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Clip-assisted therapy *versus* EUS–guided coil embolization for secondary prophylaxis of isolated gastric varices: A multicenter study

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ABSTRACT

Background and Objectives: Bleeding from isolated gastric varix type I (IGV1) is less common but more dangerous and fatal than other varices. This study compared the safety and efficacy of endoscopic clipping and cyanoacrylate injection (EC-CYA) with EUS–guided coil and cyanoacrylate injection (EUS-coil/CYA) in the secondary prophylaxis of IGV1.

Methods: A retrospective study was conducted on 131 patients with cirrhosis and a history of IGV1 bleeding who underwent either EC-CYA (n = 55) or EUS-coil/CYA (n = 76) at three medical centers. Primary outcomes were gastric variceal rebleeding and ectopic embolism. Secondary outcomes were technical success, variceal obliteration rate, cyanoacrylate volume, cyanoacrylate embolization efficiency, other causes of rebleeding, other adverse events, and mortality.

Results: In the EC-CYA group, the gastric variceal rebleeding rate (14.5% *vs*. 8.7%, P = 0.307), technical success rate (96.4% *vs*. 94.7%, P > 0.999), other causes of rebleeding rate (12.7% *vs*. 5.8%, P = 0.303), other adverse events rate (5.5% *vs*. 5.8%, P > 0.999), and mortality (12.7% *vs*. 8.7%, P = 0.467) showed no significant differences compared with the EUS-coil/CYA group. No ectopic embolism was found in either group. The EC-CYA group had a higher cyanoacrylate volume (3.14 ± 1.45 mL *vs*. 1.99 ± 0.72 mL, P < 0.001) and a higher variceal obliteration rate at first follow-up (82.23% ± 27.09% *vs*. 66.59% ± 30.28%, P = 0.032). However, the EUS-coil/CYA group was superior to the EC-CYA group in terms of cyanoacrylate embolization efficiency (2.85 ± 2.05 cm^2/mL *vs*. 1.98 ± 1.46 cm^2/mL, P = 0.044).

Conclusions: Both EC-CYA and EUS-coil/CYA are safe and effective in preventing rebleeding of IGV1. The EUS-coil/CYA has better embolization efficiency, whereas EC-CYA has better operational convenience.

Keywords: Cyanoacrylate; Coil; Endoscopic clipping; EUS; Gastric varices

INTRODUCTION

Bleeding from esophagogastric varices is a serious complication and a major cause of death in patients with cirrhosis and portal hypertension. About 35%–90% of patients rebleed after the initial bleeding episodes.[1] Among them, bleeding from gastric varices (GV) is less common than esophageal varices (EV), but has higher bleeding volume and lethality.[2,3] In particular, isolated gastric varix type 1 (IGV1) accounts for 8% of GVs but causes approximately 80% of bleeding events.[4]

Endoscopic cyanoacrylate injection, nonselective β-blockers, transjugular intrahepatic portosystemic shunt (TIPS), and balloon-occluded retrograde transvenous obliteration (BRTO) are secondary prophylaxis for gastric variceal bleeding (GVB).[5] The European Association for the Study of the Liver and the Chinese Society of Hepatology clinical practice guidelines both recommend endoscopic cyanoacrylate injection as the first-line therapy for preventing gastric variceal rebleeding.[6,7] Nevertheless, in IGV1 patients with gastrorenal shunt (GRS), endoscopic cyanoacrylate treatment carries the risk of ectopic embolism and intraoperative bleeding.

In our previous study, we found that endoscopic clipping and cyanoacrylate injection (EC-CYA) for the treatment of IGV1 with GRS resulted in no ectopic embolism, while also reducing the risk of rebleeding.[8–11] EC-CYA is a straightforward and easily performed procedure that does not require specialized EUS skills, making it more accessible for general endoscopists. To further evaluate the

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safety and efficacy of EC-CYA, we compared it with EUS-guided coil and cyanoacrylate injection (EUS-coil/CYA), which is the latest recommended treatment option in the European Society of Gastrointestinal Endoscopy (ESGE) guidelines.[12] Therefore, we collected data from patients at three liver disease centers in China to analyze the safety and efficacy of EC-CYA *versus* EUS-coil/CYA in treating IGV1 rebleeding patients with significant GRS, particularly focusing on the applicable case types, embolization efficiency and complications.

METHODS

Study population

We retrospectively analyzed the clinical data of patients diagnosed with gastrointestinal bleeding from cirrhosis and treated with endoscopic therapy (either EC-CYA or EUS-coil/CYA) between July 2019 and June 2024 in three tertiary hospitals (the First Affiliated Hospital of Anhui Medical University, the First Affiliated Hospital of Zhejiang University School of Medicine, and the Second People's Hospital of Fuyang City). The inclusion criteria were as follows: (1) age 18 years or older; (2) history of cirrhosis; (3) patients with IGV1 who had recent bleeding episodes (a. endoscopic findings of blood clots, white nipples, or erosive spots on GV; b. presence of GV with a red-color sign and absence of other bleeding sources under endoscopy); and (4) abdominal computed tomography angiography (CTA) demonstrating the presence of GRS with an internal diameter of 5 mm or more. The exclusion criteria were as follows: (1) previous endoscopic or interventional treatment of IGV1, (2) active bleeding, (3) primary prophylaxis, (4) presence of phrenic vein shunt or no shunt, (5) combined large EV, (6) advanced malignancy or multiple organ failure, and (7) portal cavernoma or portal vein thrombosis grade 2 or above.[13] This study was approved by the Ethics Committee of the First Affiliated Hospital of Anhui Medical University (No. PJ 2024-10-68), and informed consent was obtained from all participants.

Procedures

All patients underwent preoperative abdominal CTA surveillance. Endoscopic procedures were performed by an endoscopist with 10 years of experience, administering either EC-CYA or EUS-coil/CYA. Upper gastrointestinal endoscopy was performed, and the type and severity of GV and etiology of bleeding were preliminarily assessed in combination with CTA results.

Endoscopic clipping and cyanoacrylate injection

Under intravenous anesthesia, endoscopy was conducted to ascertain the flow direction of the varices. Then one or two titanium clips (Instinct; CookMedical, Bloomington, IN) were used to occlude the feeding and/or outflow vessels, which were one or both ends of the vessels. This was followed by the injection of a "modified sandwich method" into the varix post-clipping, comprising lauromacrogol–*N*-butyl 2-cyanoacrylate–lauromacrogol. Intravascular injection was determined by observing columnar backflow in the needle following puncturing GV. The volume of cyanoacrylate (Histoacryl; B. Braun, Melsungen, Germany) injected depended on the varix's diameter: 1 mL for varices up to 1 cm in diameter and 1 mL per cm for larger varices. Before and after the cyanoacrylate injection, 1–2 mL of lauromacrogol was injected. Postinjection, the firmness of the vein was palpated with the needle sheath; additional injections were administered until the varix was fully solidified [Figure 1].

EUS-guided coil and cyanoacrylate injection

After intravenous anesthesia and endoscopic examination, EUS was used to assess varices and shunts, with a varix close to the source vessel selected as the target for embolization. A standard 22G needle (Cook Medical, Bloomington, IN) was used. The size of the coil (10-mm coiled diameter, 14-cm straight lengths [Cook Medical[or 10- to 14-mm coiled diameter, 5- to 30-cm straight lengths [Boston Medical, Natick, MA], and 0.018-inch diameter) must be greater than 120% of the variceal diameter. During EUS, color Doppler flow imaging was used to observe the direction of blood flow in the target vessel, and the upstream and downstream directions of blood flow in the target area were determined. After the puncture needle was inserted into the target vessel, one or two coils were released in the downstream direction, and the "modified sandwich method" was then injected into the varix in the upstream direction. The volume of cyanoacrylate was generally 2 mL and could be reduced if the internal diameter of the target vessel was less than 8 mm or if multiple coils were placed. After the injection, variceal blood flow was monitored by color Doppler to assess the embolic effect.

Patients with medium EV underwent band ligation after successful obliteration of the IGV1 (performed during subsequent endoscopic sessions).

Follow-up

CTA and endoscopy were performed at 4-week intervals to assess the obliteration of IGV1. If the patient still required intervention, the last endoscopic protocol was continued or endoscopic cyanoacrylate was injected until the IGV1 was obliterated. An additional CTA or endoscopy evaluation was required within 3 to 6 months after IGV1 obliteration. IGV1 area for all patients at three centers and GRS diameter were accurately measured by the same experienced imaging specialist.

Definitions

(1) EVs classified into grade I (thin caliber), grade II (medium caliber), and grade III (large caliber) based on the Japanese Research Society for Portal Hypertension.[14]

(2) Rebleeding: Defined as recurrent hematemesis or melena, drop in Hb ≥ 3 g/dL, or clinical signs of hypovolemic shock.[15]

(2.1) Early rebleeding: Defined as an episode of upper gastrointestinal hemorrhage within 120 hours after the index treatment.[15]

(2.2) Late rebleeding: Defined as clinically significant bleeding after 120 hours.

(3) Variceal obliteration rate: Defined as the measurement of the degree of IGV1 obliteration by CTA. The calculation formula was as follows: (preoperative maximum variceal cross-sectional area – postoperative maximum variceal cross-sectional area)/preoperative maximum variceal cross-sectional area × 100% [Figure 2].

(4) The embolization efficiency of cyanoacrylate: Defined as the area of IGV1 that can be embolized per milliliter of cyanoacrylate. The calculation formula was as follows: (preoperative maximum variceal cross-sectional area – postoperative maximum variceal cross-sectional area)/volume of cyanoacrylate [Figure 2].

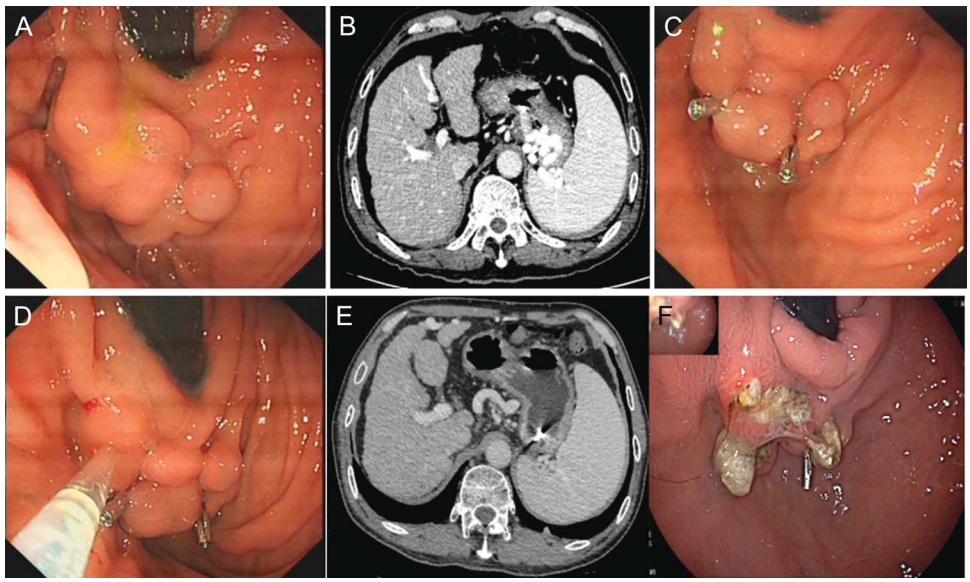

Figure 1. Endoscopic clipping and cyanoacrylate injection. (A) The endoscope revealed tumorous gastric varices. (B) Abdominal CTA clearly demonstrated the existence of a gastric varix. (C) During the endoscopy, two clips were skillfully deployed to effectively occlude the blood vessels. (D) Post-clipping, cyanoacrylate was injected into the varix using the "modified sandwich method." (E) One month after the procedure, CTA confirmed the complete occlusion of the gastric varices, with distinct areas of increased density clearly indicating the presence of titanium clips. (F) A month post-operation, endoscopy revealed a significant regression of the gastric fundus varices, accompanied by glue expulsion ulcer. CTA: Computed tomography angiography.

Outcome measures

The primary outcomes were gastric variceal rebleeding rate and ectopic embolism. Secondary outcomes were technical success, variceal obliteration rate, cyanoacrylate volume, cyanoacrylate embolization efficiency, other causes of rebleeding, other adverse events, and mortality.

Statistical analysis

Statistical analyses were conducted using IBM SPSS 26.0 (IBM Corp., Armonk, NY, USA). Quantitative data that followed a normal distribution were expressed as mean ± SD, and *t* test was used to compare between two groups. When the assumption of data normality was rejected, the median and interquartile range were presented and the Mann–Whitney *U* test was used to compare between two groups. Categorical variables were expressed as frequencies (%), and the chi-squared test or Fisher's exact test was used to compare between two groups; when categorical variables were ordered, the Mann-Whitney *U* test was used. The Kaplan-Meier method was used to analyze patient rebleeding and to plot "survival" curves, with the log-rank test used for comparisons between two groups. When baseline characteristics differed between groups, logistic regression was used to adjust for confounding factors. All statistical analyses were considered statistically significant at $P < 0.05$.

RESULTS

Baseline characteristics

A total of 166 IGV1 patients were treated with EC-CYA or EUS-coil/CYA during the study period, of which 35 patients were excluded. Finally, 55 patients with EC-CYA and 76 patients with EUS-coil/CYA were included in the study [Figure 3]. The baseline characteristics of the two groups are shown in Table 1.

Technical success and follow-up

In the EC-CYA group, the one-time technical success rate was 96.4%: one due to the clip puncturing the GV and the other due to bleeding during needle withdrawal after injection. In the EUS-coil/CYA group, the one-time technical success rate was 94.7%. There were three patients with coil installation failure and one patient with premature release of the coil into the gastric lumen. There was no difference in technical success rate between the two groups ($P > 0.999$) [Table 2].

In the EC-CYA group, a mean number of titanium clips utilized per procedure was 1.84 ± 1.30. In the EUS-coil/CYA group, a mean number of coils injected per procedure was 1.50 ± 0.79, with a mean total length coil of 15.43 ± 12.24 cm. The volume of cyanoacrylate used in the EC-CYA group was higher than that in the EUS-coil/CYA group (3.14 ± 1.45 mL *vs*. 3.14 ± 1.45 mL, $P < 0.001$).

A total of 131 patients entered follow-up after the procedure, of which 55 patients in the EC-CYA group and 7 patients were lost to follow-up in the EUS-coil/CYA group, for a total of 69 patients.

Gastric variceal rebleeding

During the follow-up period of 124 patients, 14 patients experienced gastric variceal rebleeding, all of which were late rebleeding. The gastric variceal rebleeding rates were 14.5% in the EC-CYA group and 8.7% in the EUS-coil/CYA group, with no significant difference ($P = 0.307$) [Table 2]. Logistic regression was used to control for the two factors that differed at baseline (ascites and prothrombin time) by using gastric variceal rebleeding (0 = No, 1 = Yes) as the dependent variable, and the results also showed that there was no statistically significant difference in gastric variceal rebleeding between the two groups (OR = 2.44, 95% CI: 0.48–12.41, $P = 0.284$).

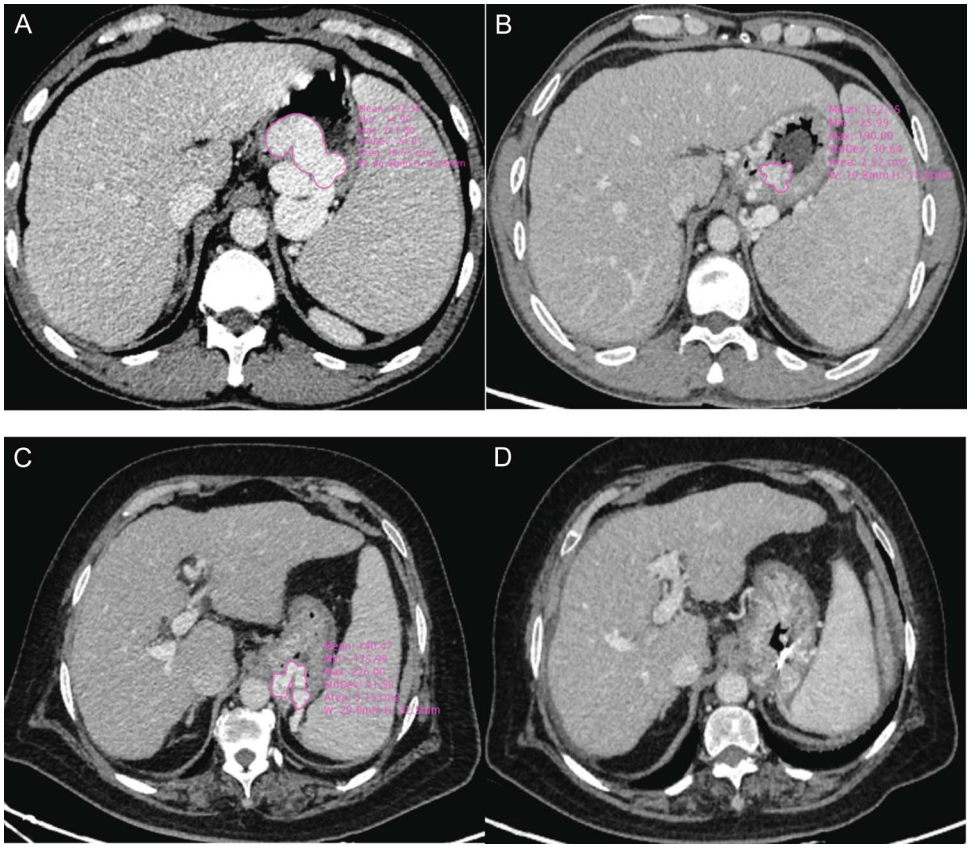

Figure 2. Measurement of IGV1 obliteration rate and cyanoacrylate embolization efficiency under abdominal CTA. First patient: (A) Preoperative CTA revealed a large GV, with the maximum cross-sectional area of the GV within the gastric wall measured at 10.63 cm^2. During surgery, 4.5 mL of cyanoacrylate was injected. (B) Postoperative CTA monitoring showed a reduction in variceal area with a measured value of 2.32 cm^2. Therefore, the IGV1 obliteration rate was calculated to be 78.17% and the embolization efficiency of cyanoacrylate to be 1.85 cm^2/mL. Second patient: (A) Preoperative CTA showed a tortuous GV, with the maximum cross-sectional area of the GV within the gastric wall measured at 5.15 cm^2, and 1.5 mL of cyanoacrylate was injected during surgery. (B) Postoperative CTA monitoring showed complete disappearance of the GV, with residual titanium clips present. Therefore, the IGV1 obliteration rate was 100%, and the embolization efficiency of cyanoacrylate was 3.43 cm^2/mL. CTA: Computed tomography angiography; GV: Gastric varices; IGV1: Isolated gastric varix type I.

Bleeding from other causes

During follow-up, 7 patients (12.7%) in the EC-CYA group and 4 patients (5.8%) in the EUS-coil/CYA group experienced bleeding from other causes. There was no statistically significant difference between the two groups (P = 0.303) [Table 2].

Combining all-cause rebleeding, Kaplan-Meier analysis showed no significant difference in the cumulative incidence of no rebleeding between the two groups [Figure 4].

Variceal obliteration rate and cyanoacrylate embolization efficiency

In the EC-CYA group, 27 patients (49.1%) underwent CTA surveillance on average of 113 days after treatment, of which 17 patients (63.0%) had achieved complete obliteration of IGV1. In the EUS-coil/CYA group, 46 patients (66.7%) underwent CTA surveillance, on average, of 34 days after treatment, of which 15 patients (32.6%) had achieved complete obliteration of IGV1. The variceal obliteration rate was higher in the EC-CYA group than in the EUS-coil/CYA group (82.23% ± 27.09% *vs*. 66.59% ± 30.28%, P = 0.032), but the embolization efficiency of cyanoacrylate was lower (1.98 ± 1.46 cm^2/mL *vs*. 2.85 ± 2.05 cm^2/mL, P = 0.044) [Table 2].

Ectopic embolism and other adverse events

All patients showed no manifestations of pulmonary embolism, such as decreased oxygen saturation, cough, dyspnea, or chest pain, during and after the operation, nor did they have clinical symptoms of cerebral embolism such as hemiplegia, hemisensory deficits, aphasia, or hemianopia. There was also no difference in the incidence of other adverse events between the two groups (5.5% *vs*. 5.8%, P > 0.999) [Table 2], and all were minor procedure-related adverse events.

Mortality

During the follow-up period, 7 patients (12.7%) in the EC-CYA group and 6 patients (8.7%) in the EUS-coil/CYA group died, with bleeding-related deaths and adverse events of end-stage liver disease predominating, and there was no difference in mortality between the two groups (P = 0.467) [Table 2].

Subgroup analysis of patients who did not undergo abdominal CTA surveillance postoperatively

A comparative analysis of baseline characteristics (including age, sex, hematological tests, Child-Pugh score, Model for End-Stage

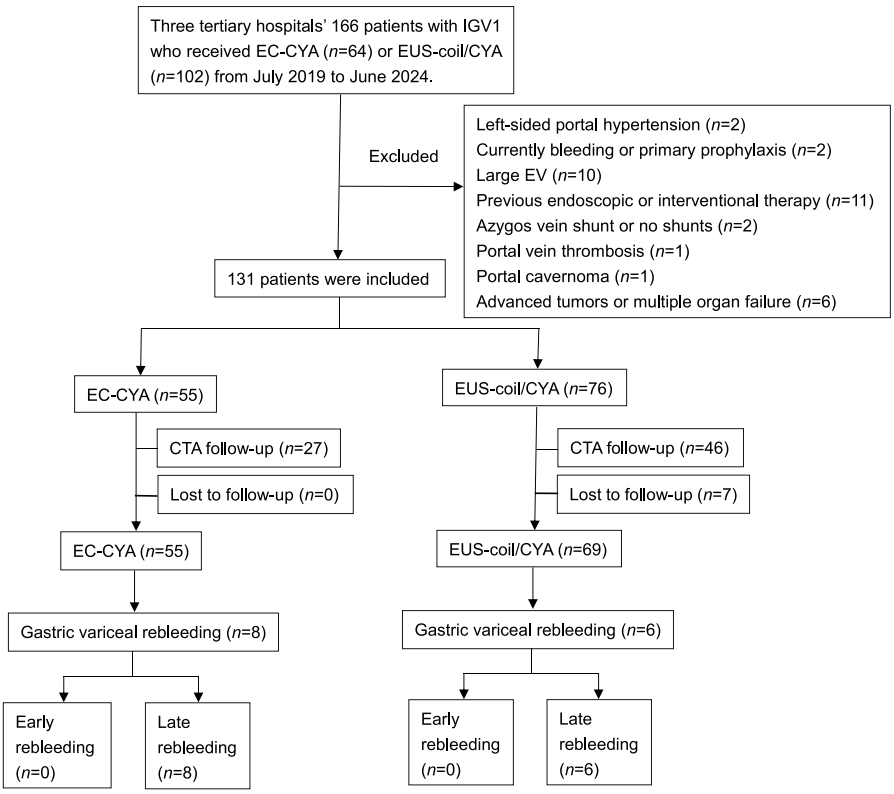

Figure 3. Flowchart demonstrating patients with IGV1 enrolled in the study who received either EC-CYA or EUS-coil/CYA. CTA: Computed tomography angiography; EC-CYA: Endoscopic clipping and cyanoacrylate injection; EUS-coil/CYA: EUS–guided coil and cyanoacrylate injection; IGV1: Isolated gastric varix type I.

Liver Disease score, and gastrorenal shunt diameter) and related factors affecting variceal obliteration (including IGV1 maximum cross-sectional area and cyanoacrylate volume) was conducted between patients who did not undergo CTA surveillance and those who did within the overall cohort. The results showed that all variables were not statistically different between the two groups ($P > 0.05$). Comparisons of the aforementioned variables were also made between patients who did not undergo CTA surveillance and those who did within the EC-CYA group and the EUS-coil/CYA group, respectively, and the results showed no statistically significant differences ($P > 0.05$). Additionally, a comparative analysis of patients who did not undergo CTA surveillance in the two groups indicated that there were no statistically significant differences in the remaining indicators ($P > 0.05$), except for prothrombin time (median, 15.30 s *vs*. 13.50 s; $P = 0.006$) and cyanoacrylate volume (3.25 ± 1.14 mL *vs*. 1.97 ± 0.76 mL, $P < 0.001$).

DISCUSSION

IGV1, especially the tumorous GV, has the characteristics of large size, high blood flow velocity, deep feeding vessels, and complex collateral circulation, which pose a high risk of bleeding and ectopic embolism during endoscopic treatment. EUS-coil/CYA blocks and embolizes the vessel from within the lumen of the GV, whereas EC-CYA clamps the vessel from outside the lumen of the GV and then embolizes it. The two modes of operation are different, but both aim to obliterate the GV and reduce ectopic embolism. EC-CYA has been performed in our centers for 6 years due to its simpler operation and lower technical difficulty, but more well-controlled studies are still needed to provide supportive evidence, especially for EUS-coil/CYA, which is the current consensus protocol.[12]

In this study, the gastric variceal rebleeding rates after intervention with the two techniques were 14.5% (EC-CYA group) and 8.7% (EUS-coil/CYA group), respectively, which appeared to be higher in the EC-CYA group, but there was no difference in statistical comparison. Furthermore, in a randomized controlled trial of EC-CYA *versus* TIPS for the treatment of IGV1 patients, we found that both methods were effective in controlling IGV1 rebleeding (14.5% *vs*. 8.8%, $P = 0.263$), and that EC-CYA did not result in ectopic embolism, and the incidence of hepatic encephalopathy was lower than that observed with TIPS.[11] It is worth noting that no patients with early rebleeding were found in either treatment group.

We observed that 2 patients (3.6%) in the EC-CYA group and 1 patient (1.4%) in the EUS-coil/CYA group developed new GVB postoperatively, indicating that persistent portal hypertension can lead to the formation of new varices despite effective obliteration of the GV in the initial treatment. In addition, 6 patients (10.9%) in the EC-CYA group and 2 patients (2.9%) in the EUS-coil/CYA group experienced bleeding of the glue expulsion ulcer. The incidence of the latter was lower than the former, although there was no difference in statistical comparisons ($P = 0.137$). During the follow-up period, bleeding due to other factors related to portal hypertension occurred in both groups. Specifically, there were 3 patients (5.5%) who bled due to EV exacerbation and 1 patient (1.8%) who bled due to colonic telangiectasia in the EC-CYA group, and 1 patient (1.4%) who bled due to portal hypertensive gastropathy in the EUS-coil/CYA group. All patients experienced symptomatic relief with appropriate treatment.

Table 1

Characteristics of the study patients.

	EC-CYA (n = 55)	EUS-coil/CYA (n = 76)	P value
Age (yr)	60.13 ± 12.07	58.57 ± 11.24	0.448
Sex (male/female)	28/27	47/29	0.212
Etiology of cirrhosis			
Hepatitis B virus	26	40	
Hepatitis C virus	5	1	
Alcoholic	5	14	0.064
Autoimmune	5	1	
Schistosomiasis	3	4	
Others	11	16	
Concomitant hepatocellular carcinoma	10	11	0.568
Albumin (g/L)	32.54 ± 5.07	33.74 ± 5.53	0.208
Total bilirubin (μmol/L)	17.28 (12.10, 23.37)	16.60 (12.00, 25.20)	0.548
Creatinine (μmol/L)	66.00 (56.00, 76.00)	66.50 (56.00, 72.00)	0.812
Prothrombin time (s)	14.90 (13.80, 16.80)	13.65 (12.70, 15.00)	0.003
Platelets ($\times 10^9$/L)	80.00 (54.00, 101.00)	92.00 (55.00, 124.00)	0.125
Ascites (present/absent)	23/32	47/29	0.023
Child-Pugh class			
A	22	43	
B	27	28	0.059
C	6	5	
Child-Pugh score	7.00 (6.00, 9.00)	6.00 (5.00, 7.00)	0.111
MELD score	8.06 ± 4.45	7.84 ± 3.66	0.054
IGV1 maximum cross-sectional area (cm^2)	8.03 ± 4.34	7.44 ± 4.37	0.242
Gastrorenal shunt diameter (mm)	11.90 (9.43, 15.21)	9.60 (7.60, 13.80)	0.490

EC-CYA: Endoscopic clipping and cyanoacrylate injection; EUS: Endoscopic ultrasound; EUS-coil/CYA: EUS–guided coil and cyanoacrylate injection; IGV1: isolated gastric varix type I; MELD: Model for End-Stage Liver Disease.

Variceal obliteration is a key factor in preventing IGV1 rebleeding and is an objective assessment of treatment efficacy. The traditional endoscopic cyanoacrylate injection technique uses palpation of the varix to ensure hardening, whereas EUS confirms IGV1 obliteration by posttreatment Doppler imaging, a more accurate method than palpation. Here, we used CTA to monitor IGV1 obliteration, which not only confirms vessel obliteration but also calculates the obliteration rate for each patient by measuring the area of varix obliteration. In this study, the variceal obliteration rate in the EUS-coil/CYA group was significantly lower than that in the EC-CYA group. Similarly, we found that the obliteration rate in the EUS-coil/CYA group was also lower than that of other scholars' studies.[16–18] Bazarbashi et al.[16] found that patients were injected with a mean number of 3.8 ± 2.9 coils per procedure, with a mean total coil length of 44.7 ± 46.1 cm and a mean cyanoacrylate volume of 2.4 ± 2.0 mL. At surveillance EUS, 74.6% of patients had evidence of diminished or obliterated Doppler flow within GV. Bhat et al. also concluded that 79 of 100 patients treated with EUS-coil/CYA who underwent EUS follow-up examinations successfully achieved complete obliteration after a single procedure.[17] Samanta et al. reported that EUS-coil/CYA treatment achieved up to 95.3% complete varix obliteration rate at 4 weeks.[18] The rate of variceal obliteration after a single procedure was low in this study, and we found the following to differ: (1) Our first treatment was performed for the target vessel only at a single puncture point and achieved complete obliteration of the vessel after puncture. In contrast, other studies tended to adopt a strategy of multiple points of coil placement and cyanoacrylate injection. This is also evident from the lower number, length of coils, and cyanoacrylate volume used in our study. Notably, the rates of gastric variceal rebleeding (8.6%) and all-cause rebleeding (14.5%) after our treatment were similar to the results of the above studies (8%–14.2% and 13.8%–16%). (2) This study used CTA to assess the degree of varix obliteration, which differs from EUS assessment in other studies and may have led to slightly different results.

To further explore the efficacy of both techniques, we analyzed the embolization efficiency of cyanoacrylate. The results showed that the variceal area embolized with cyanoacrylate per mL was 2.85 ± 2.05 cm^2 in the EUS-coil/CYA group, which was higher than that in the EC-CYA group at 1.98 ± 1.46 cm^2. EUS scan could locate and embolize the internal and external collateral vessels of the gastric wall, and rationally design the cyanoacrylate dosage, which improved the embolization efficiency of cyanoacrylate. EC-CYA could be attributed to the visual inspection of the variceal diameters leading to the higher cyanoacrylate injections, increasing cyanoacrylate per unit area, thus decreasing its embolization efficiency, as evidenced by the higher variceal obliteration rate in the EC-CYA group.

The most serious complication of endoscopic cyanoacrylate injection is ectopic embolism, commonly pulmonary and cerebral embolism. No clinically symptomatic ectopic embolism was observed in any of our IGV1 patients with GRS, especially in the EC-CYA group with higher cyanoacrylate injection. This is consistent with previous studies[9,11,19] and suggests that EC-CYA has a preventive effect on ectopic embolism. However, in a multicenter retrospective study that included 148 patients underwent EC-CYA, one case of ectopic embolism after treatment in a patient with the presence of larger IGV1 was reported.[10] Therefore, EC-CYA still needs

Table 2

Summary of outcome measurements.

	EC-CYA (*n* = 55)	EUS-coil/CYA (*n* = 69)	*P* value
Primary outcomes			
Gastric variceal rebleeding	8 (14.5%)	6 (8.7%)	0.307
Incomplete obliteration of GV	0	3	0.254
New GV	2	1	0.584
Glue expulsion ulcer	6	2	0.137
Ectopic embolism	0	0	—
Secondary outcomes			
Follow-up time (d)	700 ± 549	729 ± 577	0.347
Technical success*	53 (96.4%)	72 (94.7%)	>0.999
Surveillance CTA (*n*)	27	46	0.193
Mean time to surveillance (d)†	113 (65, 374)	34 (3, 45)	<0.001
Variceal obliteration rates (%)†	82.23 ± 27.09	66.59 ± 30.28	0.032
Volume of cyanoacrylate (mL)†	3.78 ± 1.43	2.01 ± 0.72	<0.001
Obliteration efficiency of cyanoacrylate†	1.98 ± 1.46	2.85 ± 2.05	0.044
Other adverse events	3 (5.5%)	4 (5.8%)	>0.999
Fever	3	3	
Abdominal pain	0	1	
Bleeding from other causes	7 (12.7%)	4 (5.8%)	0.303
Esophageal variceal	3	0	
Portal hypertensive gastropathy	0	1	
Colonic telangiectasia	1	0	
Agnogenic	3	3	
Mortality	7 (12.7%)	6 (8.7%)	0.467
Liver failure	1	1	
Gastrointestinal bleeding	3	3	
Sepsis	1	0	
Newly diagnosed oral cancer	0	1	
Agnogenic	2	1	

CTA: Computed tomography angiography; EC–CYA : Endoscopic clipping and cyanoacrylate injection; EUS–coil/CYA :EUS–guided coil and cyanoacrylate injection; GV: gastric varices.

*EC-CYA group (*n* = 55), EUS-coil/CYA group (*n* = 76).

†EC-CYA group (*n* = 27), EUS-coil/CYA group (*n* = 46).

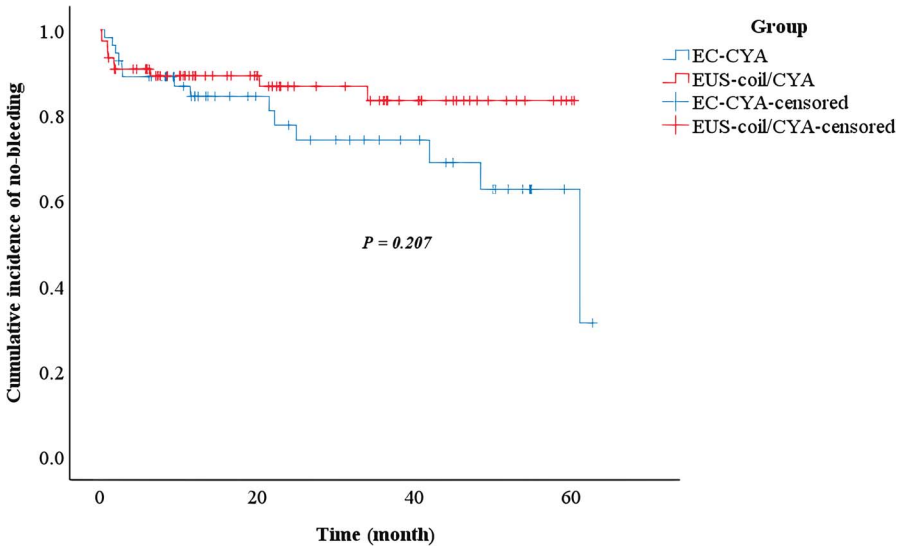

Figure 4. Kaplan-Meier curve analysis of the cumulative incidence of no-bleeding. EC-CYA: Endoscopic clipping and cyanoacrylate injection; EUS-coil/CYA: EUS–guided coil and cyanoacrylate injection.

to be used with caution in larger IGV1, and BRTO may be a viable treatment option.[20]

In this study, we utilized CTA to assess IGV1 obliteration and for the first time proposed a cyanoacrylate embolization efficiency index to assess efficacy. However, the study has limitations. First of which are the inherent flaws of retrospective studies, for instance, selection bias. Second, the postoperative CTA surveillance rates were low in both groups (49.1% *vs*. 66.7%), which could introduce potential bias. Therefore, we compared the baseline data and factors influencing IGV1 obliteration between patients who did not undergo CTA surveillance and those who did, in an effort to minimize the impact of bias. Third, the postoperative CTA surveillance time was inconsistent between the two groups (113 days *vs*. 34 days, $P < 0.001$). EUS-coil/CYA enables real-time monitoring of changes in intravascular blood flow, and thus, CTA surveillance time is relatively short. Although EC-CYA can assess vascular hardness via palpation, we extended the surveillance time to make a true judgment on the degree of variceal obliteration. Fourth, there may be some asymptomatic embolism patients, which requires the addition of lipiodol to the cyanoacrylate for tracing. However, this practice is not currently recommended.

Given the high rates of rebleeding and mortality associated with GVB, primary prevention is crucial. However, the risk/benefit ratio of treatment remains unclear due to insufficient endoscopic treatment data and the potential for serious complications, such as ectopic embolism and rebleeding after cyanoacrylate injection. The Baveno VII consensus report also advises against endoscopic intervention. Taking these factors into account, this study excluded patients without bleeding cautiously. However, for patients with high-risk factors for bleeding,[21] there is currently insufficient evidence as to whether cyanoacrylate injection, EC-CYA, or EUS-coil/CYA can be used for primary prevention.

In conclusion, EC-CYA and EUS-coil/CYA have comparable and pretty safety and efficacy for IGV1 patients with GRS. The EUS-coil/CYA has better embolization efficiency, whereas EC-CYA has better operational convenience. In medical centers where EUS-coil/CYA is not available, endoscopists can treat IGV1 patients with EC-CYA. Conversely, centers proficient in EUS-coil/CYA technology should prioritize this method for treating IGV1 patients.

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Conflicts of Interest

The authors declare no conflicts of interest for this article.

Ethical Approval

The research protocol was approved by the Ethics committee of the First Affiliated Hospital of Anhui Medical University.

Informed Consent

Informed consent was obtained from all participants

Author Contributions

Huixian Li, Wei Chen, and Wei Zhang all made equal contributions to this manuscript; Derun Kong, Hongtan Chen, and Chao Ma were responsible for the study conception and design; Huixian Li, Wei Zhang, Zhihong Wang, Wei Chen, Lingfang Shi, Xuecan Mei, and Qianqian Zhang acquired the data; Huixian Li made the statistical analysis; Huixian Li, Wei Chen, and Wei Zhang wrote the manuscript; Chao Ma, Derun Kong, and Hongtan Chen were responsible for the revision of the manuscript and study supervision; all authors issued the final approval of the version to be submitted.

Trial Registration

Chinese Clinical Trials Registry (registration number: ChiCTR240-0093249).

Data Availability Statement

Not applicable.

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