—Commentary—

EUS-guided therapy of gastric varices (with video)

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INTRODUCTION

The development of gastric varices (GVs) is a well-known complication of portal hypertension that is present in up to one-third of cirrhotic patients,[1] with an estimated 6-week mortality rate after the first bleeding index of 20%.[2] Current guidelines recommend endoscopic cyanoacrylate injection as the standard therapy for GVs,[3] despite reports of high rebleeding rates and fatal adverse events.[4,5]

EUS-guided endovascular therapies, including the injection of glue, coils, absorbable hemostatic gelatin sponges, and hybrid treatments, have been proposed for the management of GVs. However, clinical guidelines and consensus statements are pending. The present article discusses the rationale of EUS-guided endovascular treatment and reviews EUS-guided alternatives for the management of GVs.

RATIONAL FOR EUS-GUIDED ENDOVASCULAR THERAPY

EUS offers several benefits to endoscopists for the management of GVs. One of the main benefits is the precision regarding vascular targeting of the vascular structures in proximity to the gastrointestinal tract wall. Direct EUS visualization reduces the risk of perivariceal injection. Image guidance is mandatory for the injection of a device such as a coil. EUS allows the direct visualization of blood flow within the varices, enabling the detection of feeder vessels. Obliteration of such feeder vessels, which requires less glue (due to smaller diameter), should result in secondary obliteration of the feeder's tributary varices.[6] After treatment, varix obliteration can be confirmed through EUS Doppler [Figure 1]. A practical advantage of EUS is the capacity of therapeutic intervention independent of endoscopic visualization, such as in cases of active bleeding or retained food.

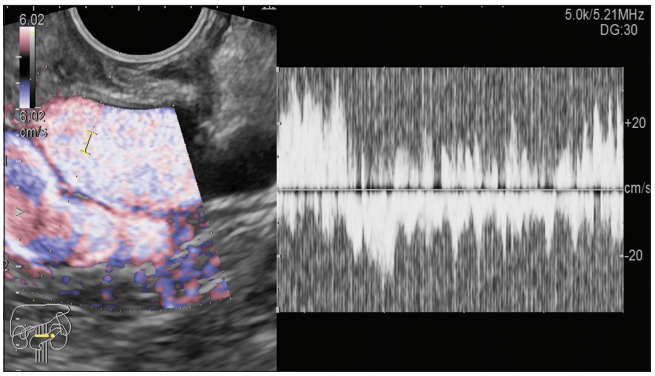

Figure 1. EUS Doppler evaluation of the gastric varix feeder vessel before EUS-guided therapy

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EUS-GUIDED GLUE INJECTION

EUS-guided fine-needle injection of cyanoacrylate was recently compared to standard direct endoscopic injection in a single-center study, confirming several benefits of EUS-guided therapy over direct endoscopic injection. These benefits were as follows: (a) a significantly lower mean volume of cyanoacrylate was required for GV obliteration, (b) a significantly higher number of varices were injected, (c) a significantly inferior rebleeding rate from GVs (8.8% *vs.* 23.7%, $P = 0.045$) was achieved, and d) a similar safety profile was maintained.[7]

EUS-GUIDED COIL DEPLOYMENT

Coiling has been applied as an alternative to cyanoacrylate glue for endoscopic treatment of GVs. When correctly sized to the diameter of the treated vessels, coils have a low risk of systemic migration. This makes coiling particularly attractive for patients with gastro-renal shunts, which have an increased risk of embolization when the glue is used.[8]

In a retrospective study comparing EUS-guided coiling *vs.* EUS-guided cyanoacrylate injection, both techniques exhibited similar obliteration rates. However, coiling was associated with a significantly inferior adverse event rate, whereas cyanoacrylate therapy was associated with a significantly higher incidence of asymptomatic pulmonary glue embolism.[9]

EUS-GUIDED DEPLOYMENT OF EMBOLIZATION COILS WITH CYANOACRYLATE INJECTION

Combined deployment of coils followed by glue injection has conceptual advantages over each alone. The deployed coil functions as a scaffold to retain the cyanoacrylate within varix, thereby reducing the risk of glue embolization [Video 1]. The combined treatment may also decrease the amount of glue needed to achieve obliteration, further decreasing the embolization risk.[10-12] In one of the most extensive series of EUS-guided combined coil and cyanoacrylate injection, a high technical and clinical success rate was noted (>99%) for hemostasis achievement in cases of active bleeding; primary and secondary bleeding prophylaxis was observed, with almost 80% of patients achieving GV obliteration within one session and only 3% of patients experiencing rebleeding after complete eradication.[10]

In a recent cost-effectiveness analysis of endoscopic cyanoacrylate injection *vs.* EUS-guided combined therapy with coiling and cyanoacrylate injection, the latter was associated with significantly higher procedural costs. However, when analyzing the costs of rebleeding management and hospitalization, EUS-guided combined therapy resulted in significantly lower costs compared to endoscopic cyanoacrylate injection therapy.[13]

In a recent randomized trial of 60 patients, EUS-guided combined coil and glue therapy was compared to EUS-guided coiling alone. Although both techniques proved to be safe, feasible, and effective for varix obliteration evaluated via EUS-Doppler, essential differences in outcomes were found. First, higher rebleeding and reintervention rates were noted in the patients treated with EUS-guided coiling alone. Similar survival periods were reported on follow-up. Second, varix disappearance on endoscopic evaluation was significantly higher in the EUS-guided combination therapy group. This was despite confirmation of absent Doppler flow after the index procedures in both groups, suggesting that endoscopic evaluation more accurately predicts varix recurrence and rebleeding events requiring reintervention.[14]

In a recent meta-analysis with data for 536 patients, EUS-guided combined therapy with coils and cyanoacrylate injection resulted in significantly superior technical and clinical outcomes compared to each performed alone. Moreover, combined therapy had a superior safety profile over EUS-guided cyanoacrylate glue injection, yet there was no difference when compared to coiling alone.[15] This supports EUS-guided combined therapy as the preferred strategy over monotherapy for the treatment of GVs.

EUS-GUIDED COIL EMBOLIZATION WITH ABSORBABLE HEMOSTATIC GELATIN SPONGES

Recently, the use of absorbable gelatin sponges was reported for combined therapy with coils in ten patients, with a 100% technical success rate and no cases of rebleeding or reintervention during a 6-month follow-up. Only one adverse event was reported (abdominal pain). There were no cases of systemic embolization.[16]

EUS-GUIDED THERAPY FOR RESCUING GASTRIC VARICES REBLEEDING

A recent retrospective study of 81 patients who experienced rebleeding after initial endoscopic cyanoacrylate injection, showed the superiority of EUS-guided therapy over the standard endoscopic therapy in terms of rebleeding and mortality rates.[20]

EUS-GUIDED VARICEALOGRAPHY OF GASTRIC VARICES

Varicealography of GVs and feeder vessels during EUS-guided endovascular therapy has a potential impact on clinical outcomes,[12] it enables to examine the portal venous system anatomy allows confirmation of intravascular location, endoscopic assessment of varix flow trajectory [Figure 2], classification of GVs as localized or diffuse, and detection of large shunts present in 38%–60% of patients,[8,17] which increase embolization risk when acrylate derivates are injected alone. In our clinical experience using varicealography in 132 patients with GV, this technique allowed us to identify four cases in which patients had porto-splenic shunts, guiding the therapy for coiling alone and to identify GVs patients with two feeder vessels.

EUS-GUIDED PORTAL VENOUS SYSTEM PROCEDURES

EUS-guided puncture of the portal vein system has the advantage of a simultaneous portal pressure gradient measurement using a digital compact manometer, which accurately reflects the degree of portal hypertension. This promising technique offers invaluable information for the management of patients with chronic liver disease and the degree of portal hypertension and is the best prognostic indicator; it may also be useful for guiding management at every phase of medical treatment.[18] Transjugular intrahepatic portosystemic shunting is a lifesaving procedure. Recently, a EUS-guided intrahepatic portosystemic shunt was created using a lumen apposing metal stent showing the feasibility and safety of this promising EUS-guided endovascular technique in porcine models.[19]

THE FUTURE

The gastrointestinal tract provides a unique window to access vascular structures in the abdomen and mediastinum. The exceptional high-resolution imaging of vascular structures afforded by EUS creates an opportunity for precise vascular access and therapy. Interventional EUS offers new exciting diagnostic and therapeutic options. Currently, we are delivering solutions and devices through a standard FNA needle. All of these methods, including coils, gel foam, and even cyanoacrylate glue, have been borrowed from the "toolbox" of our interventional radiology colleagues. In the future, the development of novel, innovative platforms dedicated to interventional EUS will occur. Randomized controlled studies validating the significant benefits of EUS-guided treatment over endoscopy-guided treatment for GVs have emerged. Randomized controlled studies have also shown hybrid treatments, such as the combination of coils and glue, to be superior to traditional monotreatments using glue or coil alone. These more complex hybrid treatments will benefit from innovative devices. A critical focus of the future will need to be advanced training in interventional EUS. Dissemination of interventional EUS can only occur with a greater focus of resources for postgraduate training opportunities. As interventional EUS disseminates, our industry partners will be incentivized to invest in the research and development of new tools and treatments.

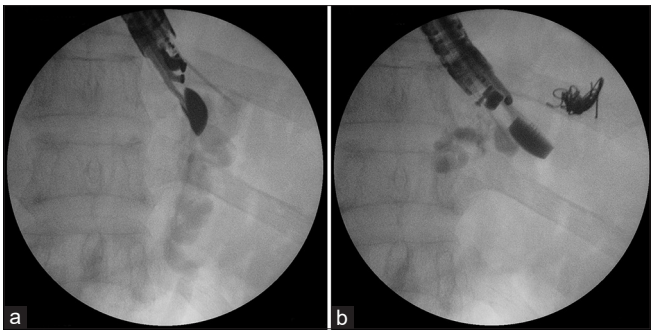

Figure 2. EUS-guided varicealography for the anatomic evaluation of gastric varices feeder vessels and blood-flow trajectory (Panel a). After coil deployment under EUS-guidance a second feeder vessel was detected under EUS-guided varicealography in the same patient (Panel b)

CONCLUSION

EUS-guided endovascular therapy has demonstrated several benefits over endoscopic therapy in the management of GV: adequate feasibility with high technical success rates, higher efficacy with superior obliteration rates for EUS-guided therapy and a higher safety profile, decreasing the risk of fatal and nonfatal adverse events.

Conflicts of interest

There are no conflicts of interest.

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