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Doctopic: Review and Opinion

Transjugular intrahepatic portosystemic shunt followed by splenectomy for complicated hepatosplenic schistosomiasis: a case report and review of the literature

Francesca Tamarozzi, Tamara Ursini, Giacomo Stroffolini, Geraldo Badona Monteiro, Dora Buonfrate, Veronica Andrea Fittipaldo, Simone Conci, Clizia Gasparini, Giancarlo Mansueto, Alfredo Guglielmi, Federico Gobbi

Hepatosplenic schistosomiasis is a complex clinical condition caused by the complications of chronic infection with *Schistosoma* species that cause intestinal schistosomiasis. Hepatosplenic schistosomiasis derives from the fibrotic reaction stimulated around parasite eggs that are transported by the mesenteric circulation to the liver, causing periportal fibrosis. Portal hypertension and variceal gastrointestinal bleeding are major complications of hepatosplenic schistosomiasis. The clinical management of hepatosplenic schistosomiasis is not standardised and a parameter that could guide clinical decision making has not yet been identified. Transjugular intrahepatic portosystemic shunt (TIPS) appears promising for use in hepatosplenic schistosomiasis but is still reported in very few patients. In this Grand Round, we report one patient with hepatosplenic schistosomiasis treated with TIPS, which resulted in regression of oesophageal varices but had to be followed by splenectomy due to persisting severe splenomegaly and thrombocytopenia. We summarise the main challenges in the clinical management of this patient with hepatosplenic schistosomiasis, highlight results of a scoping review of the literature, and evaluate the use of of TIPS in patients with early hepatosplenic schistosomiasis, to improve the prognosis.

Introduction

Schistosomiasis is a neglected tropical disease caused by infection with trematode parasites of the genus *Schistosoma*. An estimate of more than 230 million people worldwide are infected, although 440 million people globally might have the pathology caused by either concurrent infection or permanent organ damage resulting from past chronic infection.[1]

Hepatosplenic schistosomiasis is a complex clinical condition caused by the complications of chronic infection with *Schistosoma mansoni*, *Schistosoma japonicum*, or other species of parasites of the genus *Schistosoma* that cause intestinal schistosomiasis.[1] These parasites are endemic throughout the tropics, mainly in sub-Saharan Africa and Latin America where *S mansoni* is the most common species, and in east Asia where *S japonicum* and *Schistosoma mekongi* are present.[1]

After transmission through skin contact with fresh water that contains infective parasite larvae (ie, cercariae), adult parasites establish in the mesenteric veins. Here,

Key points

- Portal hypertension in hepatosplenic schistosomiasis derives from periportal fibrosis occurring as the consequence of chronic inflammatory and fibrotic reaction stimulated around parasite eggs that are transported by the mesenteric circulation to the liver, as well as spleen hyperafflux.
- Variceal bleeding is the most dangerous complication of hepatosplenic schistosomiasis. Liver function is generally preserved until late; haematochemical alterations include leukopenia and thrombocytopenia, generally not accompanied by evident haemorrhagic diathesis.
- Other than local management of varices and supportive medical treatment with β blockers, the classic surgical interventions for hepatosplenic schistosomiasis include selective portosystemic shunts, mainly distal splenorenal shunts, and non-shunt interventions such as oesophagogastric devascularisation with splenectomy. None of the surgical procedures for hepatosplenic schistosomiasis were superior and no parameter has been indentified to guide clinical management; local management of varices and medical treatment with β blockers are only supportive.
- Transjugular intrahepatic portosystemic shunt (TIPS) is a minimally invasive, interventional radiology procedure. It establishes a communication between portal and hepatic vein branches and reduces portal hypertension. Despite appearing to be promising for use in patients with hepatosplenic schistosomiasis, it is still performed in few patients. No formal indication exists for the use of TIPS in patients with hepatosplenic schstosomiasis, nor for the follow-up of patients treated with this minimally invasive procedure.
- From published case series of TIPS in hepatosplenic schistosomiasis, portal hypertension and oesophageal varices seem to be the parameters benefiting most from this intervention. These benefits encourage the evaluation of the possible application of the use of TIPS in patients with early hepatosplenic schistosomiasis to improve the patient's prognosis, even before first variceal bleeding episode, given that the association of variceal bleeding with increased risk of liver decompensation has been reported and is in turn associated with increased mortality.

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Department of Infectious-Tropical Diseases and Microbiology, IRCCS Sacro Cuore Don Calabria Hospital, Negrar di Valpolicella, Verona, Italy (F Tamarozzi PhD, T Ursini MD, G Stroffolini MD, G Badona Monterio MD, D Buonfrate PhD, V A Fittipaldo MSc, Prof F Gobbi PhD)**; Division of General and Hepatobiliary Surgery, Department of Surgical Sciences, Dentistry, Gynaecology, and Paediatrics** (S Conci PhD, Prof A Guglielmi MD)**, and Department of Radiology** (C Gasparini MD, Prof G Mansueto MD)**, University of Verona, University Hospital G B Rossi, Verona, Italy; Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy** (Prof F Gobbi)

Correspondence to:
Dr Francesca Tamarozzi, Department of Infectious-Tropical Diseases and Microbiology, IRCCS Sacro Cuore Don Calabria Hospital, Negrar di Valpolicella, Verona 37024, Italy
francesca.tamarozzi@sacrocuore.it

females produce eggs, which are excreted with the human faeces after traversing the intestinal wall. The pathophysiology of hepatosplenic schistosomiasis is different from that of cirrhosis.[2] Hepatosplenic schistosomiasis derives from the chronic inflammatory and fibrotic reaction stimulated around parasite eggs that are transported by the mesenteric circulation to the liver, where they get trapped into the small portal branches. This reaction causes the obliteration of small vessels, perivascular fibrosis, and atypical neovascularisation.[3] Embolisation of eggs over time leads to the involvement of increasingly larger portal branches, causing the characteristic periportal fibrosis—named Symmer's fibrosis or clay pipe fibrosis—and its complications, such as portal hypertension (caused by presinusoidal block and supported by hyperafflux from the spleen) with preserved hepatopetal flow, splenomegaly, hypertensive gastropathy, development of portosystemic collaterals, oesophageal varices, and upper gastrointestinal bleeding (UGB).[2,3] UGB is estimated to occur in up to 80% of people with periportal fibrosis, with a mortality rate of up to 30% per bleeding episode and a toll of 0·2 million deaths per year in sub-Saharan Africa.[1,4] Liver function is generally preserved until late in patients with hepatosplenic schistosomiasis given that the liver parenchyma itself is not replaced by fibrosis. Haematochemical alterations include thrombocytopenia and leukopenia, which have been attributed to hypersplenism or intrasplenic blood stasis. Thrombocytopenia is generally not accompanied by evident haemorrhagic diathesis and recovers, at least partly, even after spleen-preserving interventions.[5,6]

Besides local management of varices and supportive medical treatment with β blockers, the classic surgical interventions for hepatosplenic schistosomiasis include selective portosystemic shunts, mainly distal splenorenal shunts, and non-shunt interventions such as oesophagogastric devascularisation with splenectomy.[2] Currently, no procedure appears clearly superior and no parameter has been identified that could guide clinical decision making,[2] which is largely based on local expertise and experience. Generally, distal splenorenal shunts have been reported to be followed by lower rates of UGB and portal vein thrombosis but higher rates of hepatic encephalopathy compared with oesophagogastric devascularisation with splenectomy.[2] Transjugular intrahepatic portosystemic shunt (TIPS) is an interventional radiology procedure creating a communication between portal and hepatic vein branches to treat portal hypertension and reduce the risk of variceal bleeding. TIPS has been applied in patients with cirrhosis since the late 1980s, but is still rarely performed in hepatosplenic schistosomiasis and few data are available on the long-term outcome of this intervention, such as complications on the stent implant, rate of variceal bleeding, development of hepatic encephalopathy, effect on splenomegaly and haematochemical parameters, and any differences between hepatosplenic schistosomiasis caused by *S mansoni* versus *S japonicum* infection.[2]

In this Grand Round, we report one patient with hepatosplenic schistosomiasis with splenomegaly and severe thrombocytopenia, who was treated with TIPS followed by splenectomy due to the persistence of low platelet count. To our knowledge, this report is the first on TIPS followed by splenectomy in a patient with hepatosplenic schistosomiasis. We comment on the clinical aspects of this patient and update the review of the published literature on the use of TIPS in patients with hepatosplenic schistosomiasis.

Case description

In April, 2016, a 33-year-old Angolan woman arrived in Italy and attended the outpatient clinic of the Department of Infectious-Tropical Diseases and Microbiology of the Istituto di Ricovero e Cura a Carattere Scientifico Sacro Cuore Don Calabria Hospital (Negrar di Valpolicella, Verona, northeastern Italy) having complained of abdominal pain since 2013. She reported frequently observing blood in her saliva or sputum and one episode of haematemesis in 2014. She reported taking propranolol for a few months in 2014, but could not provide medical records describing the reason for prescription. She also reported a treatment with praziquantel in 1994 and having had malaria in the past. Physical examination revealed splenomegaly 4 cm beyond the rib cage. Haematochemical analyses revealed severe thrombocytopenia (43×10^9/L; normal value $130–400\times10^9$/L), leukopenia ($1·6\times10^9$/L; normal value $5·2–12·4\times10^9$/L) with moderate neutropenia ($0·6\times10^9$/L; normal value $1·9–8·0\times10^9$/L), mild lymphocytopenia ($0·8\times10^9$/L; normal value $0·9–5·2\times10^9$/L), and monocytes at the lower limit of the normal range ($0·1\times10^9$/L; normal value $0·16–1\times10^9$/L). Prothrombin time was slightly increased (international normalised ratio [INR] 1·26; normal value <1·15); aminotransferases, bilirubin, and albuminaemia were within normal ranges. Further investigations revealed sickle cell trait, latent tuberculosis (QuantiFERON interferon-γ release assay 5·32 UI/mL [negative <0·34] with no signs of active infection) and infection with *S mansoni* as assessed by the presence of parasite eggs in stool, detected by microscopy after formol ether concentration. Serology for schistosomiasis was positive (*S mansoni* IgG ELISA, Bordier Affinity Products, Crissier, Switzerland; serological index 4·05; negative <1). Testing for HIV, hepatitis C virus (HCV), hepatitis B virus (HBV), Epstein-Barr virus, syphilis, and other parasitic infections (including malaria, strongyloidiasis, other intestinal parasites, and *Schistosoma haematobium*) were negative. Chest radiograph was unremarkable. Abdominal ultrasonography and CT revealed a reduced right liver lobe (9 cm on midclavicular line; normal value 10–16 cm), with irregular margins and advanced periportal fibrosis consistent with pattern F of the Niamey-Belo Horizonte classification[7] (figure 1A),

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dilated portal vein (2 cm) with hepatopetal flow on colour doppler ultrasonography, and severe splenomegaly (bipolar length 17·5 cm; section area 104·0 cm²; figure 1B). Endoscopy showed straight small (Japanese Society for Portal Hypertension grading F1)[8] varices in the mid-lower third of the oesophagus. She received treatment for schistosomiasis with praziquantel (40 mg/kg per day in two divided doses for 3 days) and started treatment for latent tuberculosis with rifampicin plus isoniazid, prescribed for 3 months.

The evolution of haematochemical values and variceal grade from diagnosis over time is shown (figure 2). Between May, 2016, and January, 2018, the haematochemical parameters were stable overall. However, in April, 2018, platelets were decreased to 10×10⁹/L and endoscopy showed worsening of the oesophageal varices (ie, moderately enlarged, beady varices [F2]). Coproparasitology and stool PCR for *S mansoni* were repeatedly negative, but the patient was re-treated with praziquantel under the hypothesis that the worsening of the signs of portal hypertension could be not only due to the irreversible advanced periportal fibrosis, but also supported by persistent infection at a very low burden. To reduce the variceal tension and risk of bleeding, the patient started therapy with propranolol up to 40 mg twice a day, which was well tolerated. As expected, given that advanced fibrosis does not regress with parasitological cure, F2 varices were confirmed in October, 2019.

In December, 2019, the patient was admitted to the General and Hepatobiliary Surgery of Verona University Hospital where a TIPS was placed. The procedure was conducted under deep sedation, with right jugular access, with a Rosch-Uchida transjugular liver access set (Cook Medical, Bloomington, IN, USA). A 10F (Flexor Check Flow, Cook Medical, Bloomington, IN, USA) was placed in the right suprahepatic vein and a catheter with a 1 mm flexible trocar stylet was advanced inside the introducer. The track created through the liver parenchyma was dilated by balloon catheter (Mustang over the wire; Boston Scientific, Marlborough, MA, USA). The introducer was then advanced inside the portal branch and a coated stent gradually introduced over the sheath (Gore Viatorr, Flagstaff, AZ, USA). The stent was then dilated to 8 mm with a balloon catheter. Venography confirmed the patency of the shunt. The postoperative course was uneventful: 3 days after intervention, ultrasonography confirmed the patency of the shunt and the patient was discharged 5 days after intervention with a white blood cell count (WBC) 3·3×10⁹/L, platelet count 55×10⁹/L, haemoglobin 12·0 g/dL, total bilirubin 23·0 µmol/L (normal value <21 µmol/L), and ammonaemia 56 µmol/L (normal value <53 µmol/L).

In the following 18 months the patient was in good general condition, with only minor signs of portal encephalopathy, managed with lactulose and rifaximin.

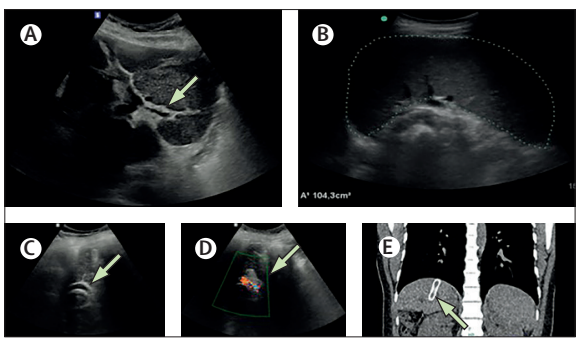

***Figure 1*: Imaging features of the patient and TIPS implant**
(A) Ultrasonography of the liver showing irregular surface and periportal fibrosis (arrow) with highly echogenic bands and streaks, extending from the portal vein bifurcation to the liver surface (pattern F of the Niamey-Belo Horizonte classification[7]). (B) Ultrasonography of the spleen showing severe splenomegaly. (C) Ultrasonography of the liver showing the TIPS device (arrow). (D) Colour doppler ultrasonography of the liver showing pervious TIPS device (arrow). (E) CT scan showing the TIPS device in the liver (arrow). TIPS=transjugular intrahepatic portosystemic shunt.

Bilirubinaemia (11·5–32·7 µmol/L) and ammonaemia (53–85 µmol/L) increased slightly, INR was 1·28–1·57, and albuminaemia was 32–40 g/L. WBC was overall stable, whereas the platelet count steadily decreased from 49×10⁹/L (January, 2020) to 14×10⁹/L (August, 2021). Antiplatelet antibodies were negative, and thrombocytopenia deriving from thrombotic microangiopathies or intravascular coagulation were excluded. Oesophageal varices were improved (F1 in March, 2020, and February, 2021). Doppler ultrasonography and CT (June, 2020, and June, 2021; figure 1C–E) showed patent, in-place TIPS device, dilated portal vein (2 cm) with 40–50 cm/s hepatopetal flow, and splenomegaly (bipolar length 18·5 cm).

In December, 2021, due to the persistent severe splenomegaly and worsening thrombocytopenia, the patient was readmitted to the General and Hepatobiliary Surgery of Verona University Hospital (Verona, Italy), where splenectomy with spleen autotransplantation was performed by positioning of one segment of splenic tissue, approximately 5 cm ×4 cm×2 cm in size and 40 g in weight, in a pouch created at the lower edge of pedunculated greater omentum. During the intervention, two platelet pools were transfused. The patient was discharged 16 days after intervention with WBC 8·8×10⁹/L, platelets 345×10⁹/L, haemoglobin 10·0 g/dL, and total bilirubin 23·4 µmol/L. Vaccinations against pneumococcus, meningococcus, and *Haemophilus influenzae* type B were performed before surgery. At discharge, doppler ultrasonography showed patent TIPS device and 28 cm/s hepatopetal portal flow. Platelet count and WBC reached normal ranges within 2–4 weeks.

From March, 2021, until the last outpatient follow-up in March, 2023, the patient referred good health, varices were stably F1, WBC maintained within normal limits, and platelets stabilised at around 95×10⁹/L. A CT scan performed in June, 2022 revealed a vascularised spleen

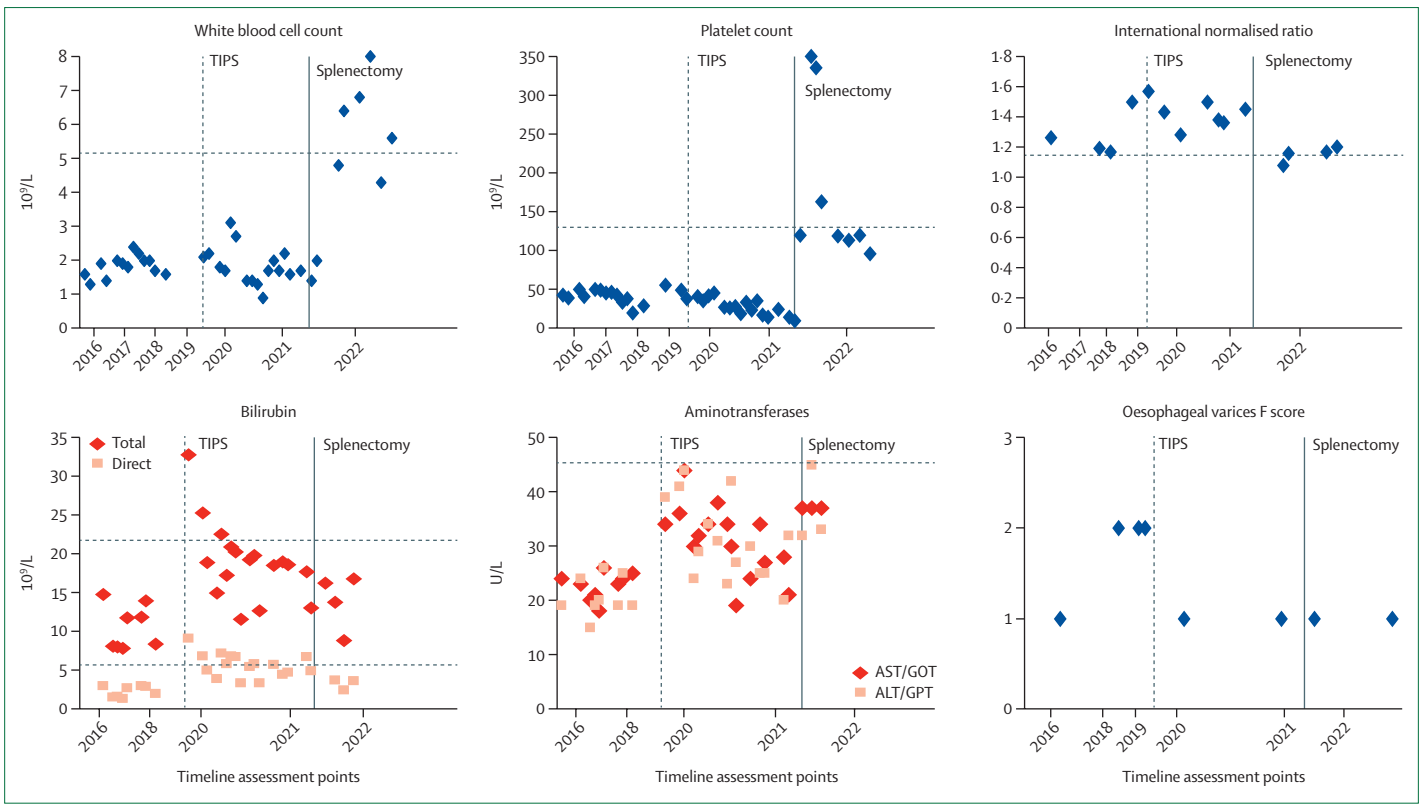

Figure 2: **Evolution of haematochemical parameters and variceal F grading[8] over time**
In relation to TIPS implant (dashed line) and splenectomy (solid line). Dotted lines indicate the lower normal values for white blood cell counts and platelet counts and the upper normal values for international normalised ratio, bilirubin, and aminotransferases. TIPS=transjugular intrahepatic portosystemic shunt.

implant, which, together with absence of Howell-Jolly bodies, indicates functionality of the autotransplanted spleen. Persistence of moderate thrombocytopenia is being monitored before more invasive procedures (ie, bone marrow aspirate) are considered.

Review and discussion

We did a scoping review of the literature to explore published literature of relevance to our case. This Grand Round specifically addressed these research areas: (1) the clinical characteristics of patients with hepatosplenic schistosomiasis managed by TIPS; (2) the main complications of TIPS in patients with hepatosplenic schistosomiasis and how they are managed; and (3) how clinical characteristics of hepatosplenic schistosomiasis evolve along the follow-up in patients treated with TIPS.

Demographic and clinical profile of hepatosplenic schistosomiasis patients managed with TIPS

Five papers (two case reports[9,10] and three case series[11–13]) published between 2000 and 2022, presented a total of 104 patients (24 female patients and 80 male patients aged 16–61 years) with hepatosplenic schistosomiasis from ten endemic countries, clinically managed with TIPS. The demographic and clinical profile of patients before TIPS is summarised (table 1). Two papers[11,12] included patients who were also described in previous publications.[14–16] Data were also extracted from these previous publications and used to complement the information reported in the other papers when needed. The species involved was *S mansoni* in 60 (58%) patients from Egypt, sub-Saharan Africa, and Brazil, and *S japonicum* in 44 (42%) of patients from China and the Philippines. 12 (12%) patients were diagnosed and managed in a non-endemic country.

Co-infection with hepatitis viruses was explicitly reported for 45 (43%) patients: HBV in 22 (21%) patients and HCV in 23 (22%) patients. 39 (38%) patients had liver cirrhosis and three (3%) patients had hepatocellular carcinoma. Among other comorbidities, the most frequent was portal vein thrombosis (27 [26%]). Three (3%) patients had Budd-Chiari syndrome. Alcohol consumption was specifically reported in two (2%) patients, metabolic syndrome in two (2%) patients, and autoimmune hepatitis in one (1%). Two patients (2%) were receiving dialysis due to renal failure.

Oesophageal varices were reported in 75 (72%) patients, the grade of which was described for only 39 (52%) patients with F3 being the most common (16 [41%] of 39). In most patients (67 [64%]), episodes of UGB were reported having occurred before TIPS intervention; in our patient, whether this occurred and how it was

	Country of origin	*Schistosoma* species	Comorbidities	Oesophageal varices	UGB	Spleen size (cm)	Laboratory tests	Ascites and hepatic encephalopathy	Child-Pugh and MELD scores	Pre-TIPS interventions
Dondelinger et al[13]										
48 patients; 38 male; ten female; mean age 44 years (range 23–61)	Egypt	*Schistosoma mansoni*	22 with HCV; eight with HBV; three with hepatocellular carcinoma; two with renal failure; 39 with cirrhosis; three with Budd-Chiari	Four F1; nine F2; eight F3; seven F4	Yes in 27 patients	17·2 ± 0·6	..	21 with refractory ascites	13 Child-Pugh A; 19 Child-Pugh B; 16 Child-Pugh C	30 variceal sclerotherapy
Grieco et al[9]										
One patient; male; age 30 years	Ethiopia	*S mansoni*	..	Yes	Yes	20·0	WBC 2·4; platelet count 47; INR 1·4; albuminaemia 3·4	Moderate ascites	Child-Pugh B7	VBL
Nordmann et al[12]										
Patient 1; male; age 19 years	Guinea	*S mansoni*	Sickle cell trait	F2	Yes	26·0	Platelet count 54; INR 1·5; albuminaemia 4·2	No	Child-Pugh 5A; MELD 11	VBL; β blockers
Patient 2; male; age 39 years	DRC	*S mansoni*	..	F3	No	16·8	Platelet count 37; INR 1·1; albuminaemia 3·8	No	Child-Pugh 5A; MELD 9	VBL; β blockers
Patient 3; male; age 28 years	Eritrea	*S mansoni*	Alcohol cons.	F3	No	26·5	Platelet count 50; INR 1·3; albuminaemia 4·6	No	Child-Pugh 5A; MELD 5	VBL
Patient 4; female; age 37 years	Madagascar	*S mansoni*	PVT	F3	Yes	13·0	Platelet count 144; INR 1·1; albuminaemia 3·3	No	Child-Pugh 6A; MELD 7	VBL; β blockers
Patient 5; male; age 19 years	Eritrea	*S mansoni*	HBV	F2	Yes	29·7	Platelet count 23; INR 1·6; albuminaemia 3·8	No	Child-Pugh 6A; MELD 15	VBL; β blockers
Patient 6; male; age 16 years	Sierra Leone	*S mansoni*	..	F3	Yes	21·0	Platelet count 20; INR 1·4; albuminaemia 3·5	No	Child-Pugh 5A; MELD 10	VBL
Patient 7; male; age 20 years	Eritrea	*S mansoni*	Gastritis	F3	No	18·8	Platelet count 52; INR 1·2; albuminaemia 4·7	No	Child-Pugh 5A; MELD 8	β blockers
Patient 8; male; age 27 years	Eritrea	*S mansoni*	..	F2	No	21·2	Platelet count 68; INR 1·4; albuminaemia 4·2	No	Child-Pugh 5A; MELD 10	VBL; β blockers
Patient 9; female; age 59 years	Philippines	*Schistosoma japonicum*	HBV; metabolic syndrome	F3	Yes	13·2	Platelet count 103; INR 1·3; albuminaemia 6·9	No	Child-Pugh 6A; MELD 13	VBL; β blockers
Patient 10; male; age 21 years	Guinea	*S mansoni*	Gastritis	F3	No	17·7	Platelet count 65; INR 1·3; albuminaemia 4·6	No	Child-Pugh 6A; MELD 14	β blockers
Patient 11; male; age 18 years	Eritrea	*S mansoni*	PVT	F3	No	19·2	Platelet count 57; INR 1·2; albuminaemia 4·4	No	Child-Pugh 5A; MELD 9	VBL; β blockers
Santo et al[10]										
One patient; male; age 41 years	Brazil	*S mansoni*	PVT; metabolic syndrome	Yes	Yes	26·0	Platelet count 51	Refractory ascites	Child-Pugh 11B	..
Huang et al[11]										
43 patients; 31 male; 12 female; mean age 58 years (range 54–61)	China	*S japonicum*	One with HCV;12 with HBV; 24 with PVT; one with alcohol consumption plus autoimmune hepatitis	Yes in 35 patients	Yes in 33 patients	16·6 ± 4·2	23 with platelet count <100; 15 with platelet count 100–300; five with platelet count >300	Eligible for TIPS if ascites is refractory or recurrent; UGB and no hepatic encephalopathy	Mean Child-Pugh 7·8; mean MELD 11·9	13 variceal treatment; 17 splenectomy

WBC and platelet count are expressed as N × 10^9/L. Albuminaemia is expressed in g/dl. F numbers refer to Japanese Society for Portal Hypertension grading.[8] HBV=hepatitis B virus. HCV=hepatitis C virus. INR=international normalised ratio. MELD=model for end-stage liver disease. PVT=portal vein thrombosis. TIPS=transjugular intrahepatic portosystemic shunt. UGB=upper gastrointestinal bleeding. VBL=variceal band ligation. WBC=white blood cell count.

Table 1: **Demographics and clinical profiles of patients with hepatosplenic schistosomiasis before TIPS, as described in the literature**

managed was unclear given that no medical records of the reported previous episode of haematemesis was available. Endoscopic management of the oesophageal varices before TIPS was reported for 57 patients (76%). Therapy with β blockers before TIPS was reported for ten (10%) patients, in which most were associated with endoscopic variceal management. Of note, in the cohort by Huang and colleagues,[11] the presence of recurrent UGB (ie, not satisfactorily managed by previous interventions) was a prerequisite for undergoing TIPS either with or as an alternative to the presence of refractory ascites. Moderate to severe splenomegaly was reported in all patients (range 13–29 cm). Azygoportal disconnection and splenectomy was reported before TIPS in 17 (16%) patients, whereas no surgical shunts were performed before TIPS.

Standardised staging of fibrosis in *S japonicum* hepatosplenic schistosomiasis was never published; however, a standardised periportal fibrosis staging for hepatosplenic schistosomiasis caused by *S mansoni* infection is available from WHO.[7] Regardless, the WHO fibrosis pattern was reported in only one patient with *S mansoni*-associated hepatosplenic schistosomiasis. Liver stiffness was measured in four patients;[15,16] however, this parameter has not been univocally associated with periportal fibrosis severity[2] and was not measured in our patient.

The haematochemical profile of our patient fitted with what is generally reported in the literature. Moderate to severe low platelet count was reported in most patients for whom this parameter was described (36 [64%] of 56 patients ranging from 20–144×10⁹/L), whereas white blood cell count was not reported for most patients and was low (1000–3700×10⁹/L) in the four patients for whom this parameter could be retrieved. INR values, reported for 12 patients, were in the upper limit of normality or slightly increased (range 1·1–1·6). Albuminaemia, also reported for 12 patients, was overall within normal ranges. When reported, Child-Pugh scores A, B, and C were roughly equally present among the patients, and the model for end-stage liver disease (MELD) score was less than 19. Ascites, absent in our patient, was reported in 27 (26%) of patients. Ascites was described in two (18%) of 11 patients with explicit or presumed absence of HBV or HCV hepatitis and at least 25 (27%) of 92 patients in the cohorts by Dondelinger and colleagues[13] and Huang and colleagues,[11] which included also co-infected patients. However, for the cohorts of these two studies, individual data could not be extrapolated, and in the cohort described by Huang and colleagues[11] refractory ascites was, together with recurrent UGB, an inclusion criterion for TIPS placement. No patient was reported to have hepatic encephalopathy before TIPS.

TIPS intervention and follow-up in the literature

Details of the follow-up after TIPS intervention are summarised (table 2). When reported, the length of time between diagnosis and TIPS intervention was between 1 week and 5 years. Unfortunately, the length of follow-up after TIPS was at maximum 24 months for most patients, with only one patient exceeding the 5-year follow-up.

TIPS placement induced a substantial (ie, >50%) reduction in portosystemic pressure gradient (PSPG) when this measure was reported. Although portal hypertension (PSPG ≥6 mm Hg) persisted in nearly all cases, in only a minority of cases post-TIPS values were still associated with risk of UGB (PSPG ≥12 mm Hg). Oesophageal varices regressed or reduced in size, as in our patient, in most patients for whom these data were reported. Rebleeding after TIPS was reported for 18 (17%) patients, 14 (78%) of whom were in the cohort described by Dondelinger and colleagues[13] who specified that rebleeding occurred in all due to shunt malfunction.

TIPS implant failed in four (4%) patients; stent complications occurring around TIPS intervention or during the follow-up were reported in all patients followed up by Dondelinger and colleagues,[13] and in a further six patients among the other studies (of these six patients, one had stent thrombosis alone, one had stent displacement and stent thrombosis, and there was no cause specified in four). In Dondelinger and colleagues,[13] early stent thrombosis was reported for five (10%) patients, but the authors also observed that "no stent showed primarily preserved function at 6 months follow-up" and all had to be revised for patency, which failed in four patients.

The different occurrence of stent thrombosis is probably because of the different stents used in the publications. Covered stent grafts have been introduced as an alternative to bare stents in TIPS, showing high primary patency rates and significant survival benefits.[17–20] The Gore Viatorr stent used in our patient and other reports (table 2) is an expanded polytetrafluoroethylene-covered nitinol stent specifically designed for TIPS with high technical success rates, low incidence of restenosis at midterm follow-up, and better survival rates.[20–22] The expanded polytetrafluoroethylene lining is biocompatible, microporous, non-thrombogenic, relatively impermeable to bile and tissue, and provides a substrate for endothelial lining, thus minimising factors known to cause stent stenosis and occlusion.[19,20,23–27] It also offers better radial compression resistance and ensures secure anchorage with minimal tissue deformation. The uncoated chainlink segments of the device allow for contralateral portal perfusion.

The increased bilirubin concentrations after TIPS, mainly attributed to haemolysis due to attrition with the implanted device, are less prominent with last-generation TIPS devices and could be because of hypersplenism, as noted by Nordmann and colleagues.[12] In our patient, bilirubin indeed reached pre-TIPS concentrations after splenectomy.

One patient underwent liver transplantation because of a major deterioration of liver function with an increased

	TIPS device	TIPS intervention complications	Follow-up length (months)	Interventions during follow-up	Oesophageal varices	UGB	Spleen size (cm)	Laboratory tests	Ascites, hepatic encephalopathy, other	PSPG (mm Hg)	Deaths
Dondelinger et al[13]											
48 patients; 38 male; ten female; mean age 44 years (range 23–61)	25 Memotherm (Angiomed, Karlsruhe, Germany); 13 Wallstent (Schneider, Bulach, Switzerland); 16 Symphony (Boston Scientific, Natick, MA, USA)	Four with intervention failures; one death; 43 with obstructions	Mean 24	43 stent revisions	16 with none; 12 with reduced; seven unchanged	Yes in 14 patients	15·1 ± 4·1	..	11 with transient hepatic encephalopathy; ten with ascites resolved	Mean 20·3 ± 6·3 before TIPS; mean 11·3 ± 5·5 after TIPS	15
Grieco et al[9]											
One patient; male; age 30 years	..	..	<1	..	..	..	..	..	..	..	..
Nordmann et al[12]											
Patient 1; male; age 19 years	Bard Luminexx (Angiomed, Karlsruhe, Germany)	Stent thrombosis	99	Stent revision	F1	No	24·0	Platelet count 58; INR 1·4; albuminaemia 4·2	None	23·0 before TIPS; 12·0 after TIPS	..
Patient 2; male; age 39 years	Gore Viatorr (Gore Medical, Flagstaff, AZ, USA)	No	45		F1–F2	No	14·0	Platelet count 41; INR 1·2; albuminaemia 2	None	23 before TIPS; 6·0 after TIPS	..
Patient 3; male; age 28 years	Bard Luminex	No	12		F0	No	..	Platelet count 40; INR 1·5	None	13·0 before TIPS; 1·0 after TIPS	..
Patient 4; female; age 37 years	Gore Viatorr	No	27		F0	No	10·0	Platelet count 227; INR 1·2; albuminaemia 3·3	None	16 after TIPS	..
Patient 5; male; age 19 years	Gore Viatorr	No	8	Liver transplantation	F1	No	17·2	Platelet count 21; INR 2·4; albuminaemia 2·0	Jaundice; hepatic encephalopathy	19·0 before TIPS; 9·0 after TIPS	..
Patient 6; male; age 16 years	Bard Luminexx	No	48		F0	No	28·0	INR 1·4; albuminaemia 3·5	None	23·0 before TIPS; 11·0 after TIPS	..
Patient 7; male; age 20 years	Gore Viatorr	No	30		F1	No	15·1	Platelet count 64; INR 1·6; albuminaemia 3·8	None	50·0 before TIPS; 27·0 after TIPS	..
Patient 8; male; age 27 years	Gore Viatorr	No	8		F1	No	21·0	Platelet count 56; INR 1·5; albuminaemia 4·3	None	15·0 before TIPS; 7·0 after TIPS	..
Patient 9; female; age 59 years	Bard Luminexx	No	34		F0	No	13·0	Platelet count 69; INR 1·2; albuminaemia 2·9	Impaired liver function; hepatic encephalopathy	24·0 before TIPS; 8·0 after TIPS	..
Patient 10; male; age 21 years	Gore Viatorr	Stent thrombosis	20	Stent revision	F1–F2	No	15·0	Platelet count 71; INR 1·7; albuminaemia 3·8	Increased liver enzymes	14·0 before TIPS; 8·0 after TIPS	..
Patient 11; male; age 18 years	Gore Viatorr	Central venous catheter sepsis; portal vein thrombosis	<1		F1	No	16·6	Platelet count 70; INR 1·2; albuminaemia 3·7	Hepatic encephalopathy	25·0 before TIPS; 13·0 after TIPS	..
Santo et al[10]											
One patient; male; age 41 years	Gore Viatorr	No	6	..	..	..	..	..	Hepatic encephalopathy	..	..
Huang et al[11]											
43 patients; 31 male; 12 female; mean age 58 years (range 54–61)	Metal plus polytetrafluoroethylene-covered stents	Four with shunt dysfunction	Mean 16 (range 17–24)	..	..	Yes in four patients	15·3 ± 2·4	Platelet count, WBC, and coagulation showed no difference from before TIPS	Two with refractory ascites; 12 with hepatic encephalopathy	Significantly reduced	Nine

Albuminaemia is expressed in g/dl. Platelet count is expressed in $N \times 10^9$/L. PSPG=portosystemic pressure gradient delta. PVT=portal vein thrombosis. TIPS=transjugular intrahepatic portosystemic shunt. UGB=upper gastrointestinal bleeding.

Table 2: **TIPS and post-TIPS follow-up of patients with hepatosplenic schistosomiasis described in the literature**

	Schistosoma mansoni (n=11)	*Schistosoma japonicum* (n=20)*	All (n=31)
Median follow-up length (range)	20 months (0–9 years)	15 months (2–27 months)	NA
Hepatic encephalopathy	2 (18%)	5 (25%)	7 (23%)
Variceal bleeding	0	3 (15%)	3 (10%)
Ascites	0	0	1 (3%)
Shunt dysfunction	2 (18%)	0	2 (6%)
Death	0	3 (15%)	3 (10%)

Data for *S japonicum* derived from Liu and colleagues.[14] NA=not applicable. TIPS=transjugular intrahepatic portosystemic shunt. *TIPS only applied if recurrent upper gastrointestinal bleeding, refractory ascites, or both, and no previous hepatic encephalopathy.[14]

Table 3: **Main outcomes after TIPS of patients with hepatosplenic schistosomiasis only**

MELD score up to 28, presumably aggravated by concomitant chronic HBV infection; no further surgical interventions after TIPS were reported for all other patients.

Different to what was observed in our patient, spleen diameter decreased after the implant in most patients for whom this parameter was reported, although the splenomegaly condition persisted. In our patient, the absence of spleen reduction could be because of the long-standing condition, a possible predominance of hypersplenism over congestion as the cause of splenomegaly, or both. On the contrary, as observed in our patient, thrombocytopenia and increased INR persisted unvaried overall when these parameters were reported. Leukocyte counts after TIPS were either not reported or were summarised as unchanged compared with preintervention values. Hepatic encephalopathy was reported in approximately 30 patients (the exact number could not be extrapolated); in our patient, hepatic encephalopathy was very mild. The Child-Pugh score was either not reported or slightly worsened and the MELD mortality risk group was unchanged in most patients for whom this information was provided, probably because of an increased rate of hepatic encephalopathy and reduction in albumin concentrations in some patients.

Death was reported for 24 (23%) patients. Cause of death was reported for 15 (31%) of the 48 patients in the cohort described by Dondelinger and colleagues:[13] one (2%) patient died during the TIPS procedure, whereas the highest mortality rate (ten [21%]) was observed within 30 days of the intervention in patients with refractory ascites and was caused by liver failure in most patients.

Hepatosplenic schistosomiasis-only patients in the literature

The two largest cohorts describing TIPS in patients with hepatosplenic schistosomiasis[11,13] included a relevant proportion (35–65%) of patients with hepatitis from other causes, mainly HBV and HCV co-infection. Unfortunately, data were aggregated, therefore it was not possible to use these cohorts to evaluate and compare main outcomes after TIPS in patients who were and were not co-infected. Therefore, outcomes after TIPS (table 3) could only be evaluated in a subset of 31 patients with hepatosplenic schistosomiasis only; 11 patients infected with *S mansoni*, described in three studies;[9,10,12] and 20 patients infected with *S japonicum*, described by Liu and colleagues.[14]

Discussion in consideration of the literature review

The impossibility to carry out an individual-patient meta-analysis, the heterogeneity of the reports, and the generally short follow-up limit the conclusions that can be drawn from the analysis of the published studies concerning the outcomes of TIPS intervention, overall and stratified by time after intervention and patients' clinical characteristics. Furthermore, as also shown with our patient, obtaining a detailed and documented clinical history from patients is often difficult, with consequent gaps in information. In addition, there is an almost complete absence of reference, in the published studies, to the grade of periportal fibrosis despite the existence of a standard classification system when caused by *S mansoni*.[7] Furthermore, due to the different pathophysiology of hepatosplenic schistosomiasis and cirrhosis, whether Child-Pugh and MELD scores, developed for cirrhosis, are also appropriate for hepatosplenic schistosomiasis is still to be determined.

Despite all these limitations, we did retrieve and carry out a synthesis of data from published information, which is useful when addressing TIPS for hepatosplenic schistosomiasis. First, portal hypertension and oesophageal varices seem to be the parameters benefiting most from TIPS. Rebleeding after TIPS in patients with only hepatosplenic schistosomiasis seems to occur in around 10% of patients (estimated at around 7% after distal splenorenal shunt[2]), with possibly a better outcome in hepatosplenic schistosomiasis caused by *S mansoni* than by *S japonicum*. This relatively small rate of bleeding is of great importance given that a large retrospective study from Brazil in 2023 showed that UGB was associated with increased risk of liver decompensation, in turn predictive of mortality,[28] and encourages to also evaluate the possible application of TIPS in early hepatosplenic schistosomiasis, even before occurrence of the first UGB episode, to improve the patient's prognosis. On the contrary, the occurrence of hepatic encephalopathy after TIPS in patients with only hepatosplenic schistosomiasis (ie, not co-infected) was higher (around 22%) than after distal splenorenal shunt (around 10%),[2] although authors generally reported that symptoms were mild and clinically manageable. In our patient, oesophageal varices were evidently reduced after TIPS and only very mild portal encephalopathy was observed, which was successfully managed with medical therapy.

Second, splenomegaly seems to be, overall, only mildly to moderately benefiting from TIPS, whereas haemato-chemical parameters related to hypersplenism, spleen congestion, or both appeared overall unchanged after the

intervention. In our patient, splenomegaly persisted after TIPS and splenectomy was considered after TIPS placement due to persistent severe thrombocytopenia. The appropriateness of this sequence of intervention (ie, splenectomy performed after TIPS in case of persistent severe signs related to the spleen function) seems to be in line with what was suggested by the authors of the Chinese cohort,[11,14] who highlighted that splenectomy significantly increased the risk of portal vein thrombosis in their cohort, which also increases the difficulty of TIPS implantation. However, it should be considered that compensatory thrombocytosis after splenectomy might also increase the risk of thrombosis, and therefore the sequence of interventions might not be fundamental.

The difficulty of a TIPS implant in hepatosplenic schistosomiasis is also because of the stiffness of the affected liver, as highlighted by Dondelinger and colleagues,[13] and also noted by the surgeons of our patient. Therefore, whether performing a TIPS implant before advanced fibrosis is reached, provided that early diagnosis is carried out, would make the procedure easier and improve patient outcome would be an important evaluation.

Search strategy and selection criteria

References were identified through MEDLINE (PubMed) and Embase databases, searched on Dec 20, 2022. We searched with Medical Subject Heading terms including the keywords "schistosomiasis", "schistosoma infection", "bilharziasis", "*Schistosoma mansoni*", "*Schistosoma japonicum*", "*Schistosoma mekongi*", "hepatosplenic schistosomiasis", "hepatic schistosomiasis", "intestinal schistosomiasis", "transjugular intrahepatic portosystemic shunt", and "TIPS". Additional articles were also searched through the reference lists of retrieved reviews and included papers. No restriction was applied regarding language and publication date. Case reports, case series, cohort studies, case-control studies, clinical trials, and systematic reviews with meta-analysis including data of patients with hepatosplenic schistosomiasis (alone or with viral hepatitis co-infection) managed by TIPS were eligible for inclusion. GS and TU reviewed titles and abstracts to identify those potentially eligible, with FT involved in case of disagreement. The diagnosis of schistosomiasis and the classification of the patient as having hepatosplenic schistosomiasis were accepted as declared by the authors of the studies. When absent, specific information on the species of *Schistosoma* involved was inferred from the geographical origin of patients, if unequivocal (eg, *Schistosoma japonicum* for patients from China).

Conclusion

TIPS is a minimally invasive procedure that appears promising for use in patients with hepatosplenic schistosomiasis but is still scarcely reported in patients. No formal indications exist regarding when to apply TIPS versus other interventions and the implementation of long-term follow-up for patients with hepatosplenic schistosomiasis. The follow-up is clearly required due to the fact that the main pathophysiological mechanism of portal hypertension in hepatosplenic schistosomiasis (ie, periportal fibrosis) will persist even after active infection has been cleared by effective antiparasitic treatment with praziquantel.[2] This requirement is also supported by the observation that portal hypertension after TIPS persisted in nearly all patients included in this Grand Round, although in only a minority of patients PSPG values were still associated with risk of UGB, which has been found to be associated with worse prognoses.[28] Consensus and wide application of standardised clinical framing of patients with hepatosplenic schistosomiasis are urgently needed to allow a rigorous evaluation and comparison of interventions in the future.

A final remark concerns the applicability of TIPS, both within and outside of endemic areas. In endemic areas, where the largest number of hepatosplenic schistosomiasis cases occur, the latest generation stents and expertise to safely place them might not be widely available. Furthermore, precise data on long-term follow-up should be obtained if envisaging the use of TIPS in populations for which attendance to long-term follow-up could be difficult. The issue of long-term effectiveness and safety applies in endemic areas, where patients might live far away from a tertiary hospital and might not be able to economically sustain the cost of regular clinical procedures, and also outside endemic areas, where patients with hepatosplenic schistosomiasis are generally migrants who are often a mobile population and difficult to harness in long-term follow-up. Finally, outside endemic areas, knowledge of schistosomiasis is scant, with attendant mismanagement and cost.[29–31] The implementation of screening tools for predicting the presence of varices, such as the Schistosma Mansoni Score or the platelet–spleen ratio,[2] and the prioritisation of early interventions, such as endoscopy and TIPS, would surely be extremely important. Clinical guidelines are urgently needed, which should be disseminated widely, not only among physicians who are experts in neglected tropical diseases, but also among clinicians with other relevant specialties (eg, gastroenterology, hepatology, and radiology).

Contributors

FG conceived the work. FT, TU, GS, and VAF searched the literature. FT, TU, GBM, DB, SC, CG, GM, AG, and FG collected and interpreted the clinical data. FT, DB, GM, and FG interpreted the literature data. All authors critically revised the manuscript, had full access to all study data, read the manuscript, and approved the final version.

Declaration of interests

We declare no competing interests.

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References

1 Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. *Lancet* 2014; **383:** 2253–64.

2 Tamarozzi F, Fittipaldo VA, Orth HM, et al. Diagnosis and clinical management of hepatosplenic schistosomiasis: a scoping review of the literature. *PLoS Negl Trop Dis* 2021; **15:** e0009191.

3 Andrade ZA. Schistosomiasis and liver fibrosis. *Parasite Immunol* 2009; **31:** 656–63.

4 Gunda DW, Kilonzo SB, Manyiri PM, Peck RN, Mazigo HD. Morbidity and mortality due to *Schistosoma mansoni* related periportal fibrosis: could early diagnosis of varices improve the outcome following available treatment modalities in sub Saharan Africa? A scoping review. *Trop Med Infect Dis* 2020; **5:** 20.

5 Petroianu A, De Oliveira AE, Alberti LR. Hypersplenism in schistosomatic portal hypertension. *Arch Med Res* 2005; **36:** 496–501.

6 Leite LAC, Domingues ALC, Lopes EP, et al. Relationship between splenomegaly and hematologic findings in patients with hepatosplenic schistosomiasis. *Rev Bras Hematol Hemoter* 2013; **35:** 332–36.

7 WHO. Ultrasound in schistosomiasis: a practical guide to the standard use of ultrasonography for assessment of schistosomiasis-related morbidity. May 20, 2000. https://iris.who.int/bitstream/handle/10665/66535/TDR_STR_SCH_00.1.pdf?sequence=1 (accessed April 20, 2023).

8 Idezuki Y. General rules for recording endoscopic findings of esophagogastric varices (1991). *World J Surg* 1995; **19:** 420–22.

9 Grieco S, Sulekova LF, Nardelli S, Riggio O, Venditti M, Taliani G. Portal hypertension related to schistosomiasis treated with a transjugular intrahepatic portosystemic shunt. *J Clin Gastroenterol* 2016; **50:** 608–10.

10 Santo MCCDE, Gryschek RCB, Farias AQ, et al. Management and treatment of decompensated hepatic fibrosis and severe refractory *Schistosoma mansoni* ascites with transjugular intrahepatic portosystemic shunt. *Rev Inst Med Trop São Paulo* 2022; **64:** e26.

11 Huang S, Liu J, Yao J, et al. Efficacy and safety of transjugular intrahepatic portosystemic shunt for the treatment of schistosomiasis-induced portal hypertension: a retrospective case series. *Eur J Gastroenterol Hepatol* 2022; **34:** 1090–97.

12 Nordmann T, Schlabe S, Feldt T, et al. TIPS and splenorenal shunt for complications of portal hypertension in chronic hepatosplenic schistosomiasis—a case series and review of the literature. *PLoS Negl Trop Dis* 2021; **15:** e0010065.

13 Dondelinger RF, Elkadi M, Taema M, Elkadi L, Ramadan M. TIPS in Egyptian hepatic schistosomiasis. In: Rossi P, Ricci P, Broglia L, eds. Portal hypertension. Heidelberg: Springer, 2000.

14 Liu J, Zhou B, Chen D, et al. Transjugular intrahepatic portosystemic shunt placement in patients with schistosomiasis-induced liver fibrosis. *Cardiovasc Intervent Radiol* 2019; **42:** 1760–70.

15 Richter J, Bode JG, Blondin D, et al. Severe liver fibrosis caused by *Schistosoma mansoni*: management and treatment with a transjugular intrahepatic portosystemic shunt. *Lancet Infect Dis* 2015; **15:** 731–37.

16 Kraef C, Arand J, Galaski J, et al. Transjugular intrahepatic portosystemic shunt (TIPS) for primary and secondary prophylaxis of variceal bleeding in hepatic schistosomiasis. *Travel Med Infect Dis* 2019; **30:** 130–32.

17 Nishimine K, Saxon RR, Kichikawa K, et al. Improved transjugular intrahepatic portosystemic shunt patency with PTFE-covered stent-grafts: experimental results in swine. *Radiology* 1995; **196:** 341–47.

18 Haskal ZJ, Davis A, McAllister A, Furth EE. PTFE-encapsulated endovascular stent-graft for transjugular intrahepatic portosystemic shunts: experimental evaluation. *Radiology* 1997; **205:** 682–88.

19 Haskal ZJ. Improved patency of transjugular intrahepatic portosystemic shunts in humans: creation and revision with PTFE stent-grafts. *Radiology* 1999; **213:** 759–66.

20 Cejna M, Peck-Radosavljevic M, Thurnher SA, Hittmair K, Schoder M, Lammer J. Creation of transjugular intrahepatic portosystemic shunts with stent-grafts: initial experiences with a polytetrafluoroethylene-covered nitinol endoprosthesis. *Radiology* 2001; **221:** 437–46.

21 Angermayr B, Cejna M, Koenig F, et al. Survival in patients undergoing transjugular intrahepatic portosystemic shunt: ePTFE-covered stentgrafts versus bare stents. *Hepatology* 2003; **38:** 1043–50.

22 Rossi P, Salvatori FM, Fanelli F, et al. Polytetrafluoroethylene-covered nitinol stent-graft for transjugular intrahepatic portosystemic shunt creation: 3-year experience. *Radiology* 2004; **231:** 820–30.

23 Saxon RS, Ross PL, Mendel-Hartvig J, et al. Transjugular intrahepatic portosystemic shunt patency and the importance of stenosis location in the development of recurrent symptoms. *Radiology* 1998; **207:** 683–93.

24 Sanyal AJ, Contos MJ, Yager D, Zhu YN, Willey A, Graham MF. Development of pseudointima and stenosis after transjugular intrahepatic portasystemic shunts: characterization of cell phenotype and function. *Hepatology* 1998; **28:** 22–32.

25 Teng GJ, Bettmann MA, Hoopes PJ, et al. Transjugular intrahepatic portosystemic shunt: effect of bile leak on smooth muscle cell proliferation. *Radiology* 1998; **208:** 799–805.

26 Nazarian GK, Ferral H, Castañeda-Zúñiga WR, et al. Development of stenoses in transjugular intrahepatic portosystemic shunts. *Radiology* 1994; **192:** 231–34.

27 Angeloni S, Merli M, Salvatori FM, et al. Polytetrafluoroethylene-covered stent grafts for TIPS procedure: 1-year patency and clinical results. *Am J Gastroenterol* 2004; **99:** 280–85.

28 Veiga ZST, Fernandes FF, Guimarães L, Piedade J, Pereira GHS. Natural history of hepatosplenic schistosomiasis (HSS) non-cirrhotic portal hypertension (NCPH): influence of gastrointestinal bleeding and decompensation in prognosis. *Trop Med Infect Dis* 2023; **8:** 145.

29 Basile G, Tamarozzi F, Salas-Coronas J, et al. Management of imported complicated urogenital schistosomiasis in Europe: a TropNet retrospective study. *J Travel Med* 2023; **30:** taac150.

30 Zammarchi L, Botta A, Tilli M, Gobbi F, Bartoloni A, Boccalini S. Presumptive treatment or serological screening for schistosomiasis in migrants from sub-Saharan Africa could save both lives and money for the Italian National Health System: results of an economic evaluation. *J Travel Med* 2023; **30:** taac140.

31 Roure S, López F, Oliva I, et al. Schistosomiasis screening in non-endemic countries from a cost perspective: knowledge gaps and research priorities. The case of African long-term residents in a metropolitan area, Spain. *PLoS Negl Trop Dis* 2023; **17:** e0011221.