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PERSPECTIVES

Gastric Variceal Bleeding: Is Endoscopic Ultrasound the Next Game Changer in the Management of Gastric Varices?

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Gastric varices (GV) are present in 15-25% of cirrhotic patients with type 1 gastroesophageal varices (GOV1) being the most common[1,2]. In comparison to esophageal varices, the incidence of gastric variceal bleeding is low (10-20%) and is not proportional to portal venous pressure as noted in the esophageal varices, which has a rebleeding rate of up to 30% noted in GV[2,3]. The GV bleeding is difficult to control due to the presence of a thick mucosal layer over the GV, which does not collapse during bleeding.

With the advent of hemodynamic studies in GV, there has been a significant change in approach and management of GV. Recently, the focus on individualized GV treatment based on hemodynamics of the portal system has increased. These hemodynamic studies and treatment options are applicable especially on the left-sided portal venous diseases, such as GV, ectopic varices and lienorenal shunt, and these treatments are not based on traditionally available endoscopic therapies. The availability of contrast computed tomography (CT) scan of the portal venous system has made it easy to delineate the anatomy of the portal venous system before planning a definitive treatment option (either primary or secondary).

At present, the standard treatments for GV are endoscopic glue injection (EGI) performed by an endoscopist and a balloon-occluded retrograde transvenous obliteration (BRTO) performed by an interventional radiologist[4-8]. Technically, BRTO is more comprehensive than and superior to EGI because the whole shunt which drains the GV can be treated by the BRTO procedure. On the other hand, in the EGI procedure, only the visible mucosal components of the varices are treated whereas the remaining submucosal varices, the shunts and the afferent and efferent drainage pathways are left untreated. EGI is the most popular method for GV treatment all over the world, but it is associated with shortcomings such as:

(i) High rebleeding rate at around 30-40% in case series[9],
(ii) Recurrence of GV after EGI,
(iii) High incidence of systemic complications, such as glue embolization and sepsis,
(iv) Increased risk for rebleeding and worsening of liver disease with each bleeding episode in situations when large volume of glue injection more per session for obliteration are given to patients with large GV,
(v) Imbalanced availability of glue for treatment across countries, and
(vi) Failure to provide direct endoscopic therapy in massively bleeding GV due to limited endoscopic view.

The rebleeding rate after EGI may increase up to 30%. The patients with rebleeding are sent for rescue therapy such as BRTO or combination of BRTO with transjugular intrahepatic portosystemic shunt (TIPS) in selected cases. The failure of therapy in EGI group of patients is probably because hemodynamic factors are not taken into consideration while deciding the treatment of GV. Thus, EGI can be considered a universal therapy in

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any situation only if the underlying portal venous anatomy, including shunts and collaterals, is not taken into account. Of note, hemodynamic studies based on imaging CT, magnetic resonance imaging (MRI), BRTO, and TIPS show that EGI cannot be treated as an all-purpose treatment method as it cannot provide satisfactory treatment in all GV cases[9]

Other than EGI, the standard of care for GV is BRTO, which is physiologically superior and definitive but it is associated with limitations and complications[10]:

(i) Free restricted movements of patient due to long-time insertion of balloon catheter in the occluded vein for 14-16 h and sometimes up to 24 h for complete occlusion of the shunt and GV[11,12],
(ii) Embolization of sclerosant and contrast material,
(iii) Systemic sepsis,
(iv) Renal vein thrombosis,
(v) Requirement for high technical expertise,
(vi) Onset of new ascites and pleural effusion in 15-20% of cases, and
(vii) Increased size of esophageal varices and increased portal hypertensive gastropathy after the shunt occlusion[13,14].

An endoscopic ultrasound (EUS) is a much superior modality in the management of GV as compared to EGI because of its added advantages over the conventional EGI method. The advantages of the EUS are as follows:

(i) EUS is equipped with color Doppler by which it can differentiate between an artery and a vein, facilitating the assessment of vascular and bleeding lesions in the gastric fundus (e.g., between gastrointestinal stromal tumors and GV);
(ii) EUS can assess shunts and collaterals outside the gastric wall, and also treat the perigastric collaterals and shunts if required, thereby physiologically achieving the cessation of blood flow in the GV, an effect somewhat similar to that of BRTO (**Figure 1**);
(iii) EUS can assess efficacy of therapy in term of cessation of blood flow within the target vessel after treatment[11-16].

EUS has been used for treatment of GV from the last decade and it has shown to be technically superior and safe. Aside from that, this low-cost treatment approach also decreases the number of sessions and morbidity related to rebleeding in GV. EUS has been shown to help in the identification of collateral veins, such as lienorenal shunt,

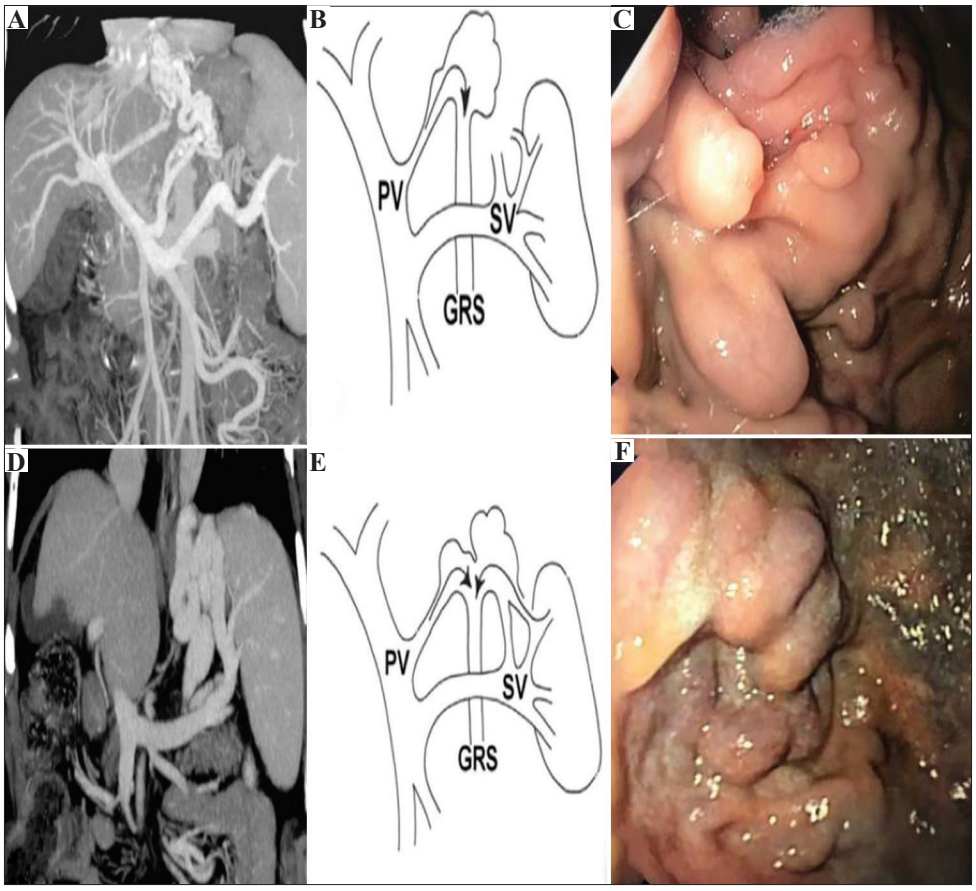


Figure 1. (A and D) Comparison of CT images of portal venous collaterals. Coronal portal venograms show the GV anatomy as well as the afferent and the efferent veins draining the system. (B) A predominant right-sided shunt in which the GV receives afferent vein from portal vein (PV) and drains directly via efferent vein, i.e. gastrorenal shunt (GRS), in renal vein. (E) A combination of right- and left-sided drainage, where the splenic vein (SV) is afferent to GV. (C and F) Endoscopic examination of gastric varices.

which facilitates the planning of treatment and therapy for these patients. It has also been used in esophageal varices assessment and EUS-guided endotherapy, as reported in a few case series.

Two recent randomized trials about EUS-based treatments were published. The first study by Lobo *et al.* compared different therapies and their combinations (EUS+glue and coil group vs. EUS+glue group). The incidence of complications in the EUS+glue group was very higher, probably attributable to the use of lipidol along with the glue. In our experience, we had discontinued treatment containing the combination of lipidol and glue as it delays the formation of clot and thrombus, thereby raising the risk for embolization. In our study, glue was used in the treatment without lipidol. Another randomized controlled trial by Medranada *et al*. compared the use between EUS+coil+glue and EUS+coil. This study concluded that the dual therapy was better in terms of safety and repeat sessions. In an meta-analysis by Babu *et al.* that compared EUS-guided therapy with conventional endotherapy, EUS-guided therapy was found to demonstrate better clinical efficacy for the treatment of gastric varices in the aspects of obliteration, recurrence, and long-term rebleeding, and may be superior to EGI[14,17-26].

Two principal mechanisms by which EUS achieves completion of therapy in GV are

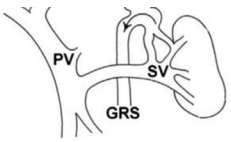
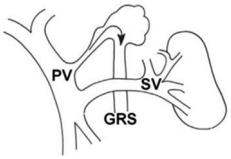
(i) Direct targeting of the mucosal GV in the gastric fundus, and
(ii) Targeting of the submucosal, perigastric collaterals, and the perforators or shunts in some situations.

Targeting of mucosal GV seems equivalent to the mechanism of EGI. The use of EUS is advantageous in this situation because the whole GV can be visualized, and the completion of therapy can be assessed at the same time, if required[14,17,18,20-23].

EUS is a modality whose functions range between EGI and BRTO. At present, there are no comparison studies between EGI, BRTO, and EUS-guided GV therapy. With the advent of better diagnostic imaging of the portal venous anatomy, the anatomy of venous drainage and collaterals can be delineated better in patients with GV. A better understanding of the anatomy, when combined with treatment modalities such as EGI, BRTO, or EUS-guided vascular treatment, helps in individualizing the therapy for the patients with GV. Glue injection is associated with complications, while other modalities such as gel foam, thrombin or coil were found to have minimal associations with complications[19-25].

The role of EUS on hemodynamics and vascular anatomy of GV is presented in Table 1, which shows that the treatment modality to be adopted for therapy can be chosen based on the anatomy, whether EUS is used alone or in combination[24,26,27]. Based on the findings from the previous studies, it is much clearer how we can decide which patients can be treated with a specific procedure.

Table 1. Hemodynamic classification of gastric varices and proposed treatment modality

Shunt/collaterals	Clinical relevance	Proposed treatment modality
Left side collaterals	• Single IGV1 or multiple small IGV1 • Chances of glue embolization are higher if either BRTO or EUS-guided therapy is done alone	• BRTO if lieno-renal shunt > 10 mm • EUS-guided therapy if no EGI
Excessive shunts (>3)	• Single draining shunt • Shunt with multiple collaterals	• BRTO, EUS-GVF, EGI • EUS-GVF, BRTO + TIPS, EGI
Single to few shunts 	• Multiple Shunts • No shunt and multiple collaterals	• EUS-PGC + GVF, TIPS, EGI • EUS-PGC ± GVF, • Neither BRTO nor TIPS is feasible, and EGI is not feasible too because the risk for embolization is high
Right side collaterals 	• Single Large GV • Multiple GV • Recurrent bleeding with shunts (absent lieno-renal shunt)	• EUS-GVF, TIPS, EGI • TIPS + BRTO, EGI (multiple sites) • EUS-PGC ± GVF • Neither BRTO nor TIPS is feasible; EGI is feasible but the risk for embolization is high

IGV1, type 1 isolated gastric varix; BRTO, balloon-occluded retrograde transvenous obliteration; EUS, endoscopic ultrasound; EGI, endoscopic glue injection; EUS-GVF, EUS-guided GV therapy targeting gastric fundus; TIPS, transjugular intrahepatic portosystemic shunt; EUS-PGC, EUS-guided GV therapy targeting perigastric collateral; +, with; ±, with or without.

GV indications for EGI procedure:

(i) Non-availability of technical expertise (BRTO or EUS).
(ii) Emergency situation, for example, hemodynamically unstable patient.
(iii) Multiple small gastric varices which are not amenable for coil placement.

GV indications for EUS-guided procedure:

(i) No lieno-renal shunt available on imaging (not amenable for BRTO)
(ii) Large perigastric collaterals
(iii) BRTO or TIPS not available
(iv) Advanced liver disease (high model for end-stage liver disease-sodium score (MELD-Na) > 18 and high Child-Turcotte-Pugh (CTP) score)

(v) Contraindications to BRTO or TIPS, such as hepatic encephalopathy, coagulopathy, moderate to massive ascites, cardiac failure, and portal vein and splenic vein thrombosis

GV indications for BRTO or TIPS

(i) Failure of endoscopic therapy
(ii) Lieno-renal shunt of > 10 mm
(iii) BRTO in predominant left-sided collaterals or TIPS in predominant right-sided collaterals

In conclusion, EUS is an emerging modality in the management of GV. The data suggest that EUS, as a treatment modality, is superior to EGI because of its association with lower incidence of complications, lesser number of treatment session required, and lower rebleeding rates. EUS can also help with determining the need to change the treatment depending on the hemodynamics of GV, whether to consider a direct treatment on gastric fundus or perigastric placement of coils.

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Conflict of interest

The author declared that he has no conflicts of interest.

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