Received: 9 May 2018 | First decision: 4 June 2018 | Accepted: 27 July 2018

DOI: 10.1111/apt.14947

WILEY AP&T Alimentary Pharmacology & Therapeutics

Variable efficacy of TIPSS in the management of ectopic variceal bleeding: a multicentre retrospective study

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Funding information
Foundation for Liver and Gastrointestinal Research Rotterdam

Summary

Background: Evidence for the efficacy of TIPSS in ectopic variceal bleeding (EctVB) is largely based on relatively small series.

Aim: To define the efficacy of TIPSS in EctVB.

Methods: Retrospective analysis of consecutive patients with chronic liver disease who presented with EctVB and received TIPSS in three tertiary centres in 1992-2016.

Results: The study included 53 patients (70% male, median age 61 years, median model for end-stage liver disease (MELD) score 11). The ectopic varices were located around the insertion of stomas (40%), duodenum (23%), rectum (17%) and at other sites (20%). Three-quarters of the patients had previously received unsuccessful medical, endoscopic or surgical therapy. The median follow-up was 14.0 months. Following TIPSS, bleeding recurred in 12 patients: 6 of 12 (50%) with duodenal varices, 2 of 9 (22%) with rectal varices and one each with stomal (1/21), intraperitoneal (1/3), hepaticojejunostomy (1/2) and ascending colon varices (1/2). The risk factors for re-bleeding were MELD score at TIPSS placement (HR: 1.081 per point; 95% confidence interval (CI): 1.012-1.153; $P = 0.034$), varices located at site other than an enterostomy (HR: 9.770; 95%CI: 1.241-76.917; $P = 0.030$) and previous local therapy (HR: 5.710; 95%CI: 1.211-26.922; $P = 0.028$). The estimated cumulative re-bleeding rate was 23% at 1 year, 26% at 3 years and 32% at 5 years. Post-TIPSS hepatic encephalopathy manifested or worsened in 16 of 53 patients (30%).

Conclusion: TIPSS provides long-term control of bleeding in most cirrhotic patients with EctVB. TIPSS is particularly effective in stomal EctVB, the most frequent cause of EctVB, but might not be as effective in duodenal EctVB.

The Handling Editor for this article was Professor Peter Hayes, and it was accepted for publication after full peer-review.

1 | INTRODUCTION

Approximately 5% of variceal bleedings occur outside the cardio-oesophageal junction and are denoted as ectopic.[1] Ectopic varices are predominantly located in the small and large intestine and around enterocutaneous stomas, but can also be present in the peritoneum, biliary tree and pelvic organs.[2] Abdominal and pelvic surgery is a well-known risk factor because postoperative adhesions and the creation of an enterostomy facilitate the formation of portosystemic collaterals.[1,2]

The management of ectopic variceal bleeding (EctVB) is challenging and not based on the results of controlled trials. Local endoscopic treatment modalities (band ligation, injection sclerotherapy, clips, argon plasma coagulation) and selective variceal embolisation frequently fail to prevent rebleeding with reported recurrence rates up to 80% within 6 months.[3,4] Surgical treatment, such as local sutures, devascularisation procedures or stoma revision with resiting, will only occasionally provide long-term control of bleeding in selected patients. The creation of surgical portosystemic shunts is associated with significant morbidity and mortality, particularly in patients with decompensated cirrhosis, and is rarely performed nowadays.[5-7]

TIPSS creation is used to treat patients suffering from EctVB.[8] Although evidence suggests that TIPSS is usually effective to prevent recurrent bleeding, research publications are restricted to patient series including only 8-28 patients.[9-13] Also, variable results have been published with respect to concomitant variceal embolisation, and the additional therapeutic value of embolisation combined with TIPSS placement remains unclear.[9,11-14]

We therefore aimed, in a multicentre cohort of patients with EctVB, to further determine the efficacy of TIPSS and to evaluate outcomes in subgroups with different types of ectopic varices. We also intended to explore the benefit of concomitant vascular embolisation of collateral vessels feeding the ectopic varices.

2 | PATIENTS AND METHODS

2.1 | Study design and data collection

We included all consecutive patients with advanced chronic liver disease, who underwent TIPSS placement for EctVB using bare metal stents or expanded polytetrafluoroethylene (e-PTFE)–covered nitinol stents (Viatorr, W.L. Gore & Associates Inc, Flagstaff, AZ, USA) in three tertiary referral centres: Erasmus MC, Rotterdam, the Netherlands, between January 1992 and December 2016; Academic Medical Center (AMC), Amsterdam, the Netherlands, between January 1998 and December 2016; and UZ Leuven, Leuven, Belgium, between January 2000 and December 2013. Demographic, biochemical clinical and survival data were collected from patient hospital records and entered into a database for statistical analysis. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in approval by the Medical Ethics Committee Erasmus MC, Rotterdam, the Netherlands, on 18 April 2017 (MEC-2017-217), stating that written informed consent was not necessary considering the retrospective study design.

2.2 | Definitions

The diagnosis of advanced chronic liver disease was based on liver histology, or a combination of clinical, biochemical and radiological findings.[15] The model for end-stage liver disease (MELD) score was calculated with the formula: $0.957 \times \log(\text{creatinine in mg/dL}) + 0.378 \times \log(\text{bilirubin in mg/dL}) + 1.120 \times \log(\text{INR}) + 0.643$.[16,17] Comorbidity with a cardiovascular condition, pulmonary condition or renal condition was defined as a condition requiring long-term medical treatment for which regular specialist follow-up care was necessary. Early TIPSS was defined as TIPSS insertion within 72 hours after an EctVB episode.[18] Bleeding was defined as a decrease in haemoglobin (Hb) by 2 g/dL (1.24 mmol/L), or the requirement of more than 2 units of packed red cells within 24 hours to stabilise Hb concentration or signs of volume depletion (systolic blood pressure below 100 mm Hg and/or heart rate above 100/min).[13] Rebleeding was defined as a single episode of clinical significant recurrent melena or hematemesis from portal hypertensive sources after day 5 that resulted in any of the following: (a) hospital admission, (b) blood transfusion, (c) drop in Hb of 3 g/dL (1.86 mmol/L) or (d) death within 6 weeks.[19]

The standard follow-up protocol for stent function differed per centre: in the Erasmus MC, a functional assessment of bare TIPSS stents with Doppler ultrasound (US) was performed 2, 7 and 30 days after placement, at 3-month intervals during the first year of follow-up, and every 6 months thereafter. Following TIPSS with covered stents, standard follow-up imaging was not performed. In the AMC, all stents were assessed at 3-7 days, 3 months, 6 months and 12 months after placement, and every year thereafter. In UZ Leuven, stent function was assessed every 6 months. In all centres, patients received an angiography with venous portal pressure measurements when shunt dysfunction was suspected based on findings during Doppler US or clinical symptoms. Shunt dysfunction was defined as shunt stenosis greater than 50% of the shunt and/or hepatic venous portal gradient higher than 12 mm Hg.[20]

2.3 | Statistical analysis

Continuous variables were reported as mean with standard deviation (SD), after visual confirmation of approximate normality, and compared using a *T* test. A median and range from the first to the third quartile (IQR, interquartile range) was computed for continuous variables with a non-normal distribution and compared using a Mann-Whitney test. Categorical variables were reported as count with proportion and compared using the chi-squared test.

The actuarial probabilities of being free of shunt dysfunction (shunt dysfunction as event, censoring at death or liver transplantation), being free of rebleeding (rebleeding as event, censoring at death or liver transplantation) and transplant-free survival (death as event, censoring at liver transplantation) after TIPSS creation were

estimated using the Kaplan-Meier method and compared using log-rank tests.

A univariable Cox regression analysis was carried out to identify risk factors for rebleeding at TIPSS placement using candidate predictor variables, hereinafter mentioned, as described in the literature and based on the clinical and research experiences of co-investigators: MELD score, location of EctVB, local treatment of the EctVB, urgency placement of TIPSS, type of stent used during TIPSS, portal pressure gradient after TIPSS placement above 12 mm Hg and concomitant embolisation.[2,11-13,18,21,22] The univariable Cox regression models were adjusted with a propensity score to take into account differences in MELD score at TIPSS placement for each individual covariate.

Furthermore, the effect of concomitant embolisation during the TIPSS procedure compared to TIPSS alone on rebleeding and mortality was analysed. For this analysis as well, a propensity score was calculated using a logistic regression model, estimating the probability to receive concomitant embolisation given the following observed baseline characteristics: MELD score, location of EctVB, type of stent used during TIPSS and urgency placement of TIPSS as predictor variables.

A two-sided $P < 0.05$ was considered significant for descriptive statistics, and a P-value <0.10 was considered significant for univariable regression models. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA).

3 | RESULTS

3.1 | Patient characteristics and TIPSS procedures

In the three centres, 53 patients received TIPSS for EctVB during the study period, representing 5.4% of the total population (n = 979) undergoing a TIPSS procedure (Figure 1). The study population consisted predominantly of males with a median age of 61 years (IQR 51-66) and a median MELD score of 11 (IQR 9-17; Table 1). The ectopic varices were most often located near the mucocutaneous junction of stomas (40%), followed by the duodenum (23%), rectum (17%) and other sites (20%). TIPSS placement was the initial treatment for EctVB in 23% of the patients. About 77% of the patients had been unsuccessfully treated for EctVB with one or multiple modalities; 24 patients (45%) had undergone previous endoscopic treatment (band ligation, injection therapy, coagulation), 22 (42%) had received vasoactive medication (nonselective beta-blockers, somatostatin, terlipressin), 9 (17%) had undergone abdominal surgery (stoma revision or relocation, bowel resection) and 1 patient (2%) had received endovascular treatment (embolisation).

TIPSS were created with a bare metal stent in 8 patients and with an e-PTFE–covered stent in 45 patients (Table 2). Hemodynamic measurements showed that the median pre-TIPSS portosystemic gradient (PSG) decreased from 14 mm Hg (IQR 10-20) to 6 mm Hg (IQR 4-7) after TIPSS placement. The post-TIPSS PSG remained above 12 mm Hg in four patients. Eighteen (34%) patients received early TIPSS and initial hemostasis was achieved in all cases.

3.2 | Clinical outcome

The median follow-up time was 14.0 months (IQR 3.8-45.9). Following TIPSS, EctVB from the same site occurred in 12 of 53 (23%) patients (Figure 2). Bleeding recurred in 1 of 21 (5%) cases with stomal varices, 6 of 12 (50%) cases with duodenal varices, in 2 of 9 (22%) with rectal varices, in 1 of 3 cases with intraperitoneal varices, in 1 of 2 cases with varices in the ascending colon and in 1 of 2 cases with varices located at the hepaticojejunostomy. The four patients with jejunal, caecal, sigmoid or umbilical vein ectopic varices remained free of rebleeding.

Most rebleeds were diagnosed shortly after TIPSS creation, in eight patients (four with duodenal varices, one with varices at the hepaticojejunostomy, one with intraperitoneal varices, one with rectal varices and one with ascending colon varices) in the first month after the TIPSS procedure (15%), in two patients (one with duodenal varices and one with rectal varices) after 1-6 months (4%) and in two patients (one with duodenal varices and one with urostomal varices) after 6 months (4%). In nine of these 12 patients, rebleeding was associated with shunt dysfunction. After TIPSS placement, the estimated cumulative ectopic variceal rebleeding rate was 23% at 1 year, 26% at 3 years and 32% at 5 years (Figure 3). Rebleeding from other sources occurred in four patients: three from gastro-oesophageal varices and one from haemorrhagic gastropathy. The univariable Cox regression to identify risk factors for rebleeding found three predicting variables: high MELD score (HR: 1.081 per point; 95% confidence interval, CI: 1.012-1.153; $P = 0.020$), EctVB located at another site than an enterostomy (HR: 9.770; 95% CI: 1.241-76.917; $P = 0.030$) and local treatment preceding TIPSS (HR: 5.710; 95% CI: 1.211-26.922; $P = 0.028$) (Table 3).

The rebleeding risk in the two main subcategories of EctVB—stomal and duodenal varices—differed markedly. A comparison of these groups with respect to aetiology of liver disease, MELD score, type of stent, concomitant embolisation, post-TIPSS PSG >12 mm Hg and established stent dysfunction did not reveal significant differences. However, age was significantly lower in patients with duodenal EctVB (54 vs 65 years, $P = 0.016$), and 11 of 12 duodenal EctVB had been treated endoscopically before TIPSS, while local endoscopic or other procedures were performed in only 2 of 21 cases with stomal EctVB ($P < 0.001$) (Figure S1).

TIPSS dysfunction was diagnosed in 6 of 8 patients with bare metal stents (75%) compared to 10 of 45 with e-PTFE–covered stents (22%) ($P = 0.011$). In six patients, shunt dysfunction was diagnosed at an elective follow-up visit and in nine patients after a rebleed. Most shunt dysfunctions were diagnosed in the first 6 months after TIPSS creation, in seven patients in the first month (13%), in 6 after 1-6 months (11%) and in three after 6 months (6%). The estimated cumulative TIPSS dysfunction rate significantly differed ($P = 0.003$) for bare metal stents (1 year: 76%; 3 years: 100%)

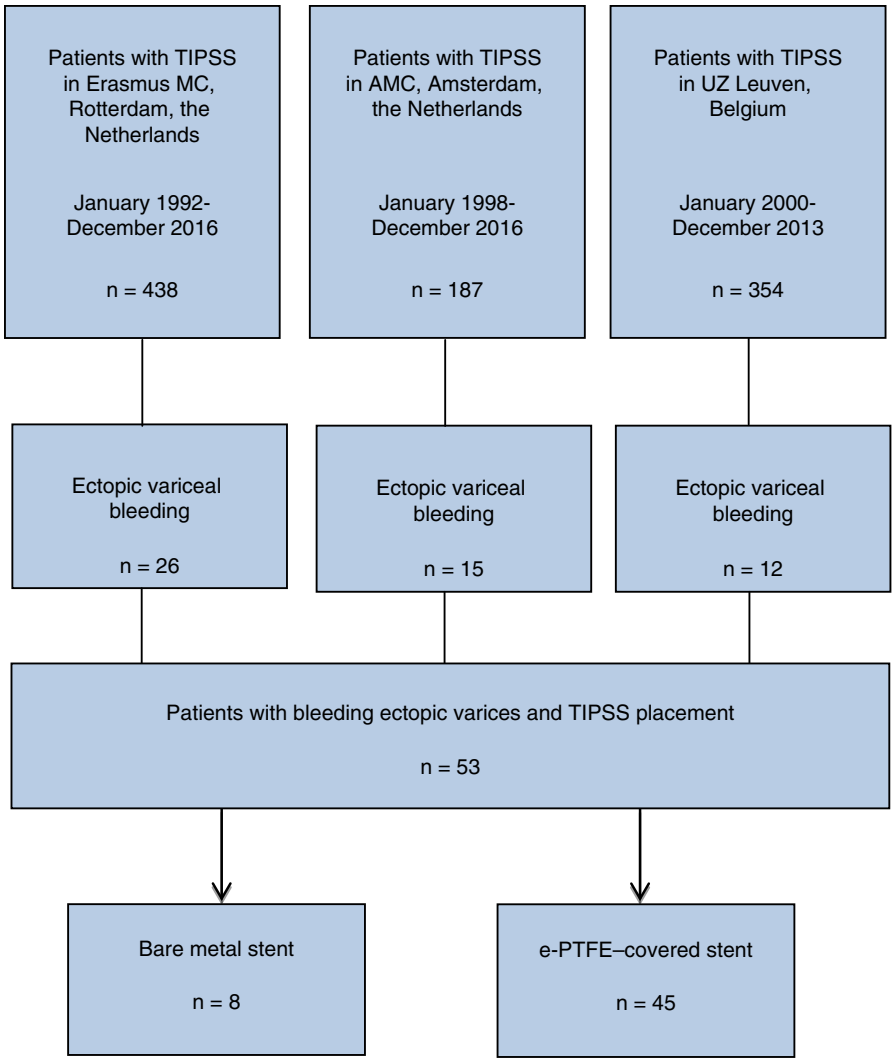


FIGURE 1 Flow diagram of inclusion. e-PTFE: expanded polytetrafluoroethylene

compared to e-PTFE–covered stents (1 year: 23%; 3 years: 24%; 5 years: 31%) (Figure 4).

A total of 31 shunt revisions were performed in the first 2 years after TIPSS creation in 13 patients. An additional stent was placed in eight patients; in four patients, angioplasty was performed (followed in two cases by additional stent placements); and in one patient, local thrombolysis was accomplished. Three patients with shunt dysfunction and rebleeding died.

Post-TIPSS hepatic encephalopathy (HE) manifested or worsened in 16 of 53 patients (30%). HE could be managed medically in 12 patients; however, in four patients radiological re-intervention was performed reducing the TIPSS diameter and improving or resolving in all cases the symptoms of HE. In no cases, a complete shunt occlusion was performed.

In this cohort, 41 patients died, five underwent liver transplantation, six were alive at the end of follow-up, and one was lost to follow-up. The causes of death were liver disease-related in 12 patients (29.3%) including three patients dying of EctVB, not liver disease-related in 12 patients (29.3%), and unknown in 17 patients (41.4%) (Figure 2). The estimated 30-day, 1-year and 5-year mortality rates were 11%, 41% and 75%, respectively (Figure S2).

3.3 | Concomitant embolisation during TIPSS

Concomitant embolisation during the TIPSS procedure was performed in 13 patients: four patients had varices located near enterocutaneous stomas, four had duodenal varices, two had rectal varices, two had intraperitoneal varices and one had varices in the ascending colon. Concomitant embolisation was performed in 4 of 9 patients with an acute bleeding and in 9 of 44 patients as a secondary prophylactic measure. There were no statistically significant differences between patients receiving embolisation and TIPSS alone with respect to age, gender, MELD score, location of varices, presentation with acute bleeding or treatment centre. After propensity score adjustment, the hazard ratio for rebleeding of concomitant embolisation compared to TIPSS alone was 0.701 (95% CI: 0.145-3.390; $P = 0.659$) and the hazard ratio for mortality was 0.776 (95% CI: 0.281-2.148; $P = 0.626$).

4 | DISCUSSION

This multicentre cohort study evaluated the efficacy of TIPSS with predominantly e-PTFE–covered stents in subgroups of patients with

TABLE 1 Clinical characteristics of the study population

	Patients with ectopic variceal bleeding (n = 53)
Male gender (%)	37 (69.8)
Age in years, median (IQR)	61 (51-66)
Aetiology of portal hypertension (%)	
Alcoholic cirrhosis	25 (47.2)
PSC/PBC/autoimmune hepatitis	11 (20.8)
Cryptogenic cirrhosis	7 (13.2)
Viral hepatitis	2 (3.8)
Other	8 (15.0)
Child-Pugh class[a] (%)	
A	34 (65.4)
B	15 (28.8)
C	3 (5.8)
MELD score,[a] median (IQR)	11 (9-18)
Portal vein thrombosis (%)	5 (9.4)
Comorbidity[b] (%)	
Previous medical history of malignancy[c]	11 (20.8)
Colorectal cancer	5
Urothelial carcinoma	3
Pancreatic cancer	2
Hepatocellular cancer	1
Lung cancer	1
Hodgkin's disease	1
Cardiovascular condition	9 (17.0)
Inflammatory bowel disease	8 (15.1)
Diabetes	6 (11.3)
Pulmonary condition	4 (7.6)
Renal condition	4 (7.6)
Medical history of gastroesophageal variceal bleeding (%)	8 (15.1)
Number of previous episodes of gastroesophageal variceal bleeding (%)	
1-3	6 (11.3)
4-6	1 (1.9)
7 or more	1 (1.9)
History of abdominal surgery (%)	36 (67.9)
Location of bleeding ectopic varices (%)	
Enterostomal[d]	21 (39.7)
Colostomy	11
Ileostomy	8
Urostomy	3
Duodenum	12 (22.6)
Rectum	9 (17.0)
Intraperitoneal	3 (5.7)
Hepaticojejunostomy	2 (3.8)
Ascending colon	2 (3.8)
Jejunum	1 (1.9)
Caecum	1 (1.9)
Sigmoid	1 (1.9)
Umbilical vein	1 (1.9)
Number of previous episodes of ectopic variceal bleeding (%)	
1-3	26 (49.1)
4-6	7 (13.2)
7 or more	20 (37.7)
Previous treatment of ectopic variceal bleeding (%)	
None	12 (22.6)
Medication[b]	22 (41.5)
Non-selective β-blocker	14
Somatostatin	12
Terlipressin	1
Endoscopic[b]	24 (45.3)
Band ligation	9
Injection therapy	17
Coagulation	2
Endovascular embolisation[b]	1 (1.9)
Surgery[b]	9 (16.9)

IQR: interquartile range; MELD: model for end-stage liver disease.
[a]Data regarding liver disease severity missing in 1 case.
[b]Patients could have multiple concomitant comorbidities or received multiple treatment modalities, either concomitant or successive.
[c]Two patients had a history with two malignancies.
[d]One patient presented with concomitant colostomy and urostomy bleeding.

bleeding from ectopic varices. The present study confirms that TIPSS was an effective treatment by completely preventing rebleeding in the large majority (77%) of cases. TIPSS was particularly effective in patients with less severe liver disease and with varices located at enterostomas. In contrast, the rebleeding risk in patients with duodenal varices was unexpectedly high.

The observed cumulative 23% rebleeding rate at 1 year is comparable with previously reported rates varying from 23% to 39%,[11-13] while the 26% rate at 2 years was considerably lower than previously reported.[12] It seems likely that the superior long-term bleeding control is attributable to the use of e-PTFE–covered stents in the large majority of cases. The actuarial risk of remaining free from rebleeding in the present series in comparison with the risk observed in TIPSS-treated gastro-oesophageal bleeding reported in two recently published studies originating from the participating centres was 77% versus 94-100% at 1 year, 74% versus 92-94% at 3 years and 68% versus 90-92% at 5 years, respectively.[22,23] Thus, the overall rebleeding risk in TIPSS-treated EctVB appears to be

TABLE 2 TIPSS procedural data

	All patients (n = 53)	Patients with bare metal stents (n = 8)	Patients with e-PFTE–covered stents (n = 45)
Pre-TIPSS placement PSG (mm Hg), median (IQR)	14 (10-20)	22 (12-26)	14 (9-19)
Post-TIPSS placement PSG (mm Hg), median (IQR)	6 (4-7)	12 (7-16)	5 (4-7)
Decrease in PSG (mm Hg), median (IQR)	8 (6-13)	8 (6-12)	8 (6-13)
Concomitant embolisation (%)	13 (24.5)	1 (12.5)	12 (26.7)
Early TIPSS placement (%)	18 (34)	4 (50)	14 (31)
Diameter stent (mm), median (IQR)	9 (8-10)	9 (8-10)	9 (8-10)

e-PTFE: expanded polytetrafluoroethylene; IQR: interquartile range; PSG: portosystemic gradient.

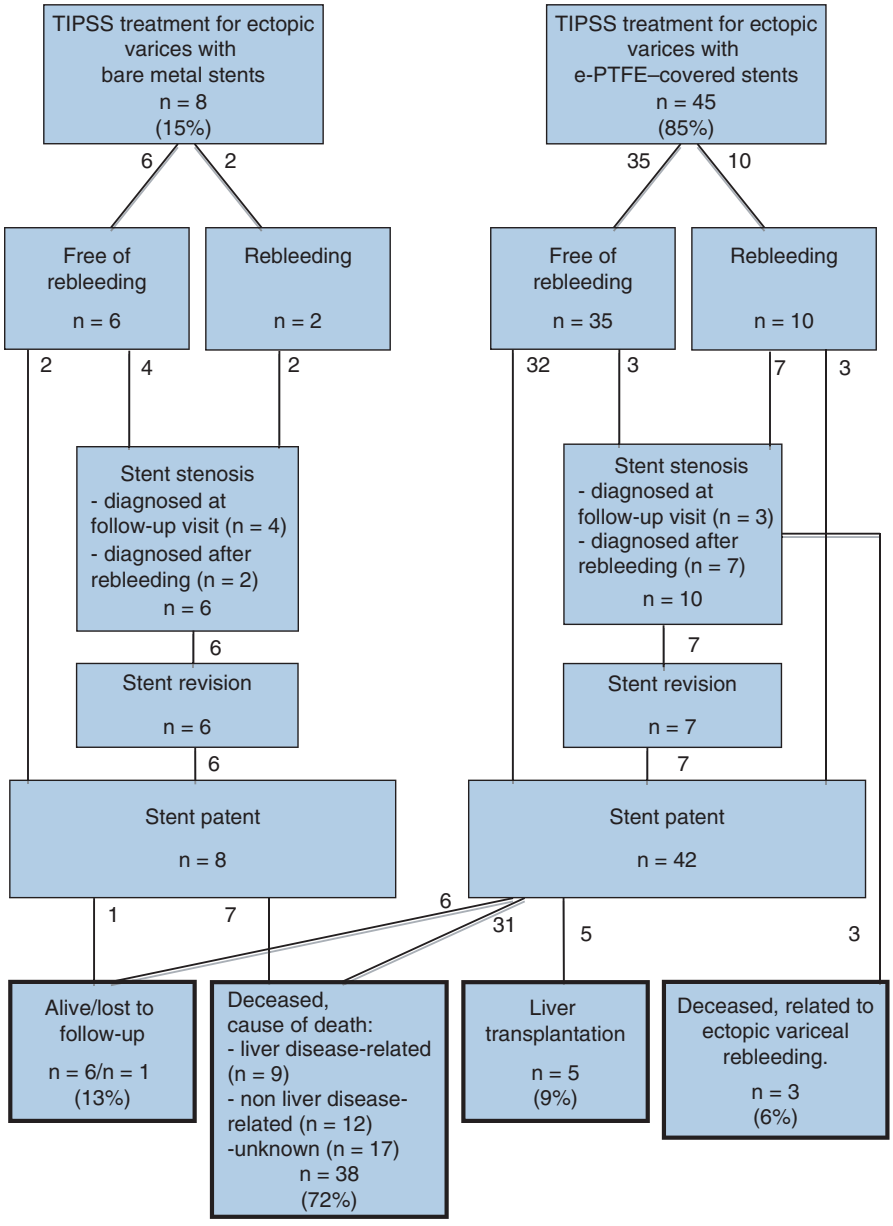


FIGURE 2 Rebleeding, stent patency and clinical outcome in patients with bare metal stents and e-PTFE–covered stents. e-PTFE: expanded polytetrafluoroethylene

higher than that in gastro-oesophageal bleeding. Our data indicate that this seems attributable to the relevant high rebleeding risk in TIPSS-treated duodenal EctVB.

In our cohort, shunt dysfunction was diagnosed in three-quarter of the patients with rebleeding and occurred three times more often in bare metal stents compared to e-PTFE–covered stents. In total,

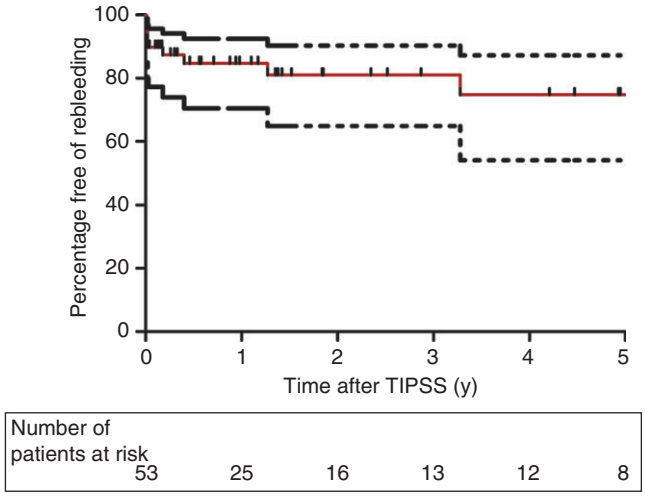


FIGURE 3 Actuarial probability (red line) with 95% confidence interval (black dashed lines) of remaining free of rebleeding following TIPSS

TABLE 3 Univariable analysis of ectopic variceal rebleeding

	HR	95% CI	*P*-value
MELD score (per point)	1.081	1.012-1.153	0.020
Location of ectopic varices[a]			
Enterostomal	1		0.030
Other site	9.770	1.241-76.917	
Previous local therapy[a]	5.710	1.211-26.922	0.028
Early placement of TIPSS[a]			
≤72 h after EctVB episode (reference)	1		0.653
>72 h after EctVB episode	0.737	0.195-2.787	
Type of TIPSS[a]			
Bare (reference)	1		0.887
e-PTFE-covered	0.9894	0.193-4.148	
Post-TIPSS PSG[a]			
≤12 mm Hg (reference)	1		0.884
>12 mm Hg	1.171	0.141-9.735	
Concomitant embolisation[a]	1.133	0.304-4.221	0.852

CI: confidence interval; e-PTFE: expanded polytetrafluoroethylene; EctVB: ectopic variceal bleeding; HR: hazard ratio; MELD: model for end-stage liver disease; PSG: portosystemic gradient.
[a]Hazard ratio adjusted with propensity score for MELD score at TIPSS placement.

TIPSS dysfunction occurred in 23% at 1-year follow-up compared to approximately 20% in the study from Kochar et al and 49% in the study from Vidal et al.[12,13] Although these rates vary notably, the trend that e-PTFE–covered stents have improved shunt patency is in line with widely reported experience.[24,25]

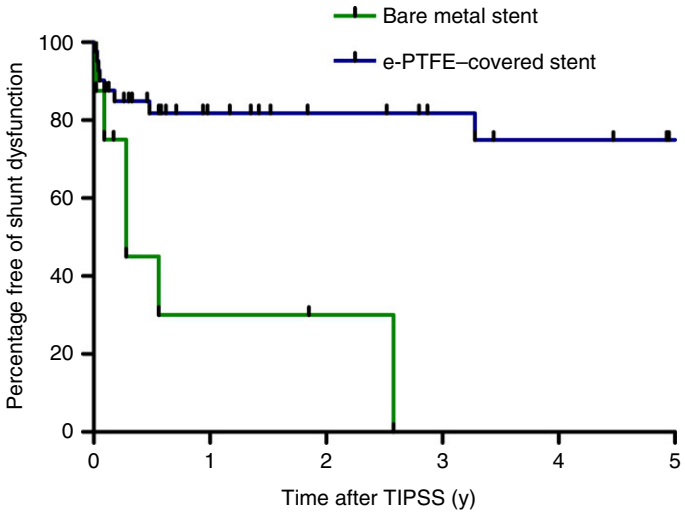
In our series, the efficacy of TIPSS in patients with duodenal EctVB, who had a disappointing 50% rebleeding risk, was relatively poor. A potential explanatory factor may be that local, but ultimately unsuccessful endoscopic therapies frequently preceded TIPSS. In our experience, endoscopic treatment, in particular repeated tissue glue injections, may lead to significant duodenal ulcerations that can be the cause of repeated bleeding in their own right. In such cases, it may be very difficult to distinguish portal hypertensive-related bleeding from other causes, and management may be troublesome. Another possibility is that local tumorous vascular ingrowth or thrombosis could cause (re)bleeding unrelated to portal hypertension. However, in our two cases with duodenal variceal bleeding and a previous diagnosis of pancreatic cancer, there was no evidence for residual or recurrent tumour. Also with respect to other malignancies, there was no indication that these were of aetiological importance. Further studies in this type of EctVB are required to further address the timing of TIPSS and whether alternative therapeutic approaches, in particular balloon-occluded retrograde-transvenous-obliteration may be a preferable strategy.[26]

The efficacy of TIPSS has to be balanced against the risk of serious side effects, in particular HE. Post-TIPSS HE manifested or worsened in 30% of our patients, which was comparable with other reported experience.[18,23,27,28] The majority of post-TIPSS HE could be managed medically, but in some cases, a stent diameter reduction was necessary. A recent report suggests that there might be an optimum of 8 mm TIPSS diameter to effectively decompress the portal system in relation to the encephalopathy risk.[29] With the knowledge that the diameter of TIPSS can passively increase after placement, improved results regarding post-TIPSS HE may be expected in the future for diameter controlled expansion stents.[30,31]

A recent meta-analysis found a nonsignificant trend towards a beneficial effect of variceal embolisation in addition to TIPSS.[14] Our data are in line with these results as embolisation did not significantly improve the probability of remaining free of rebleeding or survival. However, considering the potential selection bias occurring when embolisation of the culprit varix is not feasible and the limited number of patients treated, we were unable to reliably assess the value of embolisation as an adjunctive measure.

To the best of our knowledge, we report the largest multicentre cohort of patients with TIPSS for EctVB with predominantly e-PTFE–covered stents and our data reflect real-life practice in three university hospitals. Despite the retrospective study design, only one patient was lost to follow-up. This is the first study allowing a preliminary assessment of the efficacy of TIPSS in subgroups of EctVB, although the results should be interpreted cautiously considering the size of the patient population. Ideally, prospective trials could provide more clarity about the role of TIPSS in subgroups of EctVB as well as on the role of concomitant embolisation. However, such studies may never be performed considering the low prevalence of the disease, the heterogeneity in varices location and the technical inability to embolise all culprit collateral vessels.

In conclusion, our study demonstrates that TIPSS effectively prevents rebleeding in the majority of patients presenting with EctVB. TIPSS is particularly effective in bleeding from enterostomas, the most frequent type of EctVB. However, the results in duodenal



Number of patients at risk						
Bare metal stent	8	2	1	–	–	–
e-PTFE–covered stent	45	20	15	12	10	7

FIGURE 4 Actuarial probability of being free of shunt dysfunction: shunt dysfunction was diagnosed more often in patients with bare metal stents (green line) compared to patients with e-PTFE–covered stents (blue line) (log-rank P = 0.003). e-PTFE: expanded polytetrafluoroethylene

EctVB, with a 50 per cent rebleeding rate, were disappointing and highlight the need for alternative therapeutic approaches.

ACKNOWLEDGEMENT

Declaration of personal interests: Dr. A. Moelker received proctor fees from Cook Medical, and Terumo Corporation. All other authors declare that they have nothing to disclose regarding conflict of interest with respect to this manuscript.

Declaration of funding interests: The study was sponsored by the Foundation for Liver and Gastrointestinal Research Rotterdam (SLO).

AUTHORSHIP

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Author contributions: R.C. Oey: study concept and design, acquisition of data, interpretation of data, statistical analysis, drafting of the manuscript, final approval of the article and acting as the submission's guarantor. K. de Wit: acquisition of data, analysis and interpretation of data, drafting of the manuscript and final approval of the article. A. Moelker: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript and final approval of the article. T. Atalik: study concept and design, acquisition of data and final approval of the article. O.M. van Delden: acquisition of data, interpretation of data and final approval of the article. G. Maleux: acquisition of data, interpretation of data and final approval of the article. N.S. Erler: interpretation of data, statistical analysis, drafting of the manuscript and final approval of the article. R.B. Takkenberg: acquisition of data, interpretation of data and final approval of the article. R.A. de Man: study concept and design, interpretation of data, drafting of the manuscript and final approval of the article. F. Nevens: acquisition of data, interpretation of data and final approval of the article. H. R. van Buuren: study concept and design, interpretation of data, drafting of the manuscript and final approval of the article.

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SUPPORTING INFORMATION

Additional supporting information will be found online in the Supporting Information section at the end of the article.

How to cite this article: Oey RC, de Wit K, Moelker A, et al. Variable efficacy of TIPSS in the management of ectopic variceal bleeding: a multicentre retrospective study. *Aliment Pharmacol Ther*. 2018;48:975–983. https://doi.org/10.1111/apt.14947