

ENDOSCOPIC TREATMENT OF GASTRIC VARICES: WHEN AND HOW?

Valdés Delgado T, Rodríguez-Téllez M

UNIVERSITY HOSPITAL VIRGEN MACARENA. SEVILLE.

Abstract

Bleeding from gastric varices is less common than from esophageal varices, but when it occurs, it does so more rapidly and profusely, with higher rates of rebleeding and mortality. Therefore, understanding their complex pathophysiology and vascularization is essential, posing a significant endoscopic and therapeutic challenge.

To classify them, the Sarin classification must be used, with fundic varices posing the greatest risk of bleeding and being the focus of this controversy.

When there is active bleeding from fundic varices, treatment must be applied; however, high-quality data to choose the optimal strategy remain limited. Nonetheless, clinical practice guidelines strongly recommend treatment with cyanoacrylate via conventional gastroscopy, as it is an effective, relatively easy, and safe technique to apply in an emergency.

Special precautions must be taken when applying cyanoacrylate due to its complications, the most feared

being systemic embolisms. To minimize or even eliminate complications, the combined technique (cyanoacrylate + coils) guided by endoscopic ultrasound was developed. This treatment modality could be considered the most effective and safe technique, and although it is not yet the preferred choice for acute bleeding, it plays a fundamental role in secondary prophylaxis. It is endorsed by the ESGE guideline and has been included in the research agenda for the upcoming Baveno consensus.

Keywords: gastric varices, treatment, cyanoacrylate, combined technique.

Introduction

Gastric varices (GV) are present in approximately 20% of cirrhotic patients with portal hypertension (PH), with GV bleeding being less frequent than oesophageal variceal (EV) bleeding. However, when GVs bleed, they bleed more rapidly and profusely, leading to higher mortality (mortality rates of up to 45%), higher rates of treatment failure and thus rebleeding

Manuel Rodríguez-Téllez
University Hospital Virgen Macarena. Seville.
mrodrigueztellez@gmail.com

Valdés Delgado T, Rodríguez-Téllez M
Endoscopic treatment of gastric varices: when and how?
RAPD 2024;47(3):116-122. DOI: 10.37352/2024473.3

(rebleeding rates 35-90%)¹. All this, added to the complexity of its pathophysiology and vascularisation, presents us with a diagnostic and, above all, therapeutic challenge.

In general, the risk factors for GV bleeding are: advanced liver disease (Child B-C), GV >5 mm, GV with red dots and their location, fundic varices (FV) have a higher risk of bleeding than the rest².

As for their pathophysiology, GVs are made up of an afferent, nutritive or inflow vein and an efferent or outflow vein. This efferent vein, in 85% of cases, is formed by a decompressive portosystemic shunt, to which the systemic complications of the most widely used treatment at present, the injection of cyanoacrylate, are attributed^{3,4} (Figure 1).

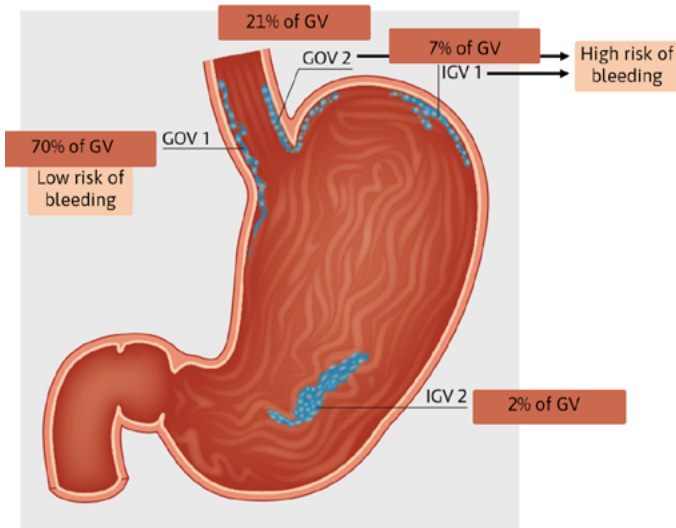


Figure 1. Sarin Classification of Gastric Varices (GV: Gastric Varices. GOV: Gastroesophageal Varices. IGV: Isolated Gastric Varices).

Classification

In order to be able to treat them correctly, it is essential to define and characterise them with criteria. There are several classifications^{5,6}, but the one used in endoscopy and endorsed by Baveno VII⁷, is the Sarin classification¹. It divides them according to their location into oesophagogastric or "junctional" varices, type GOV-1 (extending towards the lesser curvature) and GOV-2 (extending towards the fundus); on the other hand, isolated gastric varices type IGV-1 (in the fundus) and IGV-2 elsewhere. The most frequent are GOV-1 (70% of GVs) and have a lower risk of bleeding. In contrast, IGV-1 and GOV-2 are less frequent but have a high risk of bleeding, and are the origin of GV bleeding in 60-70% of cases^{7,8} (Figure 2). These FVs are the focus of this controversy.

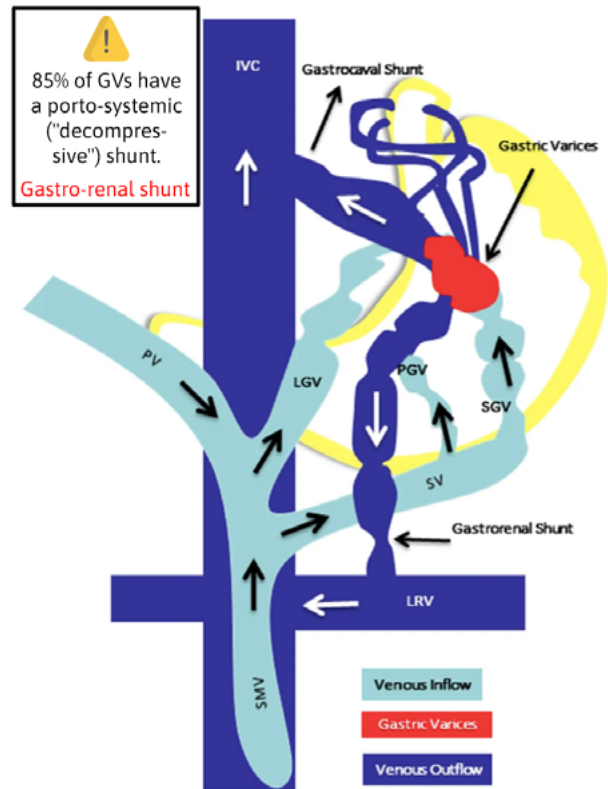


Figure 2. Vascularization of Gastric Varices (GV). Phillips et al. Figure, BMC Gastroenterol (2020). IVC: Inferior Vena Cava. LRV: Left Renal Vein. PV: Portal Vein. SMV: Superior Mesenteric Vein. SV: Splenic Vein. LGV: Left Gastric Vein. SGV: Short Gastric Vein. PGV: Posterior Gastric Vein.

Available treatments

Depending on the scenario and the techniques available in each centre, we can apply one treatment or another.

1. CONVENTIONAL GASTROSCOPY
 - Elastic bands.
 - Cyanoacrylate injection.
 - Sclerotherapy (ethanol, ethanolamine or polidocanol).
2. ECOENDOSCOPY
 - Cyanoacrylate injection.
 - Coil release.
 - Coil release + cyanoacrylate injection.
3. INTERVENTIONAL RADIOLOGY
 - TIPS (trans-jugular intrahepatic portosystemic shunt).

- BRTO (Balloon-occluded retrograde transvenous obliteration).

Different clinical scenarios

1. Gastric varicose veins with active bleeding. Treatment is always necessary.
2. Gastric varices that have bled, but at the time of gastroscopy there is no active bleeding. The treatment to be applied is secondary prophylaxis.
3. Gastric varices that have never bled. The treatment we decide on is primary prophylaxis.

Treatment of active bleeding from gastric varices

Initial assessment, resuscitation and general measures

Management of these patients should be carried out in critical or intermediate care units, at least during the first hours.

Baveno VII supports a conservative transfusion strategy, aiming for a haemoglobin of 7-8 g/dL; and avoid routine transfusion of fresh frozen plasma or platelets.

Specifically, routine orotracheal intubation prior to endoscopy is discouraged, reserving the latter for patients with altered level of consciousness or active haematemesis.

Prevention of bacterial infection remains a priority objective and intravenous ceftriaxone (1 g/24 hours) remains the most commonly used option in clinical practice. Withdrawal of proton pump inhibitors is recommended once endoscopy confirms the variceal origin of the bleeding.

Specific pharmacological haemostatic therapy of acute bleeding consists of early administration of vasoactive drugs (terlipressin, somatostatin or octreotide) as early as possible, to be maintained for 2-5 days, in addition to endoscopic treatment in the first 12 hours after stabilisation of the patient (or as soon as it is safe if instability persists). For these reasons it is considered essential that hospitals caring for patients with acute variceal haemorrhage have a gastroenterologist with experience in endoscopy available 24 hours a day⁹.

Specific endoscopic treatment

Whenever there is active bleeding at the time of gastroscopy, some endoscopic treatment should be applied.

Endoscopic options currently available to treat acute GV bleeding include sclerotherapy, endoscopic band ligation (EBL) and cyanoacrylate injection. However, high-quality data for choosing the optimal strategy remain limited, with inconsistencies between trials regarding mortality, incidence of rebleeding and adverse events.

Several systematic reviews/meta-analyses¹⁰⁻¹³ have evaluated the efficacy of cyanoacrylate injection for the treatment of GV bleeding and compared it with other endoscopic methods (sclerotherapy or EBL), with cyanoacrylate being superior in most outcomes, achieving better rates of immediate haemostasis and prevention of rebleeding.

Based on current evidence, clinical practice guidelines (ESGE and Baveno VII⁹) recommend:

1. GOV-1 and IGV-2 type GVs can be treated the same as EVs with EBL.
2. GOV-2 and IGV-1 type GVs should be treated with cyanoacrylate injection by conventional gastroscopy, achieving high rates of immediate haemostasis and low rates of rebleeding. In addition to being effective, it is easy and safe to apply in an emergency.

Cyanoacrylate is a tissue adhesive that polymerises rapidly on contact with blood and becomes a hard, acrylic material that will obliterate the varicose vein^{3,14}. In the United States it was approved by the FDA in 1998, but its use is restricted and few authorised centres are allowed to use it. Although it was first described in 1986 for the treatment of GVs by Soehendra, there are several ways of doing it and this is what makes the technique somewhat confusing and complex for endoscopists. For this reason, the endoscopy service of our hospital (Virgen Macarena University Hospital) together with the nursing staff, have developed a protocol according to our availability and experience, explaining the whole process step by step (Figure 3).

1. Lubricate the channel with acetone/silicone/lipiodol.
2. Disconnect suction.

3. Flush the injector with saline solution (SS) (approx. 1.5-2 ml).
4. Load 2 ampoules of Histoacryl (0.5 ml+ 0.5 ml) mixed with 1 ml lipiodol in a 5 ml syringe.
5. Inject the glue and rapidly push in 1.5-2 ml of SS.
6. Keep the needle inside the catheter to avoid tissue impaction (adhesive).
7. Remove the gastroscope without keeping the catheter inside the channel and then cut off the tip of the catheter so that the catheter can be removed.

severe embolism. Lipiodol is used to control the polymerisation time and, very importantly, as a contrast medium, a particularly useful advantage in cases of suspected embolisation. Although in most cases systemic emboli are asymptomatic, some studies describe up to 50% of these¹⁵⁻¹⁷.

Other complications of this technique are the formation of post-injection ulcers or fistulas, as well as systemic infections. Special mention should be made of complications related to the equipment, such as adhesion of the glue to the lens or to the gastroscope channel.

All these drawbacks of direct injection of cyanoacrylate by gastroscopy can be minimised or even eliminated by echoendoscopically guided administration, which would also allow for coil release^{15,17}.

The first time the echoendoscopy-guided coils release technique was performed to treat acute bleeding due to gastric varices was at Virgen Macarena University Hospital in Seville in 2010, by Romero-Castro *et al.*¹⁵. In 2011, Binmoeller *et al.*¹⁸ described this same technique, combined with cyanoacrylate, achieving a 96% obliteration rate of gastric varices in a single treatment session, without clinical signs of embolization with cyanoacrylate. Since this initial study, multiple retrospective studies, two randomised clinical trials and systematic reviews/analyses have been published on this topic^{19,20}, concluding that the treatment of acute GV bleeding is more effective and safe under endoscopic guidance and in combination (coils + cyanoacrylate).

Despite this evidence in the literature, for the moment, clinical practice guidelines^{7,8} do not strongly recommend this combined technique guided by echoendoscopy as the treatment of choice for acute GV bleeding. This may be due to the complexity of applying it in an emergency; these techniques are safer but only performed by expert personnel and are more expensive.

Where the recommendation for the combined echoendoscopy-guided technique is strong, on a par with the other options, is in secondary prophylaxis, which we will see later.

Persistent bleeding or early rebleeding of gastric varices

When endoscopic primary haemostasis fails or we have early recurrent bleeding we have to resort to the urgent



Cyanoacrylate injection technique. Treatment of gastric varicose veins

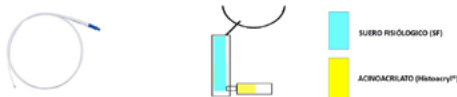
1. Eye protection for healthcare personnel and patient.



2. Disconnect suction.

3. Lubricate the channel with acetone/silicone/lipiodol.

4. Flush the injector with saline solution (SS) (approx. 1.5-2 ml).



5. Load 2 ampoules of Histoacryl (0.5 ml+ 0.5 ml) mixed with 1 ml lipiodol in a 5 ml syringe.



6. Inject the glue and rapidly push in 1.5-2 ml of SS.



7. Remove the gastroscope without keeping the catheter inside the channel and then cut off the tip of the catheter so that the catheter can be removed.

Figure 3. Cyanoacrylate Injection Technique. Virgen Macarena University Hospital.

In addition to the preparation and care during injection, special precautions must be taken with cyanoacrylate, such as in large portosystemic shunts, cardiac septal defects or hepatopulmonary syndrome, due to the risk of symptomatic and

salvage radiological techniques, TIPS or BRTO. There are very limited high level data comparing TIPS and BRTO in these situations^{21,22}. BRTO and TIPS have similar rates of technical success and adverse effects. TIPS is associated with higher rates of hepatic encephalopathy and BRTO with long-term aggravation of oesophageal varices. Due to the limited quality of comparative data, no specific selection criteria are currently available, therefore individualisation according to patient and centre experience is necessary.

Primary and secondary prophylaxis of gastric varices

Primary prophylaxis (GVs that have never bled) is performed in the same way and with the same criteria as EVs. When patients cannot receive non-selective beta-blockers (BBNS) (due to intolerance or contraindication), in the case of GOV-1 type GV, they should be treated like EVs with EBL. However, in the case of FVs, type GOV-2 or IGV-1, to date there are no firm recommendations on the endoscopic treatment of FVs in patients with intolerance to BBNS. In fact, the ESGE suggests, with a weak recommendation and low evidence, that it is equally valid not to perform any treatment or to treat them, either with cyanoacrylate injection by gastroscopy or treatment by echoendoscopy with coils + cyanoacrylate, on a case-by-case basis, and if treated, in centres with experience in the technique⁸.

In secondary prophylaxis (GVs that have bled at some point), GOV-1s are treated the same as EVs. For FVs, type GOV-2 and IGV-1, it is difficult to provide solid evidence-based recommendations due to the heterogeneity of previous research and the lack of uniform definitions or standardised outcomes. The available literature consists of case series, restricted cohort studies and a few small randomised trials, with significant selection biases²³. Therefore, the ESGE recommends an individualised approach, based on patient factors and local experience for FV eradication therapies, considering endoscopic injection of cyanoacrylate +/- BBNS, combined treatment with coils + cyanoacrylate guided by echoendoscopy, TIPS placement or BRTO⁸. A recently published network meta-analysis²⁴ suggested that BRTO may be the best intervention to prevent FV rebleeding (secondary prophylaxis), while BBNS monotherapy cannot be recommended; however, direct comparative studies are much needed.

With regard to treatments guided by endoscopic ultrasound, the target is to puncture the nutrient vessel, the perforating vein, or, failing that, the varicose vein directly. In addition, this allows us to perform it when endoscopic vision is limited by bleeding, since with Doppler we can locate the vessels and the flow, and

Doppler also allows us to check the cessation of flow when the varicose vein is obliterated (Figure 4). This can be done with different methods of obliteration: with cyanoacrylate alone, with coils alone, or with a combination of both. After a first GV treatment session, the next revision is recommended after 4-6 days and thereafter, as with EVs, every 2-4 weeks until complete GV obliteration is achieved²⁵. The steps for cyanoacrylate injection and echoendoscopically guided coil placement are explained below.

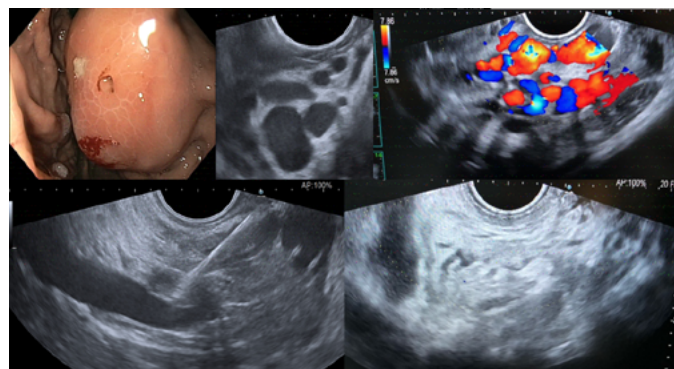


Figure 4. Example Clinical Case Dr. Romero. Placement of coils in GOV-2 varix. Gastric varix with intense Doppler flow (figure 3). Injection of 6 coils (figure 4). Complete cessation of intravariceal flow (figure 5).

Echoendoscopy-guided cyanoacrylate injection technique:

1. 22G needle purged by glucosmon.
2. Cyanoacrylate with lipiodol 1:1.
3. Avoid lateral movements with the needle inside the varicose vein.
4. Check afferent perforator: contrast or Doppler.
5. Inject 1 ml of cyanoacrylate above the muscle layer.
6. Check occlusion of the varicose vein with Doppler.

Echoendoscopy-guided coil placement technique:

1. 19 G needle.
2. Coils diameter 20% larger than the varicose vein: 8-20 mm.
3. Remove stylet and push coil with it.
4. Check intravaricose insertion of the coil.

5. As many coils as necessary.

As with EVs, patients with GV and high risk of failure to standard treatment would benefit from placement of a preventive TIPS in the first 72 hours^{7,8}.

Conclusions

1. The treatment of choice in acute bleeding of fundic varices (GOV-2 and IGV-1) is cyanoacrylate injection by conventional endoscopy.
2. Echoendoscopy-guided therapy may be particularly useful in specific situations: poor visibility and retreatment. It reduces cyanoacrylate complications and allows coil release.
3. Combined echoendoscopy-guided treatment (coils + cyanoacrylate) appears to be the most effective and safe strategy today, but well-designed controlled studies are needed to position it as the treatment of choice. This will ensure that in the coming years there will be a stronger position in the recommendations.

Finally, and by way of conclusion, the algorithm of action we follow when there is an active VG haemorrhage in the Virgen Macarena University Hospital is shown graphically (Figure 5).

Bibliography

1. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. *Hepatology*. 1992;16(6):1343-1349. doi:10.1002/hep.1840160607.
2. Kim T, Shijo H, Kokawa H, et al. Risk factors for hemorrhage from gastric fundal varices. *Hepatology*. 1997;25(2):307-312. doi:10.1053/jhep.1997.v25.pm0009021939.
3. Martínez-González J, López-Durán S, Vázquez-Sequeiros E, Albillos-Martínez A. Management of fundic varices. *Endoscopic aspects*. *Rev Esp enferm Dig*. 2015;107(8):501-508.
4. Philips CA, Ahamed R, Rajesh S, George T, Mohanan M, Augustine P. Beyond the scope and the glue: update on evaluation and management of gastric varices. *BMC Gastroenterol*. 2020;20(1):361. doi:10.1186/s12876-020-01513-7.

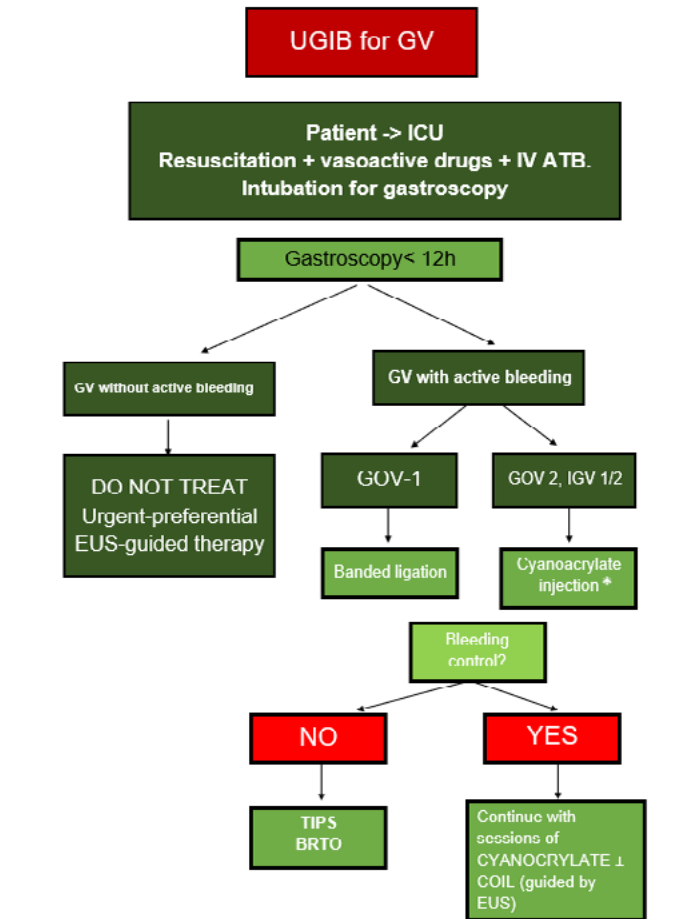


Figure 5. Algorithm for Acute Hemorrhage from Gastric Varices (GV: Gastric Varices. ICU: Intensive Care Unit. IV ATB: Intravenous Antibiotic Therapy. BRTO: Balloon-occluded Retrograde Transvenous Obliteration). * By standard endoscopy only in case of emergency without an experienced echoendoscopist available. Echoendoscopy-guided treatment (coils+/-cyanoacrylate) is preferable.

5. Arakawa M, Masuzaki T, Okuda K. Pathology of fundic varices of the stomach and rupture. *J Gastroenterol Hepatol*. 2002;17(10):1064-1069. doi:10.1046/j.1440-1746.2002.02855.x.
6. Maydeo A, Patil G. How to Approach a Patient With Gastric Varices. *Gastroenterology*. 2022;162(3):689-695. doi:10.1053/j.gastro.2021.12.277.
7. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C. Baveno VII - Renewing consensus in portal hypertension. *J Hepatol*. 2022;76(4):959-974. doi:10.1016/j.jhep.2021.12.022.
8. Gralnek IM, Camus Duboc M, Garcia-Pagan JC, et al. Endoscopic diagnosis and management of esophagogastric variceal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2022;54(11):1094-1120. doi:10.1055/a-1939-4887.

9. Téllez L, Guerrero A, Albillos A. Actualización del diagnóstico y el tratamiento de la hipertensión portal en la cirrosis según las recomendaciones de la Conferencia de Consenso de Baveno VII. *Rev Esp Enferm Dig.* 2022;114(9):534-542. doi:10.17235/reed.2022.8868/2022.
10. Ye X, Huai J, Chen Y. Cyanoacrylate injection compared with band ligation for acute gastric variceal hemorrhage: a meta-analysis of randomized controlled trials and observational studies. *Gastroenterol Res Pract.* 2014;2014:806586. doi:10.1155/2014/806586.
11. El Amin H, Abdel Baky L, Sayed Z, et al. A randomized trial of endoscopic variceal ligation versus cyanoacrylate injection for treatment of bleeding junctional varices. *Trop Gastroenterol.* 2010;31(4):279-284.
12. Chirapongsathorn S, Manatsathit W, Farrell A, Suksamai A. Safety and efficacy of endoscopic cyanoacrylate injection in the management of gastric varices: A systematic review and meta-analysis. *JGH open an open access J Gastroenterol Hepatol.* 2021;5(9):1047-1055. doi:10.1002/jgh3.12629.
13. Ríos Castellanos E, Seron P, Gisbert JP, Bonfill Cosp X. Endoscopic injection of cyanoacrylate glue versus other endoscopic procedures for acute bleeding gastric varices in people with portal hypertension. *Cochrane database Syst Rev.* 2015;2015(5):CD010180. doi:10.1002/14651858.CD010180.pub2.
14. Escorsell À, Bosch YJ. Hemorragia digestiva variceal. *Gastroenterol y Hepatol Contin.* 2005;4:97-102.
15. Romero-Castro R, Pellicer-Bautista F, Giovannini M, et al. Endoscopic ultrasound (EUS)-guided coil embolization therapy in gastric varices. *Endoscopy.* 2010;42 Suppl 2:E35-6. doi:10.1055/s-0029-1215261.
16. Romero-Castro R, Ellrichmann M, Jimenez-García VA. Endoscopic ultrasound-guided therapy of gastric varices with coils plus cyanoacrylate injection versus coiling alone: getting evidence-based data but are they comparable? *Endoscopy.* 2021;53(1):101. doi:10.1055/a-1214-6213.
17. 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. doi:10.1016/j.gie.2013.05.009.
18. 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. doi:10.1016/j.gie.2011.06.030.
19. Mohan BP, Chandan S, Khan SR, et al. Efficacy and safety of endoscopic ultrasound-guided therapy versus direct endoscopic glue injection therapy for gastric varices: systematic review and meta-analysis. *Endoscopy.* 2020;52(4):259-267. doi:10.1055/a-1098-1817.
20. McCarty TR, Bazarbashi AN, Hathorn KE, Thompson CC, Ryou M. Combination therapy versus monotherapy for EUS-guided management of gastric varices: A systematic review and meta-analysis. *Endosc ultrasound.* 2020;9(1):6-15. doi:10.4103/eus.eus_37_19.
21. Yu Q, Liu C, Raissi D. Balloon-occluded Retrograde Transvenous Obliteration Versus Transjugular Intrahepatic Portosystemic Shunt for Gastric Varices: A Meta-Analysis. *J Clin Gastroenterol.* 2021;55(2):147-158. doi:10.1097/MCG.0000000000001305.
22. Paleti S, Nutalapati V, Fathallah J, Jeepalyam S, Rustagi T. Balloon-Occluded Retrograde Transvenous Obliteration (BRTO) Versus Transjugular Intrahepatic Portosystemic Shunt (TIPS) for Treatment of Gastric Varices Because of Portal Hypertension: A Systematic Review and Meta-Analysis. *J Clin Gastroenterol.* 2020;54(7):655-660. doi:10.1097/MCG.0000000000001275.
23. Henry Z, Patel K, Patton H, Saad W. AGA Clinical Practice Update on Management of Bleeding Gastric Varices: Expert Review. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc.* 2021;19(6):1098-1107.e1. doi:10.1016/j.cgh.2021.01.027.
24. Osman KT, Nayfeh T, Abdelfattah AM, et al. Secondary Prophylaxis of Gastric Variceal Bleeding: A Systematic Review and Network Meta-Analysis. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc.* 2022;28(6):945-958. doi:10.1002/lt.26383.
25. Prieto R, Carvajal G, Álvarez E, Aponte D, Sabbagh L. Tratamiento de las várices gástricas con cianoacrilato, experiencia institucional. *Rev Colomb Gastroenterol.* 2017;31(3):223-228. doi:10.22516/25007440.94.