Gastrointestinal Bleeding as a Result of Portal Hypertension

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Jonathan Marshall

Introduction

Before leaving Prague for Oregon Health and Sciences University (OHSU), it's unlikely Josef Rosch realized how profound an affect he would have on the treatment of portal hypertension and gastrointestinal (GI) hemorrhage in the twenty-first century. The concept of transjugular intrahepatic shunt (TIPS) found its origin from the serendipitous inadvertent access to the portal system during transhepatic cholangiography to evaluate biliary obstruction. TIPS was initially tested in canine models, and the first human TIPS was performed in the early 1980s by ballooning the parenchymal tract between the hepatic vein and portal (this technique was limited by early thrombosis). By the mid-1980s, self-expanding stents were deployed within the parenchymal tract, and by the late 1990s, the introduction of the Viatorr stent graft further refined tract patency.

TIPS was initially used to treat variceal hemorrhage; however, several additional indications continue to grow in popularity including the treatment of Budd-Chiari, hepatorenal syndrome, acute and chronic portal thrombus, and mesenteric venous thrombus. Additionally, the major complication rate for TIPS is approximately 1.4% with that rate dropping at institutions performing a greater volume of the procedure.

Indications for TIPS [1]

Secondary prophylaxis of variceal bleeding
Acute variceal bleeding
Portal hypertensive gastropathy
Recurrent acute variceal bleeding
Refractory ascites
Hepatorenal syndrome
Budd-Chiari
Hepatic veno-occlusive disease
Hepatic hydrothorax
Hepatopulmonary syndrome
Portal vein thrombosis

Contraindications for TIPS [1]

Absolute	Relative
Primary prevention of variceal bleeding	Hepatoma
CHF	Obstruction of all hepatic veins
Tricuspid regurgitation	Severe hepatic encephalopathy
Multiple hepatic cysts	Uncorrectable coagulopathy INR >5
Biliary obstruction	Severe thrombocytopenia
Severe pulmonary HTN	MELD > 18, total bilirubin > 3

J. Marshall (✉)
Department of Radiology, Erie County Medical Center, Buffalo, NY, USA

© Springer Nature Switzerland AG 2019
R. Lim (ed.), *Multidisciplinary Approaches to Common Surgical Problems*,
https://doi.org/10.1007/978-3-030-12823-4_25

Technique

Conceptually, a TIPS is created by placing a stent graft in the parenchymal tract between the right hepatic vein and the undivided right portal vein. This is possible due to the anatomic orientation of the right portal vein anterior to the right hepatic vein. At the author's institution, elective TIPS are performed under general anesthesia. In cases of hemodynamically unstable variceal hemorrhage, these patients typically are intubated and paralyzed making a technically challenging procedure more manageable and allowing the proceduralist to focus on the procedure itself.

Not uncommonly and due to the nature of chronic liver disease, patients have suboptimal coagulation laboratory parameters. In the author's institution, an INR of 1.7 or less and a platelet count of >50, 000 are acceptable starting points especially given the limited effectiveness of FFP transfusions above this level [2]. Beyond these parameters, each patient should be managed on a case by case basis with attention to the acuity of the patient's condition and the risk reward associated with performing the procedure and transfusing the applicable blood products (Fig. 25.1).

Through a right or left internal jugular approach, the right hepatic vein is catheterized. Pressures are measured within the right atrium and right hepatic vein. Right atrial pressures of >20 mmHg and a mean pulmonary artery pressure of greater than or equal to 45 mmHg would be considered a contraindication as a result of increased preload as a result of TIPS venous return [3]. An occlusion balloon is advanced into the right hepatic vein, and CO_2 portovenography is performed. The occlusion balloon assisted injected allows the reflux of CO_2 through the hepatic sinusoids into the portal venules creating a blue print for access. A long metal cannula is advanced into the right hepatic vein through which a smaller less traumatic needle is advanced to gain access. Using the portovenogram as a frame of reference, a puncture is made with the Colapinto needle under fluoroscopic guidance. A syringe is attached to the back of the needle and the needle is slowly withdrawn. The return of blood signals intraluminal tip location within the portal vein. The location of the needle tip is confirmed with the injection of contrast material. Once placement within the portal vein is confirmed, stiff wire access into

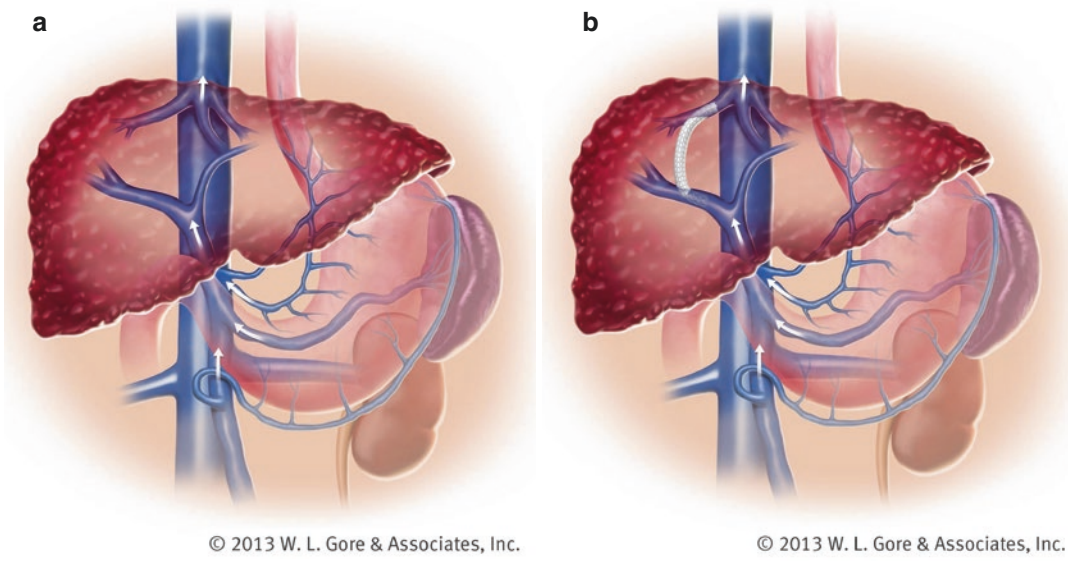

Fig. 25.1 (**a**) Diagram showing the anatomy of the systemic and portal venous systems prior to TIPS placement. (**b**) Stent deployment within the parenchymal tract creating a shunt bypass from the portal venous system into the systemic circulation. (Images courtesy of Gore USA)

the mesenteric portal system or splenic vein is obtained. The portosystemic gradient (PSG) is the measure of the difference in pressure between the portal and systemic systems. Portal hypertension is defined as being >6 mmHg [4]. The post TIPS target PSG is approximately 12 mmHg which can usually be managed with a 10 mm stent ballooned to 8 mm [5].

Cirrhotic livers tend to be stiff and fibrotic making catheter exchanges difficult. In this case, sequential balloon dilation is performed to facilitate vascular sheath placement in the main portal vein. Once sheath access to the main portal vein is obtained, portal pressures and gradients are measured, and the stent graft is deployed into the parenchymal tract (Figs. 25.2, 25.3, and 25.4).

Traditionally, bare metal stents in the form of the Boston Scientific Wallstent can be used; however, there is evidence to suggest better patency with the Gore Viatorr Endoprosthesis. The Viatorr stent has a covered component, which is deployed in the parenchymal tract to avoid bile leakage and stent occlusion, and a bare metal component which maintains flow through the portal system and averts "jailing" of the portal branches and liver infarction (Figs. 25.5, 25.6, and 25.7).

Multiple meta-analyses have demonstrated the improved benefit of TIPS vs. endoscopy in the prevention of variceal rebleeding. The rate of rebleeding in the TIPS group measured 19% vs. 44% in the endoscopy group [6].

Alternative Techniques

While the TIPS procedure has an up to 97% technical success rate in experienced hands, the orientation of the liver, right portal vein, and right hepatic vein as a result of cirrhosis and ascites can make TIPS challenging. Thrombus within the hepatic or portal veins can further complicate the procedure. A "reverse TIPS" can be performed by using an ultrasound-guided percutaneous puncture through the portal vein into the hepatic vein. A wire is then snared from a neck access, and TIPS stent graft deployment can be performed in a conventional manner.

Intravenous ultrasound (IVUS) can be used in the creation of a DIPS (direct intracaval portosystemic shunt). IVUS can guide needle puncture from the intrahepatic IVC into the portal vein. Primary patency following DIPS was measured at 100% with a follow-up range of 2 days to 30 months (mean 256 days) [7]. IVUS can also assist in portal access using conventional access from the right hepatic vein.

In the past, portal vein thrombus (either acute or chronic) was considered a contraindication to

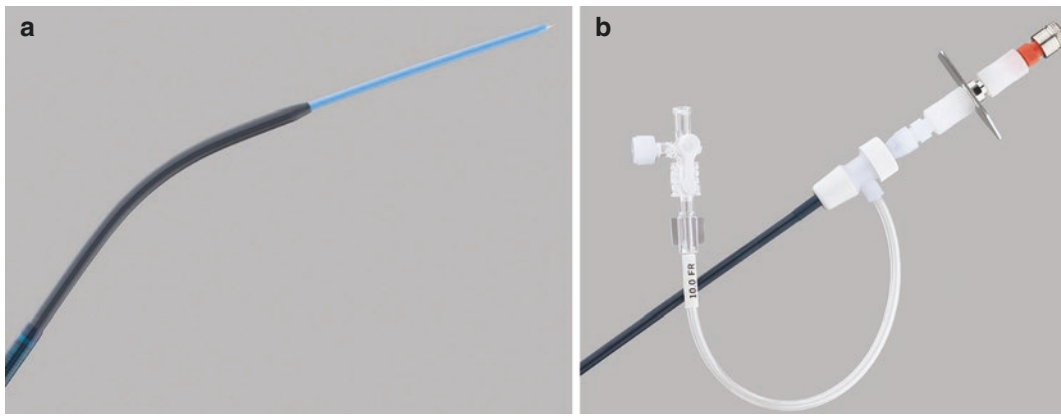

Fig. 25.2 (**a**) The Colapinto needle from the Rosch-Uchida Transjugular Liver Access Set (RUPS) from Cook Medical USA used for transjugular liver access for both diagnostic and interventional purposes. Note the curved end of the needle and smaller diameter in the event that multiple attempts at access are necessary. (**b**) Directional hub on the RUPS access sheath used to direct the needle anteriorly in the event that access is from the right hepatic vein or posteriorly if access is from the middle hepatic vein. (Images courtesy of Cook Medical USA)

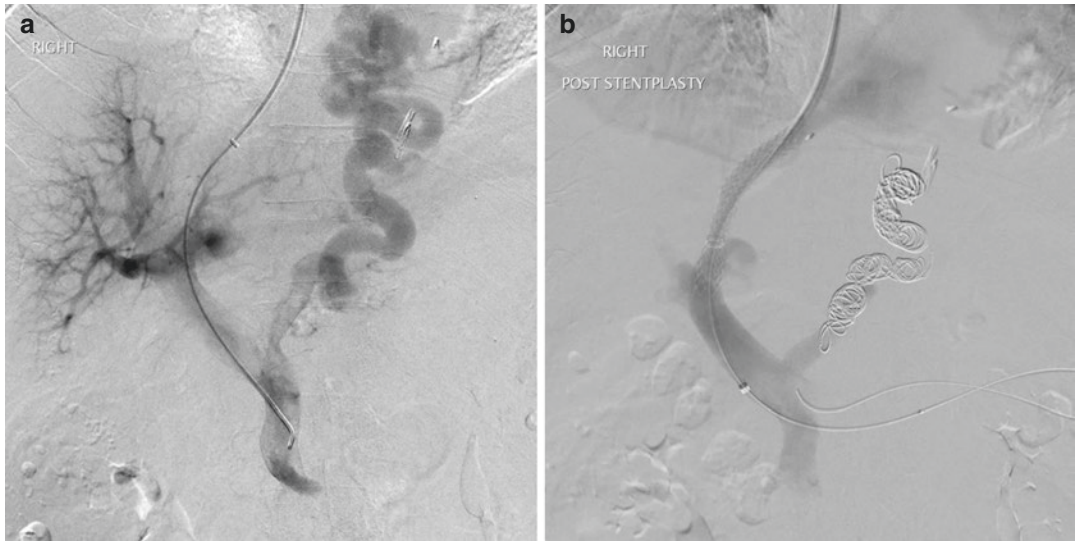

Fig. 25.3 (**a**) Demonstrates transhepatic portal access and a large gastroesophageal varix. Endoscopically placed clips are also noted; however, the varix remains widely patent. (**b**) Image following the complete endovascular coil embolization of the varix and placement of the Viatorr stent

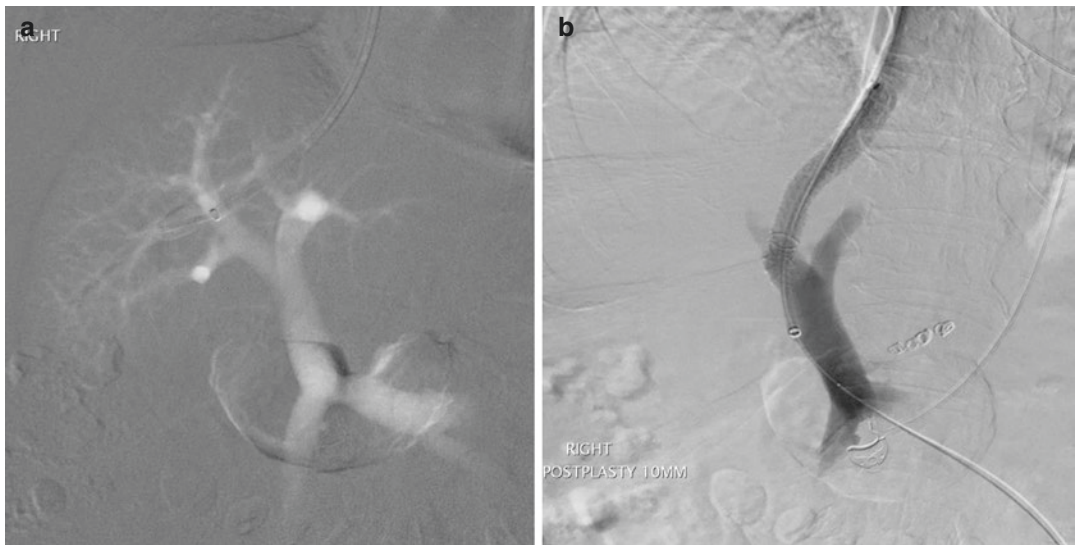

Fig. 25.4 (**a**) TIPS balloon-occluded CO_2 portovenogram is performed from the right hepatic vein with a Fogarty balloon and gentle CO_2 injection. A clear target of the "undivided right portal vein" is shown. (**b**) Same patient following TIPS placement and variceal embolization

TIPS. In the case of chronic portal vein thrombus, crossing a fibrotic cap can be difficult using hydrophilic wires and steerable catheters. Approaching the occlusion from a percutaneous access to the splenic vein can facilitate portal vein recanalization and TIPS creation by snaring the splenic access from the neck.

Acute mesenteric ischemia and infarction have mortality rates ranging from 15 to 50%. 5–15% of all cases of mesenteric ischemia are

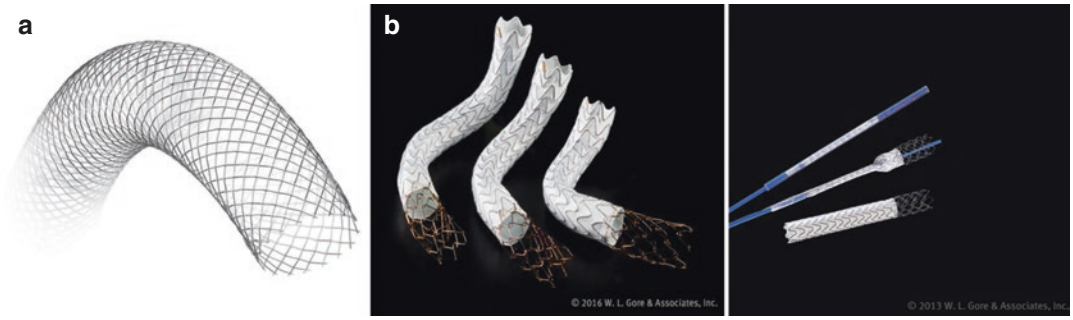

Fig. 25.5 (**a**) (above) The bare metal Boston Scientific Wallstent. (Images courtesy Boston Scientific USA). (**b**) (below) Various lengths of the Gore Viatorr with both a covered endoprosthesis and bare metal component and the deployment catheter. (Images courtesy of Gore USA)

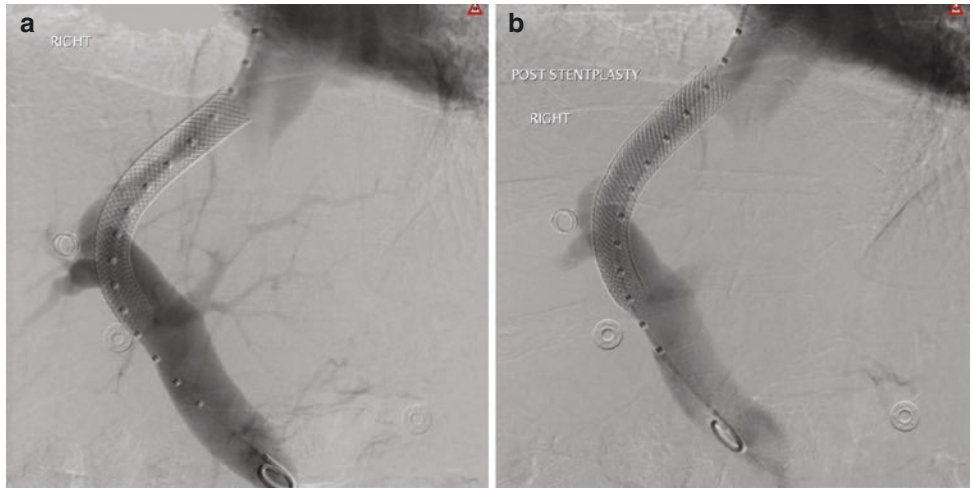

Fig. 25.6 (**a**) A 56-year-old male with alcoholic cirrhosis and refractory ascites. When the patient initially had his TIPS placed, his ascites resolved; however 6 months later, he again developed ascites which prompted a Doppler ultrasound demonstrating elevated velocities within the TIPS. Venography performed (left) demonstrates severe narrowing of the parenchymal component of the stent. The stenosis did not respond to simple balloon angioplasty. (**b**) Venographic images following the deployment of a Viabahn-covered stent within the parenchymal tract and complete resolution of the stenosis and revision of the TIPS

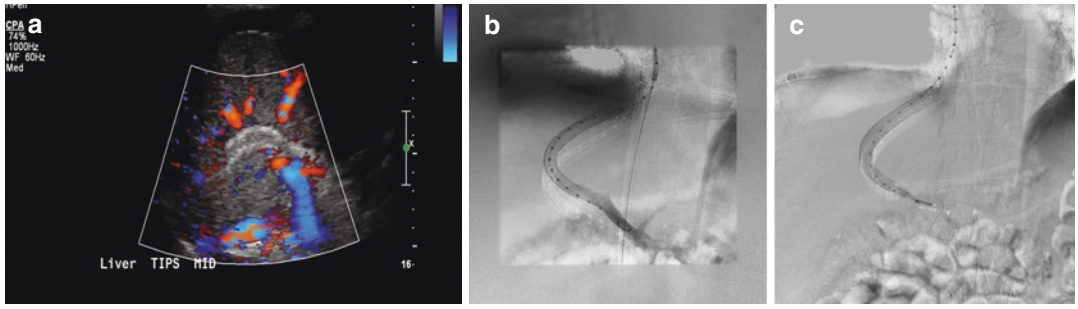

Fig. 25.7 (**a**) Color Doppler ultrasound of the TIPS postoperative day 1 without evidence of intrinsic flow within the TIPS. (**b**) Pigtail venography shows contrast refluxing into the portal vein as a result of complete thrombosis. (**c**) A Viabahn-covered stent was deployed within the parenchymal tract and contrast is seen flowing freely into the right atrium

the result of mesenteric vein thrombosis [8–11]. In the setting of portal mesenteric thrombus with continued risk of infarction and concomitant clinical decline despite systemic anticoagulation, transjugular intrahepatic portosystemic access can be used to thrombolyse the portal mesenteric system with TIPS deployment the following day. This technique can be associated with complication rates as high as 60%, but in many cases bowel resection can be avoided [12].

Esophageal Variceal Hemorrhage

The most lethal consequence of portal hypertension is esophageal variceal hemorrhage with the mortality rate within the first 2 years of the initial bleed ranging between 24% and 49% [13–18]. TIPS is considerably more successful than endoscopic therapy at preventing rebleeding (19% rebleeding in the TIPS group vs. 47% in the endoscopic therapy group). In the past, there was a belief that TIPS alone was sufficient for the treatment of acute variceal hemorrhage. Embolization at the time of TIPS has been shown to significantly reduce the rate of rebleeding versus TIPS alone (freedom from rebleed at 4 years 81% vs. 53%, respectively) [19]. A study performed by Pagan et al. challenged the use of TIPS as rescue therapy in patients with advanced liver disease and acute variceal hemorrhage. Child-Pugh B and C patients with active bleeding were randomized to vasoactive drugs with endoscopic therapy and rescue TIPS if necessary or early TIPS within 72 hours. The early TIPS groups had significantly fewer rebleeds, fewer deaths, and no difference in adverse events. Conversely, 57% of the patients in the control group that underwent rescue TIPS died [20]. It deserves mentioning that TIPS has comparable rates of encephalopathy when compared with surgical shunts.

TIPS and Hepatic Encephalopathy

While poorly understood, the postulated pathway upon which post TIPS encephalopathy develops is believed to be related to an increase in the systemic intestinally nitrogenous compounds that lack detoxification as a result of the shunt and a decrease in portal perfusion of the liver [21–25]. Following TIPS, the incidence of encephalopathy can increase as a result of increased dietary protein, other GI bleeding, sepsis, electrolyte abnormalities, or psychoactive drugs. Encephalopathy can be treated conservatively with high-fiber/protein-restricted diets (0.5 mg of protein per kilogram), with antibiotics like metronidazole or neomycin, or with zinc supplementation [26].

Hepatic encephalopathy is recognized as a complication in patients following TIPS and can occur 5–35% of the time [27]. In the majority of cases, post TIPS encephalopathy is controlled with the combination of rifaximin and lactulose. 3–7% of the time, post TIPS hepatic encephalopathy is refractory to medical and diet management and requires additional interventional management to reduce flow through the shunt [21]. Several techniques have been described for TIPS reduction including using a suture-constrained stent, deploying a stent or embolic material beside a second stent within a stent with external compression to narrow the lumen diameter, or complete embolization of a TIPS using an occlusion balloon or vascular plug or detachable coil. Gore USA has developed a controlled expansion Viatorr to control the diameter of the TIPS in a more sequential fashion. Typically, the Viatorr legacy endoprosthesis can reach its fully expanded diameter within 6 weeks despite the balloon-dilated diameter selected. The Viatorr with controlled expansion expands less than an additional 0.25 mm from its desired diameter following implantation.

Failed endoscopic therapy in the treatment of bleeding gastroesophageal varices with concomitant uncontrolled encephalopathy, severe liver failure, or technically unfeasible TIPS creation creates a complicated clinical scenario. Some studies suggest these patients can be treated with percutaneous transhepatic variceal embolization (PVTE) with partial splenic embolization (PSE) [28]. The embolization of esophageal varices without portal decompression with TIPS leads to an increase in portal pressures and as a result an increase in rebleeding rates and encephalopathy. In patients with cirrhosis and portal hypertension, a range of

60–70% of portal flow comes from the splenic vein [29]. Selective splenic infarction of 50–75% with splenic artery embolization leads to an overall decrease in portal hypertension, lower rebleeding rates, and fewer cases of encephalopathy [28].

Gastric and Parastomal Varices

Stomal or parastomal varices are associated with ileostomies and colostomies and often occur in patients with portal hypertension. Stomal variceal bleeding are uncommon, can be lethal, but in many cases can be controlled with manual compression. Manual compression is successful in focal bleeds but less helpful in diffuse high volume oozing, which occurs with those caused by portal hypertension. Endoscopy is typically only required when the culprit bleeding vein is not visible on the surface. As a result of the cirrhotic change within the liver, hepatofugal flow results in the afferent feeder from a branch of the superior mesenteric vein and the efferent branch typically draining into abdominal wall systemic venous branches that eventually drain into systemic iliofemoral branches [30].

Surgical or endoscopic therapies for bleeding stomal varices are uncommon. TIPS can be worthwhile in the treatment of bleeding stomal varices but in the long run can have a rebleed rate of 21–37% [31–33]. Coil embolization can be performed but should never involve submucosal veins since erosion can occur and delay healing. The most worthwhile techniques to control bleeding stomal varices involve the use of transvenous sclerosant obliteration using percutaneous access to portal branches within the liver, retrograde access through the systemic venous system, or using direct puncture of the varices with ultrasound guidance.

Gastric varices occur in 20–30% of patients with portal hypertension and typically have more lethal consequences as a result of higher blood volumes and flow rates with bleeding incidence as high as 25% [34, 35]. In addition, gastric varices tend to bleed at lower portosystemic gradients.

Historically it was believed that following the diagnosis of bleeding gastric varices by endoscopy, gastric varices could be decompressed with the creation of a TIPS. However, it has been shown that in 90% of cases, gastric varices are initially controlled with TIPS with rebleeding rates ranging between 13% and 53% [36, 37]. Several theories exist concerning why TIPS can be unsuccessful at treating isolated gastric varices. Importantly, Saad et al. demonstrated 0% rebleeding rates at 24 months with combined therapy using TIPS and retrograde obliteration [38]. The first published paper on balloon retrograde total obliteration (BRTO) was by Olson et al. in 1984 [39]. BRTO is performed via an internal jugular or femoral vein puncture and catheterization of the left renal vein and subsequently access to the gastrorenal shunt. A balloon is inflated at the base of the shunt to avoid reflux into the systemic venous circulation. Initially ethanolamine oleate was used, but it can cause hemolysis, hemoglobinuria, and renal tubular injury. More commonly in the United States, 3% sodium tetradecyl sulfate (Sotradecol, Angiodynamics) or polidocanol (Asclera, Merz) foam is deployed. Absolute alcohol or cyanoacrylate can also be used. BRTO requires leaving the occlusion balloon inflated for 4–24 hours to allow sclerosant dwell time. Additional described techniques include percutaneous transhepatic obliteration (PTO) also termed balloon-occluded antegrade total obliteration (BATO), coil-assisted retrograde total obliteration (CARTO), and plug-assisted retrograde total obliteration (PARTO). Occasionally, procedures can be combined using BATO technique from the portal side and BRTO from the systemic side. The goal for all of these procedures is to achieve stasis within the varices without the embolic agent entering the portal or systemic circulation.

The technical success rate of percutaneous variceal obliteration ranges from 79% to 100% [40–54]. The effectiveness of controlling active gastric variceal bleeding ranges between 91% and 100% [40, 44]. Gastric variceal obliteration has a tendency to aggravate non-gastric varices by increasing portal pressures with esophageal variceal aggravation rates at 3 years ranging from 45% to 91% [42, 48, 50, 55]. The gastric rebleed rate after successful BRTO ranges from 3.2% to

8.7%, while the global variceal rebleed rates were 19–31% [40, 43, 56].

Gastric variceal obliteration can result in resolution of encephalopathy and preservation of liver function but at the same time can aggravate global varices and ascites [44, 50, 51, 57, 58]. Overall, gastric variceal obliteration is effective, safe, and gaining popularity as a tool in the treatment of gastrointestinal bleeds as a result of portal hypertension (Figs. 25.8 and 25.9).

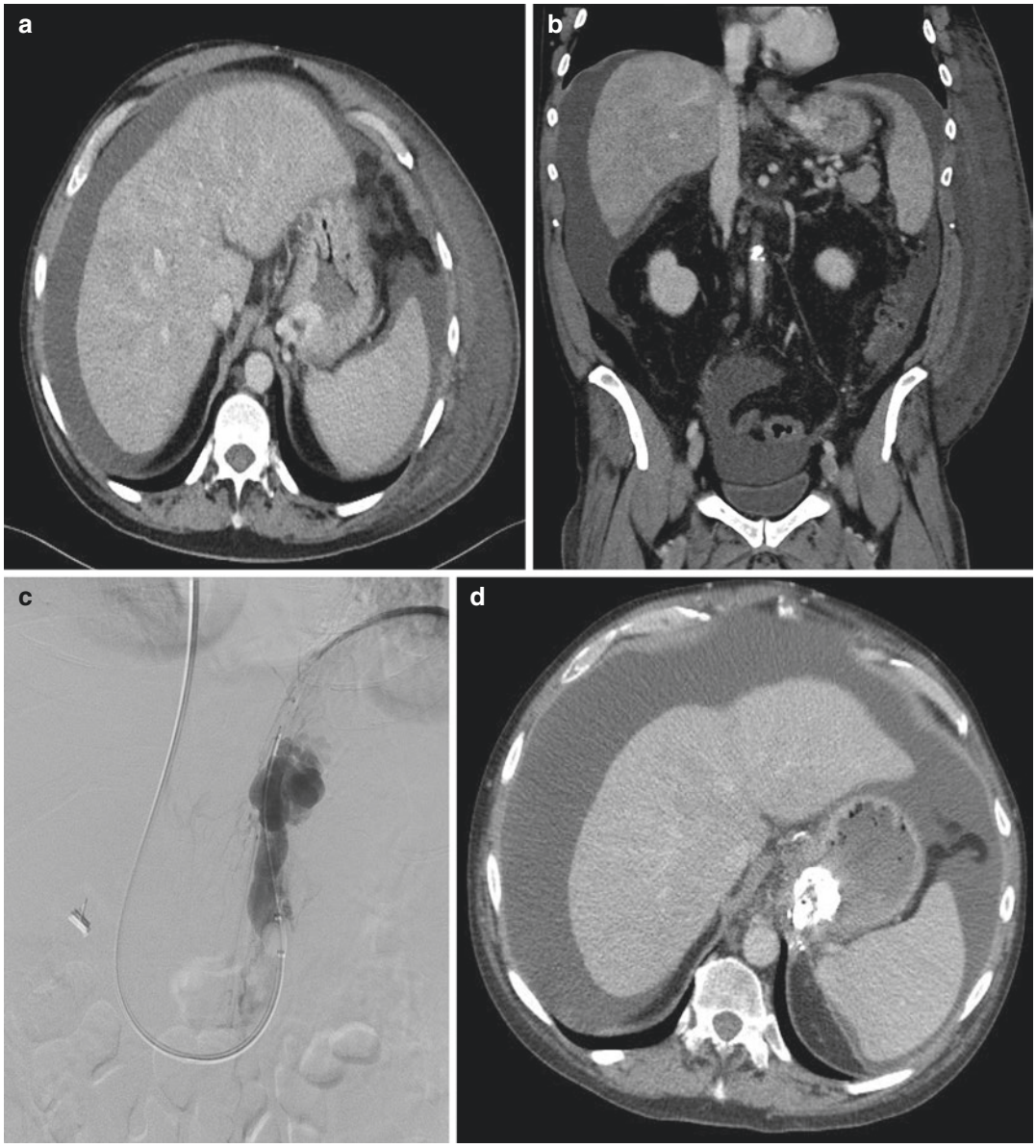

Fig. 25.8 (**a**, **b**) Axial and coronal CT scans of the abdomen demonstrate large gastric varices protruding into the lumen of the stomach in a 59-year-old male with a GI bleed that could not be controlled endoscopically. (**c**) Access to the gastric varix from a right internal jugular vein puncture and catheterization of the varix through the left renal vein. An occlusion balloon is inflated following the injection of Lipiodol and 3% Sotradecol to keep the sclerosing agent form entering the systemic system. (**d**) CT images following BRTO demonstrate complete occlusion of the varices. The patient was discharged from the hospital 3 days later

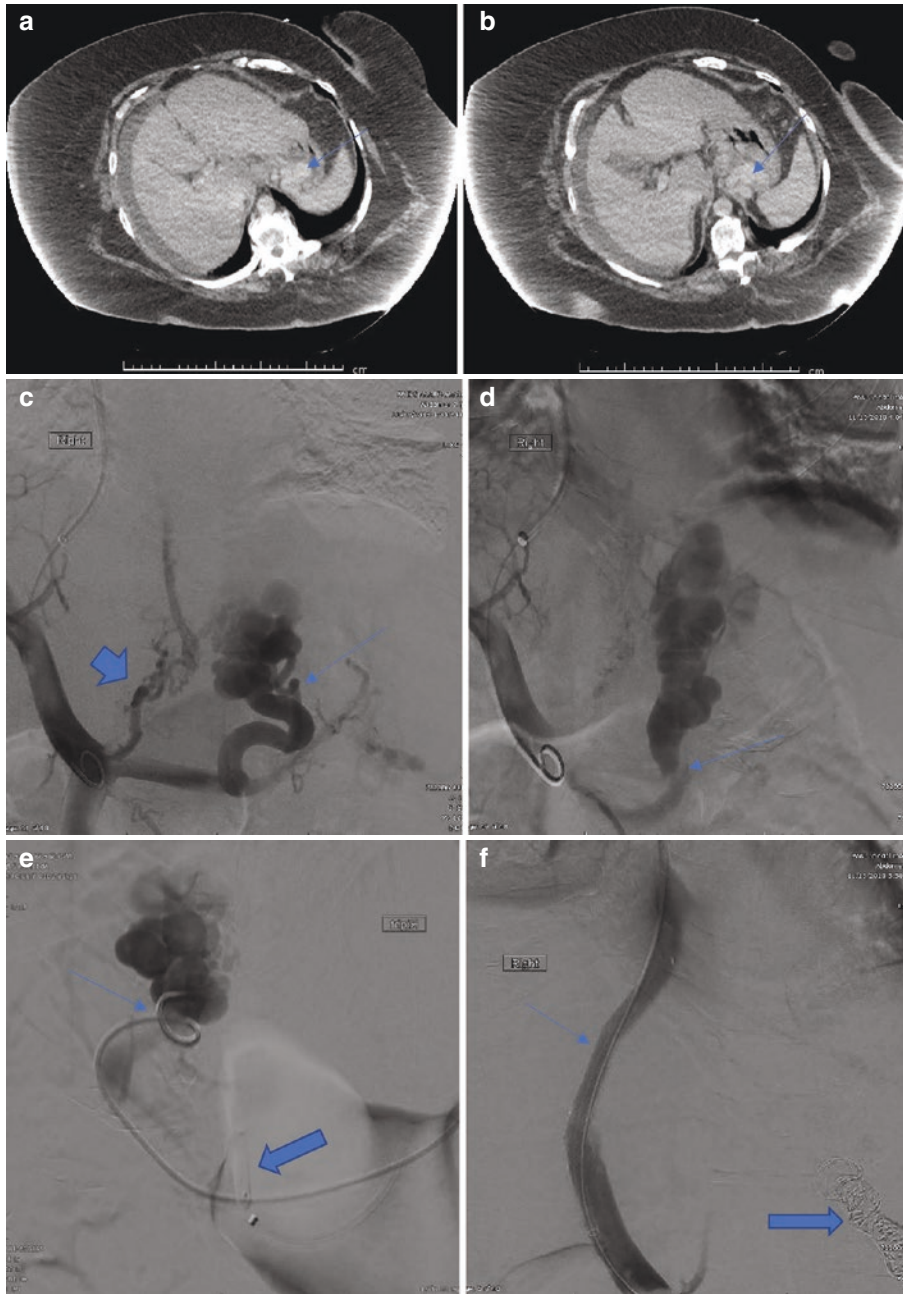

Fig. 25.9 (**a**, **b**) Demonstrate large varices (blue arrows) within the stomach with a patent splenic vein in a patient with a history of an upper GI bleed and NASH. (**c**) Angiographic images demonstrate the gastric varix (small blue arrow) filling from the splenic vein following transhepatic portal access and an esophageal varix (large blue arrow) and in (**d**) emptying of the varix into the systemic venous supply through the left renal vein on delayed images (blue arrow). (**e**) A second right internal jugular vein access was obtained, and an occlusion balloon (large blue arrow) was placed in the systemic side of the gastric varix with a catheter placed in the portal side of the varix for embolization. (**f**) Completion images demonstrating a patent TIPS (small blue arrow) with a combination of coils and 3% Sotradecol within the varix (large blue arrow). The occlusion balloon has been removed, and the esophageal varix is no longer identified. The patient was moved from the ICU to a general medical floor the next day

Conclusion

TIPS continues to be an important tool in the management of the complications of portal hypertension and specifically potentially lethal GI bleeds. New techniques including DIPS, BRTO, PTO, and CARTO are also important in patients with gastric varices which tend to bleed more or complicated hepatobiliary anatomy. TIPS continues to demonstrate low procedural complication rates, low rebleeding rates, low rates of unmanageable encephalopathy, and excellent patency rates. A majority of patients at the author's institution still receive TIPS despite endoscopic control of esophageal varices in the acute phase given the almost 50% rate of endoscopic rebleeding and the survival benefit of performing TIPS in this patient population.

Gastric varices as a result of liver disease also represent a complicated disease process. While controversial, the treatment of gastric varices in many cases requires both TIPS and BRTO. Most GI bleed patients with portal hypertension are complicated, unstable patients that require a multidisciplinary, team approach to optimize survival outcomes. Interventional radiology remains an important component of the team that should be implemented as early as possible in the management of these patients. In the situation where TIPS is not available at the hospital, endoscopy can be used to temporarily stabilize the bleeding to allow transfer to an institution where TIPS is more commonly performed.

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