

ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

Section Editor: Eugene R. Schiff, MD

Management of Cardio-Fundal Gastric Varices

Stephen H. Caldwell, MD
Division of Gastroenterology and Hepatology
University of Virginia Health Sciences Center

G&H Could you describe the etiology of gastric varices?

SC In our recently published series, approximately 10% of gastric varices were caused by splenic vein thrombosis, which is related, for the most part, to pancreatitis or cancer in the region of the splenic vein, such as pancreatic or gastric cancer. For these patients, the treatment of choice is splenectomy if possible, which is generally successful, although extensive cancer may preclude this option. Splenic artery embolization to decrease venous outflow is an alternative in this setting but carries risk of infection.

The other 90% of gastric varices, like most varices manifesting throughout the gastrointestinal tract, are caused by portal hypertension. Gastric varices in the cardio-fundus region, as opposed to the more common esophageal varices, tend to have a distinct vascular anatomy and are much more difficult to manage. Cardio-fundal gastric varices correlate approximately to Sarin class type II gastroesophageal varices and type I isolated gastric varices. Any patient with portal hypertension is at risk for gastric varices but the risk and manifestations vary, based on presumably congenital anastomoses. All of the issues discussed below are related to gastric varices developed due to portal hypertension.

Generally, although these varices seem to manifest endoscopically with multiple channels, they are often formed from one vessel coiled on itself. In the typical patient with portal hypertension and a gastric varix, the primary channel is carrying blood from the splenic vein to the left renal vein, creating a spontaneous spleno-renal shunt. This type of anatomy is often referred to as left-sided portal hypertension. The blood that flows through

these channels is usually slower and less pressurized, but of larger volume because of the cardio-fundal varices' larger diameter, in comparison to esophageal varices.

G&H How do patients with cardio-fundal gastric varices generally present?

SC These patients generally present in one of two ways: with an acute gastrointestinal bleed or via incidental discovery at the time of upper endoscopy examination. Endoscopic examinations can be prescribed for a variety of reasons but are usually performed to screen for varices.

The spontaneous spleno-renal shunts underlying the cardio-fundal varices are also often associated with recurring episodes of encephalopathy without ascites due to the presence of a relatively decompressed portal system. This clinical scenario would provide an additional signal to examine for gastric varices.

G&H What are the steps in managing cardio-fundal varices upon detection?

SC The risk of bleeding from incidentally discovered cardio-fundal gastric varices is approximately 50% over 5 years. Whether or not medical therapy with beta blockers or prophylactic endoscopic or surgical procedures reduce the risk has yet to be determined. Some physicians recommend prophylactic intervention. Unless there are extenuating circumstances such as a past history of unexplained melena, I generally recommend observation and follow-up endoscopy. The reason for this more conservative approach is that the treatment options are more limited, potentially risky, and not proven, as opposed to procedures for esophageal varices,

where there is considerable, definitive literature on the benefit of prophylactic intervention.

G&H What are the steps taken to control an acute bleed from a gastric varix?

SC The usual steps taken for a typical esophageal variceal bleed are executed for gastric variceal bleeds as well. In the United States, the patient would currently be started on octreotide (other regions utilize terlipressin) to lower the portal pressure. It is important to be cautious regarding blood volume expansion and to minimize the administration of plasma, in order to avoid engorging the varices. If the patient displays a well-defined hemostatic defect beyond simple prolongation of the INR, which may or may not be associated with a true bleeding diathesis, it should be treated with platelets and/or cryoprecipitate, particularly if the fibrinogen level is depressed. In cases of uncontrollable bleeding, the varix can be compressed with a Blakemore tube or gastric balloon.

Beyond these initial procedures, several management options exist. The patient can undergo a radiologic transjugular intrahepatic portosystemic shunt (TIPS) procedure, usually with simultaneous embolization. TIPS alone is associated with a relatively higher rebleeding rate perhaps due to the “left-sided” nature of portal hypertension which means that the varix is farther away from the site of decompression. Simultaneous embolization performed through the TIPS alleviates this problem but may not be possible in all patients. Another newer radiologic procedure called balloon retrograde transvenous obliteration (BRTO) is emerging as a viable alternative. This procedure avoids the long-term complications of TIPS (like encephalopathy) but, in our experience, requires post-BRTO endoscopic ultrasound to confirm occlusion of the varix. If there is persistent flow in the varix, this can be easily treated with cyanoacrylate.

Endoscopically, the options are more limited compared to esophageal varices but many centers in the United States are now administering various cyanoacrylate glue preparations, which are injected directly into the vein, where they polymerize, in a procedure called variceal obturation. Endoscopic obturation is as effective as TIPS in preventing rebleeding and significantly less resource intensive.

Occasionally, if the varix is small, more widely available standard endoscopic techniques can be performed. However, cardio-fundal varices are generally large and sclerotherapy has not been shown to be effective for the most part. Endoscopic banding of gastric varices, both alone and in combination with sclerotherapy, may also be used but is not as effective as cyanoacrylate therapy. Because the cardio-fundal varices are large, they are also

difficult to adequately enclose in the banding device and rebleeding after banding can be severe if the band has not completely occluded the channel. Less common procedures include temporization with the application of an endoclip, if the focus of bleeding can be definitely identified. There have also been reports of occluding the entire varix with an Endoloop. We have never attempted this procedure in our center as it appears to carry some risk of perforation or significant rebleeding.

G&H Could you describe how the cyanoacrylate procedure is performed?

SC These procedures are not widely available and are not approved by the US Food and Drug Administration but they are performed with increasing frequency because of their relative simplicity and established efficacy, as shown in series from Europe and Asia. In our published study, we used a substance called Histoacryl (enbucrilate, B Braun, Germany) mixed with an iodinated oil (Ethiodol). However, Histoacryl is not widely available in the United States so we have since switched to Indermil (US Surgical), another 4-carbon cyanoacrylate, which is used undiluted, without any oil mixture (see abstract presented by Sandhu et al at DDW 2008).

The cyanoacrylate is administered through the endoscope with a 23-gauge needle, directly into the vein. Though there is a learning curve and the procedure is not a part of basic endoscopic curriculum, it is relatively easy to learn. The greatest risk is of a piece of glue breaking off into the systemic circulation, embolizing, and causing a stroke. The risk of embolization is estimated to be about 2% with Histoacryl-Ethiodol but less with the more rapidly polymerizing Indermil preparation. There is also a risk of gluing the needle into the varix or gluing the catheter into the endoscope but these are avoidable with careful technique and we have not observed this problem in our center. From a retrospective cohort study, we have found that the short-term risk and long-term morbidity associated with cyanoacrylate obturation compare favorably to that of TIPS (per Dr. Nicholas Procaccini). Although enbucrilate obturation clearly stands alone as an effective intervention, we have also used it in conjunction with BRTO when post-procedure EUS demonstrates persistent channel patency.

G&H Could you describe how the BRTO procedure is performed?

SC BRTO is a procedure performed by interventional radiologists under fluoroscopy. It provides an alternative approach to the varix when it cannot be accessed via

TIPS or when there is contraindication to TIPS or to cyanoacrylate therapy. In BRTO, the varix is approached from the femoral vein, up the vena cava, and into the left renal vein. From there, the TIPS can be accessed where it is emptying into the renal vein. The shunt vessel can then be occluded with a balloon placed retrograde, and embolic or sclerosant material injected antegrade into the varix. However, we have seen some limitations to BRTO, in that the outflow may be occluded without actually decompressing the varix, depending on how far into the channel the sclerosant catheter can be placed. As mentioned, we use cyanoacrylate as an adjunct in this situation.

G&H Are there other factors in considering whether to utilize endoscopic (cyanoacrylate) or radiologic (TIPS, BRTO) procedures?

SC Patients with a history of thrombotic disease, prior stroke, or known intrapulmonary shunting, may be better candidates for a radiological procedure, particularly if they also have ascites, which the TIPS could manage effectively. On the other hand, if patients have a history of encephalopathy, or if they are elderly or severely obese (and cannot get on the table for a fluoroscopic procedure) or if they have cardiac dysfunction, TIPS may be contraindicated or impossible and endoscopic cyanoacrylate is then preferred. Regarding application and limitations of BRTO, the main issues are a lack of wide availability and also the possibility that the procedure may not always occlude the main channel because of variations in vascular anatomy.

G&H What are the next steps in research of these procedures?

SC There has been some sporadic interest from industry sources in the cyanoacrylate procedures. However, because of the low prevalence of the problem (a typical tertiary care center will see 1–2 of these cases per month), private industry has not been interested in supporting a controlled trial. However, it is our hope that funding will become available to compare endoscopic cyanoacrylate versus TIPS or BRTO in bleeding cardio-fundal gastric varices in order to learn how best to triage these patients.

Suggested Reading

Sandhu BS, Mogollon AD, Stravitz RT, Shiffman R, BouHaidar D, et al. A method for endoscopic obturation of gastric varices that maximizes effectiveness without risks of systemic embolization. Abstract presented at Digestive Disease Week. May 17-22, 2008. San Diego, CA. Abstract 268.

Chikamori F, Kuniyoshi N, Kagiya S, Kawashima T, Shibuya S, Takase Y. Role of percutaneous transhepatic obliteration for special types of varices with portal hypertension. *Abdom Imaging*. 2008 Jun 11. [Epub ahead of print]

Boyer TD. Transjugular intrahepatic portosystemic shunt in the management of complications of portal hypertension. *Curr Gastroenterol Rep*. 2008;10:30-35.

Park WG, Yeh RW, Triadafilopoulos G. Injection therapies for variceal bleeding disorders of the GI tract. *Gastrointest Endosc*. 2008;67:313-323.

Caldwell SH, Hespeneide EE, Greenwald BD, Northup PG, Patrie JT. Enbucrilate for gastric varices: extended experience in 92 patients. *Aliment Pharmacol Ther*. 2007;26:49-59.

Arai H, Abe T, Takagi M, Mori M. Efficacy of balloon-occluded retrograde transvenous obliteration, percutaneous transhepatic obliteration and combined techniques for the management of gastric fundal varices. *World J Gastroenterol*. 2006;12:3866-3873.

Sarin SK, Agarwal SR. Gastric varices and portal hypertensive gastropathy. *Clin Liver Dis*. 2001;5:727-767.