 shows inclusion and exclusion criteria. The PTFE-SG inner diameter was measured at 4 sites: (1) where the PTFE-SG traverses the PVW and (2) the HVW; (3) at an intraparenchymal site equidistant from PVW and HVW; and (4) at a site close to the proximal end, just before the PTFE-SG exit into inferior vena cava. The average of the largest diameters at each of the 4 sites was calculated in the entire population grouped on the basis of both the PTFE-SG nominal diameters and the dilation diameters (Supplementary Figure 2). To determine whether PTFE-SG self-expansion occurred, the average value of the maximal diameter at the 2 sites considered hemodynamically critical (ie, PVW and HVW, Supplementary Figure 2 and data not shown) was plotted for each patient against time from TIPS placement. It was considered that a PTFE-SG was stable over time if its follow-up inner diameter was within $\pm$ 0.5 mm of dilation diameter.

The study protocols conformed to the ethical guidelines of the 1975 Declaration of Helsinki. The institutional review board gave approval to collect prospective and retrospective clinical, hemodynamic, and CT data. The need for informed consent was waived for patients no longer being followed at the time of data collection.

Statistical Analysis

Results are expressed as mean $\pm$ standard deviation (or standard error if specified) or percentage. Comparisons of continuous data and proportions were performed by the Student *t* test and the chi-square test, respectively. Either Spearman rank-order or Person correlation were run to determine relationship between continuous variables. The Kaplan-Meier method was used to estimate time-related events. Patients were censored at first episode of post-TIPS PSE, first LVP after TIPS, orthotopic liver transplantation or death or last available follow-up. Differences in observed probability were assessed using the log-rank test. Post hoc competing risks analyses were also performed using Gray test, with death and orthotopic liver transplantation as competing events. A Fine and Gray competing risks proportional hazards model was used to identify risk factors for PSE in the pooled groups. Post-TIPS death/orthotopic liver transplantation were treated as the competing events. Age, sex (female vs male), pre-TIPS model for end-stage liver disease (MELD) score, TIPS indications (ascites vs rebleeding prevention), pre-TIPS PSE, PTFE-SG dilation (6 mm vs above 6 mm), and either post-TIPS PCG $<$10 mm Hg or post-TIPS decrease more than 50% were incorporated in 2 alternative models. Proportional hazards assumption of the Fine and Gray models was checked by means of graphical assessment of weighted Schoenfeld-type residuals. Finally, a propensity score analysis was performed (further details in Supplementary Table 4).

Because of its exploratory nature the study lacks a sample size calculation. PASW Statistics 20 (IBM Corp, Armonk, NY) and R 3.1.2 (The R Foundation for Statistical Computing, Vienna, Austria) were used to analyze data.

Results

Clinical Study

Between November 2009 and December 2012, a total of 117 patients had a TIPS placed, of whom 95 were included in this part of the study (Figure 1*A*). Indications for TIPS were RA in 58 (61%) patients and prevention of recurrent VH in 37 (39%) patients. In the latter group, TIPS was performed within 6 weeks of the index hemorrhage in most patients (Table 2). Mean follow-up for the whole cohort was 326 days. No patient was lost to

follow-up. Patient allocation to the different groups and clinical characteristics before and after TIPS are reported in Figure 1*A* and Table 2.

Clinical outcomes. The initial comparison was made between 42 patients with a PTFE-SG dilated to 7 or 6 mm (TG) and 53 patients with dilation ≥8 mm (CG). Patients in both groups were comparable, except that in the underdilated group RA tended to be a more frequent indication and pre-TIPS PCG was lower. No patients in either group had acute shunt occlusion. Among the 5 patients (2 in TG and 3 in CG) who underwent PCG reassessment because they still required LVP 12 weeks after TIPS placement, none required TIPS dilation (ie, PCG <12 mm Hg) and none needed further LVP 6 months after TIPS placement (Table 2). Two patients in the CG underwent TIPS reduction for persistent PSE and heart failure, respectively.

There were no cases of recurrent VH in the 37 patients in whom TIPS was placed to prevent bleeding, including those (8 out of 12) with underdilated TIPS in whom PCG did not decrease <12 mm Hg. Among the 58 patients with RA, 13 (22.4%) required at least 1 LVP during a mean follow-up of 317 days. The probability of remaining free of LVP was 74.6% (95% confidence interval [CI], 57.6.1–91.6) and 78.6% (95% CI, 62.6–94.6; $P = .728$; Gray test, $P = .923$) in the TG and CG, respectively (Figure 2*A*).

Table 2. Comparison of Clinical and Hemodynamic Characteristics of the Patients Included in the Clinical Study According to Employed Dilatation Balloon Catheters

	Standard TIPS	Underdilated TIPS	
	≥8 mm (N = 53) (CG)[a]	7 and 6 mm (N = 42) (TG)	6 mm (N = 47) (VG)
Pre-TIPS			
Alcohol as a cause, n (%)	15 (28.3)	12 (28.6)	14 (29.8)
RA as an indication, n (%)	28 (52.8)	30 (71.4)	28 (59.6)
Days from index bleeding[b] (median)	28.6 ± 24.1 (18)[c]	18.8 ± 11.6 (18)[c]	27.1 ± 18.1 (20)[c]
Male gender, n (%)	35 (66.0)	27 (64.3)	32 (68.1)
Age, *y*[b]	55.7 ± 9.5	57.8 ± 9.8	59.6 ± 10.9
MELD score[b]	13.3 ± 4.9	13.0 ± 3.9	12.3 ± 3.1
PSE, n (%)	4 (7.5)	2 (4.5)	4 (8.5)
Esophageal varices, n (%)	36 (67.9)	27 (64.3)	31 (65.9)
PCG, *mm Hg*[b]	24.7 ± 4.6	22.8 ± 3.8[d]	23.3 ± 5.1
Post-TIPS			
10-mm PTFE-SG, n (%)	45 (84.9)	30 (71.4)	37 (78.7)
Dilatation groups			
6 mm, n (%)	0 (0)	25 (59.5)	47 (100.0)
7 mm, n (%)	0 (0)	17 (40.5)	0 (0)
8 mm, n (%)	38 (71.7)	0 (0)	0 (0)
9 mm, n (%)	9 (17.0)	0 (0)	0 (0)
10 mm, n (%)	6 (11.3)	0 (0)	0 (0)
PCG, *mm Hg*[b]	10.5 ± 5.2	11.3 ± 3.7	12.6 ± 3.1[e]
PCG <12 mm Hg, n (%)	36 (67.9)[f]	21 (50.0)	23 (48.9)
PCG <10 mm Hg, n (%)	30 (56.6)	12 (28.6)[d]	11 (23.4)[e]
PCG ≥10 to <12 mm Hg, n (%)	6 (11.3)	9 (21.4)	12 (25.5)
Percent PCG decrease[b]	56.8 ± 15.1	49.0 ± 13.2[d]	44.5 ± 12.6[e]
PCG reduction >50%, n (%)	39 (73.6)	20 (47.6)[d]	17 (36.2)[e]
PCG re-evaluation during follow-up, n (%)[g]	6 (11.3)	6 (14.3)	7 (14.9)
MELD score after 30 d[b] (n)	16.3 ± 5.3 (53)	14.3 ± 4.1 (42)[d]	13.9 ± 5.1 (47)[e]
MELD score after 90 d[b] (n)	16.5 ± 4.3 (52)	14.6 ± 3.8 (38)[d]	13.6 ± 4.8 (45)[e]
MELD score after 180 d[b] (n)	15.9 ± 5.0 (48)	14.4 ± 4.3 (38)	13.8 ± 4.3 (43)[e]
MELD score at 1 y[b] (n)	15.7 ± 4.0 (43)	14.1 ± 4.4 (31)	13.5 ± 4.7 (18)
1-y probability of PSE (95% CI)	53.8 (40.2–67.8)	26.9 (12.9–40.8)[d]	22.2 (9.7–34.7)[e]
PSE severity, n (%)			
Grade II	12 (42.9)	7 (63.6)	6 (60)
Grade III	13 (46.4)	4 (36.4)	4 (40)
Grade IV	3 (10.7)	(0)	0 (0)
PSE time course, n (%)			
Episodic	23 (82.1)	9 (81.8)	8 (80)
Recurrent	4 (14.3)	2 (18,2)	2 (20)
Persistent	1 (3.6)	0 (0)	0 (0)
Triggered PSE, n (%)	6 (21.4)	3 (27.3)	3 (30)
Constipation	2 (7.1)	1 (9.1)	0 (0)
Infections	2 (7.1)	1 (9.1)	2 (20)
Dehydration (diuretic related)	2 (7.1)	1 (9.1)	1 (10)

Table 2. Continued

	Standard TIPS	Underdilated TIPS	
	≥8 mm (N = 53) (CG)[a]	7 and 6 mm (N = 42) (TG)	6 mm (N = 47) (VG)
TIPS reduction, n (%)	2 (3.8)	0 (0)	0 (0)
Esophageal varices, n (%)	2/17[h] (11.8)	2/14[i] (14.3)	3/24[j] (12.5)
HCC, n (%)	7 (13.2)	5 (11.9)	7 (14.9)
Death, n (%)	5 (9.4)	5 (11.9)	6 (12.8)
Liver disease related, n (%)	4 (80)	4 (80)	5 (83)
Liver transplant, n (%)	1 (1.9)	1 (2.4)	3 (6.3)
Follow-up, *d*[k]	348.6 ± 11.6	325.9 ± 15.1	301.2 ± 17.9

CG, control group; CI, confidence interval; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease; PCG, portocaval pressure gradient; PSE, portosystemic encephalopathy; PTFE-SG, polytetrafluoroethylene-covered stent graft; RA, refractory ascites; TG, training group; TIPS, transjugular intrahepatic portosystemic shunt; US, ultrasound; VG, validation group.

[a]Seven patients of the TG were added to the CG because of PTFE-SG dilatation to 8 mm (Supplementary Figure 1). No difference in the comparisons of CG versus TG was observed after removing these patients from the analysis.

[b]Mean ± standard deviation.

[c]Five, 1, and 3 patients in CG, TG, and VG, respectively, have been referred for TIPS after 6 weeks from index bleeding.

[d]TG versus CG, $P < .05$.

[e]VG versus CG, $P < .05$.

[f]Among the 17 patients with a PCG ≥12 mm Hg, 5 had an 8-mm PTFE-SG, 2 were dilated to 10 mm, 10 had a too advanced liver disease and/or a PCG very close to the target.

[g]PCG re-evaluation performed in the 7 patients (3, 2, and 2 in CG, TG, and VG, respectively) needing paracentesis 12 weeks after TIPS showed a PCG <12 mm Hg (none of them needed LVP 6 months after TIPS). In the remaining 12 patients, PCG re-evaluation was performed for suspicions of TIPS dysfunction at follow-up US, but none of them showed significant increase of PCG in comparison with immediate post-TIPS values.

[h]A total of 17/37 patients who had varices pre-TIPS had a post-TIPS endoscopy.

[i]A total of 14/26 patients who had varices pre-TIPS had a post-TIPS endoscopy.

[j]A total of 3/24 patients who had varices pre-TIPS had a post-TIPS endoscopy.

[k]Mean ± standard error.

During follow-up at least 1 episode of PSE occurred in 39 out of 95 patients (41%). The 1-year cumulative probability of remaining free of PSE was significantly greater in TG (73.1%; 95% CI, 59.2%–87.1%) than in CG (46.0%; 95% CI, 32.2%–59.8%; $P = .015$; Gray test, $P = .026$) (Figure 2*B*).

Post-TIPS MELD score at different time points was significantly lower in TG than in CG (Table 2).

Hemodynamic effects. In the 95 patients the mean post-TIPS decrease of PCG was −53 ± 15% (range, −22% to −93%). Post-TIPS PCG was significantly greater and the percent decrease in PCG lower in the underdilated group (Table 2). Moreover, TIPS dilation (ie, 6, 7, 8, 9, and 10 mm) inversely correlated with final PCG and directly with its percent change ($r_s = -0.285$, $P = .001$ and $r_s = 0.380$, $P = .0003$, respectively). Post-TIPS PCG <12 mm Hg[1,4,5,11,18] tended to be reached less frequently in the underdilated group, whereas PCG values <10 mm Hg, a threshold that has been associated with increased risk of PSE,[6,11] were significantly less frequent than in the standard TIPS group (Table 2).

Validation group. We separately analyzed 59 patients with TIPS placed in the same centers after completion of the initial study (Figure 1*A*). No significant differences in clinical, endoscopic, and hemodynamic baseline features were found between this 6-mm dilated VG and the TG (Table 2) or its 6-mm subgroup (Supplementary Table 1). After TIPS placement in the VG, the probabilities of remaining free of LVP (69.6%; 95% CI, 49.7.2%–93.6% vs 78.6%; 95% CI, 62.6%–94.6%; $P = .625$; Gray test, $P = .789$) and PSE episodes (77.8%; 95% CI, 65.3%–90.3% vs 79.5%; 95% CI, 62.6%–96.4%; $P = .871$; Gray test, $P = .872$) were comparable with those of the TG dilated to 6 mm (Figure 2*A* and *B*). Post-TIPS hemodynamic parameters and MELD score were also similar (Supplementary Table 1).

Risk factors for post–transjugular intrahepatic portosystemic shunt portosystemic encephalopathy. Table 3 shows the competing risk models to identify independent predictors of post-TIPS PSE. There were 49 events (PSE) and 9 competing events (death/liver transplant). Age, female sex, pre-TIPS PSE, PTFE-SG dilatation >6 mm, and post-TIPS PCG <10 mm Hg were independently associated with 1-year post-TIPS PSE. No evidence of lack of proportional hazards was found (data not shown). Supplementary Table 2 shows the multivariate models after removing patients with pre-TIPS PSE. Propensity score adjusted multivariate analyses showed PTFE-SG dilatation >6 mm and either post-TIPS PCG <10 mm Hg or post-TIPS PCG decrease more than 50% independently associated with 1-year post-TIPS PSE (Supplementary Table 3).

Supplementary Table 4 shows the comparison of main characteristics of pooled groups stratified according to PTFE-SG dilation. Supplementary Figure 3 shows the cumulative risk of PSE in patients grouped according to categorical variables and the best cutoff for age (ie, 55 years) selected after receiver operating characteristic curve analysis (data not shown). Supplementary Figure 4 shows bilirubin time course in patients stratified according to PTFE-SG dilation. Supplementary Figure 5 shows cumulative probability of remaining free of PSE

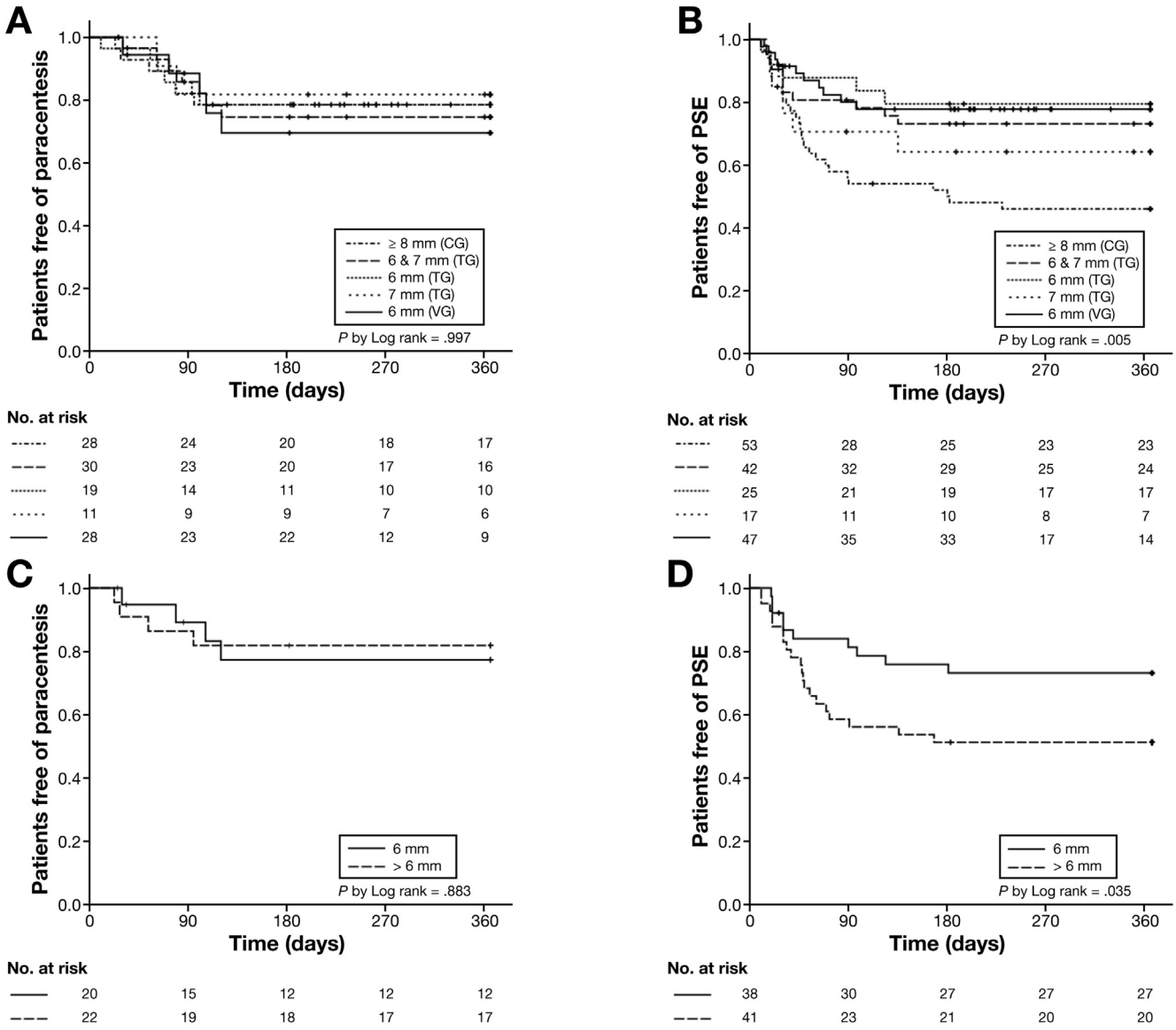

Figure 2. Cumulative probability of remaining free of LVP (*A* and *C*) and PSE (*B* and *D*) in the clinical study and imaging study groups, respectively. *A* and *C* include patients with RA; *B* and *D* include all patients. (*A*) No significant differences between paired groups were observed. (*B*) Six and 7 mm (TG) versus ≥8 mm (CG), $P = .015$; 6 mm (TG) versus ≥8 mm (CG), $P = .011$; 6 mm (VG) versus ≥8 mm (CG), $P = .002$. The remaining comparisons were not significant. No difference in the comparisons of CG versus underdilated groups was observed after removing the 7 patients dilated to 8 mm for technical reasons or for refusal of underdilated TIPS. (*C* and *D*) Patients in the 6 mm group had a PTFE-SG diameter of 6 ± 0.5 mm at PVW and/or HVW as measured on CT images obtained within 1 year after TIPS placement.

in the subgroup of patients (n = 24) with characteristics similar to those of patients enrolled in the study by Bureau et al[5] (ie, ascites as an indication, pre-TIPS MELD score below or equal to 12, no history of pre-TIPS PSE, and post-TPS PCG <12 mm Hg).

Imaging Study

A total of 226 CT scans were evaluated in this part of the study (Figure 1*B*). The mean time between PTFE-SG placement and CT scan was 252 days (median, 286; range, 1–1440 days). Supplementary Figure 2 shows average maximal diameter (ie, the largest cross-sectional inner diameter) at each of the 4 sites. PVW and HVW had the smallest diameter in underdilated PTFE-SGs, indicating that these are the hemodynamically relevant sites along the TIPS (data not shown). Therefore, diameters at these 2 sites were used to analyze stability of TIPS diameter over time in individual patients (Figure 3) and to create the groups at risk of PSE (Figure 2*C* and *D*).

Of the 8-mm PTFE-SG placed, none but one of those dilated to 6 or 7 mm self-expanded and none of those dilated to nominal diameter (8 mm) maintained this diameter (they were all under 7.5 mm at follow-up) (Figure 3*A*–*C*).

Of the 10 mm PTFE-SG placed, 74% of those balloons dilated to 6 mm underwent self-expansion to 7 (67%) or 8 mm (7%) but none to nominal diameter (Figure 3*A*). Of those dilated to 7 mm, self-expansion occurred in 32%

Table 3. Competing Risks Regression Models for 1-Year Post-TIPS PSE in the Pooled Groups of the Clinical Study (N = 142)

	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Model 1						
Indication (RA vs VH)	0.85	0.49–1.18	.570	1.03	0.59–1.79	.920
Sex (female vs male)	2.21	1.20–3.70	.009	1.91	1.07–3.40	.029
Age, *y* (1-U increment)	1.04	1.01–1.06	.004	1.04	1.01–1.07	.003
MELD score (1-U increment)	1.04	0.98–1.11	.170	1.00	0.94–1.07	.880
Pre-TIPS PSE (yes vs no)	4.21	2.24–7.91	.00001	3.83	1.96–7.49	.0001
PTFE-SG dilatation (>6 mm vs 6 mm)	2.74	1.49–5.02	.001	2.17	1.16–4.05	.01
Post-TIPS PCG <10 mm Hg (yes vs no)	2.98	1.71–5.20	.0001	1.89	1.04–3.44	.037
Model 2						
Indication (RA vs VH)	0.85	0.49–1.18	.570	0.99	0.56–1.75	.980
Sex (female vs male)	2.21	1.20–3.70	.009	1.83	1.03–3.25	.039
Age, *y* (1-U increment)	1.04	1.01–1.06	.004	1.04	1.01–1.07	.003
MELD score (1-U increment)	1.04	0.98–1.11	.170	1.01	0.95–1.07	.730
Pre-TIPS PSE (yes vs no)	4.21	2.24–7.91	.00001	4.18	2.28–7.68	.00001
PTFE-SG dilatation (>6 mm vs 6 mm)	2.74	1.49–5.02	.001	2.23	1.19–4.18	.01
Post-TIPS PCG reduction >50% (yes vs no)	2.70	1.47–4.96	.001	1.68	0.86–3.30	.130

CI, confidence interval; HR, hazard ratio; MELD, model for end-stage liver disease; PCG, portocaval pressure gradient; PTFE-SG, polytetrafluoroethylene-covered stent graft; PSE, portosystemic encephalopathy; RA, refractory ascites; TIPS, transjugular intrahepatic portosystemic shunt; VH, variceal hemorrhage.

(all to 8 mm, none to nominal diameter) (Figure 3*B*). Of those dilated to 8 mm, self-expansion occurred in 20% (all of them to 9 mm, none to nominal diameter) (Figure 3*C*). Of those dilated to 9 mm, none self-expanded (Figure 3*D*) and of those dilated to 10 mm none maintained nominal diameter (Figure 3*E*).

A follow-up PTFE-SG diameter of 6 mm (± 0.5 mm) at PVW and/or HVW on CTs performed within 1 year after TIPS placement on 79 patients included in the clinical study (Supplementary Table 5) was associated with a significantly lower incidence of PSE (Figure 2*D*) without differences in the recurrence of ascites (Figure 2*C*).

Discussion

This is the first published study demonstrating the feasibility of underdilating PTFE-SGs at diameters as low as 6 mm and indicating that this strategy is associated with a significant decrease in the incidence of post-TIPS PSE. Importantly, the lower burden of PSE was accompanied by unchanged clinical efficacy in patients with both VH and RA.

The incidence of post-TIPS PSE was inversely related to the diameter of PTFE-SG deployment, and to post-TIPS PCG. Accordingly, the percentage of patients with post-TIPS PCG <10 mm Hg, the threshold identified as predictive of post-TIPS PSE,[6,11] was significantly lower in the underdilated group. Therefore, dilation to 6 mm may be proposed as the initial option for TIPS placement, in particular in patients with risk factors for post-TIPS PSE.[2,10] These results, if confirmed in randomized trials, have the potential to change clinical practice.

Several studies have compared clinical efficacy, incidence of PSE, and hemodynamics after TIPS with different diameters, with divergent results. In 2 studies (1 early interrupted randomized[8] and 1 retrospective[18]) comparing 10 mm versus 8 mm PTFE-SG dilated to nominal diameters, patients with 8 mm PTFE-SG had similar PSE rates but lower clinical efficacy (mostly recurrence of ascites). Notably, the mean post-TIPS PCG was <10 mm Hg in both groups, making it hard to reconcile their results on clinical efficacy. Moreover, in the study by Miraglia et al,[18] 50% of patients undergoing TIPS revision during follow-up for failure to control ascites had a PCG already below the target of 12 mm Hg.[1,2,5,11,17] However, a recent large randomized study reported that 8 mm PFTE-SG had similar efficacy in preventing VH compared with 10 mm, while decreasing post-TIPS PSE independent of post-TIPS PCG.[9]

Our results are in agreement with previous studies showing a close correlation between post-TIPS PCG and the incidence of PSE.[6,11] However, finding that both post-TIPS PCG <10 mm Hg and PTFE-SG dilation to 6 mm are independent predictors of PSE indicates that underdilated TIPS may protect from PSE by mechanisms other than PCG, probably by preserving liver function. The similar efficacy of underdilated and standard TIPS on VH and RA recurrence is even more complex to explain. At least 50% of patients receiving underdilated PTFE-SG had a PCG <12 mm Hg after placement. In the remaining patients it is conceivable that a partial but substantial hemodynamic response may have been sufficient to prevent rebleeding,[9,19] similar to patients on pharmacologic prophylaxis of rebleeding.[20] However, our results on bleeding recurrence cannot be generalized to the setting of early TIPS[4] and continuous bleeding or early rebleeding.[1,2] Some patients with RA may also benefit from a partial hemodynamic response and others may benefit from further decrease in PCG because of a self-expansion albeit limited,

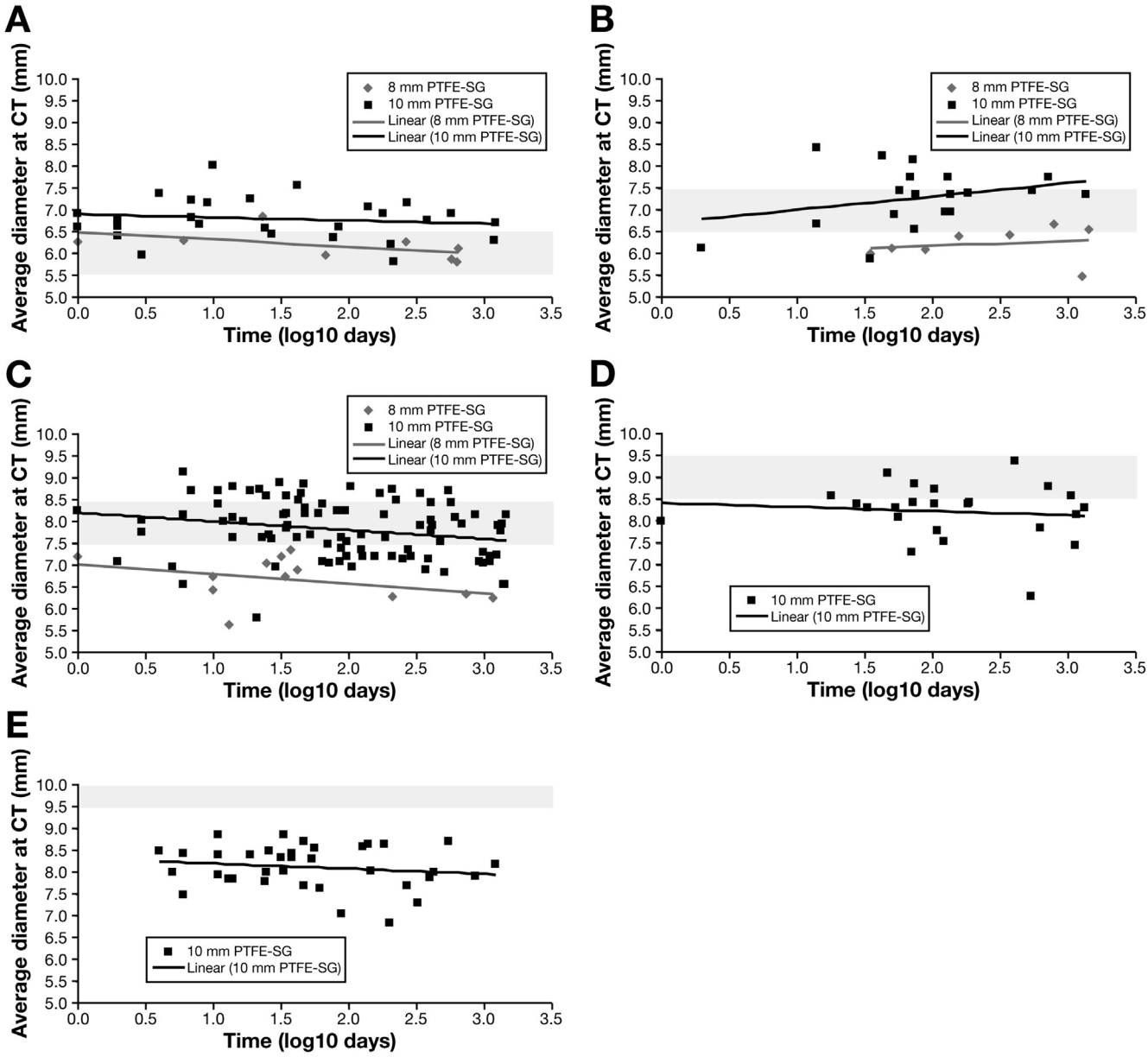

Figure 3. Relationship between average inner diameters of individual PTFE-SG dilated to different diameters and the time elapsed from TIPS placement and CT examination. The *grey areas* include cases whose average maximum diameter falls within the expected values for each dilatation subgroup ± 0.5 mm. *Solid lines* represent regression lines. Values of both regression coefficient *r* and *P* are as follow for each PTFE-SG nominal diameter group. The 8 mm group: 6 mm, $r = .27$, $P = .52$; 7 mm, $r = .05$, $P = .91$; 8 mm, $r = .42$, $P = .18$. The 10 mm group: 6 mm, $r = .01$, $P = .96$; 7 mm, $r = .42$, $P = .07$; 8 mm, $r = .17$, $P = .09$; 9 mm, $r = .07$, $P = .75$; 10 mm, $r = .01$, $P = .93$.

of PTFE-SG with time. However, the fact that some patients required LVP 12 weeks after TIPS positioning despite a reassessed PCG <12 mm Hg indicates the need to further investigate the multifactorial nature of post-TIPS RA.[1,2,18,21,22]

PTFE-SGs are believed to self-expand to nominal diameter even when not fully balloon-dilated at the time of TIPS placement, but the fate of PTFE-SG underdilation to less than 8 mm in the setting of a cirrhotic liver had not been previously explored.[13,14] Herein we showed that underdilated PTFE-SGs do not self-expand to nominal diameter, and rarely expand beyond 1 mm of the dilation diameter at the hemodynamically relevant sites HVW and PVW. Of note, deployment to 6 mm of an 8 mm PTFE-SG seems to be more stable over time compared with 10 mm PTFE-SG. If our results are confirmed, dilating to 6 mm (or using PTFE-SG with nominal diameter <8 mm) may be the recommended strategy, especially in patients with RA and in those with more compromised liver function.

A clear limitation of our study is the lack of randomization. Nevertheless, groups were comparable at baseline for most clinical parameters, including factors predictive of post-TIPS encephalopathy. A higher number of patients with RA was included in the underdilated TG, and pre-TIPS PCG was lower in the same group, likely reflecting decreased circulating blood volume secondary

to diuretic use and heart dysfunction. However, the VG, which confirmed the results obtained in the TG, was very similar to the CG in terms of indications and pre-TIPS PCG.

In conclusion, the present study shows that TIPS placement using PTFE-SGs underdilated to 6 mm is associated with a lower rate of encephalopathy and with the same clinical efficacy compared with PTFE-SG TIPS dilated to standard diameters. These results require confirmation in randomized trials.

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.2018.01.029.

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Reprint requests
Address requests for reprints to: Filippo Schepis, Department of Gastroenterology, University of Modena & Reggio Emilia, Via del Pozzo 71, Modena, I-41100, Italy. e-mail: filippo.schepis@unimore.it. Francesco Vizzutti, Department of Experimental and Clinical Medicine, University of Florence, Viale Morgagni 85, Florence, I-50134, Italy. e-mail: francesco.vizzutti@unifi.it.

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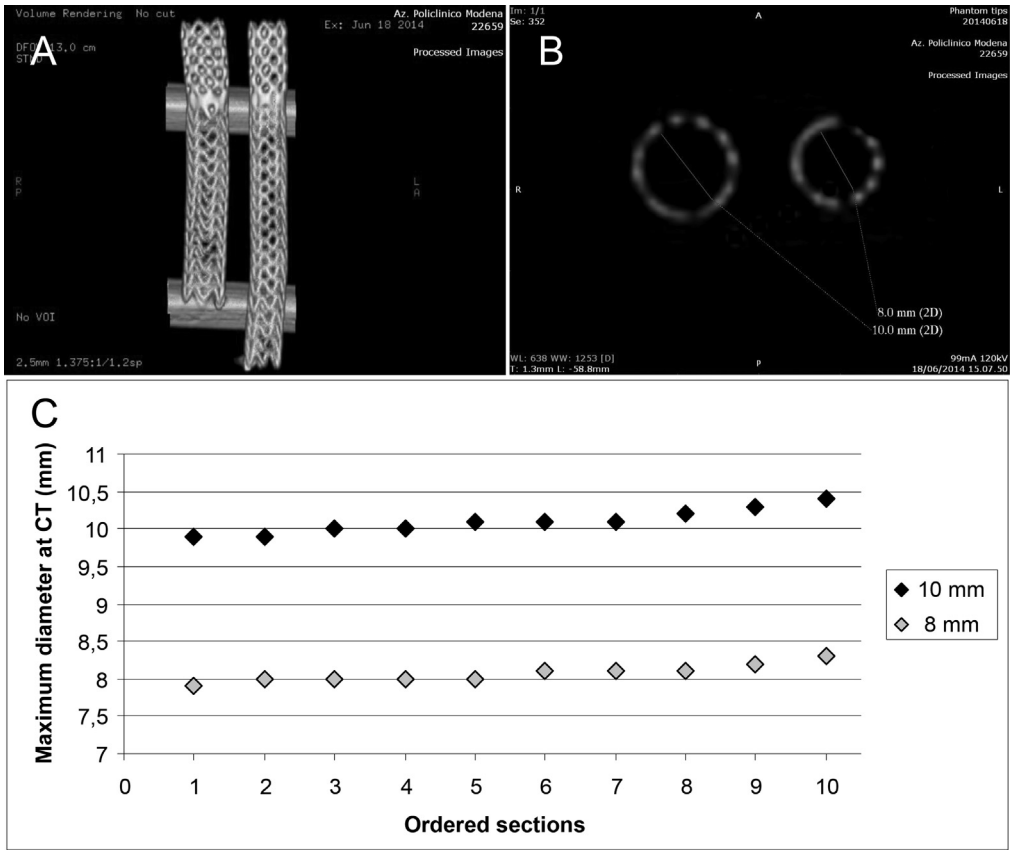
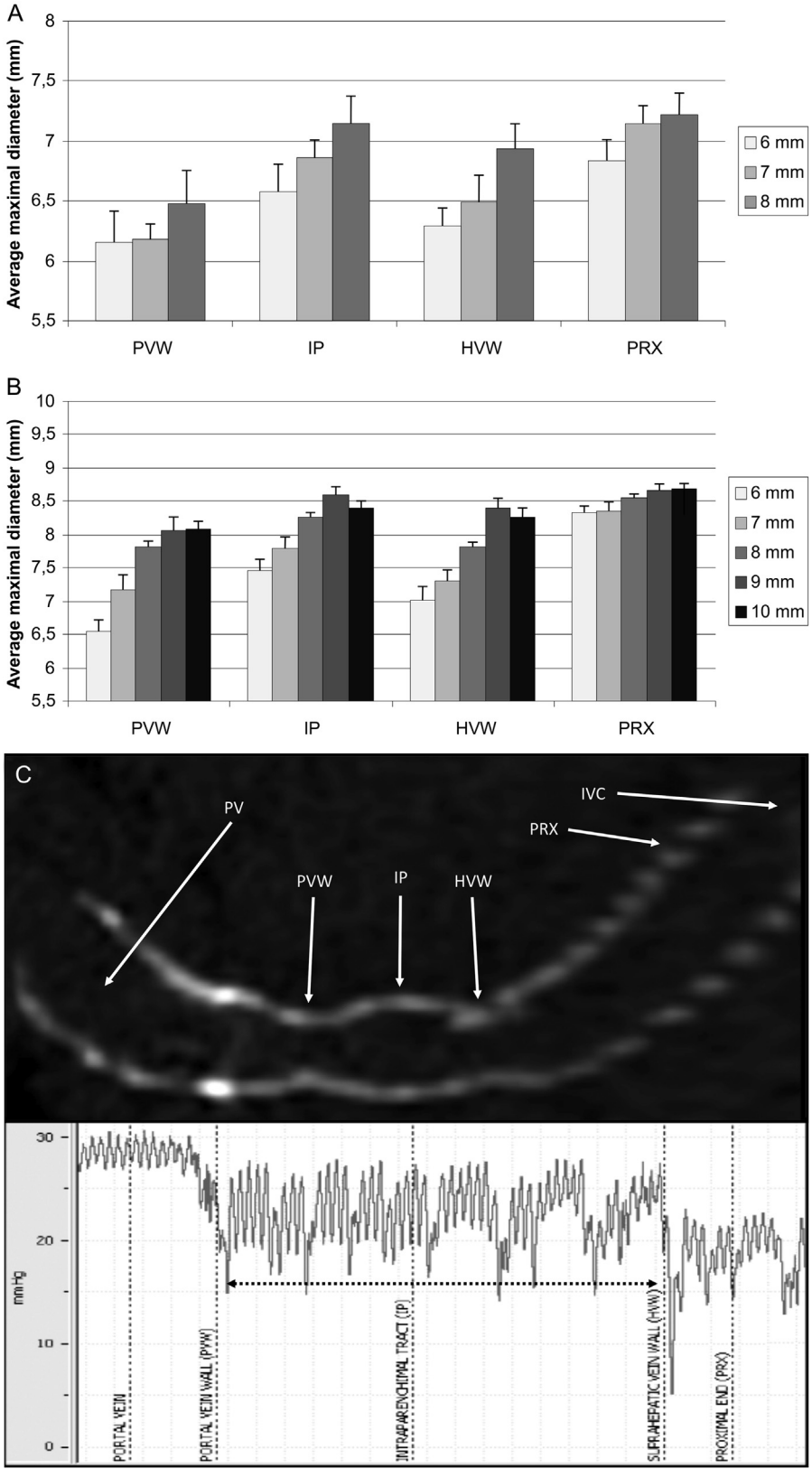
Supplementary Material and Methods

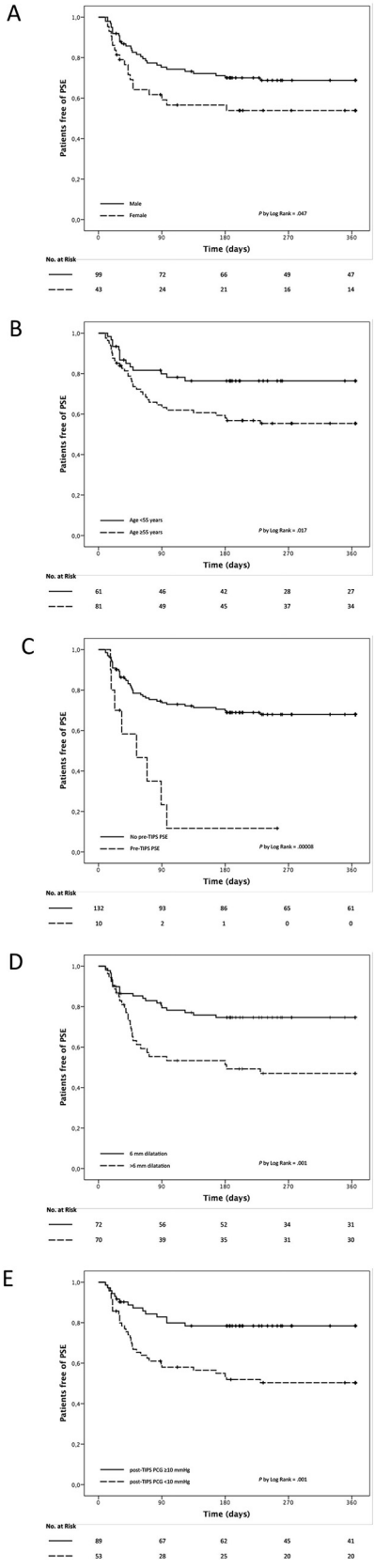
CT studies were sent in DICOM format to the coordinating Centers and analyzed by 2 independent radiologists (G.M. and L.R.) both unaware of the PTFE-SG nominal and dilatation diameters. The interobserver agreement was evaluated in the whole cohort. Quantitative analysis was performed on CT scans meeting the following quality criteria: CT scanner with $\geq$64 detectors; acquisitions timed to study venous hepatic components; slice thickness of 2.5 mm or less with an interval of 1.25 mm or less; attenuation-based automatic tube voltage limits between 120 and 500 mA; 120-kv tube current; absence of major respiratory-/motion-induced or beam hardening artifacts. To obtain homogeneous enhancement of the stent-graft lumen, wall scans were reconstructed using the venous phase of CT studies. Reformatted images of the planes perpendicular to the stent-graft at each of the 4 standard sites were obtained using Advantage Workstation 4.6 reconstruction console (GE Healthcare, Waukesha, WI) optioned with the double oblique multiplanar reconstruction application. By simultaneously working on 2 windows, it was possible to identify sections perpendicular to the stent-graft at each given point, regardless of its in vivo spatial orientation. Keeping the image centered on the lumen of the stent-graft on a pure axial plane, a paracoronal plane was selected, which contained the luminal tract to be measured. On this second image a plane orthogonal to the stent-graft was obtained and used to measure the true largest inner diameter. To minimize blooming artifacts, the window settings were adjusted at 1500 HU with a center of 300 HU.



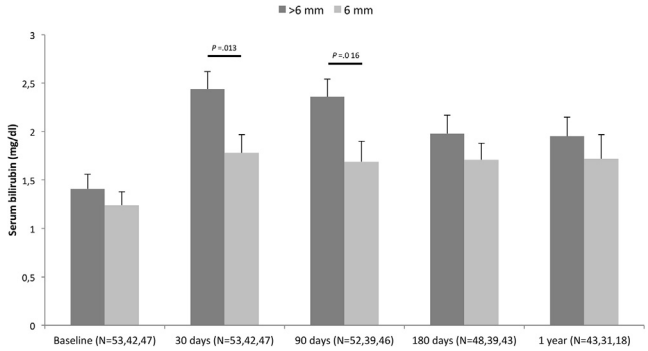
Supplementary Figure 1. (*A*) Rendering of the phantom used to test accuracy of CT measurement protocol. (*B*) Representative section of the phantom and maximum inner diameters measured at this level. (*C*) Distribution of measured inner diameters at 10 sections of the phantom. Serial measurements of a phantom were made on both 8 mm and 10 mm nominal diameter PTFE-SGs (*A*). These were released in a 37°C water bath and dilated to their nominal diameter by means of semicompliant balloon catheters (FoxCross PTA Catheter, Abbott Laboratories, Abbott Park, IL). After 2 hours at 37°C, the phantom was scanned by CT. Inner diameters of 8 mm and 10 mm PTFE-SG were measured (*B*). Means of 10 random slices orthogonal to the main axes of the PTFE-SGs were 8.08 $\pm$ 0.11 mm and 10.1 $\pm$ 0.16 mm, respectively (*C*). Deviation from the theoretical nominal diameter ranged from $-$1.3% to 3.8% (mean, 0.88 $\pm$ 1.45%) and from $-$1% to 4% (mean, 1.0 $\pm$ 1.63%), respectively.



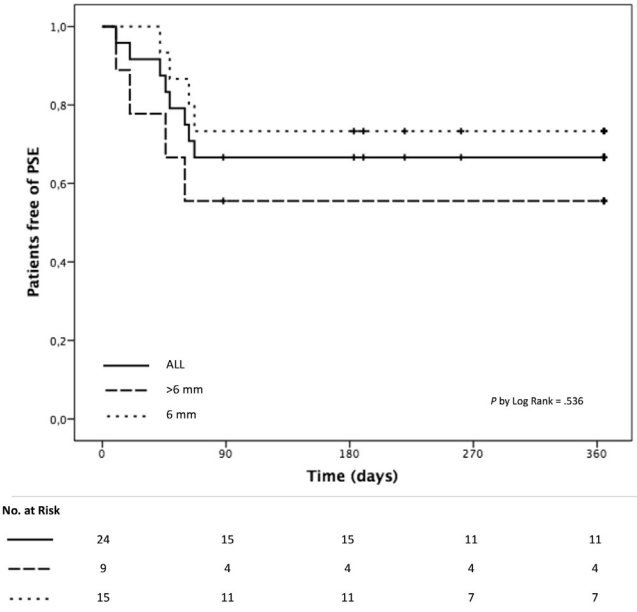
Supplementary Figure 2. Average maximal inner diameter of PTFE-SGs at each standard site after CT images processing (*A* and *B*: 8 mm and 10 mm nominal diameter PTFE-SGs, respectively). *Bars* represent mean ± standard error of different dilatation groups. In *C* an example case of implanted PTFE-SG showing a narrowing of its lumen at the level of PVW and HVW. The effects of these strictures on blood pressure curve along the PTFE-SG length are also shown (*double-headed dashed-arrow* indicates pressure values recorded along the intraparenchymal tract). Interobserver agreement regarding measurement of the inner diameter at each site of PTFE-SGs was excellent, as indicated by a coefficient for agreement of .96 (95% CI, 0.9–1.0). IVC, inferior vena cava; IP, intraparenchymal tract; PRX, proximal outflow; PV, portal vein.



Supplementary Figure 3. (*A–E*) Cumulative probability of remaining free of PSE in the entire study cohort (142 patients) stratified according to the risk factors identified by multivariate analysis.



Supplementary Figure 4. Time-course of total serum bilirubin after TIPS positioning in patients grouped according PTFE-SG dilation. In parenthesis are reported the number of patients at each time point in the control group, training group, and validation group, respectively. *Bars* represent mean ± standard error.



Supplementary Figure 5. Cumulative probability of remaining free of PSE in the subgroup of patients (N = 24) with ascites as an indication, pre-TIPS MELD score ≤12, no history of pre-TIPS PSE, and post-TPS PCG <12 mm Hg.[5] Patients are also stratified according to diameter of TIPS dilation. Follow-up (mean ± standard error): 309.6 ± 15.0.

Supplementary Table 1. Comparison of Main Clinical and Hemodynamic Characteristics of Patients Included in the Clinical Study With PTFE-SG Underdilated to 6 mm

	6 mm (N = 25) (TG)	6 mm (N = 47) (VG)
Pre-TIPS		
Alcohol as an etiology, n (%)	7 (28)	14 (29.8)
RA as an indication, n (%)	19 (76)	28 (59.6)
Days from index bleeding[a] (median)	15.5 ± 4.9 (15)[b]	27.1 ± 18.1 (20)[b]
Male gender, n (%)	17 (68)	32 (68.1)
Age, *y*[a]	55.6 ± 9.7	59.6 ± 10.9
MELD score[a]	12.6 ± 3.8	12.3 ± 3.1
PSE, n (%)	1 (4)	4 (8.5)
Esophageal varices, n (%)	16 (64)	31 (65.9)
PCG, *mm Hg*[a]	22.1 ± 3.7	23.3 ± 5.1
Post-TIPS		
10-mm PTFE-SG, n (%)	19 (76.0)	37 (78.7)
PCG, *mm Hg*[a]	11.6 ± 2.0	12.6 ± 3.1
PCG <12 mm Hg, n (%)	13 (52)	23 (48.9)
PCG <10 mm Hg, n (%)	6 (24)	11 (23.4)
PCG ≥10<12 mm Hg,	7 (28)	12 (25.5)
Percent PCG decrease[a]	46.7 ± 9.2	44.5 ± 12.6
PCG reduction >50%, n (%)	9 (36)	17 (36.2)
PCG re-evaluation, n (%)[c]	4 (16)	7 (14.9)
MELD score after 30 d (N)[a]	13.5 ± 4.9 (25)	13.9 ± 5.1 (47)
MELD score after 90 d (N)[a]	13.7 ± 4.7 (22)	13.6 ± 4.8 (45)
MELD score after 180 d (N)[a]	13.4 ± 5.0 (21)	13.8 ± 4.3 (43)
MELD score at 1 y (N)[a]	13.3 ± 5.1 (18)	13.5 ± 4.7 (18)
1-year probability of PSE, (95% CI)	20.5 (4.2–36.3)	22.2 (9.7–34.7)
PSE severity, n (%)		
Grade II	3 (60)	6 (60)
Grade III	2 (40)	4 (40)
Grade IV	0 (0)	0 (0)
PSE time course, n (%)		
Episodic	4 (80)	9 (80)
Recurrent	1 (20)	2 (20)
Persistent	0 (0)	0 (0)
Triggered PSE, n (%)	2 (40)	3 (30)
Constipation	0 (0)	0 (0)
Infections	1 (20)	2 (20)
Dehydration (diuretic related)	1 (20)	1 (10)
TIPS reduction, n (%)	0 (0)	0 (0)
Esophageal varices, n (%)	1/10[d] (10)	3/24[e] (12.5)
HCC, n (%)	3 (12)	7 (14.9)
Death, n (%)	4 (16)	6 (12.8)
Liver disease related, n (%)	3 (75)	5 (83)
Liver transplant, n (%)	1 (40)	3 (6.3)
Follow-up, *d*[f]	335 ± 15.6	301 ± 17.9

CG, control group; CI, confidence interval; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease; PCG, portocaval pressure gradient; PTFE-SG, polytetrafluoroethylene-covered stent graft; RA, refractory ascites; PSE, portosystemic encephalopathy; TG, training group; TIPS, transjugular intrahepatic portosystemic shunt; US, ultrasound; VG, validation group.

[a]Mean ± standard deviation.

[b]0 and 3 patients in 6 mm and >6 mm, respectively, have been referred for TIPS after 6 weeks from the index bleeding.

[c]PCG re-evaluation performed in the 4 patients (2 in each group) needing paracentesis 12 weeks after TIPS showed a PCG <12 mm Hg (none of them needed large-volume paracentesis 6 months after TIPS). In the remaining 7 patients, PCG re-evaluation was performed for suspicious of TIPS dysfunction at follow-up US, but none of them showed significant increase of PCG in comparison with immediate post-TIPS values.

[d]10/16 patients who had varices pre-TIPS.

[e]3/24 patients who had a post-TIPS endoscopy.

[f]Mean ± standard error.

Supplementary Table 2. Competing Risks Regression Models for 1-Year Post-TIPS PSE in the Pooled Groups of the Clinical Study After Removing Patients With Pre-TIPS PSE (N = 132)

	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Model 1						
Indication (RA vs VH)	0.89	0.48–1.64	.700	1.02	0.51–2.01	.960
Sex (female vs male)	2.63	1.20–4.07	.011	1.54	0.79–2.97	.200
Age, *y* (1-U increment)	1.04	1.01–1.07	.004	1.05	1.02–1.08	.002
MELD score (1-U increment)	1.04	0.97–1.11	.280	1.01	0.93–1.10	.770
PTFE-SG dilatation (>6 mm vs 6 mm)	2.94	1.50–5.73	.001	2.50	1.22–5.13	.012
Post-TIPS PCG <10 mm Hg (yes vs no)	2.99	1.63–5.84	.00001	2.18	1.15–4.12	.017
Model 2						
Indication (RA vs VH)	0.89	0.48–1.64	.700	0.92	0.47–1.82	.820
Sex (female vs male)	2.63	1.20–4.07	.011	1.56	0.81–3.01	.190
Age, *y* (1-U increment)	1.04	1.01–1.07	.004	1.04	1.01–1.08	.004
MELD score (1-U increment)	1.04	0.97–1.11	.280	1.02	0.95–1.10	.540
PTFE-SG dilatation (>6 mm vs 6 mm)	2.94	1.50–5.73	.001	2.42	1.13–5.19	.023
Post-TIPS PCG reduction >50% (yes vs no)	2.90	1.48–5.67	.002	1.90	0.91–3.98	.088

CI, confidence interval; HR, hazard ratio; MELD, model for end-stage liver disease; PCG, portocaval pressure gradient; PSE, portosystemic encephalopathy; PTFE-SG, polytetrafluoroethylene-covered stent graft; RA, refractory ascites; TIPS, transjugular intrahepatic portosystemic shunt; VH, variceal hemorrhage.

Supplementary Table 3. Propensity Score[a] Adjusted Multivariate Models for 1-Year Post-TIPS PSE

	HR	95% CI	*P* value
Pooled groups of the clinical study (N = 142)			
Model 1			
PTFE-SG dilatation (>6 mm vs 6 mm)	2.06	1.07–3.95	.030
Post-TIPS PCG <10 mm Hg (yes vs no)	2.54	1.40–4.59	.002
Model 2			
PTFE-SG dilatation (>6 mm vs 6 mm)	2.23	1.16–4.29	.016
Post-TIPS PCG reduction >50% (yes vs no)	2.25	1.17–4.33	.015
Patients without pre-TPS PSE (N = 132)			
Model 1			
PTFE-SG dilatation (>6 mm vs 6 mm)	2.22	1.07–4.61	.032
Post-TIPS PCG <10 mm Hg (yes vs no)	2.60	1.34–5.02	.004
Model 2			
PTFE-SG dilatation (>6 mm vs 6 mm)	2.35	1.12–4.92	.023
Post-TIPS PCG reduction >50% (yes vs no)	2.36	1.13–4.94	.023

CI, confidence interval; HR, hazard ratio; PCG, portocaval pressure gradient; PSE, portosystemic encephalopathy; PTFE-SG, polytetrafluoroethylene-covered stent graft; TIPS, transjugular intrahepatic portosystemic shunt.

[a]Propensity scores were the estimated probabilities of >6 mm PTFE-SG dilatation, calculated by means of a logistic regression model including all available pre-TIPS covariates (age, sex, pre-TIPS MELD score, TIPS indication, pre-TIPS PSE, pre-TIPS PCG). In this latter model only pre-TIPS PCG was associated to >6 mm PTFE-SG dilatation (odds ratio, 1.09; 95% CI, 1.00–1.17; $P = .0392$). A Fine and Gray model was fit using cubic polynomial smoothing based on propensity score values, PTFE-SG dilatation (>6 mm vs 6 mm), and either post-TIPS PCG <10 mm Hg or post-TIPS PCG decrease >50% as independent variables.

Supplementary Table 4. Comparison of Main Clinical and Hemodynamic Characteristics of Patients Included in the Clinical Study According to PTFE-SG Dilatation ≥6 mm at TIPS Positioning

	All (N = 142)	6 mm (N = 72)	>6 mm (N = 70)	*P* value
RA as an indication, n (%)	86 (60.6)	47 (65.3)	39 (55.7)	.320
Male gender, n (%)	94 (66.2)	49 (68.1)	45 (64.3)	.227
Age, *y*[a]	57.6 ± 10.2	58.2 ± 10.7	57.0 ± 9.7	.471
MELD score[a]	12.8 ± 4.1	12.4 ± 3.4	13.1 ± 4.3	.205
Pre-TIPS PSE, n (%)	10 (7.0)	5 (6.9)	5 (7.1)	.999
Pre-TIPS PCG, *mm Hg*[a]	23.7 ± 4.6	22.9 ± 4.6	24.5 ± 4.4	.038
Post-TIPS PCG, *mm Hg*[a]	11.5 ± 3.5	12.2 ± 2.8	10.7 ± 3.9	.006
Post-TIPS PCG <10 mm Hg, n (%)	53 (37.3)	17 (23.6)	36 (51.4)	.0009
Post-TIPS percent PCG decrease[a]	50.4 ± 14.6	45.3 ± 11.5	55.7 ± 15.7	.00002
Post-TIPS PCG reduction >50%, n (%)	76 (53.5)	26 (36.1)	50 (71.4)	.0001

MELD, model for end-stage liver disease; PCG, portocaval pressure gradient; PSE, portosystemic encephalopathy; PTFE-SG, polytetrafluoroethylene-covered stent graft; RA, refractory ascites; TIPS, transjugular intrahepatic portosystemic shunt.
[a]Mean ± standard deviation.

Supplementary Table 5. Main Clinical and Hemodynamic Characteristics of the Patients Included in the Clinical Study and Grouped According PTFE-SG Diameter Measured at CT (N = 79)

	6 mm (N = 38)[a]	>6 mm (N = 41)
Alcohol as an etiology, n (%)	11 (28.9)	13 (31.7)
RA as an indication, n (%)	20 (52.6)	22 (53.7)
Male gender, n (%)	24 (63.2)	30 (73.2)
Age, *y*[b]	57.0 ± 9.9	58.6 ± 9.4
MELD score[b]	13.5 ± 4.9	12.9 ± 4.1
Pre-TIPS PSE, n (%)	2 (5.3)	3 (7.3)
Pre-TIPS PCG, *mm Hg*[b]	23.2 ± 3.4	24.1 ± 4.1
Post-TIPS PCG, *mm Hg*[b]	11.7 ± 2.8	10.1 ± 3.4[c]
Post-TIPS percent PCG decrease[b]	47.8 ± 13.6	58.5 ± 14.9[c]
1-y probability of PSE, (95% CI)	26.7 (15.8–38.5)	48.2 (38.9–59.3)
Follow-up, *d*[d]	315.6 ± 18.7	339.6 ± 12.8

CI, confidence interval; CT, computed tomography; MELD, model for end-stage liver disease; PCG, portocaval pressure gradient; PSE, portosystemic encephalopathy; PTFE-SG, polytetrafluoroethylene-covered stent graft; RA, refractory ascites; TIPS, transjugular intrahepatic portosystemic shunt.
[a]Patients in the 6 mm group had a PTFE-SG [b] inner diameter of 6 ± 0.5 mm at PVW and/or HVW.
[b]Mean ± standard deviation.
[c]$P < .05$.
[d]Mean ± standard error.