Endoscopic Doppler Ultrasound Probe: Useful in the Management of Gastric Varices?

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Gastroesophageal varices, present in ~50% of cirrhotic patients, bleed at an annual rate of ~10%. Mortality after a hemorrhage is ~20% at 6 weeks. Although gastric varices bleed less frequently than esophageal varices, the hemorrhage is more severe, with greater mortality and more frequent rebleeding. In the Sarin endoscopic classification [1], gastric varices are categorized into four types based upon the presence of esophageal varices and location. Gastroesophageal varix type 1 (GOV 1), the most common (75%), represents a continuation of esophageal varices into the lesser curvature of the stomach. GOV 2 represents continuation of esophageal varices into the greater curvature. Isolated gastric varix type 1 (IGV 1) is the isolated gastric fundal varices that carry the highest risk of bleeding. IGV 2 is the gastric varices located outside of the cardiofundal region of the stomach. Recent practice guidelines promulgated by the American Society for the Study of Liver Disease (AASLD) recommend transjugular intrahepatic portosystemic shunt (TIPS) as the primary therapeutic choice for cardiofundal variceal bleeding and cyanoacrylate (CYA) glue injection in TIPS-ineligible patients. Endoscopic sclerotherapy is less effective in the treatment of gastric variceal bleeding compared with esophageal variceal bleeding, is associated with more adverse effects, and is associated with a higher rebleeding rate. CYA injection therapy has become the standard of care for both acute GV bleeding and rebleeding prevention due to the limited availability and high cost of TIPS in many centers across the world. This *de facto* standard, however,

appears to be based more on expediency than evidence since the quality of the data supporting glue therapy is derived from studies with small sample size and from meta-analysis which was dominated by the larger study including only GOV 1 varices [2]. Although other treatment options for the prevention of rebleeding are available, including balloon-occluded retrograde transvenous obliteration (BRTO), randomized controlled trials comparing BRTO with other therapies have not been published.

N-butyl-2 CYA (NBCA) has been used in multiple studies with hemostasis rates of 59–100% and bleeding recurrence rates of 0–40% [3]. Confirmation of gastric varix obliteration after glue injection is an important end point of the treatment. One of the most feared adverse events of CYA glue injection is systemic embolization. Factors associated with increased risk of embolization prior to the solidification of glue are over-dilution with lipiodol, excessively rapid injection, excessive glue volume, and GOV 1 isolated gastric varices with high blood flow rates [4]. Other serious adverse events noted with glue injection are sepsis, stroke, and multi-organ infarction.

Confirmation of variceal obliteration is the essential end point associated with a reduction in serious adverse events and also rebleeding risk, which in turn has been related to residual patency of treated varices [5]. Blunt probing of the variceal surface with a catheter for consistency is a widely used method to confirm obliteration of GV. This method, largely reliant on subjective assessment by experienced endoscopists, cannot predict rebleeding risk and thus has no prognostic significance. Hence, there is an urgent need for an objective method to overcome the limitations of variceal probing.

Various methods including endoscopic ultrasound (EUS)-guided CYA and/or coil deployment [6] and using lipiodol-diluted CYA and undiluted CYA have been used

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to limit volume, to confirm obliteration, and to avoid adverse events [7]. In EUS-guided CYA and/or coiling therapy, the use of color Doppler helps identify GV and also enables the operator to confirm vessel obliteration. Color Doppler not only enables precise delivery of glue into the vessel lumen even in the presence of retained food or blood in the distal esophagus, but also enables targeting of the feeder vessel rather than the varix lumen proper under EUS guidance, thereby minimizing the volume of CYA needed and potentially reducing the risk of embolization. A single session with coil and glue can obliterate GV in the majority of patients. A recent study by Bhat et al. [6] reported long-term follow-up (mean, 436 days) in 152 patients treated with a combination of EUS-guided CYA injection and coiling of GV over 6 years. Hemostasis was achieved in 151/152 cases, with a 7% rate of post-procedure complications. Ninety-three out of 100 patients who underwent follow-up EUS had confirmed obliteration of the target varix. Interestingly, only 3/93 patients experienced post-treatment bleeding from GV during a mean follow-up of 529 days. Even though several case series and retrospective studies demonstrated the excellent efficacy and safety of EUS-guided GV treatment, the high cost, the need for extensive additional training, the lengthy procedure time, the difficulties inherent in identifying the perforating vessel, the technical difficulty of deploying coils, and the unavailability of this technique in many centers limit its widespread global use.

Another simple newer technique is the use of an audible through-the-scope, non-imaging US Doppler probe in the management of GV. The audible signal produced depends on the velocity of the blood and axis of the blood flow. Furthermore, the audible signal can differentiate between arterial (high-pitched pulsatile signal) and venous (low-pitched continuous signal) blood flow. It provides objective measures useful in confirming varix obliteration and helpful in differentiating gastric varices from thickened mucosal folds and from submucosal lesions. Wong et al. [8] first reported the use of this probe in the diagnosis of gastric varices, and Salah et al. [9] reported the first case of probe-guided obliteration of GV. The use of a Doppler probe requires minimal training and does not require prior EUS experience. The major drawbacks include the need for direct visualization and that probe placement over the varix impairs its use in the presence of blood or food in the gastric fundus.

In this issue of *Digestive Diseases and Sciences*, Catron et al. [10] report the first single-center experience with audible Doppler assessment (ADA) using Doppler US probe in the management of gastric varices. The authors retrospectively compared GV obliteration and long-term outcomes in 41 patients with isolated GV (57.7%) and 30

(42.3%) with concomitant esophageal varices divided into pre-ADA and post-ADA groups. NBCA was injected without lipiodol and offered only to TIPS-ineligible cirrhotic or non-cirrhotic patients for the treatment of acute hemorrhage or for secondary prophylaxis of GV bleeding. Although the primary treatment end point was complete obliteration of the varices, end point assessment differed between the groups, with instrumental palpation used in the pre-ADA and audible Doppler in post-ADA group. The rates of hemorrhage-free survival in patients treated for acute GVH and secondary prophylaxis were not statistically significant when compared between pre-ADA and post-ADA groups. The use of ADA did not affect the adverse or clinical outcomes as compared to standard injection methods. In the ADA group, the average NBCA volume used per session was 2.5 ± 1.2 mL (range 1.0–7.5 mL), comparable to most of the earlier studies in which eradication was achieved with 2–4 injections with 1–2 mL of glue mixed with lipiodol per session [3]. Although the use of ADA did not reduce the volume of glue injected, there was a trend toward superior hemorrhage-free survival rates at 1 year in the post-ADA group compared to the pre-ADA group, a result possibly confounded by the unreported use of beta-blockers which can affect rebleeding rates. This study also demonstrates the excellent efficacy and safety of CYA glue with similar rates of all-cause mortality with or without the use of ADA. The major limitations of this study are its small sample size, its retrospective design, the comparison of two asymmetrical cohorts, and the lack of information regarding the size of the varices, which in turn is a primary factor in determining the volume of CYA injected and is also related to the probability of experiencing adverse events. Although absent blood flow, as evidenced by no audio signal, has been used in this study, there is no study examining the sensitivity of this new tool in detecting the obliteration of GV. EUS-guided CYA injection therapy, although used in numerous studies, is costly, requires technical expertise, and lacks large trials. Although this study does provide the aforementioned safety data, large randomized trials comparing the end points of GV obliteration using EUS versus audible Doppler-guided management of GV are needed in order to determine the methods that optimize variceal hemorrhage control and best prevent rebleeding.

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