American College of Radiology ACR Appropriateness Criteria[®] Radiologic Management of Gastric Varices

Variant 1:

Cirrhotic patient with active bleeding from large high-flow gastric varices, significant portal hypertension, and a MELD score of 14. CT demonstrates a large gastrorenal shunt.

| Procedure | Appropriateness Category |
|------------------------------|--------------------------|
| BRTO | Usually Appropriate |
| Endoscopic management | Usually Appropriate |
| Partial splenic embolization | May Be Appropriate |
| Surgical management | May Be Appropriate |
| TIPS | Usually Appropriate |

<u>Variant 2:</u> Cirrhotic patient with bleeding from large high-flow gastric varices with a MELD score of 20. CT demonstrates a large gastrorenal shunt.

| Procedure | Appropriateness Category |
|------------------------------|--------------------------|
| BRTO | Usually Appropriate |
| Endoscopic management | Usually Appropriate |
| Partial splenic embolization | May Be Appropriate |
| Surgical management | May Be Appropriate |
| TIPS | May Be Appropriate |

<u>Variant 3:</u> Cirrhotic patient bleeding from small, low-flow gastric varices and moderate ascites with a MELD score of 18. MRI does not demonstrate a gastrorenal shunt.

| Procedure | Appropriateness Category |
|------------------------------|--------------------------|
| BRTO | Usually Not Appropriate |
| Endoscopic management | Usually Appropriate |
| Partial splenic embolization | May Be Appropriate |
| Surgical management | May Be Appropriate |
| TIPS | Usually Appropriate |

<u>Variant 4:</u> Cirrhotic patient bleeding from large, high-flow gastric varices with hepatic encephalopathy and a MELD score of 18. MRI demonstrates a large gastrorenal shunt.

| Procedure | Appropriateness Category |
|------------------------------|--------------------------|
| BRTO | Usually Appropriate |
| Endoscopic management | Usually Appropriate |
| Partial splenic embolization | May Be Appropriate |
| Surgical management | May Be Appropriate |
| TIPS | May Be Appropriate |

Cirrhotic patient bleeding from esophageal varices and gastric varices not amenable to endoscopic management with a MELD score of 13 and a hepatic wedge pressure of 22 mmHg. CT demonstrates a small gastrorenal shunt.

| Procedure | Appropriateness Category |
|------------------------------|--------------------------|
| BRTO | Usually Not Appropriate |
| Partial splenic embolization | May Be Appropriate |
| Surgical management | May Be Appropriate |
| TIPS | Usually Appropriate |

<u>Variant 6:</u>

Cirrhotic patient bleeding from large high-flow gastric varices with a MELD score of 12 and a hepatic wedge pressure of 10 mmHg. MRI demonstrates a large gastrorenal shunt.

| Procedure | Appropriateness Category |
|------------------------------|--------------------------|
| BRTO | Usually Appropriate |
| Endoscopic management | Usually Appropriate |
| Partial splenic embolization | May Be Appropriate |
| Surgical management | May Be Appropriate |
| TIPS | Usually Appropriate |

Variant 7:

Patient with gastric variceal bleeding, found to have chronic splenic vein occlusion on MRI.

| Procedure | Appropriateness Category |
|--|--------------------------|
| BRTO | Usually Not Appropriate |
| Endoscopic management (sclerosis or cyanoacrylate injection) | May Be Appropriate |
| Partial splenic embolization | Usually Appropriate |
| Splenic vein recanalization | Usually Appropriate |
| Surgical management | Usually Appropriate |
| TIPS | Usually Not Appropriate |

Variant 8:

Patient with chronic intrahepatic and extrahepatic portal vein occlusion with cavernous transformation on CT with gastric variceal bleeding.

| Procedure | Appropriateness Category |
|--|--------------------------|
| BRTO | Usually Not Appropriate |
| Endoscopic management (sclerosis or cyanoacrylate injection) | May Be Appropriate |
| Partial splenic embolization | May Be Appropriate |
| Portal vein recanalization plus TIPS | Usually Appropriate |
| Surgical management | May Be Appropriate |

RADIOLOGIC MANAGEMENT OF GASTRIC VARICES

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Summary of Literature Review

Introduction/Background

Gastric varices are a type of portosystemic shunt that may occur in isolation or in conjunction with esophageal varices. In the setting of cirrhosis and associated portal hypertension, gastric varices accompany esophageal varices in approximately 20% of patients and are due to the concurrently elevated splenic venous pressure. In these cases, gastric varices are most often gastroesophageal in nature as opposed to isolated gastric varices [1]. With portal vein occlusion, both esophageal and gastric varices may develop in the absence of cirrhosis; in this setting, the varices are most commonly isolated gastric varices rather than gastroesophageal [1]. However, gastric varices can occur in the absence of cirrhosis and portal hypertension, most frequently related to portal or splenic vein thrombosis related to conditions such as pancreatitis. Such interruption of splenic venous outflow will result in enlargement of portosystemic collateral veins, particularly gastric varices. Regardless of the underlying etiology, gastric varices typically originate from the mid to distal splenic vein, with flow toward the left renal vein, inferior vena cava, and other intra-abdominal systemic veins.

In cases of acute gastric variceal hemorrhage, patients are initially managed with blood transfusions, correction of underlying coagulopathy, vasoactive medications, and antibiotic prophylaxis. Endoscopy is classically the initial diagnostic modality for a patient with upper gastrointestinal (GI) hemorrhage given its high accuracy in diagnosing the etiology of hemorrhage and relative efficacy in treating many types of hemorrhage. In cases of acute massive hemorrhage, balloon tamponade may be attempted on a temporary basis with the Linton-Nachlas tube [2]. In some cases, the Sengstaken-Blakemore or Minnesota tubes with inflation of only the gastric balloon and anchoring against the gastroesophageal junction might be helpful, depending on the location of the gastric varices. Classification of the distribution of gastric varices is helpful for determining the ideal treatment. Based on the Sarin classification, there are four primary types of varices that involve the stomach: Gastroesophageal varices type 1 (GOV1) extend from the esophagus into the lesser curvature, gastroesophageal varices stype 2 (GOV2) extend from the esophagus into the fundus, isolated gastric varices type 1 (IGV1) are located in the fundus, and isolated gastric varices type 2 (IGV2) are located elsewhere in the stomach [3]. Although varices extending into the lesser curvature (GOV1) are the most common type of gastric varices with cirrhosis, varices that involve the gastric fundus (GOV2 and IGV1) are much more frequent in the setting of portal or splenic vein thrombosis and are at higher risk of hemorrhage [3].

Special Imaging Considerations

Diagnosis of gastric varices is classically made on endoscopy; however, CT has been shown to detect gastric varices with high sensitivity and specificity [4,5]. Furthermore, performance of a contrast-enhanced CT or MRI is of particular importance when evaluating patients with gastric varices in order to identify the inflow and outflow because this can allow determination of the feasibility of balloon-occluded retrograde transvenous obliteration (BRTO). Similarly, identification of the presence of portal or splenic vein occlusion will determine which therapies can be considered and which will be more or less effective. Therefore, acquisition of a contrast-enhanced CT or MRI can provide crucial information for guiding therapy and thus should be obtained routinely for this patient population.

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Discussion of Procedures by Variant

Variant 1: Cirrhotic patient with active bleeding from large high-flow gastric varices, significant portal hypertension, and a MELD score of 14. CT demonstrates a large gastrorenal shunt.

Endoscopic Management

Endoscopy is an excellent modality for diagnosing and evaluating gastric varices as a source of upper GI bleeding. As with esophageal varices, endoscopic management is one of the initial considerations in the setting of gastric variceal hemorrhage [2]. Overall, there are three primary methods for endoscopic treatment of gastric varices: injection of sclerosant into the varices to induce thrombosis and occlusion (endoscopic variceal sclerotherapy), injection of cyanoacrylate into the varices to achieve obturation (endoscopic variceal obturation), and variceal ligation with standard rubber bands or other devices (endoscopic variceal ligation) [6].

Conventional endoscopic injection of sclerosant, although an effective therapy for esophageal varices, appears to be less successful in the treatment of gastric varices. Sarin et al [7] reported results for endoscopic sclerotherapy performed for actively bleeding gastric varices in 18 patients with a 67% rate for control of bleeding. There is a relative paucity of literature on endoscopic gastric variceal sclerotherapy, which has become less popular in favor of glue obturation and endoscopic ligation, which are the recommended endoscopic treatments by the most current American Association for the Study of Liver Diseases guidelines [2]. A recent meta-analysis of randomized studies comparing endoscopic variceal obturation to endoscopic variceal ligation included 194 patients [8]. Actively bleeding gastric varices were controlled more effectively with cyanoacrylate injection compared with band ligation (94% versus 80%, P = .03). Endoscopic variceal obturation had a significantly lower rebleeding rate for GOV1 (26% versus 48%, P = .04) and IGV1 (18% versus 86%, P = .02). However, control of GOV2 had similar rebleeding rates (36% versus 35%, P = .90). Complication rates were also similar. The addition of endoscopic variceal sclerotherapy to endoscopic variceal ligation may be helpful. In a randomized trial of 120 cirrhotic patients with bleeding gastroesophageal varices, the rebleeding rates were similar, but the mean number of sessions was significantly lower in patients undergoing combined endoscopic sclerotherapy and ligation compared with patients undergoing endoscopic variceal ligation alone (2.2 versus 3.4, P < .01). Highflow varices have been reported to result in significantly earlier recurrences when compared with slow-flow varices [9].

TIPS

Transjugular intrahepatic portal systemic shunts (TIPS) creation is a well-established treatment for esophageal variceal hemorrhage resulting from portal hypertension, the goal of which is to relieve the elevated portal pressures that caused the development of varices and subsequent pressurization. Although this treatment modality serves to address the underlying problem, it comes at the expense of a significant incidence of resulting hepatic encephalopathy of approximately 15% to 25%% and risk of hepatic decompensation related to diversion of portal flow away from the hepatic parenchyma, with increasing risk with a higher Model for End Stage Liver Disease (MELD) score [10]. In a recent randomized trial of covered TIPS versus endoscopic therapy with beta blockers for patients with gastroesophageal varices (82% with esophageal varices only), TIPS was found to be superior for reduction of variceal bleeding (0% rebleeding episodes after TIPS versus 37% after endoscopic/medical management, P = .001), although survival was similar [11]. Although hepatic encephalopathy was more frequent after TIPS within 1 year (35% versus 14%, P = .035), there was no significant difference after 1 year [11]. Of note, although the vast majority of TIPS data are gathered with bare metal stents, current standard of practice is with covered stents, given that shunt dysfunction has been shown to be significantly improved with covered stents in randomized trials [12].

Although data on the use of TIPS for management of gastric variceal hemorrhage are more sparse, the data are similarly supportive. To date, there are eight studies specifically evaluating TIPS for treatment of patients with portal hypertension and gastric varices with >10 patients, comprising a total of 201 patients (range for individual studies: 12–35 patients) [13-20]. Four of these studies have intrainstitutional comparisons with BRTO outcomes [15,16,18,20] and one randomized to endoscopic management [17]. Within studies, there is substantial variation in reporting, with most results based on variable durations of clinical follow-up. In six studies, TIPS were performed with bare metal stents [13-15,17-19]. In two studies analyzing patients with active gastric variceal bleeding, TIPS with a post-TIPS hepatic encephalopathy rate of 16% [13]. In the single randomized trial comparing TIPS to endoscopic management (with cyanoacrylate), the rate of gastric variceal rebleeding after TIPS was significantly lower than with endoscopic management (11% versus 38%, P = .014) with a median of 32

months of follow-up [17]. The rate of upper GI bleeding from any source was 43% versus 59%, P = .12. Although hepatic encephalopathy occurred more frequently after TIPS (26% versus 3%, P < .01), survival and other complications were similar [17].

The utilization of stent grafts for TIPS creation is expected to improve outcomes given their superior patency rates in randomized trials [12], particularly considering that over 70% of gastric variceal rebleeding occurrences after TIPS have been associated with TIPS dysfunction (TIPS stenosis or thrombosis) [17]. Two studies exclusively analyzed TIPS created with stent grafts. Kim et al [16] reported a 7% rate of rebleeding from gastric varices with a mean of 917 days of follow-up; in one patient with rebleeding 2 days after TIPS insertion, resolution was achieved with coil embolization of the varices, whereas the other patient experienced rebleeding 2 years after TIPS that was due to a TIPS stenosis, which was successfully treated with TIPS revision. Sabri et al [20] reported an 11% rate of rebleeding from gastric varices at a mean of 19.5 months of follow-up; in two of the cases, the patient had hepatic venous stenosis, which was treated successfully with revision. In the third case, the patient had normal TIPS, requiring BRTO for successful management. Of note, all three of these patients were treated with coil or plug embolization of the feeding portal vein branch during the initial TIPS procedure. The strategy of performing coil embolization of gastric varices concurrent with inserting a TIPS has been reported to result in persistent variceal patency and a substantial and surprisingly high rebleeding rate (28%) relative to those who did not undergo embolization (20%) at a median follow-up of 129 days [21]. The authors hypothesized that embolization of the dominant gastric varices is relatively ineffective because of the additional inflow veins that supply or will enlarge to supply the gastric varices. However, Jiang et al [22] reported a rebleeding rate of only 12% at a mean of 236 days with TIPS plus embolization of gastroesophageal varices. Patient selection and technique may account for the disparate differences between the two studies.

BRTO

BRTO describes transvenous sclerosis or occlusion of gastric varices via a spontaneous gastrorenal shunt. Although the original technique for occlusion of the gastrorenal shunt was described with an occlusion balloon, the use of vascular plugs (ie, PARTO) or coils (ie, CARTO) is increasing in popularity. Furthermore, various sclerosants and gelatin sponge mixtures have been utilized successfully. For the purpose of this manuscript, the term BRTO is inclusive of all of these variant techniques. BRTO has emerged as a popular method for treatment of gastric varices, which appears to convey a lesser risk of hepatic encephalopathy compared with TIPS because blood flow is not diverted from the portal system as occurs with TIPS. In fact, one of the emerging indications for BRTO is encephalopathy with the presence of a gastrorenal or gastrosplenorenal shunt [23-30]. In five studies evaluating a total of 35 patients with encephalopathy, there was resolution or significant reduction in encephalopathy in all patients [24,26-28,31]. The diversion of blood flow away from the liver with TIPS may also explain the observation of worsened MELD scores [25,32-34]. Because the BRTO procedure occludes a spontaneous hepatofugal shunt, the diversion of blood flow toward the liver [24,35-38] may help to preserve hepatic function [26,36,39]. However, it is controversial whether the Child-Pugh score remains unchanged or improves after BRTO [28,36,40]. Furthermore, the majority of authors conclude that if the Child-Pugh score improves initially in the first 6 to 9 months after BRTO, it then returns to pre-BRTO baseline levels [26,36].

Overall, the technical success rates of BRTO for patients with gastrorenal/splenorenal shunts and gastric varices range from 79% to 100% [18,26,27,35,41-52]. In most studies, gastric variceal rebleed rates of patients who had undergone a successful BRTO procedure range between 0% and 20% [18,24,26-28,35-37,41-59]. In a recent meta-analysis [60] that included 1,016 patients from 24 studies, the technical success rate was found to be 96.4%. The clinical success rate was 97.3% at a mean follow-up of 487 days, with clinical success defined as no recurrence or rebleeding from gastric varices or complete obliteration of varices on subsequent imaging. The flow velocity and flow volume in the varices have been correlated with outcomes after BRTO, with slow flow and low volume being associated with a higher success rate [61].

Procedural complications, when mentioned, include gross hematuria (15%–100% of BRTO cases) with hemoglobinuria-induced renal failure described in up to 4.8% of cases. Pulmonary embolism occurs in 1.5% to 4.1% of cases (symptomatic in 1.4%–2.5% of cases). Anaphylaxis to ethanolamine oleate (up to 5%), cardiac arrhythmias (up to 1.5%), and rapidly declining hepatic function (up to 5%–7%) have also been described. The 30-day mortality rates range from 0% to 4.1%, and the most common cause of death is progressive hepatic failure [24,26-28,30,35-38,47,51,53,55,56,59,62-64]. Notably, occlusion of gastrorenal or splenorenal shunts can aggravate sequelae of portal hypertension because these constitute portosystemic shunts that decompress the portal venous system. The aggravation of nongastric (esophageal or duodenal) varices appears to be a major

problem over the long term and is likely reflective of persistent or increasing portal hypertension following BRTO [24,26,27,30,35,37,38,47,51,53,55,62,63]. In four studies evaluating 160 patients who underwent BRTO with continuous post-BRTO endoscopic follow-up, the esophageal variceal aggravation rates (expressed as a Kaplan-Meier analysis) at 1, 2, and 3 years were: 27% to 35%, 45% to 66%, and 45% to 91%, respectively [24,32,51,55]. In another two studies evaluating 117 patients with BRTO, the percentage of patients with aggravated esophageal varices was 30% to 68%, and the percentage of patients who had bleeding esophageal varices was 17% to 24% (36%–57% of those with aggravated esophageal varices went on to have bleeding) [35,53]. In the meta-analysis by Park et al [60], the esophageal variceal recurrence rate was 33.3%. The risk of esophageal varix aggravation has been shown to correlate significantly with the total bilirubin level and a portosystemic gradient >13 [65]. Thus, pre-BRTO prophylactic esophageal banding, portosystemic gradient measurement, laboratory analysis, and post-BRTO surveillance may be helpful to avoid subsequent esophageal variceal hemorrhage. Other complications reflective of increased portal hypertension following BRTO include the development of portal hypertensive gastropathy (occurs in 5%-13%), ascites (occurs in 0%-44%), and hydrothorax/pleural effusion (occurs in 0%-8%) [24,28,36,55,59,64]. The presence of a TIPS in patients undergoing BRTO has been correlated with significantly lower ascites/hydrothorax rates and lower recurrent hemorrhage rates, although survival was similar [66]. Furthermore, concomitant performance of partial splenic embolization also can mitigate esophageal variceal aggravation as described below.

The four retrospective studies that included intrainstitutional comparison between BRTO and TIPS had a total of 133 BRTO cases and 94 TIPS cases [15,16,18,20]. The study by Choi et al [15] had an inadequate sample size for statistical comparison (BRTO: 8, TIPS: 13). Ninoi et al [18], who compared patients undergoing bare TIPS versus BRTO, reported a 1-year rebleeding rate of 20% after TIPS versus 2% after BRTO (P < .01). Furthermore, the 1-, 3-, and 5-year survival rates after BRTO were better than those after TIPS in Child-Pugh patients: 96%, 83%, and 76% versus 81%, 64%, and 40%, respectively (P = .01) [18]. However, the more recent studies comparing covered TIPS with BRTO both revealed statistically similar rebleeding rates. Sabri et al [20] reported a 1-year rebleeding rate of 11% in the TIPS group and 0% in the BRTO group (P = .25) with a hepatic encephalopathy rate of 15% and 0% (P = .12). Kim et al [16] reported a 7% and 8% rebleeding rate throughout the study duration, respectively, but with a higher rate of hepatic encephalopathy after TIPS (22% versus 0%, P = .01).

Partial Splenic Embolization

In patients with cirrhosis, the development of hypersplenism with a concomitant increase in arterial and venous flow is a commonly observed phenomenon in response to portal hypertension. This increased splenic venous flow will theoretically contribute to pressurization of gastric varices arising from the splenic vein. Accordingly, partial splenic embolization in patients with hypersplenism has been shown to result in a significant decrease in the portosystemic gradient and splenic vein flow [67]. Buechter et al [68] reviewed outcomes after partial splenic embolization in 9 patients with portal hypertension and upper GI bleeding from gastroesophageal varices or portal gastropathy, reporting a 100% resolution of hemorrhage, without any episodes of rebleeding at a mean follow-up of 6 to 52 months. The benefits of partial splenic embolization in combination with other therapies for gastric varices have been investigated in several studies. In a retrospective study comparing patients undergoing transhepatic variceal embolization with (n = 31) or without partial splenic embolization (n = 34) for patients with acute massive hemorrhage of esophagogastric varices, the recurrent rebleeding rate was significantly lower in those who underwent partial splenic embolization (6.7% versus 36.7%, respectively, P < .01) [69]. Additionally, there was a significantly higher incidence of ascites and portal gastropathy in patients who did not undergo concomitant partial splenic embolization along with variceal embolization [69]. Similarly, in a retrospective study comparing results of transingular BRTO with (n = 14) versus without (n = 19) concomitant partial splenic embolization, those undergoing partial splenic embolization had a 3-year occurrence rate of esophageal varices of 9% compared with 45% in those undergoing BRTO alone (P < .05) [55]. Waguri et al [70] also compared outcomes in patients with gastric varices after BRTO combined with partial splenic embolization (n = 10) versus BRTO alone (n = 9), reporting resolution of gastric varices in all patients but with significantly fewer cases of esophageal variceal exacerbation when partial splenic embolization was performed (60% versus 0% at 1 year, P =.01), with a similar incidence of ascites or hepatic hydrothorax between groups. In a randomized trial, 84 patients with cirrhosis, large varices, thrombocytopenia, and splenomegaly were randomized to undergo endoscopic variceal ligation with or without partial splenic embolization [71]. Patients who underwent partial splenic embolization plus endoscopic therapy had a significantly lower incidence of variceal recurrence (P = .02), variceal hemorrhage (P = .01), and death (P = .04).

Surgical Management

In patients with portal hypertension, the presence of an unpredictable and often extensive network of esophagogastric varices and other spontaneous pressurized portosystemic shunts around the portal and splenic veins render intra-abdominal surgeries to be challenging because of the risk of intraoperative hemorrhage [72]. Therefore, surgical management should be considered only at centers with substantial experience with operating in the setting of pressurized varices, such as liver transplant centers. Although rarely a first-line therapy, surgical portosystemic shunt creation has been reported to be effective in the management of gastric variceal hemorrhage. In a large randomized trial comparing endoscopic therapy with portacaval shunt creation, long-term control of hemorrhage was achieved in 97% to 100% of patients compared with only 27% to 29% with endoscopic therapy and 6% after TIPS [73]. Survival was also significantly longer after portacaval shunt creation. However, all TIPS in this study were created with bare metal stents, with a 94% rate of TIPS stenosis or occlusion, and failed TIPS revision in 93%, which is extremely disparate from results of contemporary TIPS studies with covered stents. In a clinical trial on 140 patients randomized to distal splenorenal shunt creation versus TIPS, of which over half had isolated gastric varices, there were no significant differences in rates of rebleeding, encephalopathy, or survival; however, reintervention was significantly higher in the TIPS group. Again, however, only bare metal stents were utilized in the TIPS group [74]. Therefore, in centers with appropriate experience, surgical shunt creation could be considered. For this document, it is assumed the procedure is performed and interpreted by an expert.

For similar reasons as partial splenic embolization, splenectomy can also serve to diminish blood flow into the portal venous system and by doing so potentially decrease portal venous pressures, particularly in the setting of splenomegaly with accompanying high blood flow throughput. Su et al [75] performed open splenectomy with esophagogastric devascularization in 283 patients with portal hypertension and recurrent variceal bleeding with a 3.2% incidence of rebleeding within 1 month and 4.6% incidence at full follow-up (mean 29 months). Results were compared with 196 patients who underwent TIPS, showing a significantly lower rate of rebleeding (4.6% versus 15.3%, P = .001) and encephalopathy (3.9% versus 17.3%) but with similar survival and hepatic function. Of note, a combination of bare and covered stents were utilized for TIPS creation. Cheng et al [76] reported results with laparoscopic splenectomy with esophagogastric devascularization on 204 patients with portal hypertension and variceal bleeding. The technical success rate was 92% with a mean intraoperative blood loss of 189 mL and 20% blood transfusion rate. Operative complications occurred in 49% of patients, with the majority consisting of portal vein thrombosis. The rate of rebleeding was 4% with a follow-up range of 2 to 65 months.

Finally, combined surgical procedures have also been reported as an effective strategy. Feng et al [77] reported results in 150 patients with portal hypertension and varices who underwent surgical shunt, portoazygous devascularization, and splenectomy in 100 patients, as well as 50 patients undergoing surgical shunt plus portoazygous devascularization. Although unclear whether patients presented with bleeding varices, the rate of rebleeding was reported at 2% with 1 to 7 years of follow-up.

Variant 2: Cirrhotic patient with bleeding from large high-flow gastric varices with a MELD score of 20. CT demonstrates a large gastrorenal shunt.

The key feature in this patient is the high MELD score, with all other factors being equivalent to Variant 1.

TIPS

Higher MELD scores have been correlated with worsening survival after TIPS. The 3-month mortality for patients with a MELD score ≤ 10 has been reported as 0%, whereas the 3-month mortality is 35% for MELD scores 18–24 and 66% for MELD scores of 25 or greater [33]. It has been proposed that the reason for the higher mortality after TIPS in patients with high MELD scores is the TIPS-induced decrease in portal perfusion, which may theoretically be more detrimental in patients with worse liver dysfunction. On that basis, TIPS is often avoided in patients with high MELD scores, although the causality of TIPS and mortality in patients with high MELD scores is significantly higher than those with low MELD scores in the absence of a TIPS as well [78]. Furthermore, a recent retrospective comparison of patients with TIPS versus without TIPS reported that TIPS does not independently increase the risk of death in patients with a high MELD score [79].

Endoscopic Management

A high MELD score does not impact endoscopic management; by obstructing flow through varices, there may be some theoretical increase in portal perfusion, which may be beneficial to the liver [26,36,39].

BRTO

For similar reasons, there may be theoretical benefit to BRTO by virtue of increased portal perfusion, with reports of improved hepatic synthetic function after BRTO [80].

Partial Splenic Embolization

There is no literature regarding the use of partial splenic embolization as a standalone procedure in patients with high MELD scores in the management of gastric varices. In a case series of 9 patients with lower MELD scores (range 6–14) treated with partial splenic embolization for upper GI bleeding from gastroesophageal varices or portal gastropathy, a 100% clinical success rate was reported [68]. Partial splenic embolization may also be safe and effective for patients with high MELD scores as well. In a retrospective study comparing transhepatic variceal embolization with (n = 31) or without (n = 34) partial splenic embolization, the mean MELD score was 25.9 ± 8.4 in the group undergoing partial splenic embolization. The patients undergoing partial splenic embolization had a significantly lower bleeding recurrence rate, fewer cases of ascites, fewer cases of portal hypertensive gastropathy, and less progression of their Child-Pugh score compared with patients treated with variceal embolization alone [69].

Surgical Management

For the same reasons why TIPS may theoretically be more detrimental in patients with a high MELD score, a surgical shunt may be deemed less attractive as an option; however, splenectomy should not be impacted by a high MELD score [26,36,39].

Variant 3: Cirrhotic patient bleeding from small, low-flow gastric varices and moderate ascites with a MELD score of 18. MRI does not demonstrate a gastrorenal shunt.

Endoscopic Management

The slow flow within the varices makes endoscopic management with sclerosants and embolic materials more favorable because high-flow varices are more technically challenging [6].

TIPS

The MELD score is intermediate, making TIPS mildly less attractive based on historical concerns. However, an additional benefit to TIPS in this scenario is mitigation of ascites. Using contemporary 10-mm-diameter stent grafts for creation of TIPS, the long-term need for paracentesis was reported at 31%. Using 8-mm-diameter stent grafts, the degree of ascites control was reported to be inferior (58% with need for further paracentesis, P = .003) but without differences in the incidence of hepatic encephalopathy [81].

BRTO

The absence of a demonstrable gastrorenal shunt renders this patient ineligible for BRTO. Even if a gastrorenal shunt were present, there is a substantial incidence of post-BRTO ascites in 31% of patients, which may result in worsening of ascites in this scenario [80].

Partial Splenic Embolization

As above, partial splenic embolization may decrease gastric variceal bleeding [66]. In a study of 6 patients with refractory ascites after liver transplantation, splenic artery embolization resulted in complete resolution of ascites in 5 of the patients, presumably by decreasing pressurization of the portal system [82].

Surgical Management

For the same reasons why TIPS may be theoretically more detrimental in patients with an intermediate to high MELD score, a surgical shunt may be deemed less attractive as an option; however, splenectomy should not be impacted by the MELD score [26,36,39].

Variant 4: Cirrhotic patient bleeding from large, high-flow gastric varices with hepatic encephalopathy and a MELD score of 18. MRI demonstrates a large gastrorenal shunt.

In this patient, the significant history of hepatic encephalopathy is a key discriminator.

Endoscopic Management

Endoscopic measures that result in occlusion of varices would increase portal perfusion, which could be beneficial in mitigating encephalopathy [26].

TIPS

Given the substantial incidence of worsened hepatic encephalopathy, by virtue of decreasing portal perfusion and decreased detoxification of intestinally produced bioactive compounds, TIPS would be a suboptimal choice in this patient [83].

BRTO

BRTO is likely to improve or resolve hepatic encephalopathy in addition to addressing the hemorrhage and improving hepatic synthetic function [26,80]. The presence of large varices and a large gastrorenal shunt are favorable features, but the high flow within the shunt is correlated with lower success rates [60].

Partial Splenic Embolization

Although partial splenic embolization may help to mitigate variceal bleeding [66], there are no data to suggest that partial splenic embolization as a standalone treatment affects hepatic encephalopathy. However, partial splenic embolization when combined with BRTO has been shown to result in lower serum ammonia levels and lower grades of encephalopathy [84].

Surgical Management

For the same reasons as TIPS, creation of a surgical shunt would be considered a poor choice because of the risk of uncontrollable hepatic encephalopathy [83]. However, there is no literature or theoretical reason to suggest that splenectomy would affect encephalopathy.

Variant 5: Cirrhotic patient bleeding from esophageal varices and gastric varices not amenable to endoscopic management with a MELD score of 13 and a hepatic wedge pressure of 22 mmHg. CT demonstrates a small gastrorenal shunt.

The presence of concurrently bleeding esophageal varices makes this case unique.

TIPS

TIPS has proven efficacy for both esophageal and gastric varices [11,13-20].

BRTO

Given the small gastrorenal shunt, a BRTO would be expected to be technically challenging. Furthermore, BRTO is not particularly effective for managing esophageal varices, and there is substantial literature showing that BRTO results in increased risk of early or late esophageal variceal hemorrhage [24,26,27,30,35,37,38,47,51,53,55,62,63,85].

Partial Splenic Embolization

Decreased splenic outflow into the portal system may decrease the portal pressure, which may mitigate hemorrhage [67].

Surgical Management

Surgical shunt creation or splenectomy may be effective for mitigating gastric and esophageal variceal hemorrhage [73,75].

Variant 6: Cirrhotic patient bleeding from large high-flow gastric varices with a MELD score of 12 and a hepatic wedge pressure of 10 mmHg. MRI demonstrates a large gastrorenal shunt.

This patient does not have significant portal hypertension based on the hepatic wedge pressure. Obtaining contrast-enhanced cross-sectional imaging (CT or MRI) is critical for ascertaining the presence of portal or splenic vein occlusion, which can cause severe gastric varices in the absence of cirrhosis or portal hypertension. This would be particularly crucial in determining the optimal treatment.

Endoscopic Management

Depending on technical expertise, high-flow varices can be challenging to treat with endoscopic methods [9]. For this document, it is assumed that the procedure is widely available and is performed and interpreted by an expert.

TIPS

Large gastric varices can serve as a highly effective portosystemic shunt that accordingly mitigates the portosystemic gradient [86]. In any case, diverting portal flow into a TIPS in the setting of large gastric varices would be beneficial for mitigating the risk of bleeding.

BRTO

A large splenorenal shunt is optimal for technical feasibility for performing BRTO [15], but the high flow may reduce the success rate [60].

Partial Splenic Embolization

Because partial splenic embolization has been shown to decrease portal flow and reduce the risk of variceal hemorrhage, it may be a favorable option if there is significant splenomegaly [67,68].

Surgical Management

Similar to the commentary on TIPS creation, the true portosystemic gradient is mitigated by the large gastric varices. Surgical shunt creation may help by diverting flow away from the gastric varices but may be even more effective when performed in conjunction with devascularization [87]. Similarly to partial splenic embolization, splenectomy may be helpful for decreasing flow through the varices with presumed decreased hemorrhage risk [67,68].

Variant 7: Patient with gastric variceal bleeding, found to have chronic splenic vein occlusion on MRI.

Splenic vein thrombosis may occur because of portal hypertension, pancreatitis, or a compressive mass. When occurring in the absence of portal vein occlusion, the resulting collateral development for decompression of the splenic outflow varies from portal vein occlusion in that either or both portosystemic venous collaterals or splenoportal venous collaterals can form to decompress the splenic vein. As similar with portal vein thrombosis, splenomegaly, increased splenic flow, and gastric varices can be a direct consequence of splenic vein occlusion, also referred to as sinistral portal hypertension [88].

Endoscopic Management

In patients with splenic vein occlusion, most or the entire splenic venous outflow may be via gastric varices. Although endoscopic interruption of gastric varices may be technically feasible, the abrupt distal splenic hypertension and drive for new splenic venous outflow after occlusion of the entire splenic venous outflow may encourage persistent patency or rapid development of new gastric varices. Although there is a paucity of data on endoscopic therapy in the setting of splenic vein occlusion, Liu et al [89] reported a rate of achievement of successful hemostasis of 40% after endoscopic sclerotherapy in 5 patients with splenic vein occlusion. One patient exsanguinated acutely during treatment. Sato et al [90] reported on endoscopic treatment of bleeding gastric varices using histoacryl in 3 patients with splenic vein occlusion, with successful control of bleeding in all three. However, follow-up information was not provided, and patients with severe varices were treated with alternative methods.

TIPS

Because isolated splenic vein occlusion can occur in the absence of cirrhosis, TIPS insertion would not be expected to be beneficial if the main portal vein pressure is not elevated.

BRTO

As with direct endoscopic therapy of gastric varices, the obliteration of the splenic venous drainage may be expected to be technically challenging and with suboptimal success rates [89]. Because the gastric varices comprise the sole outflow for the spleen, occlusion of the varices would also be expected to precipitate splenic congestion with worsening splenomegaly, infarction, and formation of new varices [91,92].

Splenic Vein Recanalization

When splenic vein occlusion is the etiology of sinistral hypertension, restoration of patency corrects the underlying causative problem. In a retrospective review of 11 patients with splenic vein stenosis or occlusion with gastric varices and associated bleeding, transjugular recanalization was successfully achieved in 8 patients [93]. Two were treated with angioplasty alone, with the remainder being treated with stents or stent grafts. In all patients, upper GI bleeding resolved without recurrence at a median follow-up of 17.5 months.

Partial Splenic Embolization

In the setting of splenic vein occlusion, the near entirety of splenic venous drainage will be into the gastric varices; therefore, a marked decrease in splenic volume should theoretically diminish the amount of flow and pressure within the gastric varices. Wang et al [94] performed partial splenic embolization on 14 noncirrhotic patients with gastric varices and splenic vein occlusion that was due to pancreatic pathology, resulting in diminishment or resolution of gastric varices in all patients. In the 8 patients with acute or chronic gastric bleeding, resolution of hemorrhage was achieved in all patients without recurrence. Liu et al [89] reported

outcomes in 21 noncirrhotic patients with splenic vein occlusion and gastric variceal bleeding undergoing endoscopic sclerotherapy (n = 5), splenic embolization (n = 6), or splenectomy (n = 15). Endoscopic therapy was successful in 40%, whereas splenic embolization and splenectomy were both successful in 100%, without any recurrent bleeding.

Surgical Management

Historically, splenectomy has been performed as a standard treatment for gastric variceal bleeding with sinistral portal hypertension. Because the dominant or entire source of blood flow and pressurization of gastric varices is the spleen when splenic vein occlusion is present, removal of the spleen should remove the impetus for varix development and pressurization. Thus, removal of the source of pressurization is expected to serve as definitive therapy and mitigation of hemorrhage risk. As described previously, a review of 15 noncirrhotic patients undergoing splenectomy for splenic vein occlusion and gastric variceal bleeding resulted in successful management of bleeding in all patients without recurrence [89]. In another series of 6 patients with chronic pancreatitis and splenic vein occlusion undergoing splenectomy because of bleeding gastric varices, bleeding was controlled in all patients without subsequent rebleeding at a mean of 4.8 years of follow-up [95]. However, in patients without hemorrhage, splenectomy was not found to improve outcomes in patients with gastric varices [96]. Of note, because the inferior mesenteric vein empties into the splenic vein, occlusion of the splenic vein that includes the segment between the main portal vein and inferior mesenteric vein may result in continued filling of the splenic vein and gastric varices from the inferior mesenteric vein distribution despite splenectomy.

Variant 8: Patient with chronic intrahepatic and extrahepatic portal vein occlusion with cavernous transformation on CT with gastric variceal bleeding.

One of the complications of cirrhosis and portal hypertension is the development of portal vein thrombosis that is due to the stagnation of blood flow caused by the increased resistance at the hepatic sinusoids. The development of main portal vein thrombosis will increase the existing portal hypertension within the splanchnic and splenic veins and thus can further exacerbate any existing esophageal and gastric varices. Even in noncirrhotic patients, pancreatitis, abdominal surgery, and thrombophilic states can result in portal vein thrombosis that obstructs the entire splenomesenteric venous outflow, resulting in venous hypertension of the splenic and mesenteric veins. Irrespective of the cause, the acute mesenteric venous congestion can result in venous mesenteric ischemia. Traditional thrombectomy methods can be employed, such as mechanical or pharmacologic thrombectomy, and transjugular or transhepatic access may be needed [97]. If pharmacomechanical resolution of thrombus is not performed or if spontaneous thrombolysis and recanalization does not eventually occur, the occlusion will become chronic, and esophageal, gastric, and/or ectopic varices will invariably develop to allow adequate venous drainage of the splenomesenteric system. If the intrahepatic portal veins remain patent, portal-to-portal collateral veins/cavernous transformation may develop to restore some inflow into the intrahepatic portal veins.

Endoscopic Management

Although there is a paucity of studies on endoscopic management of gastric varices specifically in the setting of portal vein occlusion, such treatment likely occurs without awareness of the underlying portal patency because imaging has historically not been routinely performed. Sharma et al [1] reported results of endoscopic variceal obturation on 162 patients who had gastric variceal hemorrhage and portal vein occlusion in comparison to 292 patients with cirrhosis. The rate of acute control of bleeding in patients with portal vein obstruction was 94%, which was found to be similar with the cirrhotic patient group (P = .05). The delayed rebleeding rate after >48 hours was also 94%, which was also similar to that of the cirrhotic patient group (P = .07) at a mean of 18.6 months of follow-up. The amount of glue used was significantly higher in patients with portal venous obstruction (P = .001).

Portal Vein Recanalization Plus TIPS

Classically, the presence of portal vein occlusion is a relative contraindication to TIPS placement because the lack of continuous flow between the TIPS and the splenomesenteric veins prevents variceal decompression, and the lack of brisk flow through the actual TIPS will result in inevitable TIPS thrombosis. Therefore, TIPS creation alone should not be performed in this setting. However, if direct continuity between the TIPS and the splenomesenteric veins recanalization, then TIPS insertion can decompress the portal venous system and associated varices.

In the largest series to date on 61 patients with chronic portal vein occlusion, Thornburg et al [98] reported a 98% technical success rate for inserting a TIPS with concomitant portal vein recanalization, with 92% achieving

patency to transplant or until the end of the study with a mean follow-up of 16.7 months. In all cases, the main portal vein was treated with angioplasty alone without stenting in order to preserve liver transplant candidacy. Although 66% of patients had esophagogastric varices, the occurrence of variceal bleeding before or after treatment were not reported. There were no cases of major hemorrhage. Luo et al [99] reported that TIPS with portal vein recanalization was successful in 92% of 22 cirrhotic patients with chronic portal vein occlusion and variceal bleeding, with 3 patients developing shunt dysfunction and recurrent variceal bleeding. The recanalized main portal vein was treated with self-expanding bare metal stents. Two patients had associated self-limited hemorrhage requiring blood transfusion. In a randomized controlled trial on 73 patients with cirrhosis and portal vein thrombosis, patients were randomized to TIPS with portal vein recanalization or endoscopic band ligation with propranolol [100]. The rate of freedom from esophageal variceal bleeding was 77.8% in the TIPS group and 42.9% in the endoscopic therapy group (P = .002) but with similar encephalopathy rates and survival. However, it is notable that the portal occlusion was not necessarily chronic and that patients with gastric varices were excluded. In a population of cirrhotic and noncirrhotic patients, Han et al [101] attempted TIPS with portal vein recanalization in 65 patients; the success rate was 72% (28 of 39) in patients with portal vein thrombosis with cavernous transformation and 100% (26 of 26) in patients without cavernous transformation. The authors concluded that it is essential to recanalize the thrombosed portal vein followed by TIPS placement. However, in several case reports, short-term TIPS patency has been reported without portal vein recanalization in patients with cavernous transformation when the TIPS can be deployed into an adequately large periportal collateral vein that effectively bypasses the occluded segment [102,103].

Although patients with cirrhosis are expected to require a TIPS with portal vein recanalization in order to bypass the high-resistance hepatic sinusoids, noncirrhotic patients may have nonpathologic hepatic sinusoids; thus, a TIPS may not be necessary in all circumstances. Marot et al [104] reported successful portal vein recanalization and stenting in 12 of 13 noncirrhotic patients with chronic portal venous occlusion to the level of the main or segmental portal vein branches. Of the 6 patients presenting with variceal bleeding, hemorrhage resolved and did not recur. Stent patency at 2 years was achieved in all 6 patients with portal occlusion extending to the left or right main portal vein compared with 4 of 6 patients with occlusion extending to the segmental branches. In 2 patients with portal vein occlusion extending even further to the distal subsegmental branches, recanalization and stenting was unsuccessful in both. These findings suggest that stent deployment is most effective when the portal vein occlusion is limited to the main and right or left portal vein to ensure adequate flow through the stent; otherwise, TIPS creation may be needed to ensure adequate portal flow and patency after recanalization. Qi et al [105] reported outcomes after TIPS with portal vein recanalization in 20 noncirrhotic patients with chronic portal vein occlusion and variceal bleeding in which the success rate was 35% with a variceal rebleeding rate of 14% in patients with successful TIPS. Klinger et al [106] reported a 77% portal vein recanalization success rate in 17 noncirrhotic patients with chronic portal vein thrombosis, with treatment including angioplasty, stent deployment, and/or TIPS creation, depending on the degree of portal flow, with a resulting 2-year patency rate of 70%.

BRTO

There is a paucity of literature on BRTO with portal vein occlusion. Generally, BRTO in this settting can have grave consequences because the gastric varices may be the sole or dominant outflow for the entire splenomesenteric circulation; thus, occlusion of this outflow could result not only in splenic engorgement and infarction, it could also result in mesenteric venous thrombosis and acute venous mesenteric ischemia [92]. One small case series of 2 patients described successful BRTO in a noncirrhotic patient with subacute portal vein thrombosis with complete resolution of gastric varices on endoscopy 105 days postprocedure and on CT 5 months postprocedure. The second patient had chronic portal vein occlusion with cavernous transformation and splenic vein thrombosis that was due to necrotizing pancreatitis with multiple failed endoscopic treatments of her gastric varices [107]. BRTO was again successfully performed, with resolution of variceal bleeding and continued complete obliteration of varices at 6 months.

Partial Splenic Embolization

Because partial splenic embolization should decrease flow into gastric varices, some degree of mitigation of active bleeding and rebleeding risk is expected, as shown for patients with portal hypertension and splenic vein occlusion above. However, robust literature is lacking. In a case report, the authors described a patient with severe portal hypertensive gastropathy with oozing on endoscopy with portal thrombosis and cavernous transformation who was treated with partial splenic embolization. Two months later, there was improvement in the appearance on endoscopy, and at 1 year post-treatment, there were no additional episodes of bleeding [108].

Surgical Management

For similar reasons in portal hypertension and sinistral portal hypertension, splenectomy is expected to decrease venous inflow into the portal system and thereby decrease portal hypertension and hemorrhage from gastric varices. Surgical portosystemic shunts would also be expected to have similar results in patients with portal hypertension or sinistral portal hypertension. The Rex-bypass shunt, which allows bypass of the occluded segment from the superior mesenteric vein to the left portal vein, has been shown to be effective in relieving both esophageal and gastric varices, with a patency rate of 86% over a follow-up period ranging from 6 to 64 months [109]. Creation of a splenorenal or mesocaval shunt has also been reported as a method for decompressing the portal venous system in the setting of portal vein occlusion [110].

Summary of Recommendations

- Variant 1: BRTO, endoscopic management, or TIPS is usually appropriate for a cirrhotic patient with active bleeding from large, high-flow gastric varices, significant portal hypertension, a MELD score of 14, and a large gastrorenal shunt. These procedures are equivalent alternatives (ie, only one procedure will be performed to effectively manage the patient's care).
- Variant 2: BRTO or endoscopic management is usually appropriate for a cirrhotic patient with bleeding from large, high-flow gastric varices with a MELD score of 20, and a large gastrorenal shunt. These procedures are equivalent alternatives (ie, only one procedure will be performed to effectively manage the patient's care).
- Variant 3: Endoscopic management or TIPS is usually appropriate for a cirrhotic patient bleeding from small low-flow gastric varices and moderate ascites with a MELD score of 18 and no gastrorenal shunt. These procedures are equivalent alternatives (ie, only one procedure will be performed to effectively manage the patient's care).
- Variant 4: BRTO or endoscopic management is usually appropriate for a cirrhotic patient bleeding from large, high-flow gastric varices with hepatic encephalopathy, a MELD score of 18, and a large gastrorenal shunt. These procedures are equivalent alternatives (ie, only one procedure will be performed to effectively manage the patient's care).
- Variant 5: TIPS is usually appropriate for a cirrhotic patient bleeding from both esophageal and gastric varices that are not amenable to endoscopic management, with a MELD score of 13, a small gastrorenal shunt, and a hepatic wedge pressure of 22 mmHg.
- Variant 6: BRTO, endoscopic management, or TIPS is usually appropriate for a cirrhotic patient bleeding from large, high-flow gastric varices with a MELD score of 12, a hepatic wedge pressure of 10 mmHg, and a large gastrorenal shunt. These procedures are equivalent alternatives (ie, only one procedure will be performed to effectively manage the patient's care).
- Variant 7: Partial splenic embolization, splenic vein recanalization, or surgical management is usually appropriate for a patient with gastric variceal bleeding and chronic splenic vein occlusion. These procedures are equivalent alternatives (ie, only one procedure will be performed to effectively manage the patient's care).
- Variant 8: Portal vein recanalization plus TIPS is usually appropriate for a patient with chronic intrahepatic and extrahepatic portal vein occlusion with cavernous transformation and gastric variceal bleeding.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at <u>https://acsearch.acr.org/list</u>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

Appropriateness Category Names and Definitions

| Appropriateness Category Name | Appropriateness Rating | Appropriateness Category Definition |
|--------------------------------------|---------------------------|--|
| Usually Appropriate | 7, 8, or 9 | The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk- benefit ratio for patients. |
| May Be Appropriate | 4, 5, or 6 | The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal. |
| May Be Appropriate (Disagreement) | 5 | The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned. |
| Usually Not Appropriate | 1, 2, or 3 | The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable. |

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The ability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.