Communication from the ASGE Technology Committee

TECHNOLOGY STATUS EVALUATION REPORT

ASGE American Society for Gastrointestinal Endoscopy

Endoscopic devices and techniques for the management of gastric varices (with videos)

Prepared by: the ASGE Technology Committee

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This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

Background and Aims: Gastric variceal bleeding occurs less commonly than bleeding from esophageal varices (EVs), although it is associated with higher morbidity and mortality. Bleeding from gastroesophageal varices type 1 (GOV1) is treated like EVs. In contrast, other forms of gastric variceal bleeding, including gastroesophageal varices type 2 (GOV2) and isolated gastric varices types 1 (IGV1) and 2 (IGV2), are treated with varying endoscopic approaches. Nonendoscopic methods include transjugular intrahepatic portosystemic shunt (TIPS) or balloon-occluded retrograde transvenous obliteration (BRTO). This technology report focuses on endoscopic management of gastric varices (GVs).

Methods: The MEDLINE database was searched through August 2022 for relevant articles by using key words such as gastric varices, glue, cyanoacrylate, thrombin, sclerosing agents, band ligation, topical hemostatic spray, coils, EUS, TIPS, and BRTO. The article was drafted, reviewed, and edited by the American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee and approved by the Governing Board of the ASGE.

Results: Endoscopic injection with cyanoacrylate (CYA) glue has been the primary endoscopic method to treat GVs. EUS-guided angiotherapy with CYA glue and coil embolization has emerged as an alternative method enabling improved detection of GVs with a high technical success for targeting and obliterating GVs. Combining CYA glue with coil therapy allows the coil to act as a scaffold for the glue, reducing the risk of glue embolization and improving outcomes. Alternative injectates or topical treatments have been described but remain poorly studied.

Conclusions: The mainstay paradigm for the endoscopic management of gastric variceal bleeding is the injection of CYA glue. The published success of EUS-guided angiotherapy using CYA glue with or without embolization coils has increased our treatment armamentarium. (Gastrointest Endosc 2025;101:496-510.)

(footnotes appear on last page of article)

The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methods are used, with a MEDLINE literature search to identify pertinent clinical studies on the topic and a Manufacturer and User Facility Device Experience (U.S. Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported adverse events of a given technology. Both are supplemented by accessing the "related articles" feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases data from randomized controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and web-based publications, proprietary publications, and informal

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communications with pertinent vendors. Technology status evaluation reports are drafted by 1 or 2 members of the American Society for Gastrointestinal Endoscopy Technology Committee, reviewed and edited by the committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. For this review, the MEDLINE database was searched through August 2022 for articles related to endoscopic therapy of gastric varices by using additional relevant key words such as "gastric varices," "Sarin classification," "cyanoacrylate," "thrombin injection," "interventional EUS," "topical hemostasis," "EUS-guided coil embolization," and "EUS-guided glue injection," among others. Technology status evaluation reports are scientific reviews provided solely for educational and informational purposes. Technology status evaluation reports on emerging technologies are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any treatment or payment for such treatment.

Gastric varices (GVs) are diagnosed in approximately 20% of patients with portal hypertension but bleed less commonly than esophageal varices (EVs), accounting for 2% to 5% of all acute variceal bleeds.[1] Gastric variceal bleeding is associated with higher rates of uncontrolled bleeding, recurrent bleeding, transfusion requirements, and mortality compared with esophageal variceal bleeding.[1-5] Treatment goals include immediate therapy to manage acute bleeding, to prevent early recurrence within 5 days (secondary prophylaxis), and to prevent 6-week mortality.[1-5]

Traditionally, acute gastric variceal bleeding has been challenging to treat endoscopically; however, advances in endoscopic therapy have resulted in alternative treatment options to endovascular approaches such as transjugular intrahepatic portosystemic shunt (TIPS) and balloon-occluded retrograde transvenous obliteration (BRTO). BRTO involves retrograde cannulation of the left renal vein accessed through the jugular or femoral vein, followed by balloon occlusion and slow infusion of sclerosant vascular plugs (ie, plug-assisted retrograde transvenous obliteration) or deployment of embolization coils (ie, coil-assisted retrograde transvenous obliteration) to obliterate the gastrorenal or splenorenal collateral and fundal varices.[6]

In patients with portal venous thrombosis ± splenic venous thrombosis, in the absence of a splenorenal or gastrorenal shunt, partial splenic embolization to decrease the spleen's contribution to elevated portal pressures is yet another strategy. Current American Association for the Study of Liver Diseases practice guidelines recommend the use of TIPS for bleeding from GVs that are either not endoscopically manageable or bleed recurrently despite pharmacologic and endoscopic interventions.[7]

TIPS is especially useful in patients with a known high portal pressure gradient without the presence of large portosystemic shunts. BRTO is considered for the management of fundal varices with large gastrorenal or splenorenal collaterals.[6] Although TIPS increases the risk of hepatic encephalopathy, BRTO has the potential to improve hepatic encephalopathy but at the expense of increased portal pressure and worsening of adverse events such as ascites or bleeding from EVs.[7]

CLASSIFICATION OF GVs

It is essential to understand the relevant vascular anatomy when determining an optimal intervention for hemostasis of GVs including traditional endoscopic, EUS-guided, and interventional radiologic alternatives.[3] GVs communicate as vascular collateral between the portal and systemic circulation (Fig. 1), commonly through the left gastric–azygos veins (gastroesophageal venous system) into the superior vena cava or through a gastrosplenic shunt and the inferior vena cava through the inferior phrenic veins (gastrophrenic venous system), or sometimes both. These drainage systems generally correspond to the endoscopic classification system proposed by Sarin et al.[1] This classification (Fig. 2) categorizes GVs based on their relationship with EVs and the location within the stomach. Junctional varices, also known as gastroesophageal varices (GOVs), are essentially an extension of EVs into the stomach arising from the left gastric vein. They are further subclassified based on their location into type 1 (GOV1; lesser curvature) and type 2 (GOV2; greater curvature). In contrast, nonjunctional varices are isolated GVs (IGVs) and are further subclassified into type 1 (IGV1; fundus) and type 2 (IGV2; outside of fundus). The blood supply for IGVs is typically from the short and posterior gastric veins, and they are often associated with large gastrorenal shunts originating below the lamina propria in the gastric submucosa.[1]

The classification of GVs has implications for determining the risk of bleeding and dictates the ideal therapeutic approach and predicted response to treatment.[8,9] GOV1 are treated like traditional EVs as described in a previous American Society for Gastrointestinal Endoscopy (ASGE) guideline document and are thus not discussed further.[10] This Technology Status Evaluation Report reviews the current endoscopic technologies and approaches for management of other GVs.

TECHNOLOGY UNDER REVIEW

Endoscopic therapy is often considered for the initial treatment of gastric variceal bleeding. The various endoscopic treatment modalities for gastric variceal bleeding include sclerotherapy, band ligation, obturation with glue, thrombin injection, hemostatic spray, and EUS-guided approaches

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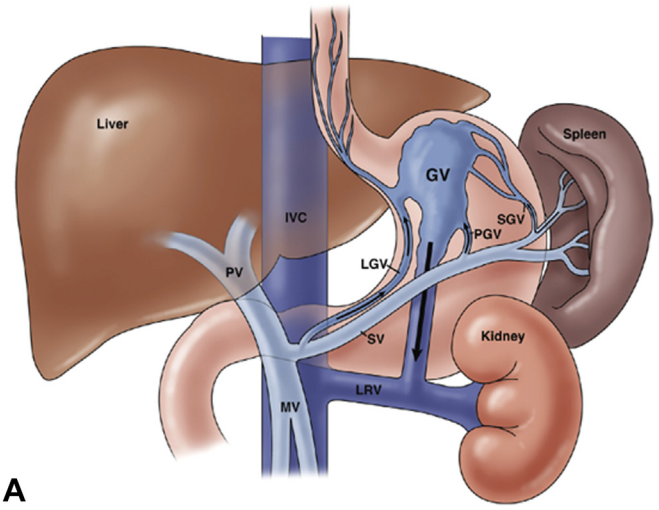

Figure 1. The vascular anatomy of the gastric variceal system demonstrating the gastric varix (GV) with the afferent vasculature (venous inflow) from the LGV, SGV, and PGV and the efferent vasculature (venous outflow) into the LRV forming the GV complex. *IVC,* Inferior vena cava; *PV,* portal vein; *LGV,* left gastric vein; *MV,* mesenteric veins; *LRV,* left renal vein; *SV,* splenic vein; *PGV,* posterior gastric vein; *SGV,* short gastric veins. (From Garcia-Pagán JC, Barrufet M, Cardenas A, et al. Management of gastric varices. Clin Gastroenterol Hepatol 2014;12:919-28, with permission.)

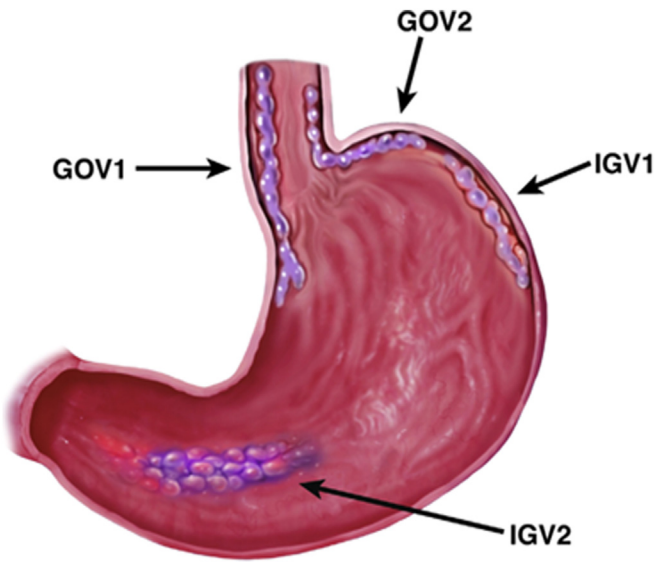

Figure 2. Sarin's classification of gastric varices. *GOV1*, Gastroesophageal varices type 1 (extension of esophageal varices along the lesser curvature of the stomach; *GOV2*, gastroesophageal varices type 2 (extension of esophageal varices along greater curvature of the stomach); *IGV1*, isolated gastric varices type 1 (exist in the gastric fundus and do not extend into the esophagus or the cardia); *IGV2*, isolated gastric varices type 2 (varices that occur outside the fundus of the stomach. (From Garcia-Pagán JC, Barrufet M, Cardenas A, et al. Management of gastric varices. Clin Gastroenterol Hepatol 2014;12:919-28, with permission.)

with glue injection and/or coil embolization. Injectants are U.S. Food and Drug Administration (FDA)-approved medications used in an off-label manner when applied for the endoscopic management of gastric variceal bleeding. Importantly, endoscopic management of acute gastric variceal hemorrhage cannot be undertaken until patients undergo resuscitative efforts and are deemed hemodynamically stable, including administration of prophylactic antibiotics using a third-generation cephalosporin or fluoroquinolone in patients with underlying cirrhosis.[8,9]

Endoscopic assessment and intervention typically occur within the first 12 to 24 hours after presentation. Treatment goals are to control active bleeding and urgently treat other high-risk stigmata of hemorrhage for GVs (eg, platelet plugs, adherent clots, or flat spots on EGD), prevent recurrent bleeding, interrupt the blood flow to the GV, and obliterate the GV for definitive hemostasis.

Endoscopic sclerotherapy

Sclerosants are synthetic chemicals or fatty acid derivatives that cause thrombosis and endothelial damage, leading to fibrosis and vascular obliteration. Endoscopic sclerotherapy (EST) was historically used for management of esophageal variceal hemorrhage but has since been supplanted by band ligation therapy. EST has also been studied for treatment of bleeding GVs; however, the use of sclerosing agents for the management of GOV2 and IGVs is not recommended when compared with alternative techniques because of a lack of efficacy and safety for this indication.

Several sclerosing agents are available (eg, ethanolamine oleate, sodium morrhuate, sodium tetradecyl sulfate, polidocanol ethanol or phenol) that are used in varying concentrations and volume. A previous ASGE technology status evaluation report discussed endoscopic variceal sclerotherapy indications and technique for injection.[10,11]

Endoscopic variceal ligation

Endoscopic variceal ligation (EVL) is the preferred initial therapeutic technique for management of EVs; however, it is not recommended as the first-line treatment for fundal type GVs for several reasons. First, the large size of GVs preclude complete capturing of the varix into the ligation cap. Second, thick overlying gastric mucosa with deeper vascular channels often results in incomplete eradication and a higher rate of postligation ulcers with resultant bleeding. If preferred treatment methods such as cyanoacrylate (CYA) glue or EUS-guided coil embolization are not available, EVL can be performed in the acute bleeding setting as a temporizing therapy to bridge to more definitive treatment methods.

Cyanoacrylate glue

CYAs are synthetic glues that rapidly polymerize into hard substances on contact with weak bases, such as water or blood.[12] Injection of CYA glue has become the standard endoscopic treatment for gastric variceal bleeding.[13,14] Injection of CYA glue is more effective and safer than EVL and EST in the context of acute bleeding and prevention

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of recurrent bleeding.[15,16] A previously published ASGE technology status evaluation report described the use of CYA glue in GI endoscopy.[12]

Several CYAs with different chemical structures and physical properties are available (Table 1). All these CYA formulations are considered off-label in the United States when used for endoscopic applications.[12] N-butyl-2-cyanoacrylate (4 carbon compounds) have a faster polymerization rate compared with 2-octyl-cyanoacrylate and N-butyl-2-cyanoacrylate plus methacryloxysulfolane (8 carbon compounds). N-butyl-2-cyanoacrylate–only compounds are sometimes mixed with Lipiodol (Ultra Fluid; Guerbert, Roissy, France), an oil-based radiopaque contrast agent allowing fluoroscopic visualization to confirm intravascular delivery of the glue.

Of note, the addition of Lipiodol to CYA glue is not widely used because of its unclear clinical benefit and delayed rate of polymerization, thus theoretically increasing the risk of systemic embolization.[12,15] Fluoroscopy can be used to visualize the distribution of the injectate when Lipiodol is mixed with CYA glue, potentially helping the endoscopist identify a safer, low-flow injection site as opposed to higher flow sites that may present an increased risk of embolic adverse events. When used, CYA–Lipiodol mixtures vary from .5 mL to .8 mL in a 1:1 proportion.

A standardized technique for glue injection for GVs has been proposed with demonstrated efficacy and safety[15] (Table 2 and Videos 1 and 2, available online at www.giejournal.org). Endoscopy staff and patients should use protective eyewear during glue preparation and injection.[12] The distal end of the endoscope should be lubricated, and the working channel of a large-channel endoscope is usually flushed with either silicone, olive oil, or Lipiodol to prevent glue adherence and scope damage.

A large-bore sclerotherapy needle (21 or 23 gauge) is primed with sterile water. Normal saline solution is not recommended as a primer because it may polymerize the glue prematurely. The CYA glue is drawn up in low-volume (2-3 mL) syringes, and several additional low-volume syringes filled with sterile water are prepared for flushing. A Luer lock catheter is recommended to allow rapid injection and prevent spraying of the injectate. Varices with bleeding or stigmata of bleeding are targeted first. Adjacent varices without stigmata can be treated during the same session or subsequent sessions. The targeted vessel is initially punctured with a saline solution–primed sclerotherapy needle followed by injection of .5-mL or 1.0-mL aliquot of CYA glue.[17]

Injecting first where the varix arises from the gastric wall, which is the furthest point away from the most bulging area of the varix, and then toward the more bulging area is advised. Severe back bleeding can occur if the most bulging area is injected initially. The ideal injection rate has not been determined, with experts advocating for injecting the CYA glue over 30 seconds, because a more-rapid injection will likely increase the embolization rate and a slower injection rate increases the risk of needle occlusion.[18]

There should be no resistance and no mucosal bulge during CYA glue delivery becasue this may indicate perivariceal injection. Glue injection is followed by a sterile water flush to remove the remaining CYA glue from the injection catheter into the GVs. The volume of flush is equivalent to the catheter dead space (typically 1.0-1.5 mL) and should be determined before the procedure for the specific catheter chosen. A maximum of 3 mL of sterile water flushing into larger varices may be needed after each injection. A back and forth vibration of the needle catheter during glue and water injection can reduce the risk of needle adherence in the varix. The needle is then retracted from the GVs, followed by flushing with additional sterile water to keep the needle patent. Endoscopists should refrain from withdrawing the injection catheter into the endoscope channel and avoid suctioning extruded glue into the endoscope for a minimum of 20 seconds to avoid endoscope damage. After several minutes, the injected varix is palpated with the injection catheter. If the varix remains soft, injection is repeated with 1-mL aliquots of CYA glue until the varix hardens, confirming obliteration. On average, 4.0 mL (range, 1-13 mL) of CYA glue is required.

Subtotal occlusion of GVs occurs within minutes of injection and total occlusion within hours followed by gradual necrosis of the overlying mucosa with a cast of the glue extruding into the gastric lumen within 3 months. Repeat endoscopy is generally performed at 2- to 4-week intervals to assess obliteration of the GV with additional injection of CYA glue until complete obliteration of the varix is accomplished. One to 3 sessions are needed on an average to achieve variceal obliteration. Surveillance endoscopy should be considered every 3 to 6 months after complete variceal obliteration is achieved; however, the optimal surveillance interval is unknown.[12,15,16]

Endoscopic thrombin injection

Human thrombin injection has been studied as an alternative to CYA glue because it may be technically easier to use without concerns for endoscope damage and with less risk of systemic embolization and treatment-induced gastric ulceration. Thrombin converts fibrinogen to fibrin, resulting in a fibrin clot to achieve hemostasis. Human-derived thrombin is commercially available in the United States as a standalone thrombin (Evithrom; Ethicon, Somerville, NJ, USA). Human thrombin is also available as a hemostatic matrix in conjunction with an absorbable gelatin sponge (Floseal [Baxter International Inc, Deerfield, Ill, USA] and Surgiflo [Ethicon]), in fibrin sealants (Tisseel [Baxter International Inc] and Evicel [Ethicon]), or as an onsite preparation from local blood banks (Table 3). There is no standard concentration for injection. For example, 1 study used the human thrombin portion of Tisseel reconstituted in calcium chloride to a volume of 2 mL and further diluted in sterile water for a total volume of 5

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TABLE 1. List of different commercially available cyanoacrylate glue preparations

Trade name	Manufacturer	Active component	Sold as	Polymerization rate	Lipiodol	Cost per ampule (U.S.$)	Available in the United States
Histoacryl	TissueSeal	N-butyl-2-cyanoacrylate	.5-mL liquid/ampule	Faster	Optional	27	Yes
Dermabond	Ethicon	2-Octyl-cyanoacrylate	.7-mL liquid/ampule	Slower	No	25	Yes
Glubran 2	GEM, Italy	N-butyl-2-cyanoacrylate + methacryloxysulfolane	.25-, .5-, and 1-mL liquid/ ampule	Slower	Optional	Not available	No
Liquiband	McKeeson	N-butyl-2-cyanoacrylate	.4-, .5-, and .8-mL liquid/ampule	Faster	No	30	Yes
Leukosan	BSN Medical	Blended 2-octyl and N-butyl cyanoacrylate	.7-mL liquid/ampule	Faster	Optional	30	No
SurgiSeal	Adhezion Biomedical	2-Octyl-cyanoacrylate	.35-mL ampule	Slower	No	20	Yes
DermaFlex	Chemence	2-Octyl cyanoacrylate	.7-mL liquid/ampule	Slower	Optional	26	Yes
Swiftset	Medtronic	N-butyl-2-cyanoacrylate	.8-mL ampule	Faster	No	33	Yes

The polymerization rate is variable and increases with glue concentrations. An example is that the initial polymerization time for N-butyl cyanoacrylate and Lipiodol has been evaluated between 5 and 10 seconds.[62]

TABLE 2. Technique for glue injection of gastric varices

Steps	Technique
Preinjection preparation	
1	Patient and all healthcare providers participating in the procedure wear eyewear to protect from CYA glue splash
2	Coat the tip and accessory channel of the endoscope with Lipiodol or silicone to minimize glue adherence
3	Determine the dead space of a large-bore injection catheter (21-23 gauge)
4	Prime the large-bore sclerotherapy needle (21-23 gauge) with sterile water or Lipiodol
5	Prepare CYA glue in 2- to 3-mL syringes and separate syringes with sterile water for flushing
6	Attach the Luer lock syringe containing the CYA glue to the injection catheter
Injection technique	
7	Puncture the targeted varix and inject 1.0-mL aliquots per puncture. Injection should flow without resistance or mucosal elevation indicating intravascular access
8	Flush the needle with sterile water (dead space volume) to clear the glue from the catheter
9	Retract the needle from the varix and wait a few minutes for glue polymerization
10	Palpate the varix with the catheter to confirm the varix has hardened
11	If the varix is still soft on palpation, repeat the injection steps until the varix hardens on repeat palpation

CYA, Cyanoacrylate.

mL, resulting in an effective concentration of 200 IU/mL.[19] Intravariceal injection was performed in aliquots of 1 mL into the varix. After thrombin administration, the needle was retracted and pressure applied with the injection device sheath for at least 1 minute to tamponade the varix. The varix was observed for another minute to confirm hemostasis. The average dose of injected thrombin per endoscopy was 1100 IU (range, 200-3000 IU).[19]

Topical hemostatic powders

Topical hemostatic agents may be used to temporarily control active bleeding in GVs but are not indicated for definitive therapeutic intervention for GVs. Four powder-based topical hemostatic agents are available: Hemospray (also known as TC-325; Cook Medical Inc, Winston-Salem, NC, USA), EndoClot PHS (Olympus America, Center Valley, Pa, USA), Nexpowder (Medtronic, Minneapolis, Minn, USA), and Ankaferd Blood Stopper (AndIlac, Istanbul, Turkey), which is not available in the United States (Table 4).[20]

Hemospray was FDA cleared in May 2018 for use in non-variceal GI bleeding and was discussed in a previous ASGE technology assessment report.[21] The Hemospray system consists of a delivery catheter (either 7F or 10F, both 220-cm long) connected to an integrated handle that contains the hemostatic powder, CO_2 cartridge, CO_2 activator knob, flow valve, and a trigger button. Once the CO_2 cartridge is activated, the spray is applied in short 1- to

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TABLE 3. List of different commercially available human thrombin preparations available for medical use

Trade name	Manufacturer	Material/composition	Sold as	Cost per ampule (U.S.$)	Available in the United States
Surgiflo	Ethicon	Human thrombin and porcine gelatin	8 mL Surgiflo Hemostatic Matrix Kit with thrombin	300	Yes
Floseal	Baxter	Human thrombin and bovine gelatin	5 or 10 mL	450 or 650	Yes
Recothrom	Baxter	Recombinant thrombin (genetically modified Chinese hamster ovary cell line)	5000 units or 2000 units per vial	103 or 412	Yes
Evithrom	Ethicon	Thrombin, topical (human)	800-1200 IU/mL in 2-, 5-, or 20-mL vials	82, 117, or 458	Yes
Tisseel (fibrin sealant)	Baxter	Human thrombin and human sealer protein	Thrombin component 400-625 units/mL; other components included in kit are 2, 4, or 10 mL	193, 322, or 778	Yes
Evicel (fibrin sealant)	Ethicon	Human thrombin and biologic active component 2 (human fibrinogen)	Thrombin component 800-1200 IU/mL in kit of 2, 4, or 10 mL	4 mL = 302	Yes

TABLE 4. List of commercially available hemostatic powders

	Average cost (U.S.$)
Hemospray (Cook Medical Inc, Winston-Salem, NC, USA)	2500
EndoClot PHS (Olympus America, Center Valley, Pa, USA)	2600*
Nexpowder (Medtronic, Minneapolis, Minn, USA)	750

*EndoClot air compressor is a separate added purchase.

2-second bursts to the bleeding site.[21] In patients with GVs, a more diffuse approach is generally applied unless an area of spurting is seen.[22] There is no universal protocol defining the amount of Hemospray needed to achieve hemostasis for GVs; however, manufacturer recommendations should be followed not to exceed 3 Hemospray devices per patient.

Ankaferd Blood Stopper is a combination of plant extracts used in traditional Turkish medicine that is available in liquid form (AND İlaç, Istanbul, Turkey). The product is instilled or flushed onto the bleeding areas by a catheter. Current studies in the treatment of GVs apply 7 mL to 25 mL of Ankaferd Blood Stopper to form a gray-yellow coagulum in the stomach that when effective achieves hemostasis within minutes. Currently, there are no published reports of EndoClot or Nexpowder in the treatment of GVs.[23]

EUS-guided angiotherapy

EUS offers diagnostic and therapeutic advantages over conventional endoscopy for the treatment of GVs. EUS offers real-time Doppler imaging enabling detection and precise targeting of perforating and collateral vessels that often account for uncontrolled or recurrent gastric variceal bleeding.[18] EUS can distinguish varices from prominent gastric folds and other confounding submucosal lesions, increasing the rate of gastric variceal detection by 6-fold.[24] GVs can be confirmed with EUS when direct endoscopic visualization is obscured by active bleeding, and EUS facilitates the accurate delivery of a hemostatic agent into the varix, minimizing paravariceal injection. EUS may also precisely direct therapy into either the largest vein in a gastric variceal bundle or the perforating vessel, theoretically resulting in more-effective treatment with a reduced quantity of the hemostatic agent.[25] Finally, Doppler US can assess the adequacy of treatment (eg, decreased or cessation of blood flow) in real time. This approach may result in improved rates of gastric variceal obliteration and fewer endoscopic sessions, thus translating into a reduction in interval recurrent bleeding [26-28]

EUS-guided injectables. Under EUS guidance, the targeted vessel and its course can be mapped to determine the ideal injection site as well as locations to avoid.[18] Some studies recommend endosonographic venography using 5 to 10 mL of water-soluble contrast to confirm the intravascular location and to study varix flow trajectory (afferent or efferent) under fluoroscopy.[29,30] The properties and application techniques for the various CYA glues were discussed above. In contrast to conventional endoscopic glue injection, EUS guidance uses a more dilute 2:1 mixture of 2-octyl-cyanoacrylate and Lipiodol when using a 22-gauge needle versus a 2.5:.5 mixture when using a 19-gauge needle. The FNA needle is preloaded with CYA glue to avoid the need to remove the stylet once the needle is in the vessel, thus minimizing the risk of glue occlusion within the needle.

Given the risk of systemic embolization of CYA glue and potential damage to the echoendoscope, alternative hemostatic agents have been proposed for EUS-guided

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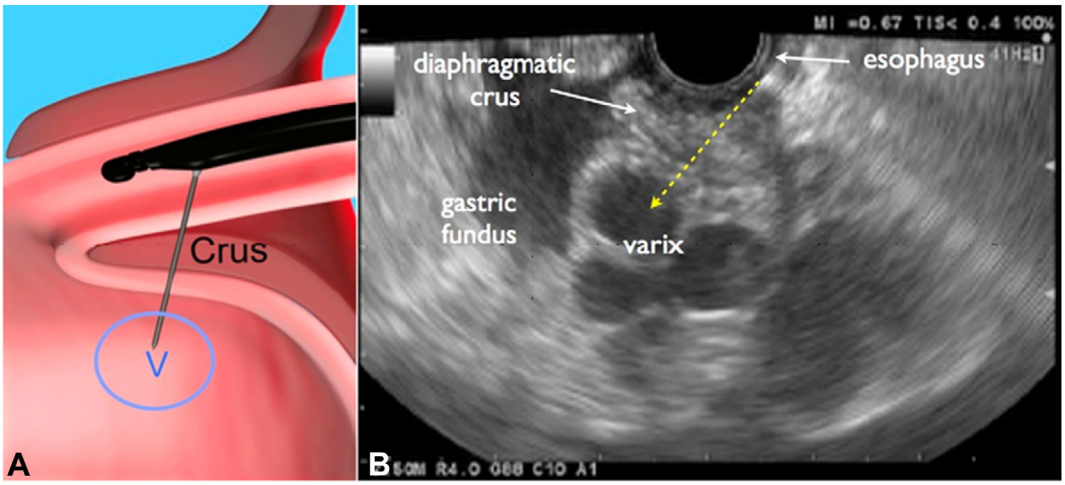

Figure 3. Transcrural approach to gastric fundal varices. **A,** Anatomic diagram. **B,** EUS view. The *yellow dashed line* is the direction of the injection needle. *V*, Fundal varix. (From Cameron R, Binmoeller CF. Cyanoacrylate applications in the GI tract, Gastrointest Endosc 2013;77:846-57, with permission.)

injection.[31] Injection of thrombin has been reported until the gastric variceal flow is obliterated on color Doppler or until a maximum of 10,000 IU of thrombin is administered.[31] Other hemostatic agents studied include an absorbable gelatin sponge that is a collagen-based material widely used in interventional radiology and surgery.[29] EUS can be used to inject 1 to 3 mL of the absorbable gelatin sponge (Gelfoam [Pfizer, New York, NY, USA] or Surgiflo [Ehticon]) as a liquid slurry for obliteration of the GV (mixed with a 1:1 solution of saline solution and contrast).[29]

EUS-guided coil embolization with or without CYA glue injection. Coil embolization is a hemostatic technique adopted from interventional radiology. Coils (Tornado and Nester Embolization Coils; Cook Medical Inc) are made of a nickel-based super alloy (magnetic resonance imaging conditional up to 3 T) and contain radially expanding synthetic fibers that induce clot formation and hemostasis (Table 5). These fibers can serve as a scaffolding for CYA glue polymerization and prevent glue embolization when injected in the same endoscopic session.[32] The space-occupying effect of the coil along with CYA glue retention by the coil's synthetic fibers augments obliteration of the varix with less volume of CYA glue required.[33]

Embolization coils range in length from 2 to 15 mm with coiled diameters of 12 to 20 mm. Selection is based on the diameter of the varix. The diameter of the predeployment coils should be approximately 1.2- to 1.6-fold of the diameter of the targeted vessel to reduce the risk of coil migration.[18] Coils can be deployed through a 22-gauge needle (.018-inch coil) or a 19-gauge needle (.035-inch coil). The smaller diameter 22-gauge FNA needle provides greater ease of use and a theoretical reduction in bleeding at the needle puncture site.[34]

The echoendoscope is usually positioned either in the distal esophagus in an antegrade manner (transesophageal–transcrural approach) or in the gastric fundus (transgastric approach) to treat fundal GVs (ie, GOV2).[35] The transesophageal–transcrural approach avoids visualization issues from gastric contents (blood and food), and the thick fibromuscular diaphragmatic crus serves as a stabilizing backboard to prevent back bleeding.[36] This approach also eliminates difficulties related to echoendoscope retroflexion in the stomach (Fig. 3).[33]

Water instillation of the gastric fundus can improve acoustic coupling and aid in visualization of gastric fundal varices. Doppler is used to anatomically delineate the variceal network with the intent of targeting the feeding (perforator) vessel when possible.[18] Some endosonographers consider it difficult to accurately identify the feeder vessel in the conglomerate of vessels and instead prefer to target the largest vessel in the variceal complex.[37]

Coil loading requires removal of the needle stylet, which is then used to advance the coil from its original sheath into the FNA needle lumen. Once the coil is loaded, the needle is inserted through the echoendoscope channel and advanced into the target vessel (Video 3, available online at www.giejournal.org). If there is concern for coil migration, some experts advocate puncturing through and through the vessel wall to anchor the coil a short distance into the deeper tissue.[18] The stylet can be used to advance the coil while minimally retracting the needle, thus anchoring the coil into the vessel wall. This technique mitigates migration but ensures placement of the bulk of the coil within the vessel lumen. Like initial deployment, the final portion of the coil can be anchored in the near vessel wall. Doppler imaging after coil insertion aids in assessing the response to treatment and the potential need for further therapy[18]

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TABLE 5. List of commercially available coils for medical use

Type of coil	Compatible with	Sizes available	Cost (U.S.$)
Micro Nester coils	22-gauge needle	Diameters: 2, 3, 5, 6, 8, and 10 mm Lengths: 3, 5, 7, and 14 cm	170-194
Nester coils	19-gauge needle	Diameters: 3, 4, 6, 8, and 10 mm Lengths: 7, 14, and 20 cm	194-253
Tornado platinum embolization micro-coils	22-gauge needle	Diameters: 3, 4, 5, 6, 7, and 8 mm Lengths: 2, 3, and 4 cm	194
Tornado platinum embolization coils	19-gauge needle	Diameters: 4, 5, 6, and 7 mm Length: 3 cm	194

OUTCOMES AND COMPARATIVE EFFECTIVENESS DATA

There is marked heterogeneity in published studies on this topic, specifically regarding enrollment criteria, primary versus secondary prophylaxis, initial versus rescue therapy, subtypes of GVs (eg, GOV1, GOV2, IGV1), therapies provided (number or volume of coils, glue, combination therapy), target structures (superficial vs feeding vessel), number of treatment sessions, duration of follow-up, and veracity of assessment for adverse events. This makes generalizable conclusions regarding available treatments and comparative effectiveness difficult to interpret. There are 3 main clinical scenarios for gastric variceal therapy: incidentally diagnosed GVs without prior bleeding (primary prophylaxis), actively bleeding GVs (acute treatment), and elective treatment of previous gastric variceal bleeding (secondary prophylaxis).

Endoscopic sclerotherapy

Endoscopic therapy for GVs requires more sessions and a larger volume of sclerosant because of the larger size and higher flow rates compared with EVs.[2] Small observational studies reported immediate hemostasis with EST in 60% to 100% of acute gastric variceal bleeding; however, there were higher recurrent bleeding rates (20%-89%) because of low complete obliteration rates for GOV2 (70.4%) and IGV1 (46.7%)[1,2,5,38,39] Thus, EST of GVs is relegated to hemostasis for acute bleeding when other more-efficacious treatments are unavailable.

Endoscopic variceal ligation

One meta-analysis of 7 studies comparing CYA glue with EVL treatment for acute gastric variceal bleeding noted superior hemostasis (odds ratio [OR], 2.32; 95% confidence interval [CI], 1.19-4.51) and a longer gastric variceal recurrent bleeding–free period when using CYA glue (hazard ratio, .37; 95% CI, .24-.56).[39] There were no significant differences in mortality, number of treatment sessions to eradication, or procedure-related adverse events. All 7 studies in the meta-analysis included GOV1 patients; however, 5 studies did not include patients with IGV1. A second meta-analysis including 3 randomized controlled trials comparing CYA glue with EVL demonstrated superior hemostasis for control of active gastric variceal bleeding (OR, 4.44; 95% CI, 1.14-17.30; $P = .032$) and a lower recurrence rate of GVs (OR, .26; 95% CI, .11-.61; $P = .002$). CYA glue was better than EVL for prophylaxis of IGV1 recurrent bleeding (OR, .06; 95% CI, .01-.58; $P = .015$); however, this was not observed for GOV2 (OR, .91; 95% CI, .23-3.62; $P = .895$).[40] A third Cochrane meta-analysis compared CYA glue with EVL for treatment of acute gastric variceal bleeding.[41] There was no significant difference between the use of CYA glue and EVL in control of bleeding (92.5% vs 83.7%; relative risk, 1.07; 95% CI, .90-1.27) and bleeding-related mortality (23.7% vs 27.6%; relative risk, .83; 95% CI, .52-1.31). Notably, there were lower recurrent bleeding rates for CYA compared with EVL (18% vs 29.9%; relative risk, .60; 95% CI, .41-.88).[41]

Endoscopic CYA glue injection

Acute bleeding. A retrospective cohort study evaluated the efficacy and safety of CYA glue injection for acutely bleeding GVs.[15] All 131 patients with bleeding fundal varices treated with injection of CYA glue (N-butyl-2-cyanoacrylate) achieved immediate hemostasis and obliteration of the GV after a mean of 1 treatment session (range, 1-3 sessions). There were no procedure-related adverse events or recurrent bleeding of the GV within 30 days of the procedure. The late recurrent bleeding–free rate at 1, 3, and 5 years was 94.5%, 89.3%, and 82.9%, respectively.[15]

A randomized trial compared treatment of acute gastric variceal bleeding with CYA glue (n = 37) with TIPS (n = 35). Obliteration of GVs was superior in the CYA group (51% vs 20%, $P < 0.01$); however, the recurrent bleeding rate was lower with TIPS (11% vs 38%, $P = .014$). Of note, the recurrent bleeding rate with CYA glue was higher compared with other studies. Adverse events including hepatic encephalopathy were expectedly higher in the TIPS group compared with the CYA group (25.7% vs 2.7%, $P < .01$).[42] A second retrospective study noted similar recurrent bleeding rates with CYA glue (n = 61) and TIPS (n = 44) at 72 hours (6.9% vs 9.5%), 3 months (10.6% vs 20.7%), and 1 year (10% vs 25%). TIPS resulted in significantly greater morbidity (hepatic encephalopathy,

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TIPS stenosis, and acute renal failure) compared with CYA glue (41% vs 1.6%, $P < .0001$).[43]

Primary prophylaxis. A single-center study evaluated primary prophylaxis with CYA glue for large fundal GVs (GOV2 and IGV1).[44] Patients were randomized to CYA glue injection (n = 30), a nonselective beta-blocker (n = 29), or no treatment (n = 30). CYA glue was more effective than beta-blocker therapy in preventing incident gastric variceal bleeding with a rate of 13% for CYA glue compared with 28% for the beta-blocker ($P = .04$) and 45% for no treatment ($P = .003$). Improved survival was noted in the CYA group compared with the no-treatment group (90% vs 72%, $P = .05$). Although CYA glue may be more effective for primary prophylaxis to prevent gastric variceal bleeding, Baveno VI and American Association for the Study of Liver Diseases guidelines recommend nonselective beta-blocker therapy.[7,13]

Secondary prophylaxis. A randomized trial for secondary prophylaxis of GVs (GOV2 or IGV1) compared the injection of CYA glue (n = 33) with beta-blocker treatment (n = 34) and found significantly lower recurrent bleeding rates (15% vs 55%, $P = .004$) and mortality rates (3% vs 25%, $P = .03$) favoring CYA glue.[45] A retrospective study showed that most patients (77.8%) undergoing secondary prophylaxis on follow-up endoscopy required only 1 injection of CYA glue for obliteration.[46] Overall cumulative survival rates between studies for patients treated with CYA glue at 6 months were 92.1% and at 1, 3, 5, 6, and 10 years were 66.9% to 84.2%, 64.2%, 45.3% to 60.4%, 43%, and 55.5%, respectively.[46-48]

Endoscopic thrombin injection

A meta-analysis that included 11 studies using human or bovine thrombin for GVs yielded a pooled early recurrent bleeding rate of 9.3% (95% CI, 4.9-17) and a late recurrent bleeding rate of 13.8% (95% CI, 9-20.4). The pooled rescue therapy rate after injecting thrombin was 10.1% (95% CI, 6.1-16.3), and the pooled 6-week gastric variceal–related mortality rate was 7.6% (95% CI, 4.5-12.5). After injecting thrombin into bleeding GVs, the pooled adverse event rate was 5.6% (95% CI, 2.9-10.6).[49] Insufficient data remain to support thrombin efficacy compared with standard CYA glue therapy; thus, thrombin injection should not be considered as a first-line approach for the treatment of gastric variceal hemorrhage.

Topical hemostatic powder

Topical hemostatic powder has been used to control acute variceal bleeding, although this remains an off-label approach. Hemostatic powder may have a role as a temporary measure in stabilizing the patient. It is important to reiterate that urgent arrangements should be made thereafter for a definitive therapeutic intervention if hemostatic powder is used. Small studies have shown that the application of TC-325 achieved initial hemostasis in 88% to 100% of active bleeders, followed by more definitive therapy in 12 to 24 hours.[22] A small case series also reported the use of Ankaferd Blood Stopper as a bridge to more definite therapy.[23]

EUS-guided angiotherapy

Monotherapies (EUS-guided CYA glue or coils). A multicenter retrospective study compared EUS-guided coil injection (n = 11) with EUS-guided injection of CYA glue (n = 19) among consecutive patients with gastric fundal varices (GOV2 and IGV1).[50] Thirty-three percent were experiencing active hemorrhage at the time of treatment application, whereas others were treated for primary or secondary bleeding prophylaxis. One week after initial EUS-guided therapy, a repeat EUS was performed to verify eradication of the GVs, and the same therapy was repeated if needed. There was no difference in the main outcome measures of variceal obliteration (91% vs 100%, not significant) or mean number of treatment sessions to obliteration (1.3 vs 1.5, not significant) for the coil and CYA groups, respectively. No recurrences of GVs were observed in either group over a 17-month follow-up. Adverse events were significantly higher in the CYA group (58% vs 9%, $P = .01$), although 9 of the 11 adverse events in this group were asymptomatic pulmonary glue embolization noted on routine postendoscopy CTs.

A single-center retrospective study reported the outcomes of EUS-guided thrombin injection (600-10,000 IU) in 8 patients with active gastric variceal bleeding (n = 3) or as primary prophylaxis (n = 5).[31] Hemostasis was reported in 2 of the 3 bleeding patients with 1 failure requiring emergent TIPS. Immediate endosonographic gastric variceal obliteration was initially noted in both patients with successful hemostasis and all 5 of the primary prevention patients; however, 1 patient showed recurrent variceal flow on surveillance EUS. No recurrent bleeding was observed, and no procedure-related AEs were reported.

Combination therapy (EUS-guided CYA glue injection and coiling). A single-center retrospective study evaluated the efficacy of combined EUS-guided CYA glue injection and coil embolization treatment of gastric fundal varices. Therapy was provided to patients with active bleeding (5%), history of recent bleeding (69%), and as primary prophylaxis (26%).[35] The procedure was technically successful in 151 of 152 patients (99%). Treatment-related adverse events included mild postprocedure abdominal pain in 4 of 125 patients (3%), minor delayed bleeding in 4 of 125 patients (3%) from coil and/or glue extrusion, and clinical signs of pulmonary embolization in 1 patient (1%). The pulmonary embolization was possibly related to the CYA glue, but the delay of 7 days after treatment adds uncertainty. Among 100 patients with follow-up EUS examinations, 93% had confirmation of complete obliteration of GVs by Doppler analysis. Once obliteration was achieved, long-term follow-up (mean, 529 days; range, 30-2043) demonstrated a very low post-treatment recurrent bleeding rate of 3%.

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In the only single-center observational study evaluating 80 patients specifically undergoing primary prophylaxis for high-risk GVs (size >10 mm and/or with cherry red spot) with EUS-guided CYA glue injection and coil embolization with 100% technical success, post-treatment gastric variceal bleeding was seen in 2 (2.5%), and there was no need for emergent TIPS in any patients. The authors estimated that the cost of EUS-guided CYA glue injection and coil embolization was less than half of the cost of inpatient hospitalization for gastric variceal bleeding, suggesting a need for further randomized trials to explore its role in primary prophylaxis.[51]

A single-center randomized trial compared combination EUS-guided CYA glue injection and coil embolization (n = 30) with EUS-guided coil embolization alone (n = 30) for the treatment of GVs (GOV2 and IGV1) with active bleeding (10%) or as primary (12%) or secondary prophylaxis (78%).[52] Procedural technical success was 100% in both treatment groups, and clinical success, defined as obliteration of the GVs, was 100% of the combined CYA–coil group compared with 90% in the coil embolization monotherapy group ($P = .12$). EUS Doppler evaluation more accurately determined that varix obliteration as the immediate gastric variceal thrombosis rate determined by EUS Doppler interrogation was significantly higher than was appreciated by endoscopic appearance. Also, during a median follow-up of 14.5 months (range, .6-31.2), the EUS-guided CYA–coil group compared with the coil monotherapy group had significantly lower rates of recurrent bleeding (3.3% vs 20%, $P = .04$), reduced varix reappearance (13.3% vs 46.7%, $P < .001$), and reintervention (16.7% vs 40%, $P = .01$). There was no significant difference between the 2 treatment arms in terms of mortality (30% combined therapy vs 26.7% coil only, $P = .9$) or adverse events (6.7% combined therapy vs 3.3% coil only, $P = .5$).[52]

A meta-analysis including 11 studies (randomized controlled trials, 2; prospective case series, 1; and retrospective analyses, 8) totaling 536 patients with active or recent gastric variceal bleeding compared 3 endoscopic treatments: EUS-guided CYA glue injection, combined EUS-guided CYA glue injection and coil embolization, and EUS-guided coil embolization.[53] The overall technical success, clinical success, and adverse event rates were 100% (95% CI, 98-100), 97% (95% CI, 92-100), and 14% (95% CI, 6-23), respectively.[53] On subgroup analysis, combined EUS-guided CYA glue injection and coil embolization resulted in improved technical and clinical success compared with either CYA glue alone (100% vs 97% [$P < .001$] and 98% vs 96% [$P < .001$]) or coil embolization alone (99% vs 97% [$P < .001$] and 96% vs 90% [$P < .001$]). Combined CYA glue injection and coil embolization resulted in lower adverse event rates compared with CYA glue alone (10% vs 21%, $P < .001$), and comparable rates with coil embolization alone (10% vs 3%, $P = .057$).

A 2020 meta-analysis of 23 studies totaling 851 patients compared treatment outcomes for EUS-guided gastric variceal therapies (EUS-guided coil embolization, EUS-guided glue injection, and combined EUS-guided coil embolization and glue injection) with CYA glue injection using a standard endoscopic approach.[54] Clinical efficacy was comparable between EUS-guided therapies and standard endoscopic CYA glue approaches in terms of bleeding control (94% vs 91%, $P = .4$), early recurrent bleeding (7% vs 5%, $P = .7$), and late recurrent bleeding (12% vs 17%, $P = .1$). EUS-guided therapy was superior in terms of obliteration of GVs (84% vs 63%, $P = .02$) and recurrence rate of GVs (9% vs 18%, $P = .06$). A subgroup analysis for gastric variceal recurrence demonstrated superior outcomes for the combined EUS-guided coil–CYA therapy with a rate of 5.2% ($P < .01$) compared with EUS-guided CYA and EUS-guided coil groups.

SAFETY AND PROCEDURE-RELATED ADVERSE EVENTS

Traditional hemostasis: sclerotherapy, band ligation, and topical hemostatic agents

Recurrent bleeding ranging from 36% to 87% and serious adverse events can occur commonly using sclerosing agents for GV treatment.[11] Adverse events include pyrexia, retrosternal chest pain, abdominal pain, dysphagia, bleeding, ulceration, and perforation.[2,11,55] EVL is associated with increased recurrent bleeding compared with other modalities and ulcer formation that can result in severe hemorrhage.[1,20] Hence, CYA glue or other modalities are preferred for GV management, especially fundal type varices.

No adverse events have been reported to date with the use of topical hemostatic agents to control gastric variceal or ectopic variceal bleeding. Limitations of topical hemostatic agents include blockage of the applicator delivery system or accessory endoscope channel. Looping of the endoscope may hinder the soft catheter sheath, disrupting the visual field if further endoscopic hemostasis methods are needed, and there is a theoretical risk of air embolism.[20,56]

Endoscopic CYA glue injection

Technical challenges with CYA glue delivery include premature blockage or entrapment of the injection needle within the varix and glue adherence to the endoscope or working channel. A higher occurrence of these issues has been found with the injection needle adhering to the varix with the use of rapidly polymerizing undiluted CYA glue (5.03%) compared with slowly polymerizing formulations such as CYA glue mixed with Lipiodol (.8%). This occurs more commonly if several injections or GVs are treated during the same session. Glue adherence to the endoscope can be minimized by using a proper injection

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technique and coating the distal tip and accessory channel of the endoscope with a lubricant (eg, silicone oil or Lipiodol). In the event of CYA glue adherence to the endoscope or its components, manufacturer recommendations should be followed, which may include the use of acetone for removal.

The most serious adverse event after glue injection therapy is systemic embolization.[15] Factors that may increase glue embolization include dilution of CYA glue with Lipiodol, rapid injection, injection in large-volume aliquots, and IGV1 contrasted with GOV2 because of higher blood flow rates. Consequences of CYA glue embolization are pulmonary embolism, acute kidney injury, splenic infarction, and splenic and portal vein thrombosis. Embolization into the arterial circulation through a patent foramen ovale or arteriovenous pulmonary shunt can result in a cerebrovascular accident or multiorgan infarction. A high frequency of subclinical pulmonary embolization was reported in 1 series with 58% of patients treated with N-butyl-2-CYA diluted 1:1 with Lipiodol.[25] In a study of 140 patients, only 6 patients (4.3%) had radiographic evidence of pulmonary embolism, of which 4 had respiratory symptoms.[57] In a larger series of 753 patients, only .7% of those treated with CYA glue had a distant embolization (1 pulmonary, 1 brain, and 3 splenic).[58]

Transient pain and fever after CYA glue injection commonly occur in up to 90% of patients.[12] Sepsis from CYA glue embolization serving as a nidus of infection has been reported.[59] CYA glue may less frequently lead to gastric ulceration, major gastric variceal bleeding, mesenteric hematoma, hemoperitoneum, and bacterial peritonitis. Visceral fistulization from the stomach into the pleura or mediastinum also may occur after unintentional paravariceal injection.[60]

Endoscopic thrombin injection

Human thrombin is used over bovine thrombin since the FDA placed a black box warning in 1996 on all bovine thrombin products because of abnormal hemostasis, ranging from asymptomatic laboratory alterations to severe bleeding and/or thrombosis.[61] No adverse events directly attributable to human thrombin injection, and specifically no bleeding secondary to postinjection ulceration, have been reported. This is a key advantage of thrombin therapy over sclerosants or tissue adhesives. Thrombin may be used for a bridge to more definitive therapy, in secondary prevention, or in patients where TIPS is precluded.[19]

EUS-guided angiotherapy

A meta-analysis reported a pooled rate of mild and moderate adverse events of 5.9% and 5.7%, respectively. The most commonly reported adverse events were sepsis and/or bacteremia, distant organ CYA glue embolism (5.6%), postprocedure fever, and postprocedure pain.[54] The pooled rate of all-cause mortality with EUS-guided therapy and with gastric variceal bleeding was 13.1% and 7.7%, respectively.

EASE OF USE AND TRAINING CONSIDERATIONS

Given the length and complexity of gastric variceal endoscopic treatment, general anesthesia should be considered given the risk of active bleeding and for airway protection, and prophylactic intravenous antibiotics are recommended in the acute bleeding settting.[34] Studies addressing the necessary training required to achieve proficiency in the various hemostatic maneuvers applied for gastric variceal treatment are lacking. The echoendoscope has a smaller aspiration channel, which limits the suction capability during active hemorrhage and potentially compromises EUS imaging. Given the limited range for retroflexion with echoendoscopes, approximation to the fundal mucosa is often difficult, and transesophageal targeting of fundal varices may be required. Most endoscopists are familiar with injection techniques within the GI tract; however, CYA can be technically challenging to use for the endoscopist, nursing staff, and endoscopy technicians because it requires meticulous preparation and setup of equipment and glue components. Familiarity with the sequence of delivery is also crucial for safe and efficient use.[12] Topical hemostatic agents are easy to apply in difficult to access locations but lead to a transient reduction in endoscopic visualization and possible interference with other treatment modalities if hemostasis fails.

EUS-guided angiotherapy should be performed by appropriately trained endosonographers. Fluoroscopic guidance can be considered to monitor for immediate embolization; however, through-the-scope Doppler imaging can also be used to confirm occlusion of the GV. The portability of through-the-scope Doppler imaging makes it a useful alternative to fluoroscopy in hemodynamically unstable patients in the intensive care unit.[34] Extreme care must be undertaken to clean the echoendoscope thoroughly after CYA glue injection to prevent glue from getting lodged within the working channel.

FINANCIAL CONSIDERATIONS

List prices of commonly used hemostatic devices in the United States are shown in Tables 3 through 5. Device costs for most clinical enterprises are lower than list prices because of purchasing agreements. Current Procedural Terminology (CPT) codes for endoscopic hemostasis are as follows:

- 43255 EGD, flexible, transoral; with control of bleeding, any method
- 43243 EGD, flexible, transoral; with injection sclerosis of EVs/GVs
- 43244 EGD, flexible, transoral; with band ligation of EVs/GVs
- 43255 with Healthcare Common Procedure Coding System code C1052 (as of January 1, 2021) EGD with hemospray

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- For EUS-guided coil embolization with or without CYA glue, the code most relevant to EUS-guided angiotherapy is 43253 (EUS-guided transmural injection)

For unlisted CPT codes, a letter providing a clear description of the nature, need, time required, necessary equipment for the procedure, and supporting medical literature should be submitted to the insurance carrier. The letter should state why billing cannot be addressed with the standard CPT codes and suggest a reasonably comparable CPT code based on work relative value units and percentage of a reasonably similar CPT code.

Cost analysis of EUS-guided coil embolization versus EUS-guided CYA glue injection

The costs of medication used in Europe including a value added tax of 10% are €55.20 (U.S.$72.30) for 1 mL Histoacryl/Lipiodol and €143.5 (U.S.$187.00) for 1 mL Glubran/Lipiodol. Independent of the length, 1 coil costs €75.9 (U.S.$99.4). Based on these costs, successful obliteration of GVs with CYA glue has a mean cost of €151.60 ± 13.90 (U.S.$198.60 ± 18.20; range, €99.40-298.10 [U.S.$130.10-390.40]). Treatment with coils was significantly more expensive with a mean of €441.60 ± 90.30 (U.S.$578.50 ± 118.30; range, €151.80-986.70 [U.S.$198.90-1293]; $P = .003$). Additional costs for the prolonged hospital stay need for EUS-guided CYA glue injection were not considered.

AREAS FOR FUTURE RESEARCH

EUS-guided therapy for the treatment of GVs requires further refinement as many questions remain regarding the injection technique, materials for injection, and ideal follow-up intervals. Currently, EUS-guided vascular interventions are performed using standard endoscopic accessories, and available tools are borrowed from the interventional radiology armamentarium. The development of dedicated devices specifically designed to facilitate EUS-guided therapies for hemostasis are needed. Experience with EUS-guided therapies could also help us better understand GVs, perhaps serving to identify the characteristics of lower flow more readily and safer sites for traditional CTA glue injection monotherapy. Ideally, comparative outcomes data in randomized trials should address the clinical efficacy and cost-effectiveness of EUS and traditional endoscopic hemostasis techniques (eg, CYA glue injection monotherapy) before widespread adoption is recommended into clinical practice. Local expertise will remain a primary factor in determining the appropriate therapy. In many practice settings, the availability of endoscopists comfortable with traditional CYA glue injection monotherapy may be limited. The optimal training pathways for gaining proficiency in advanced EUS-guided techniques such as EUS-guided coil embolization need further study but could become a standard element of an advanced endoscopy curriculum at centers with a dedicated interest in endohepatology. Given the potentially catastrophic nature of gastric variceal bleeding, the potential benefit of both primary and secondary prophylactic approaches, endoscopic or angiographic alternatives, remain fertile ground for further study.

SUMMARY

GVs are associated with higher morbidity and mortality when compared with EVs. Therapeutic management of patients with GVs depends on local expertise and should be approached in a multidisciplinary manner incorporating input from therapeutic endoscopists, interventional radiologists, and hepatologists. The control of bleeding in acute gastric variceal hemorrhage can be challenging. GOV1 are typically treated like EVs with banding, whereas CYA glue injection and EUS-guided coil embolization has emerged as preferred endoscopic treatments for other forms of GVs (GOV2, IGV1, and IGV2) in the acute bleeding setting and as secondary prophylaxis to prevent recurrent bleeding. Older endoscopic methods using sclerosing injectants or band ligation for GOV2 and IGV can temporize by providing acute hemostasis. Still, these approaches are no longer recommended as definitive therapy because of suboptimal efficacy and safety. A limited body of literature suggests a role for primary prophylaxis, but additional data are needed. Endoscopic methods may be favored over TIPS by avoiding associated long-term adverse events, such as hepatic encephalopathy. EUS enables improved detection of GVs and allows precisely targeted therapies, potentially offering higher technical success and gastric variceal obliteration rates with a reduced incidence of systemic embolization compared with endoscopic CYA glue injection alone. The endoscopic approaches discussed in this document offer an essential option for patients who are not candidates for interventional radiology approaches such as TIPS or BRTO in the setting of gastric variceal bleeding.

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Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; BRTO, balloon-occluded retrograde transvenous obliteration; CI, confidence interval; CPT, Current Procedural Terminology; CYA, cyanoacrylate; EST, endoscopic sclerotherapy; EV, esophageal varix; EVL, endoscopic variceal ligation; FDA, U.S. Food and Drug Administration; GOV1, gastroesophageal varices type 1; GOV2, gastroesophageal varices type 2; GV, gastric varix; IGV1, isolated gastric varices type 1; IGV2, isolated gastric varices type 2; OR, odds ratio; TIPS, transjugular intrahepatic portosystemic shunt.

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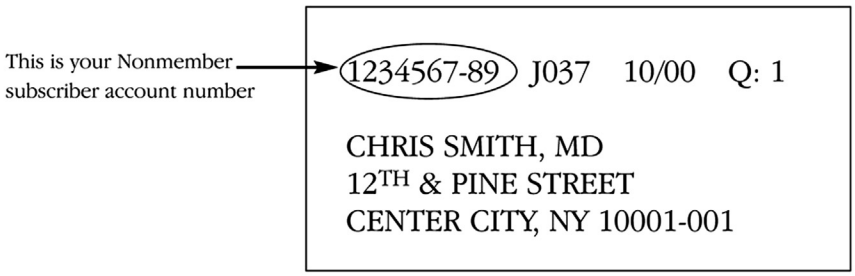

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