

Bleeding ectopic varices—treatment with transjugular intrahepatic porto-systemic shunt (TIPS) and embolisation

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Background/Aims: Bleeding ectopic varices due to cirrhosis can be difficult to manage. We report our experience of uncontrolled bleeding from ectopic varices treated with transjugular intrahepatic porto-systemic shunt (TIPS).

Methods: We selected the 21 cirrhotics who underwent TIPS for bleeding ectopic varices from our database: Child-Pugh grade A (2), B (11) and C (8). Site of bleeding was rectal (11), colonic (2), ileal 1, jejunal 1, duodenal 1, and stomal (5).

Results: TIPS was performed successfully in 19/21 (90%) patients. All except 1 had either a reduction in portosystemic pressure gradient ≤ 12 mmHg ($n=12$) or reduction by 25–50% of baseline ($n=6$). TIPS alone was used in 12/19; 7 of these 12 had no further bleeding; 5 (42%) rebled within 48 h, and had embolisation, 4 without further bleeding. In 7 of 19, TIPS and embolisation were performed together: 2 patients (28%) rebled; further embolisation stopped the bleeding.

Conclusions: Ectopic varices do rebleed despite a reduction of porto-systemic pressure gradient ≤ 12 mmHg or by 25–50% of baseline, following TIPS. Embolisation stopped bleeding in all but 1 patient. We recommend performing embolisation at the time of the initial TIPS to control bleeding from ectopic varices.

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1. Introduction

Portal hypertension is a common complication of liver cirrhosis. Typical sites of variceal formation are the oesophagus and stomach. However, varices can occur along the entire gastro-intestinal tract: duodenum, jejunum, ileum, colon, and rectum, usually in relation to previous abdominal surgery and are commonly denoted as ectopic varices. Stomal varices after fashioning of an ileostomy, colostomy and ileal conduits are a further site of ectopic varices.

Ectopic varices are an infrequent cause of bleeding (5% of all variceal bleeding) [1] but in contrast may be difficult to diagnose, and may not be amenable to standard local

therapy due to their inaccessibility. Even when they can be reached with an endoscope, our experience has been similar to others, in that banding or sclerotherapy of large rectal varices can leave an ulcer, which then rebleeds [1]. In addition, the relative infrequency of patients with ectopic variceal bleeding means that experience tends to be reported either as single cases, or small series. This is particularly true for transjugular intrahepatic porto-systemic shunt (TIPS), for which there are 37 case reports [2–40] and only 2 series of 12 patients [17] and 9 [28].

We report our experience of bleeding ectopic varices in cirrhotic patients treated with TIPS to lower portal pressure and using the stent as a conduit for selective embolisation of collaterals feeding the ectopic varices.

2. Patients

We reviewed our database of 360 TIPS procedures and selected the 21 patients who underwent TIPS for bleeding ectopic varices between 1993

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and 2003. Patients' characteristics are shown in Tables 1 and 2. Mean age was 51 years \pm 16.3. The cause of cirrhosis was alcohol in 12, cryptogenic in 5, post-OLT - HBV re-infection in 1, HCV infection in 1, primary sclerosing cholangitis in 1 and autoimmune hepatitis in 1. Child-Pugh grade was A in 2, B in 11 and C in 8.

All the patients presented with melaena and not haematemesis, but all were investigated by upper endoscopy, excluding oesophageal/gastric fundal variceal bleeding or any other cause of bleeding from the stomach and oesophagus.

Sites of bleeding were duodenal varices in 1 patient, rectal varices in 11 patients, colonic/caecal varices in 2 patients, stomal varices in 5 patients, ileal varices in 1 patient, and jejunal varices in 1 patient.

Diagnosis was made by upper endoscopy in 1 (duodenal varices); by colonoscopy in 12 (11 rectal, 1 colonic/caecal varices); by direct vision of the stoma or stomal endoscopy in 5. The diagnosis of ectopic varices was confirmed in all cases by portal venography at the time of TIPS placement by the identification of abnormal splanchnic vessels feeding from either superior or inferior mesenteric veins via hepatofugal flow. In 3 patients repeated endoscopy failed to show a source of bleeding, and delayed venous phase splanchnic arteriography was necessary to reveal ileal, jejunal and colonic variceal bleeding, respectively. Stomas had been fashioned after colectomy secondary to toxic megacolon in 1 patient and secondary to rectal carcinoma in the other 4 patients.

Bleeding was considered clinically significant by the following criteria: decrease of haemoglobin by ≥ 2 g/dl, or requirement of more than 2 units of packed red cells within 24 h to stabilise haemoglobin concentration or signs of volume depletion (systolic blood pressure below 100 mmHg and/or heart rate above 100/min). All these patients had clinically significant bleeding. 13 of these had active bleeding despite 24 h of vasoactive therapy (terlipressin 1–2 mg/4 h or octreotide 50 μ g/h) and subsequently they underwent emergency TIPS in order to arrest bleeding. 8 patients presented with recurrent clinically significant bleeding episodes, requiring repeated blood transfusion, and an elective TIPS was performed.

Mean transfusion before TIPS was 10.7 ± 6.7 units of blood. In those who rebled mean transfusion after TIPS was 9.3 ± 5.1 units. Portosystemic

pressure gradient was defined as the difference between the portal and the central venous pressure measured in the right atrium.

2.1. Procedure

The technique of TIPS used in our centre has been described previously [41] Memotherm stents (Angiomed, Karlsruhe, Germany) were used in all cases; Tract dilatation was to a diameter of 8, 10, or 12 mm and was dependent on final portal pressure gradient, age of patient, and the presence of encephalopathy.

Patients who showed persistent variceal filling after reducing portosystemic pressure gradient < 12 mmHg (or by 25–50% of baseline) or who had early rebleeding after TIPS were managed with variceal embolization with stainless steel coils and/or 100% alcohol and/or gel foam.

Continued or early rebleeding following TIPS within the same hospital admission led to urgent repeat upper endoscopy or colonoscopy and repeat TIPS venography. Doppler ultrasonography, to check on shunt function, was carried out before discharge, at 3–6 month intervals, and whenever shunt dysfunction was suspected clinically. Portal venography and shunt dilatation were performed when there was radiological or clinical evidence of shunt dysfunction, and routine venography was performed at 12 months.

3. Results

TIPS was performed successfully in 19/21 (90%) patients. (Fig. 1). Before TIPS mean right atrial pressure (RA) was 10.9 ± 6.7 mmHg, mean portal vein pressure (PV) was 32 ± 10.2 mmHg, and mean portosystemic pressure

Table 1
Characteristics of cirrhotic patients with uncontrolled bleeding from ectopic varices

Pt No.	Age	Sex	Aetiology of liver disease	Child-pugh classification and score	MELD score	Units of blood transfused before/after TIPS	Oesophageal/gastric varices (grade)
1	42	M	Cryptogenic	B 8	12	12	Oesophageal varices
2	36	F	Cryptogenic	B 7	2	9	Previous sclerotherapy for variceal bleeding
3	64	M	Post OLT HBV	B 8	22	4	Gastric varices
4	51	F	Alcohol	B 9	13	6	Oesophageal varices
5	37	F	Alcohol	C 12	20	15/15	Oesophageal varices
6	57	F	Primitive sclerosing colangi-tis	B 8	18	6	Gastric varices
7	68	M	Alcohol	C 10	23	8	Oesophageal varices
8	60	M	Alcohol	C 11	40	7	No varices
9	60	F	Alcohol	C 12	8	9	Oesophageal varices
10	76	M	Cryptogenic	A 6	14	6	Gastric varices
11	19	M	OLT for autoimmune hepa-titis. Recurrence	B 8	9	13/8	Oesophageal varices
12	76	M	HCV	A 6	0	8	No varices
13	76	F	Cryptogenic	C 10	6	8	Oesophageal varices
14	43	F	Alcohol	B 9	12	23	Oesophageal varices
15	21	F	Cryptogenic	B 8	2	33/5	Oesophageal varices
16	43	F	Alcohol	C 11	22	14/12	Oesophageal varices
17	46	M	Alcohol	C 10	11	8	Previous banding for oesophageal varices
18	52	M	Alcohol	B 9	3	11	No varices
19	54	F	Alcohol	C 12	24	8	Gastric varices bleeding
20	35	F	Alcohol	B 8	21	4	No varices
21	52	M	Alcohol	B 8	14	14	Previous banding for oesophageal varices

Table 2
Source of bleeding, TIPS and embolisation procedures and follow up in cirrhotic patients with uncontrolled bleeding from ectopic varices

Pz No.	Source of bleeding	Emergency/ elective TIPS	Pre TIPS porto-sys-temic pressure gradient	Post TIPS porto-sys-temic pressure gradient	Reduction (%)	Embolisa-tion	Rebleed-ing	Time interval between TIPS and rebleed-ing (h)	Emboli-zation post rebleed-ing	Follow up (interval from date of TIPS)
1	Ileostomy	Emergency	21	14	33	No	Yes	36	Yes	Died due to liver failure 4 months later
2	Rectum	Emergency	19	7		No	No			Died due to sepsis 3 years later
3	Ileostomy	Elective	23	5		No	No			Died due to sepsis 15 days after TIPS.
4	Rectum	Emergency	31	7		No	No			Well after 26 months.
5	Caecum	Emergency	21	17	19	No	Yes	24	Yes	Died after 3 months due to hepato-renal syndrome and liver failure
6	Ileostomy	Elective	–	–		–				Died bleeding 3 weeks after TIPS was attempted
7	Rectum	Emergency	–	–		–				Died bleeding 10 h after TIPS was attempted
8	Ileostomy	Emergency	24	6		No	No			Died the day after TIPS due to sepsis
9	Rectum	Elective	27	14	48	No	No			Died 2 years later
10	Ileum	Elective	10	5		No	No			Well at 3 months
11	Colon	Emergency	11	8		No	Yes	48	Yes	Encephalopathy at 1 month. Well at 2 years
12	Rectum	Elective	14	8		Yes	No			Well at 2 years
13	Rectum	Elective	23	14	39	Yes	No			TIPS occlusion followed by melaena at 14 days (dilated). Well at 12 months
14	Rectum and gastric varices	Emergency	29	17	41	No	No			Retinal haemorrhage at 3 months. Well at 6 months
15	Duodenum	Emergency	20	2		No	Yes	24	Yes	TIPS stenosis followed by melaena at 14 days (dilated). Well at 1 year
16	Jejunum + rectum	Emergency	18	7		Yes	Yes	72	Yes	Acute Respiratory Distress Syndrome and sepsis after TIPS. Died after 25 days.
17	Rectum	Emergency	27	16	41	Yes	No			Well at 7 months
18	Colostomy	Emergency	19	8		Yes	Yes	240	Yes	Died due to sepsis at 17 days
19	Rectum; Gas-tric fundus	Emergency	26	15	42	No	Yes	48	Yes	Well at 6 weeks
20	Rectum	Elective	16	12		Yes	No			Well at 6 weeks
21	Rectum	Elective	19	10		Yes	No			Encephalopathy-required TIPS reduction stent at 4 weeks

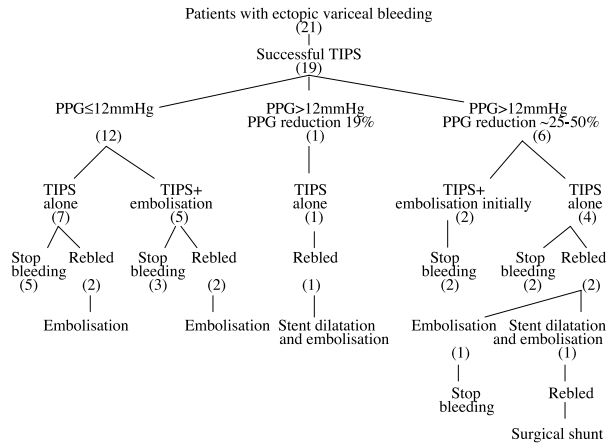


Fig. 1. Description of patients with ectopic variceal bleeding treated with TIPS.

gradient was 21 ± 5.7 mmHg. Post TIPS placement mean right atrial pressure (RA) was 12.5 ± 5.6 mmHg, mean portal vein pressure (PV) was 22.2 ± 8 mmHg, and mean portosystemic pressure gradient was 10.3 ± 4.6 mmHg.

In 12 of 19 patients (63%) we obtained a post TIPS portosystemic pressure gradient ≤ 12 mmHg. In 6 patients (No. 1, 9, 13, 14, 17, 19) post procedural portosystemic pressure gradient was > 12 mmHg, but with a drop between 33 and 48% of baseline. In only 1 patient (No. 5) was a reduction of portosystemic pressure gradient of 19% from baseline, with a pre TIPS portosystemic pressure gradient of 21 mmHg and a post TIPS portosystemic pressure gradient of 17 mmHg.

TIPS alone was the initial treatment in 12 of 19 patients (63%). In 7 of these 12 patients (58%), TIPS was enough to arrest haemorrhage and to prevent rebleeding. However, 5 of the 12 (42%) rebled within 48 h: in 2 patients (No. 11, 15) post TIPS portosystemic pressure gradient was < 12 mmHg; in 2 (No. 1, 19) portosystemic pressure gradient was > 12 mmHg after TIPS but with a drop of 33% and 42% from baseline, respectively; in one patient (No. 5) the portosystemic pressure gradient change post TIPS was 19%. In this patient TIPS stent dilatation, in addition to embolisation with coils was used. Portosystemic pressure gradient dropped to 7 mmHg and no further rebleeding occurred. In the remaining 4 patients who rebled early despite achieving haemodynamic targets, embolisation with coils was performed and in 3 no further bleeding occurred. In the remaining patient (No. 1), despite embolisation, there was repeated bleeding. Therefore stent dilatation reducing portosystemic pressure gradient < 12 mmHg was performed, but rebleeding occurred again. A further 3 sessions of embolisation, were used but bleeding recurred; a surgical porto-caval shunt was necessary to arrest bleeding.

In the other 7 of 19 patients, TIPS and embolisation were performed at the initial TIPS placement. In 5 patients (No. 12, 16, 18, 20, 21) we obtained a portosystemic

pressure gradient ≤ 12 mmHg. In the other 2 patients (No. 13, 17), portosystemic pressure gradient was > 12 mmHg, but with a drop of 39 and 41% from baseline, respectively. 2 patients rebled (28%) (No. 16 and 18), despite portosystemic pressure gradient < 12 mmHg. Both needed a further embolisation session and both subsequently stopped.

Fig. 2 shows the actuarial probability of being free of bleeding (Kaplan–Meier estimates).

In 2 patients (No. 6, 7), portal vein puncture was unsuccessful and a stent was not placed. One had an extremely small liver and was bleeding from ileostomal varices. During the procedure, there were 3 perforations of the liver capsule, which were successfully blocked with coils. The patient died at home after 3 weeks, after further bleeding episodes. In the other patient, there was rectal variceal bleeding presenting 20 days after having sclerosis for oesophageal varices. The TIPS procedure was unsuccessful during which there were 2 capsular punctures that were successfully blocked with coils and the patient died after 10 h, with continued bleeding from rectal varices.

3.1. Follow up

There were 4 deaths within 6 weeks from TIPS due to sepsis and progressive liver failure (No. 3, 8, 16, 18). Other deaths during follow up were 1 (No. 5) who died after 3 months due to hepato-renal syndrome and liver failure; 1 (No. 2) who died at 3 years following sepsis and 1 (No. 1) who died due to hepatic failure after 4 months following a surgical portal-caval shunt.

The 7-days, 6 weeks, 3 month and 6 month rates of survival mortality were 96%; 78, 74 and 65%, respectively (Fig. 3 Kaplan–Meier estimates).

Only 2 patients (No. 13 and 15) required TIPS revision for occlusion of the stent. One patient has required stent reduction for encephalopathy (No. 21), and a further patient had lactulose responsive encephalopathy.

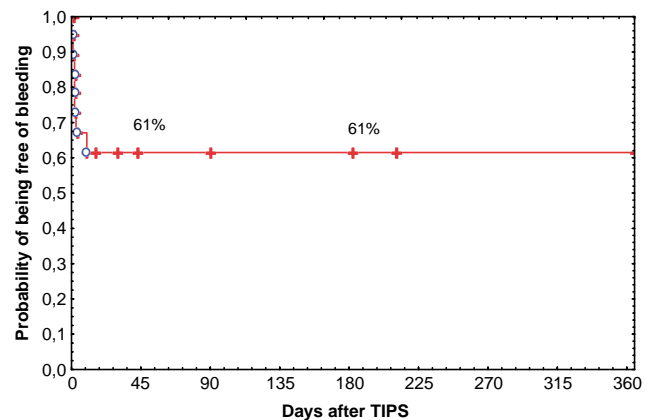


Fig. 2. Actuarial probability of being free of bleeding (Kaplan–Meier estimates). [This figure appears in colour on the web.]

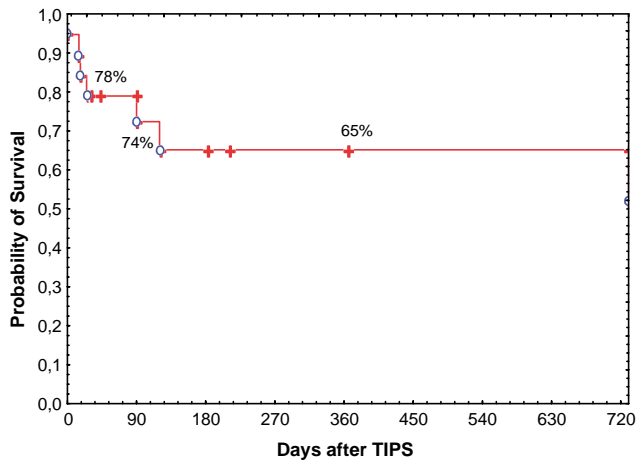


Fig. 3. Actuarial probability of survival (Kaplan–Meier estimates). [This figure appears in colour on the web.]

4. Discussion

Bleeding from ‘ectopic varices’ may be difficult to manage [1]. A recent review has suggested that when medical therapy has failed, embolisation should be used first, before proceeding to TIPS [1]. However, long term results of embolisation or local surgery alone are disappointing, as collaterals reform, and rebleeding occurs and the risk of porto-mesenteric thrombosis is high. Portal-caval surgery in sick cirrhotic patients has a high morbidity and mortality. Treatment with sclerotherapy or band ligation, especially for rectal varices, has been proposed, but results are often disappointing, because of the risk of massive haemorrhage after sloughing of the occluded varices a few days after therapy and because of persistence of portal hypertension. In our cohort, TIPS combined with embolisation was an effective therapy for controlling haemorrhage from ectopic varices. Indeed, only 1 patient of 19 (6%) continued to bleed despite a portosystemic pressure gradient reduction < 12 mmHg with TIPS, and numerous sessions of embolisation. A surgical shunt was necessary as rescue therapy for this patient.

Embolisation appeared well tolerated and we had no complications. There is however one reported case of paradoxical cerebral emboli after TIPS and coils embolisation for treatment of duodenal varices [4].

However, our experience with respect to portal pressure has not mirrored the medical literature. Patients with recurrent oesophago-gastric bleeding, despite beta-blockers and endoscopic therapy, can be treated successfully with TIPS according to Casado et al [42], reducing portosystemic pressure gradient < 12 mmHg, or more than 50% from baseline, (although gastric variceal bleeding with portal pressure gradients below 12 mmHg has been reported by the Edinburgh group [43]). Rossle [44] demonstrated that a 50% reduction in the pressure gradient protected patient from rebleeding. A reduction by 25% or more was also effective

with a probability of rebleeding of only 7% and the potential benefit of less risk of encephalopathy and liver failure.

In 18 of 19 patients (95%), we obtained a post TIPS portosystemic pressure gradient ≤ 12 mmHg or a drop in portosystemic pressure gradient by 25–50% of baseline, but this did not universally prevent early rebleeding: 7 of 19 patients (37%) rebled after TIPS \pm embolisation (5 in the group treated initially solely with TIPS and 2 patients in the TIPS and embolisation at the same session). In this group, only 1 patient did not have an optimal portosystemic pressure gradient reduction (post TIPS portosystemic pressure gradient of 17 mmHg with a drop of 19% from baseline).

In 12 of 19 pt (63%) variceal embolisation was performed for controlling haemorrhage, in addition to optimal portosystemic pressure gradient reduction: in 5 patients the embolisation followed further bleeding after initial TIPS placement.

In particular all the patients who rebled, including the 4 with portosystemic pressure gradient < 12 mmHg, had varices some distance from the portal vein, and it was our impression that for ectopic varices, the ‘12 mmHg rule’ does not apply. These patients characteristically had blood flow away from the portal vein at the site of varices and required embolisation. Indeed, our technique of measuring right atrial pressure and portal vein pressure may actually have over-read the true intrabdominal portal pressure gradient, as the free IVC pressure is always either equal or more than right atrial pressure.

The available experience of other groups treating bleeding ectopic varices with TIPS is hampered by the large number of single case reports [2–40], and only 2 series [16,27]. In total 63 patients are reported: 47 patients of 63 were initially treated just with TIPS and 16 also had embolisation together with the TIPS.

Nine patients of the 47 (19%) rebled. It is not always clear if the rebleeding occurred early after TIPS, i.e. failure to control bleeding, rather than rebleeding due to shunt occlusion. In 16 patients who had contemporaneous embolisation, 9 stopped bleeding, but 7 rebled (44%). In 2, a second session of embolisation was necessary to stop haemorrhage. Therefore, in total of 47 of 63 cases (75%) in the literature bleeding was stopped either with TIPS alone or TIPS and embolisation. All reports except four [13,19,22,26] document an optimal portosystemic pressure gradient reduction, either to ≤ 12 mmHg or by 25–50% of baseline value, so that 14 of 63 (22%) rebled despite achieving these targets. 2 of the four that do not document an optimal portosystemic pressure gradient reduction rebled.

Our success rate is therefore similar to that in literature. Ectopic varices may rebleed despite a reduction of portosystemic pressure gradient < 12 mmHg or by 25–50% of baseline value with TIPS. Adding embolisation to TIPS appears to reduce the risk of rebleeding in ectopic varices or can be useful to control bleeding in a patients with a portosystemic pressure gradient < 12 mmHg.

Furthermore, we believe that our experience and that of the literature suggest that the optimal management of bleeding ectopic varices could be to use embolisation with TIPS at the same sitting. This refines the algorithm published by Norton et al [1]. The stent-shunt provides a conduit to embolise ectopic varices and could prevent further collateralisation. Embolisation together with a target reduction at portal pressure would be a reasonable therapeutic aim.

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