CLINICAL PRACTICE UPDATE

AGA Clinical Practice Update on Management of Bleeding Gastric Varices: Expert Review

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Management of bleeding gastric varices (GV) presents a unique challenge for patients with portal hypertension. Despite over thirty years of diagnostic and treatment advances standardized practices for bleeding GV are lacking and unsupported by adequate evidence. There are no definitive natural history studies to help with risk assessment or prospective clinical trials to guide clinical decision making. Available literature on the natural history and management of gastric varices consists of case series, restricted cohort studies, and a few small randomized trials, all of which have significant selection biases. This review summarizes the available data and recommendations based on expert opinion on how best to diagnose and manage bleeding from gastric varices. Table 1 summarizes our recommendations.

Keywords: Gastric Varices; Portal Hypertension; Endoscopic Cyanoacrylate; BRTO; TIPS.

Gastric varices (GV) represent a complex collection of vascular shunts between the portosplenic venous system and the systemic veins of the abdomen and thorax. Owing to the heterogeneity of these shunts, their diagnosis, prognosis, and management are variable (Table 1). The prevalence of GV is estimated between 17% and 25% in patients with portal hypertension (pHTN) in comparison with esophageal varices (EV), which are present in up to 85% of these patients.[1–3] Although EV are more prevalent and bleed more frequently, hemorrhage from GV bleeding is often more severe, with an incidence of 16%–45% at 3 years, and associated with higher mortality.[1,2,4] Similar rates of bleeding and mortality from GV are reported for patients with noncirrhotic compared with cirrhotic pHTN.[5–9]

Endoscopic Classification OF GV

Though natural history data for GV bleeding exist, classification and risk stratification has been challenged by the small number of patients studied and lack of validated predictive models for bleeding. In practice, most gastroenterologists use the Sarin classification with the main distinction being cardiofundal vs lesser curvature GV.[1] However, the vascular supply and corresponding therapy for GV and EV are often different so a merged classification, such as Sarin's, can be problematic for therapeutic planning purposes. An alternative nomenclature for GV (Figure 1) based on location within the stomach is clearer and facilitates correlation with vascular imaging (Figure 1).

GV can also be classified by risk of bleeding. While Sarin has identified cardiofundal GV as being higher risk for bleeding, other groups have identified GV size, presence of a red mark, or discoloration as risk factors of bleeding, analogous to the North Italian Endoscopic Club criteria for predicting EV bleeding.[10–12] Based on this, we recommend adding an estimate of variceal size and high-risk stigmata (discolored marks, platelet plugs) to the Sarin classification when describing GV.[1,2,10]

Owing to their rare nature, lack of good investigational data, and the need for more complex, multidisciplinary management, we have excluded discussion of distal GV from this review.

The Importance of Cross-Sectional Imaging and Multidisciplinary Discussion

Consistency of the vascular anatomy of EV makes a universal treatment approach with band ligation or transjugular intrahepatic portosystemic shunt (TIPS) viable. In contrast, the vascular anatomy of GV can be highly variable and therefore not always amenable to one particular treatment option.[13]

Descriptive studies evaluating portomesenteric venous structures have shown significant differences between vascular anatomy of GV and EV and suggest that GV may bleed at lower portal pressures, possibly related to the presence of so-called left-sided circulation from a gastrorenal shunt (GRS).[14–17] A classification system has

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Table 1. Recommendations for Management of Bleeding GV: BPA Statements

BPA 1	Endoscopic classification systems for the appearance of GV should not be used for purposes of guiding primary prophylaxis of GV bleeding.
BPA 2	Initial medical management of bleeding GV should be performed according to current practice guidelines for portal hypertensive bleeding.
BPA 3	Goals of initial endoscopic evaluation include identification of the bleeding source and classification of the variceal bleeding site. Initial therapy for bleeding GV should focus on acute hemostasis for hemodynamic stabilization with a plan for further diagnostic evaluation and/or transfer to a tertiary care center with expertise in GV management.
BPA 4	Following initial endoscopic hemostasis, cross-sectional (MR or CT) imaging with portal venous contrast phase should be obtained to determine vascular anatomy, including the presence or absence of portosystemic shunts and gastrorenal shunts.
BPA 5	Determination of definitive therapy for bleeding GV should be made based upon endoscopic appearance of the gastric varix, the underlying vascular anatomy, presence of comorbid portal hypertensive complications, and available local resources. This is ideally done via a multidisciplinary discussion between the gastroenterologist or hepatologist and the interventional radiologist.
BPA 6	In cases in which definitive endoscopic therapy is favored, CA injection of bleeding GV is the treatment of choice. CA injection should be performed without the addition of plant-based oils such as lipiodol.
BPA 7	Following definitive endoscopic treatment of bleeding GV with CA injection, endoscopy should be performed every 2–4 wk to repeat CA injection as needed. Once the GV is completely treated with no further need for CA injection, endoscopic reevaluation should occur within 3–6 mo and then yearly thereafter.
BPA 8	TIPS placement may be used in management of GV bleeding when there is significant inflow to the GV from the coronary vein and/or significant comorbid complications from pHTN.
BPA 9	When TIPS is utilized for management of GV bleeding, endovascular sclerosis and/or direct embolization of GV should also be performed when feasible.
BPA 10	When a gastrorenal shunt is present, local expertise is available, and when severe comorbid complications of pHTN are absent, BRTO is the optimal endovascular therapy for management of GV bleeding.
BPA 11	Following BRTO for bleeding GV, short-interval (48 h) endoscopic assessment of the GV should be performed to ensure that vascular flow has been obliterated. If residual vascular flow is detected after BRTO for bleeding GV, CA injection should be performed. Cross-sectional imaging with CT or MR, should be performed within 4–6 wk from the procedure and subsequently as clinically indicated to confirm GV obliteration and evaluate for potential vascular complications.
BPA 12	When BRTO is performed to treat GV bleeding, surveillance endoscopy should be performed to assess and treat EV that may be exacerbated by increased portal pressures.

BPA, best practice advice; BRTO, balloon-occluded retrograde transvenous obliteration; CA, cyanoacrylate; CT, computed tomography; EV, esophageal varices; GV, gastric varices; MR, magnetic resonance imaging; pHTN, portal hypertension; TIPS, transjugular intrahepatic portosystemic shunt.

previously been defined (Figure 2), and we recommend using this to map vascular anatomy prior to any definitive therapy for bleeding GV to guide management discussions.[13,17] The presence of portosystemic shunts, splanchnic vein thromboses, other portal hypertensive complications, or other organ system failures or abnormalities should inform treatment options. For example, patients with noncirrhotic pHTN related to splenic vein thrombosis may best be managed with splenectomy, an option likely to be delayed or missed with endoscopic evaluation alone.[18] Therefore, cross-sectional imaging with either computed tomography or magnetic resonance imaging using portal venous phase of contrast is necessary in planning definitive therapy for GV.

Management of bleeding GV is best done through a collaborative, multidisciplinary approach including hepatologists, interventional radiologists, and interventional endoscopists. When feasible, patients with bleeding GV should be treated at centers resourced with these specialists.

Primary Prophylaxis

Given the relative rarity of GV compared with EV, and less robust data regarding endoscopic and clinical predictors of bleeding risk, demonstration of benefit with specific approaches to primary prophylaxis is lacking. Available data are challenged by heterogeneity in patient populations studied, predictive risk factors assessed, and definitions utilized for bleeding outcomes. While available data are intriguing, without validation of these outcomes, practice guidelines have not supported any form of primary prophylaxis for GV.[19]

Initial Medical Management

Clinical presentation of acute GV hemorrhage is indistinguishable from other causes of acute upper gastrointestinal bleeding, though bleeding episodes do
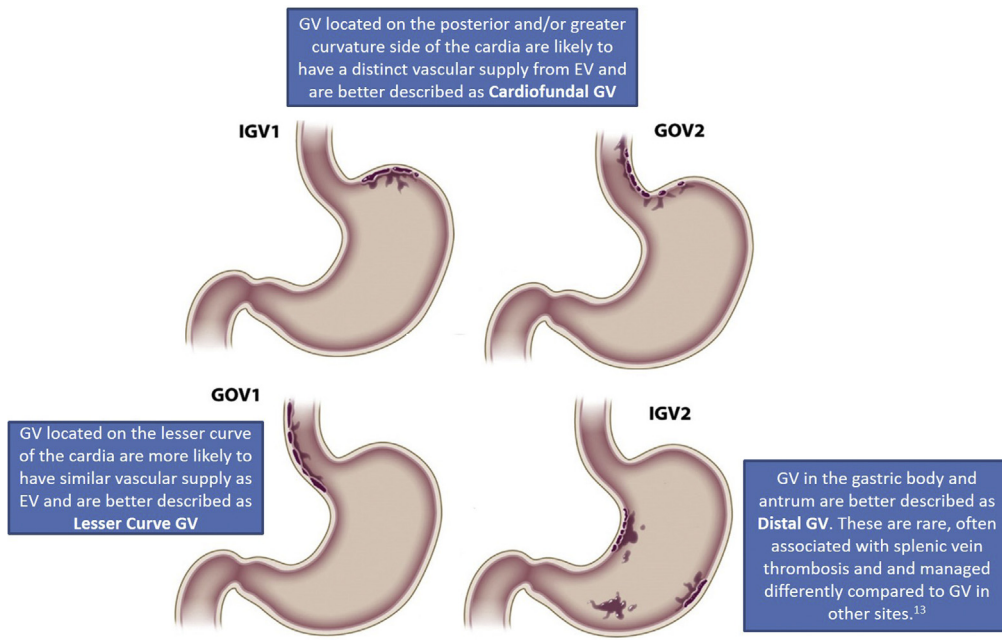
Figure 1. Recommended endoscopic classification system for GV. Although the Sarin classification is most commonly used in clinical practice, we recommend a simpler and intuitive classification system that includes cardiofundal GV, lesser curve GV, and distal GV. GOV1, gastroesophageal varices 1; GOV2, gastroesophageal varices 2; IGV1, isolated gastric varices 1; IGV2, isolated gastric varices 2.

tend to be more severe (greater transfusion requirements and higher mortality) compared with EV bleeding.[1,20] Initial management of patients with suspected pHTN bleeding should adhere to current practice guidelines, as summarized in Table 2.[3,19,21–29] Figure 3 represents a proposed algorithm for addressing GV bleeding based on both endoscopic and vascular anatomy.

Initial Endoscopic Evaluation and Temporizing Methods

The initial endoscopic evaluation should confirm bleeding source and attempt classification of variceal bleeding site. Preprocedural administration of a promotility agent and utilization of a therapeutic endoscope or advanced suctioning device are advised, as intragastric blood frequently obscures the cardia or fundus and underlying GV. Once the fundus is clear and GV identified, a standard classification system should be applied. It is also important to fully classify the presence of EV at the time of endoscopy per standard guidelines, as definitive therapies for bleeding GV vary in their effect on subsequent EV bleeding risk.[3,19,21]

Initial therapy for bleeding GV should focus on acute hemostasis for hemodynamic stabilization with a plan for further diagnostic evaluation or transfer to a center with expertise in GV management. Temporizing measures to halt active bleeding are often not the definitive treatment of choice to prevent rebleeding from GV, whereas definitive measures such as endoscopic cyanoacrylate injection (ECI) or endovascular treatments are often not feasible in the acute, diagnostic setting.

When active GV bleeding is encountered, any available therapy should be employed to stop the bleeding based on the resources available to the endoscopist and local expertise. Endoscopic sclerotherapy with alcohol-based agents (eg, ethanolamine) achieve marginal initial hemostasis, high incidence of early rebleeding, and risk development of deep ulcerations.[3,30–32] As such, we do not recommend this modality unless no other options are available. Band ligation, while inferior to cyanoacrylate for long-term bleeding control of cardiofundal GV, can result in initial hemostasis rates of 45%–93% and thus is a reasonable temporizing modality but must be followed by a more definitive therapy.[33,34] For lesser curve GV, band ligation not only is a temporizing measure, but also is often the best definitive therapy, given their similarity to EV. There are case reports of other endoscopic modalities in achieving initial hemostasis for bleeding GV, but there are insufficient data for efficacy and safety to endorse these approaches.[35–38] We do not recommend the routine use of procoagulants, such as activated factor VII, owing to risk for thrombotic complications and absent data to support efficacy in GV bleeding. Although ECI can be highly effective in achieving initial hemostasis, the logistics involved in performing ECI limit its utility during the initial diagnostic endoscopic examination. Additionally, defining the vascular anatomy (ie, the presence of thrombosis or shunting) may affect the results of ECI; therefore, we would not recommend its use as a temporizing measure absent other options.

Gastric compression balloons (Sengstaken-Blakemore tube or Linton-Nachlas tube) are highly effective at temporizing bleeding from cardiofundal and lesser curve GV, but the acquisition of competency in this procedure is hindered by the relative rarity of GV bleeding events.[16,39] Specific details on balloon placement and avoiding certain pitfalls can be found in prior publications.[16,40] When utilizing this approach, we recommend inflating only the gastric balloon and proceeding to definitive therapy as quickly as possible because
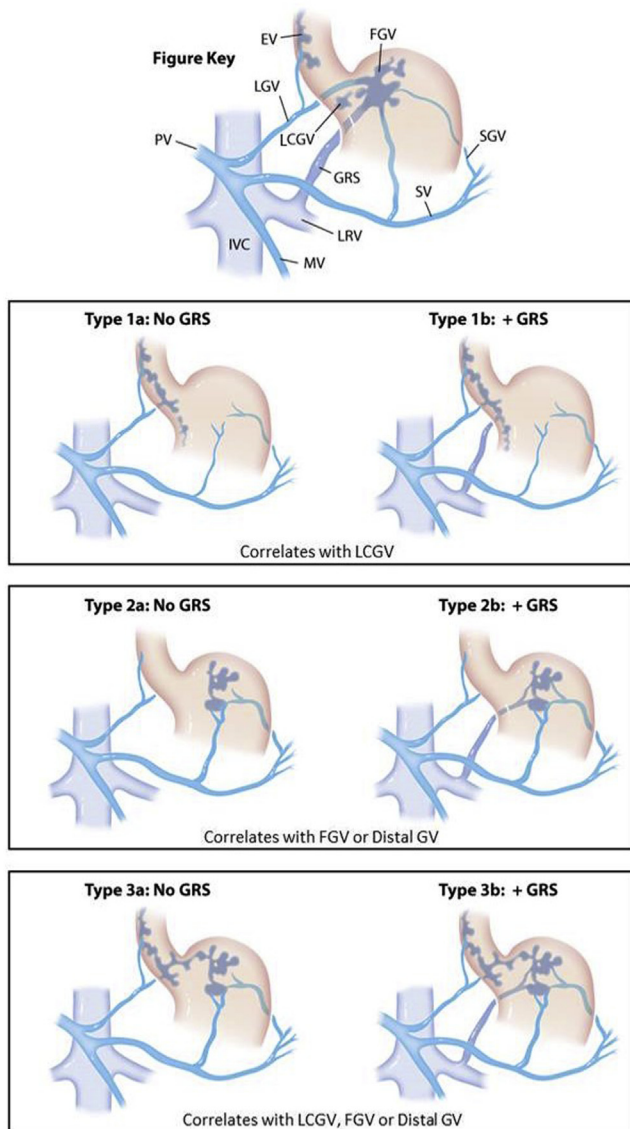
Saad-Caldwell Classification

Figure 2. Recommended vascular classification system for GV. The Saad-Caldwell classification system[17] describes variations of afferent flow into the GV as well as efferent flow through portosystemic shunts. FGV, fundal gastric varices; IVC, inferior vena cava; LCGV, lesser curve gastric varices; LGV, left gastric vein; LRV, left renal vein; MV, mesenteric vein; PV, portal vein; SGV, short gastric veins; SV, splenic vein.

prolonged balloon tension may precipitate mucosal breakdown.

Definitive Endoscopic Management for Bleeding GV

Current international guidelines recommend endoscopic therapy as the preferred definitive modality for GV bleeding, though much of this is based on poor-quality data.[19] Of the various endoscopic approaches to therapy for GV,[30–39] the most widely accepted method remains ECI.[15,41–45] Since it was introduced in the 1980s, ECI has been shown to be effective at preventing both early and late rebleeding, with fewer complications compared with alcohol-based sclerotherapy or band ligation.[42–44]

Studies comparing endoscopic interventions for GV have not stratified outcomes by classification (ie, lesser curve GV vs cardiofundal GV), limiting conclusions regarding the efficacy of therapeutic approaches according to type of GV. Large size and mass-like configuration of cardiofundal GV can make band ligation difficult, while injection of cyanoacrylate into the deeper submucosal varices represents a physiologically superior technique. Therefore, we recommend that ECI be considered the only definitive endoscopic therapy for cardiofundal GV. Alternatively, lesser curve GV, which typically extend from EV, typically respond well to band ligation, given their similarity to EV. If imaging to classify underlying vascular anatomy is available prior to definitive therapy, band ligation can be planned prospectively; without pre-endoscopic determination of vascular anatomy, it is reasonable to pursue band ligation in the acute setting for bleeding GV located on the lesser curve.

The best method of ECI is highly debated, with multiple publications supporting various techniques.[41–45] The success of any method of ECI for GV is influenced by choice of cyanoacrylate formulation, use of co-mixture agents, preparation of materials, and steady, uniform injection delivery. Currently, no formulation of cyanoacrylate is Food and Drug Administration approved for use as a long-term implant into vascularized human tissue; however, in practice, it is routinely used to treat GV. Direct comparative studies of ECI techniques have not been undertaken, and most reports derive from case series. Ideally, the specific cyanoacrylate agent should favor the fastest polymerization time to avoid embolization and inducing GV bleeding. Based on limited prior data, the 4 carbon (butyl) preparations of cyanoacrylate polymerize much faster than the 8 carbon (octyl) preparations and have more data to support their use.[46] Plant-based oils, such as lipiodol, were previously used to determine radiographic success with ECI. We do not advocate adding plant-based oils to cyanoacrylate for injection of bleeding GV, as radiographic confirmation of success is unnecessary and this method may increase distal embolization risk.[46] Supplementary Figure 1 outlines procedural details of ECI.

Complications specific to ECI include embolization of the glue thrombus, impaction of the needle into the GV, exacerbation of bleeding, portal vein thrombosis, and infection. The most reported and feared complication is glue embolization leading to pulmonary embolus or stroke. However, in the largest series of ECI to date, the embolization rate was 0.7%.[47] Many studies have defined embolization events through incidental radiographic identification of very small regions of lipiodol uptake within the lungs. Rates of clinically significant embolization leading to symptoms, need for

anticoagulant therapy, or death are very rare.[47] Impaction of the injector needle into the GV has only been reported in case reports, not in larger series, suggesting that although this is possible, it may be related to endoscopist experience, outlining the need for specific training in these techniques.[48] Likewise, induction of GV bleeding with needle injection into a pressurized system is rare and, if the glue is injected immediately after needle insertion, should not exacerbate bleeding (see Supplementary Figure 1). Portal and splenic vein thrombosis are also extremely rare.[47] Last, infections have been reported (in case series) primarily in patients presenting with active bleeding (who should receive antibiotic prophylaxis per practice guidelines).[3,19,21]

ECI should only be performed by endoscopists who have undergone specific training and have experienced interventional radiologists available in the event of complication. Endoscopic ultrasound (EUS)–guided procedures have been developed to improve precision and safety of ECI. Borrowing from interventional radiology techniques, EUS-guided interventions involve placement of hemostatic coils and/or glue into the varices via fine needle aspiration needle.[49–52] Large case series have demonstrated efficacy and safety of this technique, but it has not been directly compared with standard ECI. Potential advantages of an EUS-based approach include real-time assessment of Doppler flow and reduced embolization risk. Further evaluation of EUS techniques, optimal coil and needle selection, and outcomes in comparison with ECI are necessary before routine use can be recommended.

Follow-up to endoscopic management of GV should mimic that of endoscopic management for EV. Although data suggest that rebleeding occurs late (months) after the index bleed, prompt endoscopic reassessment may reduce these events. For both lesser curve and cardiofundal GV, we recommend repeat endoscopic evaluation every 2–4 weeks until obliteration is complete. At follow-up, palpation of a previously treated cardiofundal GV should be performed with a blunt tipped instrument or Doppler probe. Areas noted to dimple or invert merit repeat ECI. For lesser curve GV, band ligation should be repeated as per EV eradication. After endoscopically confirmed GV eradication, repeat endoscopic assessment should be performed within 3–6 months and then yearly thereafter. For de novo or recurrent GV on long-term (>12 months) follow-up, we recommend repeating cross-sectional imaging and discussing the case in a multidisciplinary fashion to explore potential mechanisms contributing to the change in GV and alternative treatment options such as an endovascular approach.

Definitive Endovascular Management of GV

Endovascular therapy for bleeding GV was introduced over 30 years ago, when the vascular anatomy was defined by Watanabe and colleagues.[14] Balloon-occluded retrograde transvenous obliteration (BRTO) was developed in the mid-1990s and has undergone multiple iterations to optimize success.[53,54] Around the same time, the TIPS procedure was also applied to the management of GV.[56,57] Determining the optimal procedure for endovascular treatment of GV is hampered by heterogeneity of prior studies and lack of uniform imaging or population selection. Likewise, determining when endovascular therapies are best used over endoscopic intervention is fraught with insufficient evidence; however, we will outline the advantages and risks of each. Endovascular management of GVs should only be performed as treatment for proven GV bleeding, either electively or emergently (after or during the first sentinel bleed, respectively).

TIPS for Management of GV

TIPS is an effective therapy to reduce portal pressure, halt active EV bleeding, and prevent rebleeding.[55–58] Although not as efficacious in patients with GV, it has shown success in initial hemostasis and rebleeding.[59–61] Prior studies of TIPS for bleeding GV have reported reduced rebleeding compared with ECI, but failure to effectively delineate between lesser curve and cardiofundal GV profoundly limits assessment of TIPS utility.[60,61] Cardiofundal GV bleed at lower portal pressures and further reduction of portal pressures with TIPS may allow for up to 50% of GV to rebleed.[18] While direct comparisons of TIPS with ECI suggest similar efficacy in initial hemostasis with slightly better rates of long-term rebleeding with TIPS, they also suggest added costs and increased complications (encephalopathy) with TIPS placement.[60,61] In contrast to cardiofundal varices, TIPS placement should be favored for bleeding from lesser curve GV that is refractory to band ligation or for patients with recurrent bleeding, similar to management of EV.

The risks of TIPS (hepatic encephalopathy and hepatic ischemia) may be greater in the presence of a GRS, often associated with cardiofundal GV.[62] In a meta-analysis comparing TIPS and BRTO for management of cardiofundal GV, there were no significant differences in initial hemostasis rates or procedure-related complications, but BRTO had less rebleeding and encephalopathy.[63] For cardiofundal GV, TIPS is most efficacious in combination with direct embolization or endovascular sclerosis to ensure GV obliteration.[64] In some cases, portal hypertensive complications (ascites, EV) may be too severe for BRTO to be feasible. In those cases, TIPS allows for decompression of the portal system with direct endovascular sclerosis to the GV itself.[64]

Endoscopic examination should be performed 1 month after TIPS to ensure resolution of the GV. Without direct obliteration of cardiofundal GV, continued flow through the varices is likely following TIPS (though GV that are shrinking may not require additional therapy). Stable or enlarging cardiofundal GV merit subsequent ECI or BRTO. Following TIPS, therapy with ECI carries an increased risk for glue embolization or portal vein

Table 2. Evidenced-Based Algorithm for Initial Management of Suspected Portal Hypertensive Bleeding

Assess circulatory status[3,21,22]	Ensure adequate vascular access (2 large-bore peripheral intravenous cannulae or central venous access) and provide fluid resuscitation (colloid or crystalloid).
Assess respiratory status[19,22]	Tracheal intubation advised for active hematemesis, inability to maintain or protect airway, and as needed to provide optimal sedation to complete endoscopic examination and therapy.
Vasoactive drug administration[3,23–25]	• Administration associated with reduced mortality and transfusion requirements. • Octreotide (somatostatin analog) initial intravenous bolus of 50 μg (can be repeated in first hour if ongoing bleeding). • Continuous intravenous infusion of octreotide 50 μg/h for 2–5 d (may stop after definitive hemostasis achieved). • Somatostatin analogs inhibit gastric acid secretion (co-administration of proton pump inhibitor not required).
Antibiotic prophylaxis[26]	• Prophylactic antibiotics reduce infections, rebleeding, and mortality. • Intravenous ceftriaxone 1 g/24 h (maximal duration 7 d).
Restrictive red blood cell transfusion[3,27]	• Transfuse at Hgb threshold of 7 mg/dL and goal maintenance Hgb of 7–9 mg/dL. • Restrictive transfusion associated with favorable effect on hepatic venous pressure gradient, decreased mortality, and decreased rate for early rebleeding.
Evaluate coagulation parameters[3,28]	• GV bleeding is precipitated by portal hypertension rather than a bleeding diathesis. Measuring and characterizing the hemostatic profile in cirrhosis is complex and high-quality data to guide practice are limited. • Overuse of blood products in cirrhosis carries significant risk, including precipitation of portal venous thrombosis. • Owing to conflicting data in the literature, there is no data-driven specific international normalized ratio or platelet cutoff in which procedural bleeding risk is reliably increased; therefore, specific transfusion cutoffs cannot be recommended. • Although low fibrinogen levels have been associated with increased bleeding risk in critically ill patients with cirrhosis, a specific threshold for transfusion has not been clinically validated. Cryoprecipitate and fibrinogen factor replacements are low-volume products effective at increasing fibrinogen levels, but a specific recommendation for transfusing these products cannot be made at this time.
Urgent endoscopic assessment for source of bleeding and provision of initial hemostasis[3,21,29]	• Following stabilization of circulatory and respiratory status, within 12 h of presentation (as soon as possible). • Consider administration of erythromycin before emergency endoscopy (250 mg intravenous, 30–120 min before) to optimize visualization (check QT interval prior to administration).
Intensive inpatient setting[19]	Patients with acute variceal hemorrhage should be managed within the intensive care unit or other well-monitored units, given the risk for mortality and complexity of care required.

Hgb, hemoglobin.

thrombosis and, as such, BRTO is favored. Alternatively, subsequent direct GV embolization through the patent TIPS can be pursued. When TIPS is combined with direct obliteration of GV, then follow-up endoscopy should include a through-the-scope audible Doppler probe or EUS to evaluate for persistent flow in the GV. If present, ECI can be performed to "complete" therapy with subsequent endoscopic follow-up, as noted previously. If lesser curve GV persist after TIPS, then subsequent band ligation should be performed until eradication.

BRTO for Management of Cardiofundal GV

Conventional BRTO is a procedure in which cardiofundal GV are approached with an indwelling occlusive balloon from the systemic veins via a GRS. Up to 85% of cardiofundal GVs are associated with a left-sided spontaneous portosystemic shunt (GRS), which drains the GV and empties in the left renal vein, but conventional BRTO has also been described via less common portosystemic shunts.[17] In an attempt to reduce the dwell time of the balloon and shorten procedure duration, accelerated BRTO techniques have been developed in which the indwelling balloon is replaced with permanent alloy-based hardware such as coils (CARTO [coil-assisted retrograde transvenous obliteration]) or vascular-plugs (PARTO [plug-assisted transvenous obliteration]).[54] These modalities are not supported with the same volume of data as conventional BRTO, and although they are physiologically plausible, it is unclear if outcomes are equivalent.
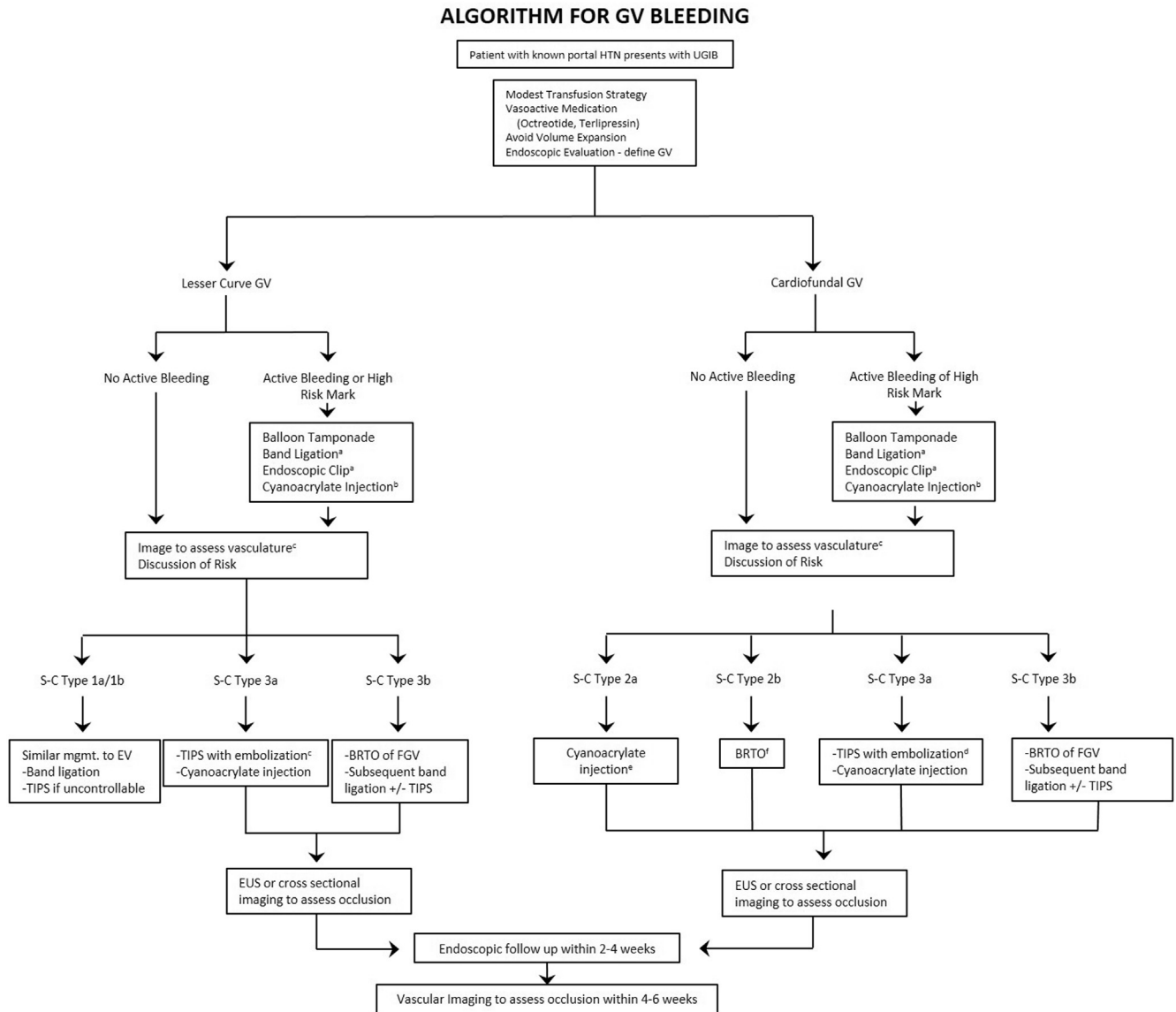
ALGORITHM FOR GV BLEEDING

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                    ┌─────────────────────────────────────────┐
                    │ Patient with known portal HTN presents   │
                    │ with UGIB                                 │
                    └─────────────────────────────────────────┘
                    ┌─────────────────────────────────────────┐
                    │ Modest Transfusion Strategy              │
                    │ Vasoactive Medication                    │
                    │   (Octreotide, Terlipressin)             │
                    │ Avoid Volume Expansion                   │
                    │ Endoscopic Evaluation - define GV        │
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Figure 3 algorithm:

Lesser Curve GV
- No Active Bleeding
- Active Bleeding or High Risk Mark → Balloon Tamponade / Band Ligation[a] / Endoscopic Clip[a] / Cyanoacrylate Injection[b] → Image to assess vasculature[c] / Discussion of Risk
  - S-C Type 1a/1b → Similar mgmt. to EV / -Band ligation / -TIPS if uncontrollable
  - S-C Type 3a → -TIPS with embolization[c] / -Cyanoacrylate injection
  - S-C Type 3b → -BRTO of FGV / -Subsequent band ligation +/- TIPS
  - → EUS or cross sectional imaging to assess occlusion

Cardiofundal GV
- No Active Bleeding
- Active Bleeding of High Risk Mark → Balloon Tamponade / Band Ligation[a] / Endoscopic Clip[a] / Cyanoacrylate Injection[b] → Image to assess vasculature[c] / Discussion of Risk
  - S-C Type 2a → Cyanoacrylate injection[e]
  - S-C Type 2b → BRTO[f]
  - S-C Type 3a → -TIPS with embolization[d] / -Cyanoacrylate injection
  - S-C Type 3b → -BRTO of FGV / -Subsequent band ligation +/- TIPS
  - → EUS or cross sectional imaging to assess occlusion

→ Endoscopic follow up within 2-4 weeks

→ Vascular Imaging to assess occlusion within 4-6 weeks

Figure 3. Recommended algorithm for multidisciplinary approach to management of GV. [a]Temporizing options should be chosen based on local expertise and available resources; [b]Cyanoacrylate injection is often not feasible in the acute setting and is more safely used as definitive treatment once imaging has been obtained. [c]In patients with lesser curve GV alone, some cases may sufficiently be treated similar to EV without imaging to assess underlying vasculature. However, in cases of active bleeding, multifocal GV, or concerns for thrombosis or shunt, then imaging should follow initial endoscopic assessment and temporizing measures. [d]TIPS alone is often insufficient to control bleeding from cardiofundal GV and should be combined with direct embolization. [e]In the absence of a GRS cyanoacrylate injection is the best option for managing cardiofundal GV. [f]In the presence of a GRS, BRTO is the best option for managing cardiofundal GV absent severe complications of pHTN. S-C, Saad-Caldwell.

BRTO, with all its technical variations, is a safe and effective treatment for bleeding GVs, with cessation of active bleeding in over 90% of cases and very low rebleeding rates.[54,65–67] Unfortunately, there are no randomized controlled studies with adequate sample size to validate these retrospective results. The intention-to-treat rebleed rate from GVs after BRTO is consistently <5%–7% at 1 year.[67] However, the overall upper gastrointestinal bleeding rate is higher and varies considerably in retrospective studies. The most common cause of post-BRTO bleeding is EVs that are commonly exacerbated after BRTO; up to 30%–35% will progress in size after the procedure.[68,69]

Other complications following BRTO include development or exacerbation of ascites or hepatic hydrothorax.[70] Clinically evident or symptomatic ascites or hydrothorax requiring an intervention occur in approximately 15% of patents within a year after BRTO and are present in up to 35%–40% of patients by imaging.[71] On the contrary, hepatic encephalopathy improves significantly after BRTO, and its incidence is 0%–5% at 1 year after the procedure. In fact, one of the indications of BRTO is type B (portosystemic shunt related) hepatic encephalopathy.[70–73] Contrary to the acutely depressed liver function that can be seen after TIPS, liver synthetic function may actually improve after BRTO due to the

increase in portal blood flow to the liver, though no impact on patient outcomes has been demonstrated.[74]

EUS should be performed within 48 hours after BRTO to confirm obliteration of GV, evaluate for exacerbation of EV, and obtain a new baseline after the procedure. Subsequent endoscopic surveillance is dependent on findings and need for additional management of EV. Minimal areas within the GV that are not obliterated will usually thrombose spontaneously within 1–2 months post-BRTO. Four to 6 weeks after the procedure, a clinic visit coupled with laboratory evaluation and contrast-enhanced computed tomography or magnetic resonance is recommended.[75] This imaging serves to confirm obliteration of the gastric variceal system, evaluate for new shunts, and identify complications such as splenic vein thrombosis, portal vein thrombosis, or compromise of the left renal vein from hardware or sclerosant. An additional contrast-enhanced computed tomography or magnetic resonance should be performed at 3 and 6 months and subsequently as clinically indicated.

We recommend repeat upper endoscopy within 2 weeks of BRTO in patients with high-risk EV at the time of BRTO and within 4–6 weeks for those patients with low-risk EV. Treatment of EV, as needed, should then follow standard guidelines based on endoscopic findings and risk assessment.[3]

Conclusions

Bleeding GV is a rare complication of portal hypertension but is typically more severe with higher mortality than other portal hypertensive bleeding. The diagnostic and treatment algorithms of bleeding GV are complex and require a multidisciplinary team approach to management, often at a tertiary care center where multiple options for therapy are available. Given the heterogeneity of prior research and lack of uniform definitions or standardized outcomes in this field, it is difficult to provide strong, evidence-based recommendations. Large studies to define the natural history of GV, risk factors for bleeding, and optimal diagnostic and therapeutic interventions are needed to improve understanding and management of this condition.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2021.01.027.

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Preparation

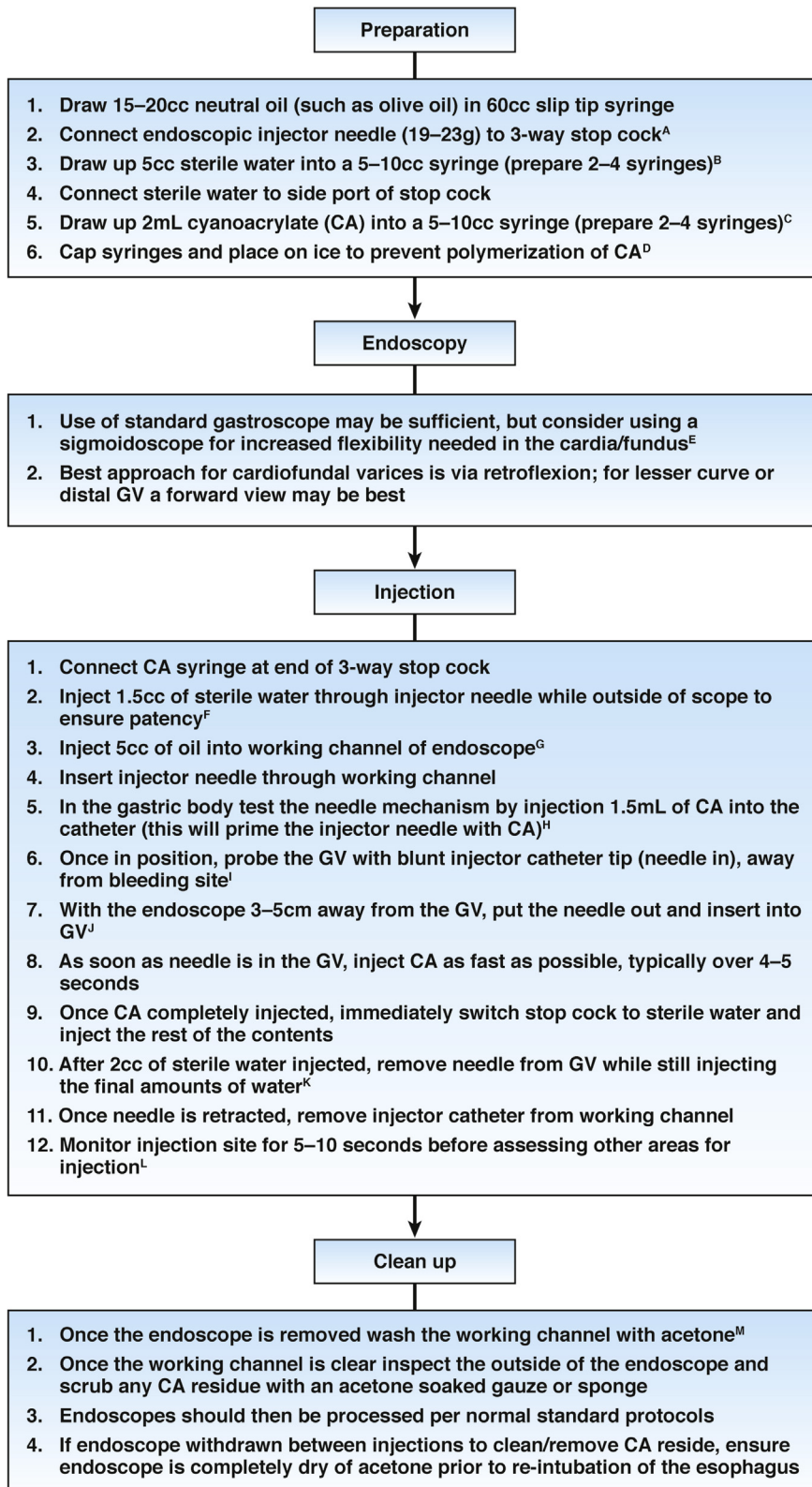1. Draw 15–20cc neutral oil (such as olive oil) in 60cc slip tip syringe
2. Connect endoscopic injector needle (19–23g) to 3-way stop cock[A]
3. Draw up 5cc sterile water into a 5–10cc syringe (prepare 2–4 syringes)[B]
4. Connect sterile water to side port of stop cock
5. Draw up 2mL cyanoacrylate (CA) into a 5–10cc syringe (prepare 2–4 syringes)[C]
6. Cap syringes and place on ice to prevent polymerization of CA[D]

Endoscopy

1. Use of standard gastroscope may be sufficient, but consider using a sigmoidoscope for increased flexibility needed in the cardia/fundus[E]
2. Best approach for cardiofundal varices is via retroflexion; for lesser curve or distal GV a forward view may be best

Injection

1. Connect CA syringe at end of 3-way stop cock
2. Inject 1.5cc of sterile water through injector needle while outside of scope to ensure patency[F]
3. Inject 5cc of oil into working channel of endoscope[G]
4. Insert injector needle through working channel
5. In the gastric body test the needle mechanism by injection 1.5mL of CA into the catheter (this will prime the injector needle with CA)[H]
6. Once in position, probe the GV with blunt injector catheter tip (needle in), away from bleeding site[I]
7. With the endoscope 3–5cm away from the GV, put the needle out and insert into GV[J]
8. As soon as needle is in the GV, inject CA as fast as possible, typically over 4–5 seconds
9. Once CA completely injected, immediately switch stop cock to sterile water and inject the rest of the contents
10. After 2cc of sterile water injected, remove needle from GV while still injecting the final amounts of water[K]
11. Once needle is retracted, remove injector catheter from working channel
12. Monitor injection site for 5–10 seconds before assessing other areas for injection[L]

Clean up

1. Once the endoscope is removed wash the working channel with acetone[M]
2. Once the working channel is clear inspect the outside of the endoscope and scrub any CA residue with an acetone soaked gauze or sponge
3. Endoscopes should then be processed per normal standard protocols
4. If endoscope withdrawn between injections to clean/remove CA reside, ensure endoscope is completely dry of acetone prior to re-intubation of the esophagus

Supplementary

Figure 1. Recommended method for endoscopic cyanoacrylate (CA) therapy. [A]Two-milliliter aliquots allow a good volume of CA to be injected without increasing risk of embolization, needle impaction, or need for many repeated injections. [B]Placing the syringe of CA on ice helps prevent polymerization of the glue within the syringe. Once the glue is drawn into syringes, proceed with the endoscopy as soon as possible to avoid this. [C]Sterile water should be used over normal saline, as saline may interact with CA and cause rapid polymerization within the injector catheter. All of your materials and tools should be tested in an ex vivo setting prior to ever performing endoscopic CA injection in a patient. [D]You should not use an injector needle <23 gauge, as the CA is increasingly difficult to inject through smaller-gauge needles. [E]A flexible sigmoidoscope (not often used in modern practice) typically has increased flexibility as compared with a gastroscope and allows for easier access to the posterior wall of the cardia and fundus for CA injection. [F]This is to ensure that the injector needle is patent and working correctly before you insert into the working channel. A 23-gauge injector needle holds approximately 1.5 mL of fluid within the catheter, and you should inject just enough to see water leave the tip of the needle. [G]Oil is used to coat the working channel to prevent glue embolization within the endoscope. [H]Injecting 1.5 mL into the catheter clears the sterile water from your injector catheter and primes it with CA so that once you begin injection CA is immediately in contact with the inside of the vessel. [I]We recommend injecting away from a suspected site of bleeding to avoid inducing bleeding with needle insertion. [J]This distance is recommended to avoid splash-back of CA on the endoscope. [K]Ideally, this will clear the injector needle of any remaining CA and help avoid needle impaction into the gastric varices (GV) while removing the needle. [L]Some oozing from the site is expected but is typically minimal and self-limited. [M]Acetone (nail polish remover) is a strong astringent that will help break up polymerized CA.