ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: Todd H. Baron, MD

Endoscopic Ultrasound–Guided Coil and Glue Injection for Gastric Variceal Bleeding

Kenneth F. Binmoeller, MD
Medical Director
Interventional Endoscopic Services
California Pacific Medical Center
San Francisco, California

G&H How common is variceal bleeding in patients with gastric varices?

KB There are approximately 7000 cases of gastric variceal bleeding per year. The prevalence and risk of bleeding from gastric varices are much lower compared to esophageal varices, but gastric variceal bleeding tends to be more severe and is associated with higher mortality. The mortality from a bleed ranges from 30% to 50% and depends on various factors, including the size of the varices (with larger varices carrying a higher risk), endoscopic stigmata of bleeding (ie, red wale marks), and the severity of the patient's underlying liver disease (with increased risks seen in patients with Child-Pugh class B or C, or a high Model for End-Stage Liver Disease score).

G&H What is the difference between junctional and nonjunctional gastric varices?

KB Junctional varices are located at the cardia, or the junction of the stomach to the esophagus. Also known as gastroesophageal varices (GOVs), they are essentially an extension of esophageal varices into the stomach and appear as rope-like columns. GOVs and esophageal varices have the same anatomy, pathophysiology, and blood source; they arise from the left gastric vein and originate from the lamina propria. Nonjunctional gastric varices are isolated to the stomach; thus, they are also referred to as isolated gastric varices (IGVs). IGVs originate below the lamina propria in the submucosa, and are most commonly found in the fundus. Their source of blood flow is derived from the short and the posterior gastric veins. Often, IGVs are associated with large gastrorenal shunts.

The Sarin classification of gastric varices further categorizes GOVs and IGVs into 2 types each according to their location in the stomach and their relationship with esophageal varices. Type 1 GOVs are located only at the junction (lesser curve), and are an extension of esophageal varices. Type 2 GOVs extend from the junction toward the fundus along the greater curve. Type 1 and type 2 IGVs are located in the fundus and elsewhere, respectively (Figure 1). It is important to understand these classifications because the risk of bleeding as well as the approach and response to treatment differ significantly.

> Cyanoacrylate glue injection is currently recommended as first-line treatment for IGVs.

G&H What treatment approaches are currently available to manage GOV and IGV bleeding?

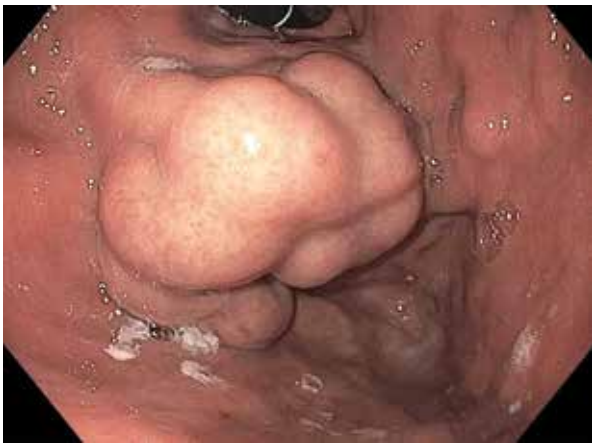

Figure 1. Large, type 1 isolated gastric varices are located in the fundus.

Figure 2. An endoscopic ultrasound image showing deployment of a coil through a 19-gauge needle. Cyanoacrylate glue injection immediately follows coil placement.

KB Treatment can be divided into radiologic and endoscopic approaches; surgical shunting is no longer performed. Radiologic treatments consist of transjugular intrahepatic portosystemic shunt (TIPS) and balloon-occluded retrograde transvenous obliteration (BRTO). TIPS works well to treat type 1 GOVs in patients who are refractory to band ligation, as the shunt reduces the portocaval pressure gradient. However, this approach is not effective for IGVs due to the association of the varices with gastrorenal shunts. Instead, IGVs can be treated with BRTO, which was developed in Japan and is popular in Asia, because this procedure targets the large gastrorenal shunts that supply blood to the gastric varices. A radiologist inflates an angiographic balloon to occlude the shunt and then injects a sclerosant, which remains in the shunt network to further occlude gastric varices. Currently, very few hospitals in the United States use this treatment approach.

Different modalities exist under endoscopic treatment. Sclerotherapy, which is nearly obsolete, involves injection of a sclerosant into a varix. Band ligation has replaced sclerotherapy for the treatment of type 1 GOVs and involves application of a rubber band to a varix in order to strangulate the blood flow. This approach is not recommended for IGVs, as varices in the fundus are larger in size, are located in the submucosa, and have a thick overlying mucosa, making it difficult to suck the entire varix into the band. If the varix and its contralateral wall cannot be captured entirely, blood flow still exists and can result in massive bleeding (ie, hemorrhage). The worldwide standard of care for the treatment of IGVs is a variant of sclerotherapy that uses a glue injection in place of a sclerosant. Under endoscopic guidance, a liquid monomer called cyanoacrylate glue is injected via a needle into the varix. After coming into contact with blood, the glue polymerizes and solidifies into a hard substance, plugging up the varix.

G&H What is the role of endoscopic ultrasound–guided coil and glue injection in the treatment of gastric variceal bleeding?

KB Cyanoacrylate glue injection is currently recommended as first-line treatment for IGVs. However, this procedure carries a risk of embolization, as the glue can flow through the bloodstream before it solidifies. The risk of embolization is low, but it has occurred and can result in serious morbidity and mortality. The coil is a response to this limitation. The coil has synthetic fibers attached to it, and the concept behind its use was that these fibers could slow down the flow of blood in the vessel and promote blood-clot formation, thus occluding the vessel. I hypothesized that if a coil were deployed into a varix and followed with glue injection, the glue would attach to the synthetic fibers and would be bound at the site of the coil, preventing the glue from embolizing. I tested that hypothesis in ex vivo studies by placing a coil in a jar of heparinized blood and then injecting the glue. All of the glue attached to the coil fibers, leaving none of the glue in the jar. The procedure was then used in patients, and study results demonstrated that the coil is a very effective method in reducing the risk of embolization.

Coil deployment can be performed under fluoroscopic guidance, but endoscopic ultrasound (EUS) guidance is a more practical and easy-to-use imaging modality. An endoscopist no longer has to be dependent on an endoscopic view of the varix; the stomach can be full of

blood or food, and EUS allows the endoscopist to visualize the targeted varix, as well as the main feeder vessel to the varix, and precisely place the coil and deliver the glue (Figure 2). Additionally, EUS guidance can be used with Doppler, which provides information regarding the blood flow rate inside the varix and whether the varix has been completely treated.

G&H Is this modality gaining traction in clinical use?

KB Yes. Placing a coil before cyanoacrylate glue injection is simply a modification of glue injection, which has already been embraced worldwide as the standard of care for fundal varices. It is easier for clinicians to accept a modified version of a well-established treatment than a completely new procedure, such as the use of coils alone to achieve vessel occlusion. However, only endoscopists who are skilled in using EUS are able to perform this treatment, which may limit its dissemination.

G&H What adverse events are associated with EUS-guided coil and glue injection?

KB The main adverse event of cyanoacrylate glue injection is embolization, which is what the coil is aiming to prevent. It is possible that embolization could still occur if the glue were not to attach to the coil fibers and float away. In my more than decade-long experience of using combined coil and glue injection, only 1 patient developed pulmonary embolization after undergoing this procedure. Interestingly, the event occurred a week after the patient was discharged rather than immediately; a piece of the glue may have broken off and traveled to the lungs, or the embolization may not have even been related to the glue. Another potential risk is the transmission of infection into the bloodstream, which is why patients are given periprocedural antibiotics.

Clinicians should not wait until a gastric varix bleeds to treat it due to the high mortality rate.

G&H What do the data show regarding the short- and long-term outcomes of EUS-guided coil and glue injection?

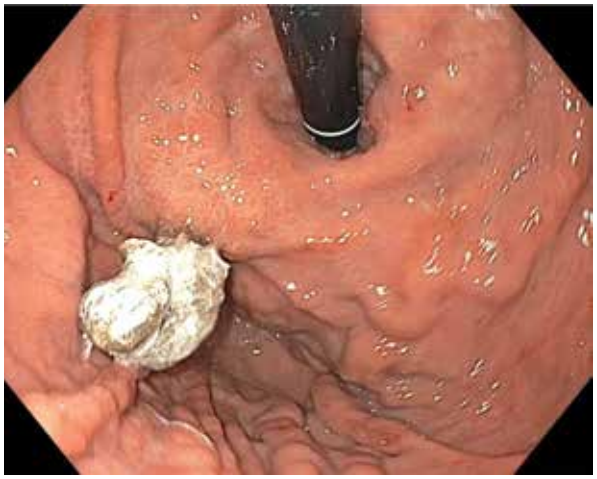

Figure 3. A follow-up endoscopy 1 month after endoscopic ultrasound–guided coil embolization shows a coil-glue conglomerate extrusion from obliterated gastric varices.

KB My colleagues and I published the results of a pilot study of 30 patients in 2011 that were very encouraging. The mean follow-up was 193 days (range, 24-589 days). Among 24 patients, 23 (96%) achieved variceal obliteration after 1 treatment session. Four patients (16.6%) experienced rebleeding, none of which was associated with the varices. No procedure-related complications occurred, and no symptoms or signs of embolization following cyanoacrylate glue treatment were reported. In 2016, we published results of a long-term follow-up study (mean, 436 days; range, 30-2043 days) in 152 patients. Among 100 patients who were followed up with EUS examinations, 93 achieved complete variceal obliteration. Recurrent bleeding occurred in 3 of 93 patients (3%), and 4 of 125 patients (3%) experienced mild abdominal pain following the procedure. Another 4 patients (3%) had minor delayed upper gastrointestinal bleeding from coil or glue extrusion, and 1 patient (1%) reported pulmonary embolization, which I mentioned previously. Overall, we were able to demonstrate that EUS-guided coil and glue injection is a very safe and effective treatment for gastric variceal bleeding.

It is important to note that this procedure is used to treat the varices that are at highest risk for bleeding, and the underlying cause of varices—portal hypertension—still exists. Therefore, patients should be followed up annually with EUS so that any new varices, including those that have not bled or are at risk for bleeding, can be treated prophylactically (Figure 3). Clinicians should not wait until a gastric varix bleeds to treat it due to the high mortality rate.

G&H What are the next steps in research?

KB It would be beneficial to conduct a randomized, controlled trial comparing standard cyanoacrylate glue injection using a freehand technique under endoscopic guidance to EUS-guided coil and glue injection. Ideally, the trial would utilize computed tomography scans in patients undergoing either type of treatment, so we could learn whether the coil and glue treatment is achieving its objective of reducing, if not eliminating, the risk of embolization. The goal is to make this modified approach the new standard of care. Currently, the data are anecdotal, but reports have started to surface from other centers employing EUS-guided coil and glue treatment. A large comparison trial would help clinicians understand the importance of having an alternative modality that can further benefit patients.

Dr Binmoeller has no relevant conflicts of interest to disclose.

Suggested Reading

Bhat YM, Weilert F, Fredrick RT, et al. EUS-guided treatment of gastric fundal varices with combined injection of coils and cyanoacrylate glue: a large U.S. experience over 6 years (with video). *Gastrointest Endosc*. 2016;83(6):1164-1172.

Binmoeller KF, Weilert F, Shah JN, Kim J. EUS-guided transesophageal treatment of gastric fundal varices with combined coiling and cyanoacrylate glue injection (with videos). *Gastrointest Endosc*. 2011;74(5):1019-1025.

Fujii-Lau LL, Law R, Wong Kee Song LM, Gostout CJ, Kamath PS, Levy MJ. Endoscopic ultrasound (EUS)-guided coil injection therapy of esophagogastric and ectopic varices. *Surg Endosc*. 2016;30(4):1396-1404.

Romero-Castro R, Ellrichmann M, Ortiz-Moyano C, et al. EUS-guided coil versus cyanoacrylate therapy for the treatment of gastric varices: a multicenter study (with videos). *Gastrointest Endosc*. 2013;78(5):711-721.

Wani ZA, Bhat RA, Bhadoria AS, Maiwall R, Choudhury A. Gastric varices: classification, endoscopic and ultrasonographic management. *J Res Med Sci*. 2015;20(12):1200-1207.

Weilert F, Binmoeller KF. Endoscopic management of gastric variceal bleeding. *Gastroenterol Clin North Am*. 2014;43(4):807-818.