Efficacy and safety of endoscopic glue injection in acute peptic ulcer bleeding

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Abstract

Background: Optimal management of peptic ulcer bleeding remains a clinical challenge.

Objectives: To evaluate the efficacy and safety of endoscopic glue injection (EGI) for acute peptic ulcer bleeding.

Design: Single-center retrospective study.

Methods: This study (October 2015–December 2024) included adults (⩾18 years) with high-risk peptic ulcer bleeding (Forrest Ia–IIa) treated with EGI using n-butyl α-cyanoacrylate ester or standard endoscopic treatment (SET) involving contact thermal therapy and hemoclips. The primary endpoint was the rebleeding within 7 days, and the secondary endpoints included rebleeding within 30 days, 30-day all-cause mortality rate, occurrence of adverse events (AEs), and length of hospital stay and intensive care unit (ICU) stay. Risk factors for rebleeding within 7 days were also analyzed.

Results: A total of 148 patients were included (EGI: 57; SET: 91). The rates of rebleeding within 7 days were 8.77% (EGI) versus 20.88% (SET; $p = 0.067$), and within 30 days were 8.77% versus 21.98%, respectively ($p = 0.043$). The 30-day all-cause mortality rate was 0.0% for EGI versus 1.1% for SET ($p = 1.000$). AEs—including Mallory–Weiss syndrome, esophageal blood blister, pulmonary embolism, hemorrhagic shock, cardiovascular or cerebrovascular events, infections, multiple organ failure, and lower limb thrombosis—did not differ significantly between groups (all $p > 0.05$). Mean hospital stay was shorter in the EGI group (10.91 ± 12.40 vs 15.38 ± 10.91 days; $p = 0.002$); ICU stay was similar ($p = 0.153$). Forrest classification Ia (odds ratio (OR) = 8.294; $p = 0.013$) and kidney disease (OR = 24.257; $p = 0.003$) were independent risk factors for rebleeding within 7 days.

Conclusion: EGI may be an effective and safe treatment for acute peptic ulcer bleeding, significantly reducing 30-day rebleeding and shortening hospital stay compared with SET. Clinicians should exercise heightened vigilance and consider more intensive monitoring or preventive strategies for patients with Forrest classification Ia ulcers or underlying kidney disease, who are at increased risk of early rebleeding.

Plain language summary

Endoscopic glue injection for acute peptic ulcer bleeding

EGI may be an effective and safe treatment for acute peptic ulcer bleeding, significantly reducing 30-day rebleeding and shortening hospital stay compared with standard endoscopic treatment. Clinicians should exercise heightened vigilance and consider more intensive monitoring or preventive strategies for patients with Forrest classification Ia ulcers or underlying kidney disease, who are at increased risk of early rebleeding.

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Introduction

Peptic ulcer bleeding refers to the occurrence of hematemesis and/or melena and/or unexplained decrease in hemoglobin in patients, and subsequent endoscopic examination confirms that the source of bleeding is chronic peptic ulcer.[1] Peptic ulcer bleeding typically affects the stomach and duodenum and is mainly triggered by *Helicobacter pylori* (HP) infection and nonsteroidal anti-inflammatory drugs (NSAIDs).[2,3] The estimated annual incidence rate of peptic ulcer bleeding is 19.4–57.0 per 100,000 people.[4] The average 7-day recurrence rate of bleeding is 13.9%, and the average 30-day mortality after bleeding is 8.6%.[4] Hemostasis failure and ulcer rebleeding are major issues in peptic ulcer bleeding, inducing long hospital stays, high mortality rates, and high incidence of complications.[3] In recent decades, China has achieved remarkable progress in reducing the mortality rate associated with peptic ulcer disease, suggesting improvements in therapeutic interventions such as endoscopic hemostasis and medical management.[5]

The European Society of Gastrointestinal Endoscopy Guideline indicates that Forrest classifications Ia (active bleeding), Ib (oozing bleeding), and IIa (nonbleeding visible ulcer) have a high risk of rebleeding and require active endoscopic treatment.[6] The treatment of epinephrine injection plus contact thermal or mechanical therapy is used as first-line treatment for Forrest classifications Ia and Ib. For Forrest classification IIa, contact or noncontact thermal therapy, mechanical therapy, or injection of sclerosants and combination or noncombination of adrenaline injection can be chosen.[6] In previous high-quality randomized trials, standard endoscopic treatment (SET) was defined as epinephrine injection followed by contact thermal therapy or placement of hemoclips.[7] Ample evidence suggests that for patients with Forrest classification Ia, Ib, and IIa ulcers, any endoscopic hemostatic treatment is superior to drug therapy alone,[8,9] and more than 90% of cases can achieve hemostasis.[10] However, for certain complex or high-risk patients, especially those with large vessel exposure or lesions that are difficult to clamp, the risk of rebleeding remains high, posing a considerable challenge to clinical management.

Endoscopic glue injection (EGI) using cyanoacrylate is widely applied for gastric variceal bleeding, achieving rapid polymerization and vessel obliteration. However, according to a Cochrane systematic review, the certainty of the evidence was very low, and estimates on all-cause and bleeding-related mortality, failure of intervention, and adverse events (AEs) remain highly uncertain.[11] Based on its characteristics, EGI may have an effect on peptic ulcer bleeding; however, research on its safety, effectiveness, and long-term efficacy is lacking. Therefore, the research question of this retrospective cohort study was: In patients with acute peptic ulcer bleeding, does EGI achieve effective and safe hemostasis compared with standard SET?

Methods

Study design and participants

We conducted a single-center retrospective cohort study at Qingdao University Affiliated Hospital, including inpatients who underwent emergency endoscopic examination for acute ulcer gastrointestinal bleeding.

Inclusion criteria. (1) Hospitalized patients aged 18 years and above, regardless of gender, with symptoms of vomiting blood and/or black stool and with manifestations of blood loss, such as dizziness, sweating, palpitations, shock, were included. (2) The patient was diagnosed with peptic ulcer with acute bleeding,[1] and endoscopic findings showed Forrest Ia–IIa ulcer rebleeding, with a high risk of rebleeding. (3) SET or EGI was performed. As this was a retrospective study, the use of epinephrine injection prior to endoscopic therapy was not consistently recorded, and therefore was not included as a defining criterion for SET. In our study, SET was defined as contact thermal therapy or placement of hemoclips, with or without prior injection therapy, in accordance

with the routine clinical practice at our center. SET includes the use of contact thermal therapy and placement of hemoclips, with or without prior injection of diluted adrenaline.

Exclusion criteria. The following cases were excluded: (1) those highly suspected of tumor bleeding or with pathological indication of cancer; (2) bleeding caused by esophageal–gastric variceal bleeding, Mallory–Weiss syndrome, Dieulafoy's lesion, or other vascular lesions; (3) those with abnormal coagulation function, increased prothrombin time by more than 3 s, and platelet count less than 80×10 (3)/μL; (4) combined gastrointestinal perforation requiring surgical intervention; (5) bleeding caused by previous gastroscopy procedures, such as biopsy, polypectomy, submucosal dissection, dilation; (6) pregnant or lactating women.

The study protocol was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University, with approval number (QYFY WZLL 29902) and approval date April 2025. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[12]

Study treatments

EGI group

(1) Preparation conditions: On the basis of their basic condition, the patients underwent endoscopic treatment under intravenous anesthesia or regular gastroscopy.
(2) Equipment and consumables: An Olympus Q26 endoscope, a disposable endoscope injection needle (specification: 23G, needle core length: 5 mm), and *n*-butyl α-cyanoacrylate ester (Beijing Kangpaite tissue adhesive) were used.
(3) Operation steps:
(1) The bleeding point was identified and fully exposed under gastroscopy.
(2) The assistant prefilled the injection needle with 0.25–0.5 ml Kangpaite tissue glue and 3.5 ml air after saline flushing, ready for use. The operator inserted the needle into the target vessel at the ulcer base.
(3) Once blood reflux was observed, the glue was injected at a steady speed, the needle withdrawn within 3 s, and the puncture site briefly compressed. Hemostasis was defined by cessation of bleeding or local mucosal blanching. If the first attempt failed, injection was repeated. Persistent bleeding was managed with alternative endoscopic, interventional, or surgical treatments as appropriate.

The operation process of endoscopic tissue glue injection for hemostasis was shown in Figure 1.

SET group

(1) Hemoclips: The goal of hemostasis was achieved by using endoscopy to locate the hemostatic clip at the bleeding site and clamp the blood vessel or bleeding point.[13]
(2) Contact thermal therapy: In contact thermocoagulation, thermal energy was utilized to raise tissue temperature, which in turn caused tissue denaturation and coagulation, leading to blood vessel contraction or closure and achieving the effect of hemostasis.[14]

Outcome measures and follow-up

The baseline characteristics collected included age, sex, Forrest classification, Rockall score, ulcer location, mean ulcer size, comorbidities, smoking status, alcohol consumption, HP infection, and the use of antiplatelet agents, anticoagulants, NSAIDs and proton pump inhibitor.

The primary end point was the rebleeding within 7 days. In accordance with the suggestion of Laine et al.,[15] a preliminary assessment of rebleeding was conducted 7 days after the end of endoscopic treatment. Rebleeding was defined as the occurrence of any of the following: (i) clinical presentation of hematemesis or melena; (ii) hemodynamic instability; (iii) a decrease in hemoglobin >2 g/dL after transfusion; (iv) transfusion requirement of more than 4 units of blood; or (v) endoscopic visualization of active bleeding at the previously treated site.[16]

The secondary end points included the incidence of rebleeding within 30 days and 30-day all-cause mortality, the occurrence of AEs, and the length of hospital stay and intensive care unit (ICU) stay. AEs related to gastrointestinal bleeding and endoscopic treatment include cardiovascular and

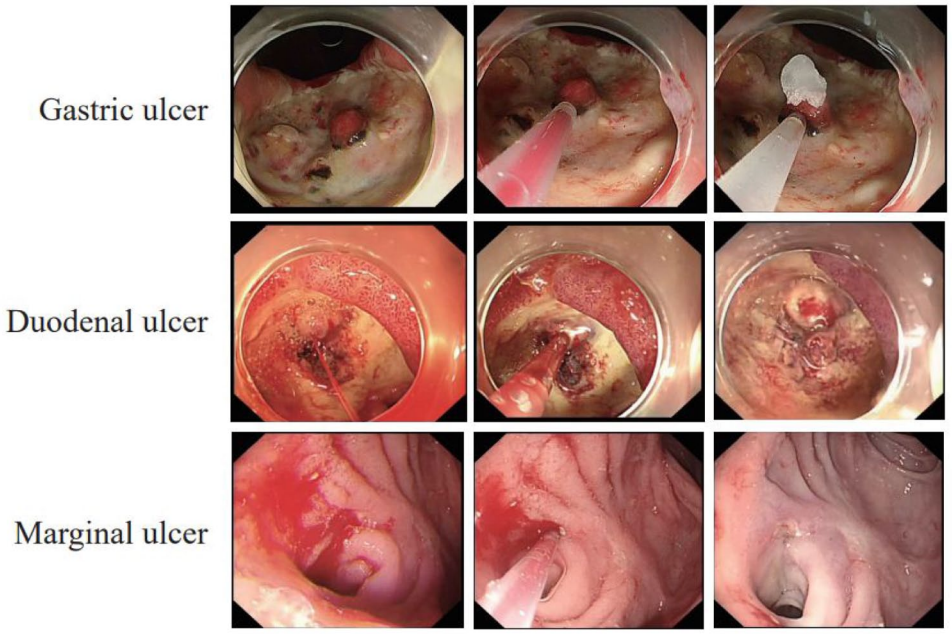


Figure 1. The operation process of endoscopic tissue glue injection for hemostasis.

cerebrovascular accidents, perforation, infection, hemorrhagic shock, multiple organ failure, and lower limb thrombosis.[2,6,17]

All patients were followed up by telephone to assess the occurrence of rebleeding and whether follow-up endoscopy had been performed.

Statistical analysis

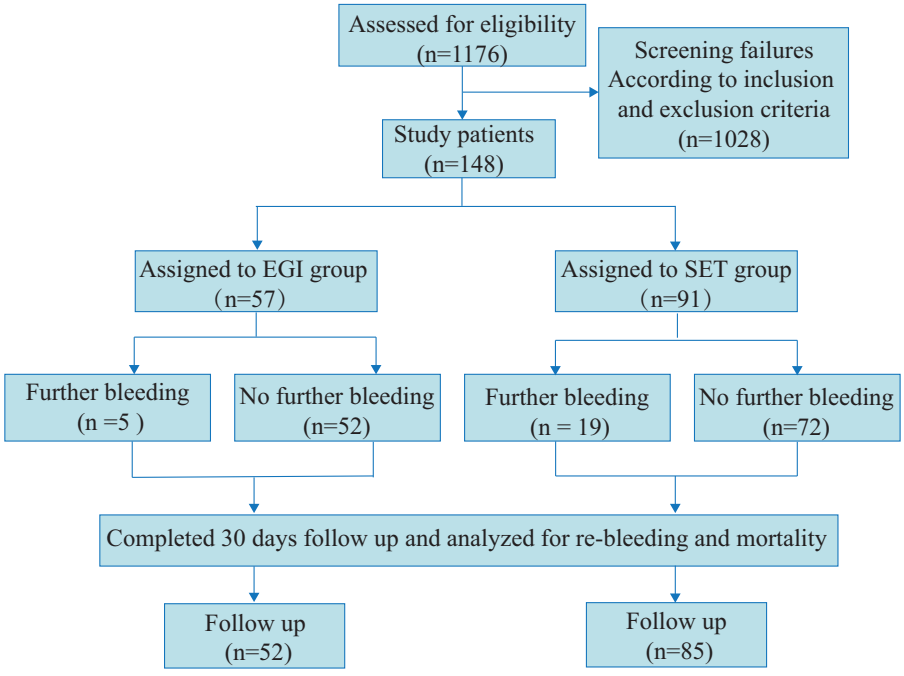
In this study, the normality test for continuous variables was conducted using the Kolmogorov–Smirnov test.[18] For data that followed a normal distribution, *t*-test was used for intergroup comparison; for data that did not follow a normal distribution, the Mann–Whitney *U* test was used for nonparametric testing.[19] The comparison of categorical variables was conducted using Chi-square test or Fisher's exact test, and the appropriate method was selected on the basis of data distribution.[20] To control for potential confounding factors and assess the independent effects of each variable on the results, we used multivariate logistic regression and calculated the odds ratios (ORs) and their 95% confidence intervals (CIs).[21] The statistical significance level was set to $p < 0.05$. When the p value was less than 0.05, the difference between groups was considered statistically significant.

Results

The screening process and baseline characteristics of patients

From October 2015 to December 2024, a total of 1176 patients with peptic ulcer bleeding were screened for eligibility. Based on the inclusion and exclusion criteria, 148 hospitalized patients with acute upper gastrointestinal ulcer bleeding who underwent endoscopic treatment were ultimately enrolled in the study, including 57 patients in the EGI group and 91 patients in the SET group. The participant enrollment and screening process was shown in Figure 2 and the annual number of cases per year demonstrated a fluctuating upward trend (Table S1).

The average age of the queue was 58.87 ± 14.54 years, ranging from 18 to 84 years old. The proportion of male patients was comparable (84.21% vs 83.52%, $p = 0.911$). Forrest classification showed similar distribution between groups: Ia (52.63% vs 37.36%), Ib (24.56% vs 43.96%), and IIa (22.81% vs 18.68%; $p = 0.055$). Based on Rockall scores, the proportion of medium-risk patients was 75.44% in the EGI group and 82.42% in the SET group, while high-risk patients accounted for 24.56% and 17.58%, respectively ($p = 0.401$). Ulcer locations were comparable,



EGI: Endoscopic Glue Injection; SET: Standard Endoscopic Treatment.

Figure 2. The participant enrollment and screening process.

including gastric (43.86% vs 48.35%), duodenal (43.86% vs 40.66%), marginal (8.77% vs 9.89%), and compound ulcers (3.51% vs 1.10%). The proportion of ulcers ⩾15 mm was 35.09% in the EGI group and 28.57% in the SET group ($p = 0.467$). No significant differences were found in comorbidities: cancer (10.53% vs 20.88%), ischemic heart disease (7.02% vs 8.79%), liver disease (12.28% vs 7.69%), cirrhosis (8.77% vs 6.59%), acute liver failure (1.75% vs 2.20%), renal disease (5.26% vs 6.59%), acute kidney injury (1.75% vs 3.30%), or chronic kidney disease (CKD; 3.51% vs 3.30%; all $p > 0.05$). Among those tested for HP infection, positivity was observed in 25.00% of the EGI group and 19.61% of the SET group ($p = 0.388$). Smoking rates were 38.60% versus 37.36%, and alcohol consumption was 28.07% versus 31.87% ($p = 0.508$ and 0.382, respectively). Bleeding-risk medications, including antiplatelet drugs (5.26% vs 6.59%), anticoagulants (1.75% vs 0.00%), and NSAIDs (7.02% vs 8.79%), showed no significant between-group differences ($p = 1.000$, 1.000, and 0.768, respectively). The results were shown in Table 1.

Rebleeding rates and all-cause mortality rate within 30 days

The initial hemostatic treatment for the SET group included hemostatic clips ($n = 70$), electrocoagulation hemostasis ($n = 14$), and electrocoagulation combined with hemostatic clips ($n = 7$) for hemostasis. The rebleeding rates within 7 days in the EGI and SET groups were 8.77% and 20.88%, respectively. Although the rebleeding rates within 7 days in the EGI group were lower than those in the SET group, no statistically significant difference existed between the two groups ($p = 0.067$). In the subgroup analysis based on Forrest classification, no difference in the rebleeding rates within 7 days was identified between the EGI and SET groups (all $p > 0.05$). Six patients in the SET group and five patients in the EGI group were lost to follow-up within 30 days. The risk of rebleeding within 30 days in EGI was significantly lower than that in SET ($p = 0.042$), but no significant difference in all-cause mortality rate within 30 days was observed between the two groups ($p = 1.000$). The results were shown in Table 2.

Table 1. Baseline characteristics of patients.

Variables/group	EGI (*N* = 57) (*n*, %)	SET (*N* = 91) (*n*, %)	*p*-Value
Age, years, mean ± SD	61.00 ± 13.80	57.54 ± 14.90	0.256
Male sex, *n* (%)	48(84.21)	76(83.52)	0.911
Forrest classification, *n* (%)			
Ia	13(22.81)	17(18.68)	0.055
Ib	14(24.56)	40(43.96)	
IIa	30(52.63)	34(37.36)	
Rockall scores, *n* (%)			
Medium risk	43(75.44)	75(82.42)	0.401
High-risk	14(24.56)	16(17.58)	
Peptic ulcers, *n* (%)			
Gastric ulcer	25(43.86)	44(48.35)	0.771
Duodenal ulcer	25(43.86)	37(40.66)	
Marginal ulcer	5(8.77)	9(9.89)	
Compound ulcer	2(3.51)	1(1.10)	
Mean ulcer size (SD), mm			
Ulcer size ⩾15 mm, *n* (%)	20(35.09)	26(28.57)	0.467
Coexisting disease, *n* (%)			
Cancer	6(10.53)	19(20.88)	0.119
Ischemic heart disease	4(7.02)	8(8.79)	0.768
Liver disease	7(12.28)	7(7.69)	0.395
Cirrhosis	5(8.77)	6(6.59)	0.337
Acute liver failure	1(1.75)	2(2.20)	1.000
Renal disease	3(5.26)	6(6.59)	1.000
AKI	1(1.75)	3(3.30)	1.000
CKD	2(3.51)	3(3.30)	1.000
HP infection, *n* (%)			
Positive	7/28(25.00)	10/51(19.61)	0.388
Not detected	29(50.88)	40(43.96)	
Smoking, *n* (%)	22(38.60)	34(37.36)	0.508
Alcohol consumption, *n* (%)	16(28.07)	29(31.87)	0.382
Bleeding-risk medications, *n* (%)			
Antiplatelet drugs	3(5.26)	6(6.59)	1.000
Anticoagulants	1(1.75)	0(0.00)	1.000
NSAID	4(7.02)	8(8.79)	0.768

Imbalanced between groups ($p < 0.05$).
AKI, acute kidney injury; CKD, chronic kidney disease; EGI, endoscopic glue injection; HP, *Helicobacter pylori* infection; NSAID, nonsteroidal anti-inflammatory drug; SD, standard deviation; SET, standard endoscopic treatment.

Table 2. The incidence of rebleeding within 7 and 30 days.

Variables/group	EGI (*N* = 57) (*n*, %)	SET (*N* = 91) (*n*, %)	*p*-Value
Rebleeding within 7 days	5(8.77)	19(20.88)	0.067
No bleeding within 7 days	52(91.23)	72(79.12)	
Rebleeding within 30 days	5/52(9.62)	21/85(24.71)	0.042[a]
No bleeding within 30 days	47/52(90.38)	64/85(75.29)	
30 Day all-cause mortality rate	0/52(0.00)	1/85(1.18)	1.000
Lost to follow-up	5(8.77)	6(6.59)	
Subgroup analysis of rebleeding within 7 days according to Forrest classification			
Ia	0/13(0.00)	4/17(23.53)	0.087
Ib	1/14(7.14)	11/40(27.50)	0.160
IIa	4/30(13.33)	4/34(11.76)	1.000

[a]Imbalanced between groups ($p < 0.05$).
EGI, endoscopic glue injection; SET, standard endoscopic treatment.

Among the 24 patients who experienced rebleeding within 7 days, except for 2 patients who received conservative treatment, all others received remedial treatment. One patient received hemostatic clips and interventional treatment, one patient received EGI and hemostatic clips, and one patient underwent surgical treatment after intervention treatment. In addition, three patients underwent hemostatic clips or electrocoagulation hemostasis, three patients underwent EGI, and three patients underwent surgical treatment. Ten patients underwent interventional treatment.

AEs, hospital stay, and ICU stay

AEs related to gastrointestinal bleeding and endoscopic treatment included Mallory–Weiss syndrome, esophageal blood blister, pulmonary embolism, hemorrhagic shock, cardiovascular or cerebrovascular events, infections, multiple organ failure, and lower limb thrombosis. No statistically significant differences in the incidence of these AEs existed between the two groups (all $p > 0.05$). The results were shown in Table S2.

The length of hospital stay was 15.38 ± 10.91 days in the SET group and 10.91 ± 12.40 days in the EGI group, with a significant difference between the two groups ($p = 0.002$). The ICU stay was 4.51 ± 8.70 days in the SET group and 5.91 ± 13.63 days in the EGI group, with no significant difference between the two groups ($p = 0.153$).

Given the nonnormal distribution of hospital and ICU stay durations, Spearman's rank-order correlation analysis was used to assess the relationships between AEs and hospital and ICU stays. Significant positive correlations were observed between hospital stay and multiple organ failure, lower limb thrombosis, infection, cardiovascular or cerebrovascular events, and hemorrhagic shock. Likewise, significant positive correlations were determined between ICU stay and multiple organ failure, lower limb thrombosis, infection, and hemorrhagic shock. These findings suggest that patients who experience these AEs likely require prolonged hospitalization and intensive care.

Analysis of risk factors for rebleeding within 7 days

Age, sex, Forrest classification, Rockall risk classification, ulcer location, comorbidities, smoking, and alcohol consumption history were included as potential risk factors in a multivariate logistic regression analysis. Because of the limited number of patients tested for HP infection, this variable was excluded from further analysis. In the stepwise

logistic regression analysis, although Forrest classification IIa classification was statistically significant in the univariate analysis ($p = 0.004$), it was excluded from the final model because of collinearity with other variables or a lack of additional explanatory contribution during stepwise selection.

In multivariate logistic regression analysis, Forrest classification Ia (OR = 8.294, 95% CI: 1.576–43.644, $p = 0.013$) and kidney disease (OR = 24.257, 95% CI: 2.857–205.074, $p = 0.003$) were independent risk factors for rebleeding within 7 days. The model demonstrated a good fit, as supported by both the Omnibus test and the Hosmer–Lemeshow goodness-of-fit test ($\chi^2 = 5.177$, $p = 0.739$), and the regression coefficients were statistically significant. The results were shown in Table 3.

Follow-up outcomes

Among the 148 patients, 6 patients in the SET group and 5 patients in the EGI group were lost to follow-up within 30 days. Unfortunately, one person died from multiple organ failure. Sixty-five patients (30 in the SET group and 35 in the EGI group) underwent gastroscopy follow-up. The overall follow-up rate was 43.92%, with a mean interval of 142.11 days between the bleeding episode and the follow-up endoscopy. Among them, nine cases in the SET group and nine cases in the EGI group were found to have stage A2 or above ulcer lesions again, with no significant difference between the groups ($p = 0.358$).

Discussion

This study retrospectively evaluated the effectiveness and safety of EGI in the treatment of peptic ulcer bleeding. The results showed that although the rebleeding rate within 7 days of EGI treatment for peptic ulcer bleeding was not lower than that in the SET group, the rebleeding rate within 30 days was significantly lower. Forrest classification Ia and kidney disease are independent risk factors for rebleeding within 7 days. In terms of safety, the incidence of AEs and ICU stay in the EGI group was insignificantly different from that in the SET group, but the length of hospital stay was significantly lower.

The 2019 guidelines of the British Society of Gastroenterology emphasize that adrenaline injection alone is insufficient and should be followed by definitive hemostatic methods, such as mechanical or thermal therapy, to achieve effective and durable hemostasis.[22] Endoscopic thermal therapy stops bleeding by causing tamponade and coagulation of the bleeding vessel. Clips close the vessel by mechanical compression.[23,24] The hemostatic mechanism of EGI involves the rapid polymerization of cyanoacrylate upon contact with blood, resulting in the formation of a solid plug that embolizes the target vessel and achieves hemostasis.[25] Research on the use of tissue glue for peptic ulcers is currently limited. Among 18 patients with failed endoscopic hemostasis for gastroduodenal ulcer bleeding who subsequently received cyanoacrylate injection, the hemostasis success rate was 94.4%, with no reported complications or device-related injuries associated with cyanoacrylate use.[26] A small sample descriptive study found discovered that cyanoacrylate glue is particularly effective and safe for Forrest classification IIa and IIb peptic ulcer.[25] The rebleeding rate of patients with refractory high-risk peptic ulcer bleeding receiving endoscopic injection of cyanoacrylate is significantly lower than that of patients receiving perivascular injection.[27] Unlike previous studies that lacked a SET control group, our research incorporated this comparison to enhance the robustness of the findings.

Endoscopic injection of cyanoacrylate is widely used for gastric varices, but it is associated with the systemic embolization risk, ulcer bleeding at the injection site, peritonitis, rebleeding, and even death.[28,29] The same concern restricts the application of EGI in the treatment of peptic ulcer bleeding. In our study, EGI did not increase the incidence of AEs such as pulmonary embolism, cardiovascular and cerebrovascular accidents, and lower limb thrombosis compared with SET, indicating its safety. Normally, migrated glue particles may travel from gastric varices through the gastrorenal and splenorenal veins into the inferior vena cava, subsequently reaching the right side of the heart and entering the pulmonary circulation. The lungs usually act as a filter, trapping the embolized glue and resulting in pulmonary embolism.[30] Only in rare cases—such as in patients with atrial septal defects, patent foramen ovale, or pulmonary arteriovenous malformations—can the glue particles bypass the pulmonary filter and enter the systemic circulation and may lodge in arteries, such as the cerebral, splenic, or coronary

arteries, leading to catastrophic events, such as cerebral infarction or myocardial infarction.[30] The occurrence of thrombotic complications—such as acute myocardial infarction, ischemic stroke, and lower limb deep vein thrombosis—in patients with gastrointestinal bleeding is primarily associated with hypovolemia, anemia, and prolonged immobilization or enforced bed rest following the bleeding episode, particularly among elderly individuals with underlying atherosclerotic disease.[31–33]

The Forrest classification has predictive value for rebleeding of peptic ulcers.[34] Forrest classification Ia is a risk factor for rebleeding after endoscopic treatment of peptic ulcers, which is consistent with the results of another retrospective cohort study.[35] Kidney disease is a also risk factor for gastrointestinal rebleeding. Gastrointestinal bleeding is a serious complication in patients with end-stage renal disease, with a fivefold higher risk than that in patients without CKD.[36] Among CKD patients, gastric ulcer (37%) and duodenal ulcer (23%) are the most common causes of upper gastrointestinal bleeding.[36] The mechanism may be related to anticoagulants used for extracorporeal circulation during hemodialysis, high prescription rates of antiplatelet drugs, impaired platelet aggregation function, and abnormal interactions between platelets and vascular walls caused by the accumulation of uremic toxins.[36] Therefore, we recommend that patients with peptic ulcer bleeding complicated with kidney disease should pay special attention to the risk of rebleeding.

Ulcers with a fibrotic base or those in difficult locations may not respond well to conventional therapies (e.g., hemoclips or thermal coagulation). In such cases, alternative treatments should be considered.[24] Cyanoacrylate injection may be a promising and generally safe salvage therapy for peptic ulcer bleeding refractory to conventional endoscopic treatment, although high-quality randomized controlled trials are still lacking.[26,37,38] A recent case report demonstrated that EUS-guided reinjection of cyanoacrylate can precisely target the bleeding vessel tract and significantly reduce the risk of inadvertent injection into surrounding tissues or ectopic embolism.[39] This also points out the direction for improving the safety of endoscopic SET treatment for peptic ulcer bleeding.

Table 3. Analysis of risk factors for rebleeding within 7 days.

Variables	OR (95% CI)	*p*-Value
Age	0.973 (0.930–1.017)	0.223
Sex	0.693 (0.109–4.401)	0.697
Forrest classification		
Ia	8.294 (1.576–43.644)	0.013[a]
Ib	4.622 (0.974–21.922)	0.054
Rockall scores	2.126 (0.571–7.912)	0.261
Peptic ulcers		
Gastric ulcer	0.027 (0.000–4.204)	0.160
Duodenal ulcer	0.025 (0.000–4.204)	0.148
Marginal ulcer	0.123 (0.001–18.926)	0.415
Compound ulcer	0.000 (0.000–0.000)	1.000
Mean ulcer size	2.866 (0.822–9.994)	0.099
Coexisting disease		
Cancer	0.684 (0.126–3.715)	0.660
Ischemic heart disease	0.151 (0.018–1.279)	0.083
Renal disease	24.257 (2.857–205.974)	0.003[a]
Liver disease	1.215 (0.183–8.072)	0.841
Smoking	3.530 (0.827–15.074)	0.089
Alcohol consumption	0.866 (0.197–3.802)	0.849
Bleeding-risk medications		
Antiplatelet drugs	5.877 (0.296–116.717)	0.245
Anticoagulants	935033585.000 (0.000–.)	1.000
NSAID	2.722	0.717

[a]Imbalanced between groups ($p < 0.05$).
CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drugs; OR, odds ratio.

Advantages and limitations

This study, based on a relatively large sample size, compared the efficacy and safety of EGI and SET for peptic ulcer bleeding. Independent risk factors for rebleeding were evaluated, highlighting the need for strengthened management in high-risk patients. However, several limitations should be acknowledged: (i) This was a retrospective cohort study, which may be subject to selection bias and

information bias, thereby limiting the ability to infer causal relationships. (ii) The data were derived from a single medical center, which may affect the generalizability of the results. (iii) Only about half of the patients underwent testing for HP infection and follow-up endoscopy, and there was considerable variability in the timing of follow-up. HP infection is one of the major etiological factors in the development of peptic ulcer disease.[40] These limitations restrict the ability to systematically evaluate HP as a risk factor for rebleeding, as well as to assess long-term outcomes and the incidence of posttreatment ulceration at the injection site. Therefore, a randomized controlled trial with standardized follow-up protocols is warranted to validate the findings of this study.

Conclusion

This study retrospectively evaluated the efficacy and safety of EGI in treating peptic ulcer bleeding. The results indicate that EGI is not inferior to traditional treatment in terms of hemostatic effect and significantly shortens hospitalization time without increasing the risk of AEs, demonstrating good clinical application potential. Endoscopic Forrest classification Ia and kidney disease are independent risk factors for rebleeding within 7 days. Thus, individualized management strategies for high-risk populations urgently need to be strengthened. Prospective studies are needed in the future to validate the clinical value and scope of application of EGI.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University, with approval number (QYFY WZLL 29902) and approval date April 2025. Given the retrospective design of the study and the use of anonymized data, the requirement for informed consent was waived by the Ethics Committee.

Consent for publication

Not applicable.

Author contributions

XingSi Qi: Investigation; Methodology; Project administration; Writing – original draft.

Li Jia: Methodology; Supervision.

ShiDong Wang: Conceptualization; Formal analysis.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Supplemental material

Supplemental material for this article is available online.

References

1. Laursen SB, Jørgensen HS, Schaffalitzky de and Muckadell OB. National consensus on management of peptic ulcer bleeding in Denmark 2014. *Dan Med J* 2014; 61: 1–10.

2. Orpen-Palmer J and Stanley AJ. Update on the management of upper gastrointestinal bleeding. *BMJ Med* 2022; 1: e000202.
3. Lu M-H and Chiang H-C. Turn over the new leaf of the treatment in peptic ulcer bleeding: a review of the literature. *Therap Adv Gastroenterol* 2024; 17: 259–261.
4. Lau JY, Sung J, Hill C, et al. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. *Digestion* 2011; 84: 102–113.
5. Xie X, Ren K, Zhou Z, et al. The global, regional and national burden of peptic ulcer disease from 1990 to 2019: a population-based study. *BMC Gastroenterol* 2022; 22: 1–13.
6. Gralnek IM, Stanley AJ, Morris AJ, et al. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline—update 2021. *Endoscopy* 2021; 53: 300–332.
7. Pittayanon R, Khongka W, Linlawan S, et al. Hemostatic powder vs standard endoscopic treatment for gastrointestinal tumor bleeding: a multicenter randomized trial. *Gastroenterology* 2023; 165: 762–772.e2.
8. Laine L and McQuaid KR. Endoscopic therapy for bleeding ulcers: an evidence-based approach based on meta-analyses of randomized controlled trials. *Clin Gastroenterol Hepatol* 2009; 7: 33–47.
9. Barkun AN, Martel M, Toubouti Y, et al. Endoscopic hemostasis in peptic ulcer bleeding for patients with high-risk lesions: a series of meta-analyses. *Gastrointest Endosc* 2009; 69: 786–799.
10. Jung DH, Park CH, Choi SI, et al. Comparison of a polysaccharide hemostatic powder and conventional therapy for peptic ulcer bleeding. *Clin Gastroenterol Hepatol* 2023; 21: 2844–2853.e5.
11. Rios Castellanos E, Seron P, Gisbert J, et al. Endoscopic injection of cyanoacrylate glue versus other endoscopic procedures for acute bleeding gastric varices in patients with portal hypertension. *Cochrane Database Syst Rev* 2015; 2015(5): CD010180.
12. Von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting. *J Clin Epidemiol* 2007; 147: 573–578.
13. Shung DL and Laine L. Upper gastrointestinal bleeding—review of current evidence and implications for management. *Aliment Pharmacol Ther* 2024; 59: 1062–1081.
14. Tanabe S. Endoscopic hemostasis for nonvariceal upper gastrointestinal bleeding. *Dig Endosc* 2022; 34: 61–63.
15. Laine L, Spiegel B, Rostom A, et al. Methodology for randomized trials of patients with nonvariceal upper gastrointestinal bleeding: recommendations from an international consensus conference. *Am J Gastroenterol* 2010; 105: 540–550.
16. Sung JJY, Luo D, Wu JCY, et al. Early clinical experience of the safety and effectiveness of Hemospray in achieving hemostasis in patients with acute peptic ulcer bleeding. *Endoscopy* 2011; 43: 291–295.
17. Saleem S and Thomas AL. Management of upper gastrointestinal bleeding by an internist. *Cureus* 2018; 10(6): e2878.
18. Ghasemi A and Zahediasl S. Normality tests for statistical analysis: a guide for non-statisticians. *Int J Endocrinol Metab* 2012; 10: 486–489.
19. Kim TK. *T* test as a parametric statistic. *Korean J Anesthesiol* 2015; 68: 540.
20. Mchugh ML. The Chi-square test of independence lessons in biostatistics. *Biochem Med* 2013; 23: 143–149.
21. Bewick V, Cheek L and Ball J. Statistics review 14: logistic regression. *Crit Care* 2005; 9: 112–118.
22. Banks M, Graham D, Jansen M, et al. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. *Gut* 2019; 68: 1545–1575.
23. Stanley AJ and Laine L. Management of acute upper gastrointestinal bleeding. *BMJ* 2019; 364: 1–15.
24. Laine L, Barkun AN, Saltzman JR, et al. ACG clinical guideline: upper gastrointestinal and ulcer bleeding. *Am J Gastroenterol* 2021; 116: 899–917.
25. Ye Y, Liu L and Xu L. Preliminary exploration of the application of cyanoacrylate glue in Forrest IIa and IIb peptic ulcer hemorrhage. *Surg Endosc* 2025; 39: 3155–3166.
26. Repici A, Ferrari A, De Angelis C, et al. Adrenaline plus cyanoacrylate injection for treatment of bleeding peptic ulcers after failure of conventional endoscopic haemostasis. *Dig Liver Dis* 2002; 34: 349–355.

27. Mou H, Zou C, Shi G, et al. Endoscopic cyanoacrylate injection therapy for refractory high-risk peptic ulcer bleeding by conventional endoscopic therapy. *Scand J Gastroenterol* 2023; 58: 331–338.

28. Florencio de, Mesquita C, Antunes VLJ, Milioli NJ, et al. EUS-guided coiling plus glue injection compared with endoscopic glue injection alone in endoscopic treatment for gastric varices: a systematic review and meta-analysis. *Gastrointest Endosc* 2025; 101: 331–340.e8.

29. Gralnek IM, Duboc MC, Garcia-Pagan JC, et al. Endoscopic diagnosis and management of esophagogastric variceal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2022; 54: 1094–1120.

30. Michael PG, Antoniades G, Staicu A, et al. Pulmonary glue embolism: an unusual complication following endoscopic sclerotherapy for gastric varices. *Sultan Qaboos Univ Med J* 2018; 18(2): e231–e235.

31. Arahata M and Asakura H. Antithrombotic therapies for elderly patients: handling problems originating from their comorbidities. *Clin Interv Aging* 2018; 13: 1675–1690.

32. Pemmasani G, Ashwath A, Aronow WS, et al. Six-month cardiovascular prognostic impact of type 1 and type 2 myocardial infarction in patients hospitalized for gastrointestinal bleeding. *Eur J Intern Med* 2023; 116: 51–57.

33. Szymanski TW, Weeks PA, Patel CJ, et al. Risk of pump thrombosis and stroke in patients with continuous-flow left ventricular assist devices and gastrointestinal bleeding. *Artif Organs* 2020; 44: 1171–1175.

34. De Groot NL, van Oijen MGH, Kessels K, et al. Reassessment of the predictive value of the Forrest classification for peptic ulcer rebleeding and mortality: can classification be simplified? *Endoscopy* 2014; 46: 46–52.

35. Cha B, Noh JH, Ahn JY, et al. Clinical outcomes of patients with benign peptic ulcer bleeding after an emergency endoscopy based on patient location. *Dig Dis Sci* 2023; 68: 1539–1550.

36. Costa-Moreira P, Vilas-Boas F, Teixeira Fraga A, et al. Particular aspects of gastroenterological disorders in chronic kidney disease and end-stage renal disease patients: a clinically focused review. *Scand J Gastroenterol* 2020; 55: 129–138.

37. Grassia R, Capone P, Iiritano E, et al. Non-variceal upper gastrointestinal bleeding: rescue treatment with a modified cyanoacrylate. *World J Gastroenterol* 2016; 22: 10609–10616.

38. Oleas R and Robles-Medranda C. Endoscopic treatment of gastric and ectopic varices. *Clin Liver Dis* 2022; 26: 39–50.

39. Tan W, Sheng J, Huang Z, et al. EUS-guided cyanoacrylate glue injection for the management of refractory bleeding from postglue ulcer following gastric varices treatment (with video). *Endosc Ultrasound* 2024; 13: 382–384.

40. Almadi MA, Lu Y, Alali AA, et al. Peptic ulcer disease. *Lancet* 2024; 404: 68–81.