Precise application of topical tranexamic acid to enhance endoscopic hemostasis for peptic ulcer bleeding: a randomized controlled study (with video)

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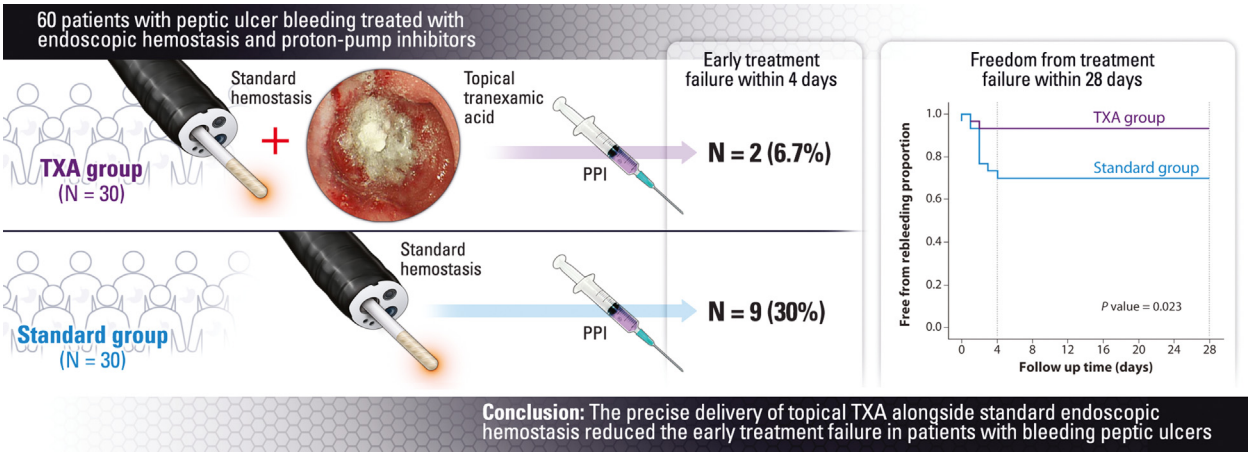
GRAPHICAL ABSTRACT



Background and Aims: Peptic ulcer recurrent bleeding occurs in 20% to 30% of patients after standard endoscopic hemostasis, particularly within 4 days after the procedure. The application of additional tranexamic acid (TXA) to the ulcer may enhance hemostasis. This study investigated the effectiveness of TXA powder application on bleeding ulcers during endoscopic hemostasis.

Methods: This study enrolled patients who had peptic ulcer bleeding between March 2022 and February 2023. After undergoing standard endoscopic therapy, the patients were randomly assigned to either the TXA group or the standard group. In the TXA group, an additional 1.25 g of TXA powder was sprayed endoscopically on the ulcer. Both groups then received 3 days of high-dose (8 mg/h) continuous infusion proton pump inhibitor therapy. Second-look endoscopy was conducted on days 3 to 4. The primary end point of early treatment failure was defined as ulcer recurrent bleeding within 4 days or major stigmata of recent hemorrhage on the second-look endoscopy.

Results: Sixty patients (30 in each group) with peptic ulcer bleeding and balanced baseline characteristics were randomly assigned to a treatment group. The early treatment failure rate was lower in the TXA group (6.7%) than in the standard group (30%) ($P = .042$). The freedom from treatment failure periods for 4 and 28 days was significantly longer in the TXA group than in the standard group ($P = .023$). No adverse events from TXA were recorded.

Conclusions: The precise delivery of topical TXA alongside standard endoscopic hemostasis reduced the early treatment failure rate in patients with bleeding peptic ulcers. (Clinical trial registration number: NCT05248321.) (Gastrointest Endosc 2023;98:755-64.)

(footnotes appear on last page of article)

Peptic ulcer bleeding, the most common cause of upper GI (UGI) bleeding, has a high mortality risk.[1] The standard therapy for acute peptic ulcer bleeding combines proton pump inhibitor (PPI) and endoscopic therapies.[2] Endoscopic hemostasis, which includes local epinephrine injection, heater probe coagulation, use of hemostatic clips, and/or band ligation, is highly effective in hemostasis, with an overall immediate success rate of 85% to 95%.[3] However, 20% to 30% of patients experience recurrent bleeding within 30 days after standard endoscopic hemostasis, particularly those with Rockall scores $\geq$6.[3,4] Studies have indicated that early recurrent bleeding primarily occurs within the first 4 days after therapy.[5,6] How to prevent early recurrent peptic ulcer bleeding remains an unresolved clinical problem.

Tranexamic acid (TXA) is a well-known antifibrinolytic agent that inhibits fibrin degradation by binding to tissue plasminogen, thereby preventing blood clot lysis and reducing bleeding.[7] Because TXA is a conventional drug, it is cheap and easily available. Studies have shown that TXA reduces blood loss and the need for transfusions in patients with surgical bleeding and also prevents mortality caused by traumatic bleeding.[8-10] However, the use of TXA for GI bleeding remains controversial. Review articles have shown that although TXA may be effective in reducing mortality, its hemostatic ability is inconsistent.[11,12] The Haemorrhage Alleviation with Tranexamic Acid–Intestinal System (HALT-IT) trial, a randomized controlled trial of 12,009 patients, found that systemic TXA did not prevent deaths from GI bleeding.[13]

Because TXA has antifibrinolytic effects on the bleeding site, however, local administration of TXA is expected to have higher efficacy than intravenous administration.[8,14] A recent study showed that topical administration of TXA had a better postoperative blood-conserving effect than intravenous administration during spine surgery.[15] In addition, local mouth washing with TXA bleeding after tooth extraction can prevent oral bleeding.[16] Moreover, local administration of TXA may reduce blood loss and systemic adverse effects in surgery more effectively than intravenous use.[17]

On the basis of the aforementioned findings, we hypothesized that precise endoscopic TXA spraying on a bleeding ulcer site may enhance hemostasis and prevent recurrent bleeding. Therefore, this study investigated the effectiveness and safety of topical TXA powder administration in patients with peptic ulcer bleeding after standard endoscopic therapy.

METHODS

Study setting and design

This single-center randomized controlled pilot study was conducted at National Cheng Kung University Hospital and was approved by the hospital's Institutional Review Board (A-BR-110-085). The study was registered at ClinicalTrials.gov (NCT05248321). Patients with confirmed peptic ulcer bleeding treated with endoscopy were recruited. The results are reported in this article in accordance with the Consolidated Standards of Reporting Trials statement.

Informed consent was obtained from all participants included in the study, and all individuals agreed to the use of the obtained data.

Selection of participants

This study enrolled patients aged $\geq$20 years who had peptic ulcer bleeding with major stigmata of recent hemorrhage (SRH) detected by EGD at our hospital. The study excluded patients with poor renal function (serum creatinine >2.9 mg/dL), tumor ulcer bleeding, allergies to TXA, and/or acute thromboembolic events within 1 week or who were unable to temporarily halt antiplatelet or anticoagulation treatment.

Study procedure

All the enrolled patients underwent standard endoscopic hemostasis by local injection of diluted epinephrine combined with heater probe coagulation, use of hemostatic clips, and/or band ligation.[2,3] After the standard treatment (Fig. 1A-C), the patients were randomly assigned to either a standard group or a TXA group. The patients in the standard group received no additional treatment after standard endoscopic therapy. By contrast, an additional 1.25 g of TXA powder was applied to the peptic ulcer sites of the patients in the TXA group before endoscopic completion (Fig. 1D and E). The pharmacologists opened 5 Transamin capsules (250 mg per capsule, Daiichi Sankyo Taiwan Ltd, Taipei, Taiwan) to collect 1.25 g of TXA powder. This powder was then delivered through a functional powder delivery system (7F polyethylene catheter with 1-3 L/min of airflow from the hospital's air source as the propelling power) (Video 1, available online at www.giejournal.org). Both groups then received a 72-hour continuous infusion of high-dose PPI (8 mg/h) therapy. All patients then underwent a second-look EGD on day 3 or 4 after the initial endoscopy (Fig. 1F).

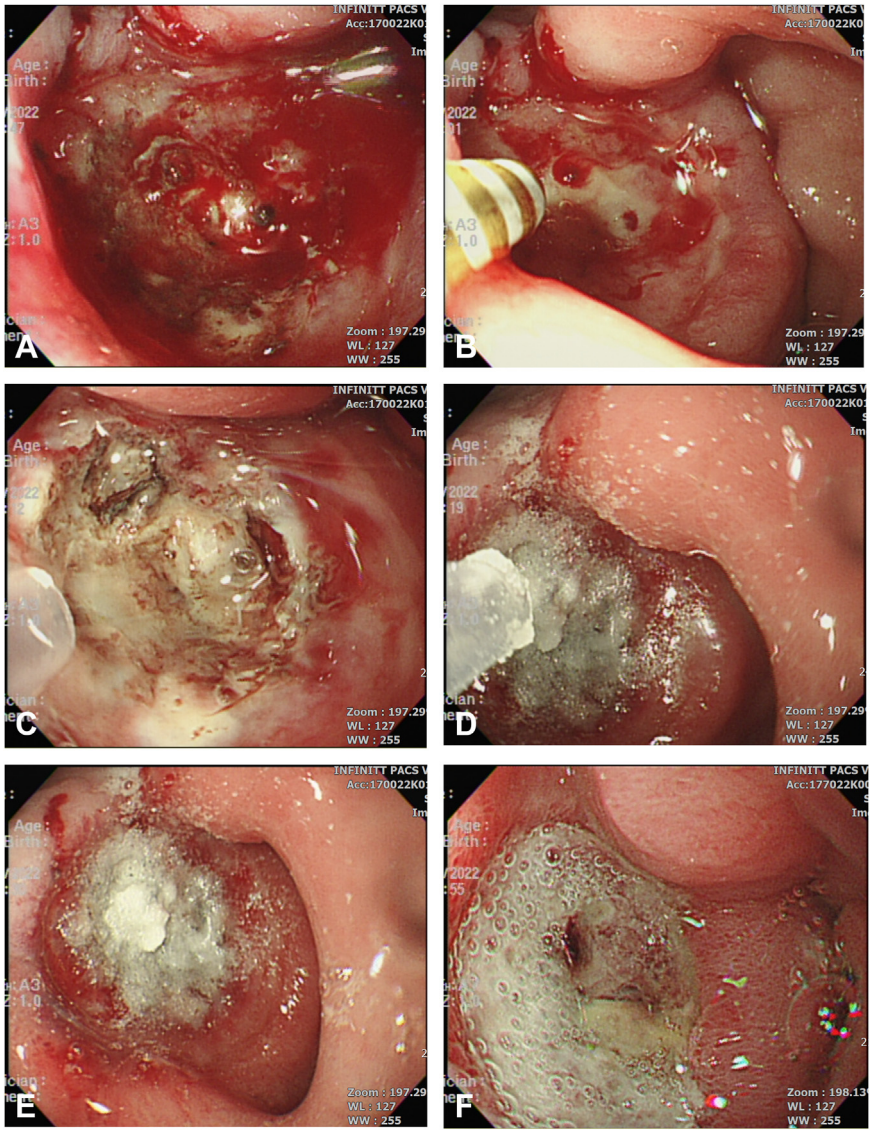


Figure 1. A, Duodenal ulcer (3 cm) with 2 bleeding visible vessels at duodenal bulb. **B,** Heater probe coagulation applied after endoscopic epinephrine injection. **C,** Bleeding ceased after standard endoscopic hemostasis. **D,** Tranexamic acid powder (1.25 g) sprayed on duodenal ulcer. **E,** Tranexamic acid powder rapidly clotted after exposure to moist environment in intestine. **F,** Second-look EGD on day 3 indicated healing duodenal ulcer with flat red appearance.

The patients with Rockall scores ≥6 received oral PPI therapy twice daily for 11 days, followed by once-daily PPI for at least 3 months.[18] Patients with Rockall scores <6 received once-daily PPI for at least 3 months.

Patients receiving antiplatelet or anticoagulant therapies for cardiovascular or cerebrovascular diseases discontinued their treatments 3 days after the initial EGD. The antiplatelet or anticoagulant treatments were resumed after the second-look EGD.

Patient allocation

All enrolled patients underwent standard endoscopic therapy. The patients were subsequently assigned to either the standard or TXA group following a block randomization with a 1:1 allocation ratio. Block randomization ensures a balance in small sample sizes across groups over time.[19] The number of participants from the 2 groups was balanced equally between the blocks. The blocks (1-10) were randomly chosen by drawing straws by an endoscopy assistant other than the group members to determine each patient's assignment into either group.

Outcome measurement

Because most peptic ulcer recurrent bleeding occurs within 4 days after endoscopic hemostasis,[5,6] the primary outcome in the current study was early treatment failure of the index ulcer within 4 days after the initial endoscopic treatment.[20] Treatment failure was defined as the following:

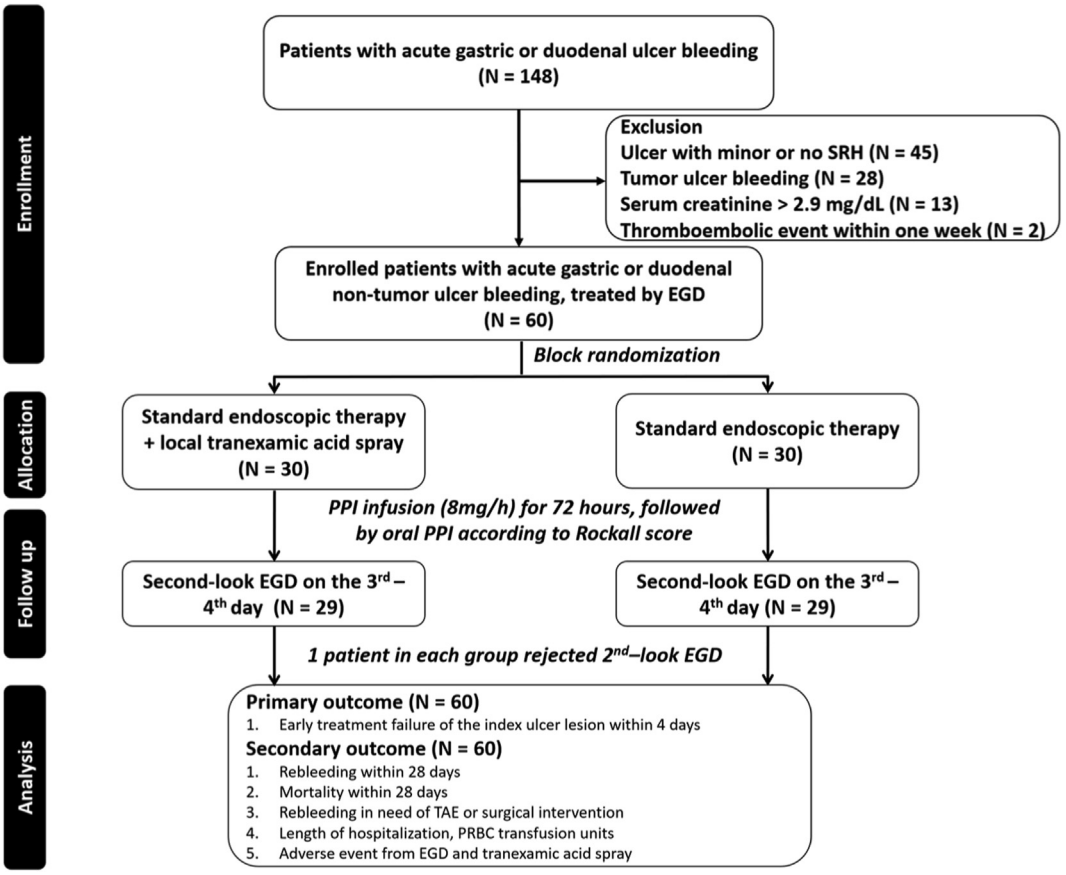


Figure 2. Study flowchart. *SRH*, Stigmata of recent hemorrhage; *PPI*, proton pump inhibitor; *TAE*, transarterial embolization; *PRBC*, packed red blood cell.

(1) index ulcer recurrent bleeding, symptoms of which include continuous melena, hematochezia, bloody drainage from a nasogastric tube, hemodynamic instability (systolic blood pressure < 90 mm Hg; heart rate >120 beats/min), and a drop in serum hemoglobin >2 g/dL with a subsequent EGD confirming major SRH of the index ulcer; (2) index ulcer with major SRH requiring repeated endoscopic hemostasis during the second-look EGD; or (3) index ulcer recurrent bleeding requiring transarterial embolization (TAE) or surgery before the second-look EGD.

Secondary outcomes included the following: (1) index ulcer recurrent bleeding within 28 days; (2) index ulcer recurrent bleeding requiring TAE or emergent surgery; (3) the duration of hospitalization; (4) transfusion units of packed red blood cells; (5) mortality; and (6) severe adverse events due to TXA (eg, seizures, thromboembolic events).

Statistical analysis

We established an early treatment failure rate of 35% and a relative odds ratio of 5 for the additional TXA based on data from related studies. Because the participant dropout rate was estimated to be 10%, this study required 60 participants, with a minimum of 30 in each group, to achieve statistical significance. The baseline and outcome data were analyzed by using the Student t test, the Mann-Whitney *U* test, Pearson's χ^2 test, or the Fisher exact test depending on the data characteristics. Univariate and multivariate logistic regression models were implemented to predict the relationships between risk factors and the occurrence of recurrent bleeding events. The log-rank test was used to compare the Kaplan-Meier curves of the 2 study groups in the freedom from treatment failure analysis. Statistical analysis was conducted by using SPSS version 25.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA) or SAS version 9.4 (SAS Institute, Inc, Cary, NC, USA).

RESULTS

Between March 2022 and February 2023, a total of 401 patients with upper GI bleeding were admitted to our hospital. Of these patients, 148 had gastric or duodenal ulcer bleeding and were screened for enrollment. As shown in Figure 2, patients with tumor-related ulcer bleeding (n = 28) or those with only minor or no SRH (n = 45) were excluded. In addition, 13 patients with serum creatinine levels >2.9 mg/dL and 2 with thromboembolic events within 1 week were also excluded. Finally, 60 patients who had

non-tumor ulcer bleeding with major SRH met the enrollment criteria for randomization. Fourteen (23.3%) of these patients had gastric ulcer bleeding, and 46 (76.7%) had duodenal ulcer bleeding. The EGD view revealed that 2 (3.3%) ulcers were active spurting bleeds (Forrest classification Ia), 20 (33.3%) were active oozing bleeds (Forrest classification Ib), 33 (55%) were ulcers with nonbleeding visible vessels (Forrest classification IIa), and 5 (8.3%) were ulcers with adherent clots (Forrest classification IIb). After receiving standard endoscopic treatment, 30 patients in each group were randomly assigned to the TXA group and the standard group.

Among the enrolled patients, 11 (18.3%) experienced early treatment failure within 4 days. One patient experienced severe clinical recurrent bleeding and underwent TAE and surgery before the second-look EGD. Another patient had recurrent bleeding after the second-look EGD on day 4. Nine patients were diagnosed with an index ulcer with major SRH requiring endoscopic treatment during the second-look EGD; among these 9 patients, 2 had Forrest classification Ia, 5 had Forrest classification IIa, and 2 had Forrest classification IIb.

The 2 groups did not differ significantly with respect to baseline characteristics, comorbidities, or endoscopic findings (Table 1). The clinical and endoscopic outcomes are listed in Table 2. For the primary outcome, the early treatment failure rate was lower in the TXA group than in the standard group (6.7% vs 30%, respectively; $P = .042$). The periods of freedom from treatment failure for both 4 days and 28 days were significantly longer in the TXA group than in the standard group ($P = .023$) (Fig. 3). Moreover, the results indicated a trend of higher severity of Forrest classification on the second-look EGDs in the standard treatment group compared with the TXA group ($P = .056$). The incidence rate of major SRH on the second-look EGDs was higher in the standard group than in the TXA group (26.7% vs 3.3%, $P = .025$).

Regarding the secondary outcomes, the results indicated a decreased recurrent bleeding rate within 28 days in the TXA group compared with that of the standard group; however, this finding did not reach statistical significance (6.7% vs 23.3%, respectively; $P = .145$). One patient in each group underwent emergent TAE and surgery for pseudoaneurysm bleeding from a branch of the gastroduodenal artery. The 9 patients who had index ulcers with major SRH underwent successful endoscopic salvage treatment. The 2 groups did not differ in their durations of hospitalization or in the transfusion units of packed red blood cells received. No patient in either group experienced recurrent bleeding within 28 days during the follow-up period after the salvage treatment or second-look EGD. One patient in the TXA group died of progressive pneumonia on day 15 of hospitalization; otherwise, no patient experienced GI perforation, seizure, or a thromboembolic event.

Table 3 evaluates the effects of risk factors interfering with early treatment failure of a bleeding peptic ulcer. The univariate analysis indicated that the topical TXA spray was associated with a lower rate of early treatment failure (relative risk [RR], .17; 95% confidence interval [CI], .03-.85; $P = .032$) and that acute kidney injury was associated with a higher rate of early treatment failure (RR, 6.05; 95% CI, 1.49-24.51; $P = .012$). The multivariate analysis indicated that the topical TXA spray was the only independent factor that prevented early treatment failure (RR, .10; 95% CI, .01-.87; $P = .037$).

DISCUSSION

To the best of our knowledge, this study was the first to evaluate the hemostatic effect of topical TXA powder spray on bleeding peptic ulcers. This randomized controlled pilot study showed that precise application of the TXA spray significantly reduced the early treatment failure rate of bleeding peptic ulcers. The results also revealed that the topical TXA spray could downgrade the severity of Forrest classification on the second-look EGD. Moreover, a topical 1.25 g TXA powder spray in patients with preserved renal function was safe and led to no severe adverse events.

Systemic TXA therapy has been shown to effectively reduce blood loss and mortality due to surgery or trauma.[8-10] However, its role in UGI bleeding remains under debate. The HALT-IT trial enrolled 12,009 patients who had GI bleeding between 2013 and 2019 and intravenously administered 4 g of TXA to the experimental group over 24 hours.[13] The investigators found that GI bleeding–related deaths were similar between the TXA and placebo groups (3.72% vs 3.77%, respectively). Another retrospective study that evaluated the hemostatic effect of systemic TXA on 386 patients with peptic ulcer bleeding indicated no effect on the recurrent bleeding rate, duration of hospitalization, or incidence of blood transfusions.[21] These findings suggest that the systemic administration of TXA does not prevent GI bleeding or related mortality.

Pharmacodynamic analyses have suggested that local administration of TXA may yield more potent hemostatic effects than systemic administration.[22,23] Studies have shown the effects of topical TXA.[15-17] A meta-analysis of 5 studies involving 603 patients concluded that the combined use of intravenous and topical TXA was more effective than intravenous TXA alone in primary total knee or hip arthroplasty.[24] Another study of 104 patients undergoing elective spinal surgery indicated that the patients who received topical TXA had less postoperative blood loss and needed fewer blood transfusions than those who received intravenous TXA.[15]

Two studies have investigated the effect of topical TXA solution for the treatment of UGI bleeding. Karadaş et al[22] administered 2 g of a TXA solution through a nasogastric

TABLE 1. Baseline characteristics

Characteristic	Tranexamic acid group (n = 30)	Standard group (n = 30)	*P* value
Age, mean ± SD, y	68.9 ± 15.7	72.3 ± 14.4	.394
Sex, male:female	20:10	23:7	.567
Ulster site, gastric:duodenal	6:24	8:22	.761
Ulcer size, cm			
Mean ± SD	1.3 ± .5	1.4 ± .8	.308
≥2:<2	5:25	6:24	1.000
Hypotension, n (%)	4 (13.3)	2 (6.7)	.671
Hematemesis, n (%)	8 (26.7)	2 (6.7)	.080
Rockall score			
Median (IQR)	6 (5-7)	6 (5-7)	.913
≥6:<5	19:11	19:11	1.000
Forrest classification			.096
Ia (spurting vessel)	1	1	
Ib (active oozing)	10	10	
IIa (NBVV)	19	14	
IIb (adherent clot)	0	5	
Endoscopic treatment			.346
Heat probe coagulation	19	15	
APC	2	3	
Clipping	9	8	
Rubber band ligation	0	1	
Heat probe + clipping	0	3	
Serum test, mean ± SD			
Platelet, $10^3/\mu L$	267.6 ± 93.6	236.7 ± 90.9	.200
Hemoglobin, g/dL	10.1 ± 2.6	9.3 ± 2.7	.236
Creatinine, mg/dL	.9 ± .4	1.0 ± .4	.146
PT-INR	1.2 ± .2	1.2 ± .3	.772
Albumin, g/dL*	3.4 ± .6	3.2 ± .6	.384
Comorbidity, n (%)			
Liver cirrhosis	3 (10)	3 (10)	1.000
Cardiovascular disease	11 (36.7)	8 (26.7)	.580
Acute kidney injury	7 (23.3)	11 (36.7)	.399
Use of antiplatelet/anticoagulant	11 (36.7)	10 (33.3)	1.000
Use of NSAID	8 (26.7)	11 (36.7)	.580
Helicobacter pylori status			.807
Positive	2 (6.7)	1 (3.3)	
Negative	23 (76.7)	22 (73.3)	
Not performed	5 (16.7)	7 (23.3)	

SD, Standard deviation; *IQR*, interquartile range; *NBVV*, nonbleeding visible vessels; *APC*, argon plasma *coagulation*; *PT-INR*, prothrombin time–international normalized ratio; *NSAID*, nonsteroidal anti-inflammatory drug.
*Sixteen patients in the tranexamic acid group and 12 patients in the standard group did not have serum albumin level measurements.

tube as an additional treatment; however, their results indicated no significant reduction in mortality or recurrent bleeding. Similarly, Rafeey et al[23] endoscopically applied 1 g of a TXA solution to the surface of peptic ulcers, which yielded no significant effect on peptic ulcer recurrent bleeding. Those 2 results do not support the application of topical TXA for UGI bleeding treatment. We hypothesized that the lack of positive results in those studies may have been caused by the inability of the TXA solution to adhere to the bleeding site.

TABLE 2. Clinical outcomes of patients after endoscopic treatment

Outcome	Tranexamic acid group (n = 30)	Standard group (n = 30)	*P* value
Early treatment failure	2 (6.7%)	9 (30%)	.042
Second-look EGD*			.056
Forrest classification			
Forrest Ia	0	2 (6.7%)	NA
Forrest Ib	0	0	1.000
Forrest IIa	0	5 (16.7%)	NA
Forrest IIb	1 (3.3%)	1 (3.3%)	1.000
Forrest IIc	16 (53.3%)	14 (46.7%)	.599
Forrest III	11 (36.7%)	7 (23.3%)	.263
Major SRH† (Ia-IIb)	1 (3.3%)	8 (26.7%)	.025
Rebleeding within 28 d	2 (6.7%)	7 (23.3%)	.145
Treatment failure salvage			.345
Endoscopic hemostasis	1 (3.3%)	8 (26.7%)	
TAE and/or surgery	1 (3.3%)	1 (3.3%)	
Rebleeding after salvage therapy	0	0	1.000
Hospitalization, median (IQR), d	5 (4-7)	6 (4-8)	.664
RBC transfusion during hospital stay, median (IQR), U	2 (0-4)	3 (0-8)	.445
RBC transfusion after endoscopic therapy, median (IQR), U	2 (0-4)	2 (0-5)	.793
Mortality			
All-cause mortality	1	0	1.000
Bleeding-related death	0	0	1.000
Severe adverse events			
GI tract perforation	0	0	1.000
Seizure	0	0	1.000
Thromboembolic event	0	0	1.000

SRH, Stigmata of recent hemorrhage; *TAE*, transarterial embolization; *IQR*, interquartile range; *RBC*, red blood cell.
*One patient in the tranexamic acid group accepted TAE and surgery before the second-look EGD. One patient in the standard group had no major SRH during the second-look EGD but had recurrent bleeding on day 4. One patient in the standard group and one patient in the tranexamic acid group rejected the second-look EGD.
†Major SRH includes Forrest classification Ia, Ib, IIa, and IIb.

Hemospray Endoscopic Hemostat (Cook Medical, Bloomington, Ind, USA) was approved in 2018 for use in facilitating endoscopic hemostasis and reducing recurrent bleeding. Hemospray is a nonabsorbable powder that produces a mechanical tamponade by forming an adhesive covering to seal a peptic ulcer.[25] The current study endoscopically applied TXA powder precisely onto peptic ulcers. Similar to Hemospray, the moistened TXA powder in this study adheres to an ulcer surface to expand its local effect, as shown in Figure 1 and in the accompanying Video 1. Furthermore, the topical TXA protects against additional injury to the ulcer from gastric acid. This study therefore showed the effectiveness of topical TXA in preventing treatment failure in patients with bleeding peptic ulcers.

Furthermore, the current study evaluated the adverse effects of TXA powder spray to ensure patient safety. The HALT-IT trial found a .6% seizure rate and a 1.4% thromboembolic event rate in patients receiving 4 g of systemic TXA.[13] By contrast, no patients in our TXA group experienced seizures or thromboembolic events within 28 days, likely because of the lower TXA dose (1.25 g) and the exclusion of patients with serum creatinine levels >2.9 mg/dL.[26] Regarding airflow concerns, one study reported a GI perforation rate of approximately .7% with Hemospray.[25] Our TXA powder spray flow rate was set at 1 to 3 L/min, which was lower than that of Hemospray and similar to the airflow rate of the EGD[27]; no patients experienced GI perforation.

However, notably, this randomized pilot study had several limitations. First, the sample comprised 60 patients at a single medical center. This small sample size was determined to evaluate the early treatment failure rate; however, the evaluation of adverse events may require a larger sample size for validation. Second, 9 patients (30%) in the standard group had early treatment failure; although this rate was high, it was consistent with corresponding rates in relevant clinical trials (ie, 42.4% and 28.6%).[28,29] Third, the current randomized trial was not double blinded. Because the clinical caregivers were

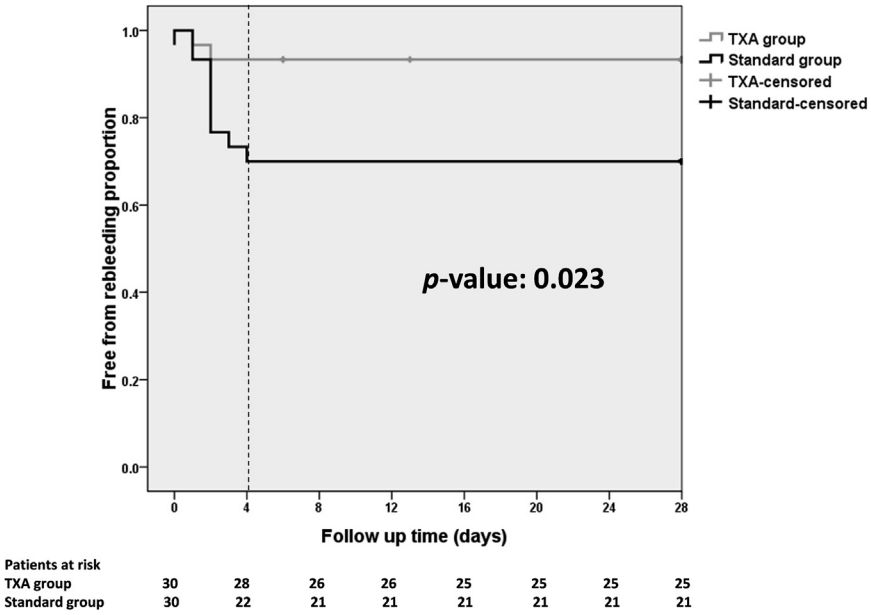


Figure 3. Kaplan-Meier curves of freedom from treatment failure for TXA and standard groups within 28 days. *TXA*, Tranexamic acid.

not prohibited from reviewing the endoscopic images, they may have detected the patients' grouping. However, because both groups underwent high-dose PPI infusion for 72 hours, no imbalance of crucial nonprotocol interventions occurred. Therefore, the bias risk was deemed low in accordance with the Cochrane risk-of-bias tool.[30] Fourth, the TXA powder used in this study for each patient was collected from 5 Transamin capsules. Each capsule contains 250 mg of TXA as the

TABLE 3. Risk factors interfering with early treatment failure of a bleeding peptic ulcer within 4 days

	Early treatment failure, n (%)		Univariate analysis		Multivariate analysis	
	Yes (n = 11)	No (n = 49)	RR (95% CI)	*P* value	RR (95% CI)	*P* value
Baseline						
Age ≥65 y	8 (72.7)	33 (67.3)	1.29 (.30-5.54)	.729		
Male sex	6 (54.5)	37 (75.5)	.39 (.10-1.51)	.172		
Manifestation						
Hematemesis	1 (9.1)	9 (18.4)	.44 (.05-3.93)	.466		
Hypotension	3 (27.3)	3 (6.1)	5.75 (.98-33.68)	.052	8.27 (.59-116.8)	.118
Rockall score ≥6	9 (81.8)	29 (59.2)	3.10 (.61-15.91)	.174		
AKI occurrence	7 (63.6)	11 (22.4)	6.05 (1.49-24.51)	.012	3.47 (.70-17.19)	.127
Ulcer size ≥2 cm	3 (27.3)	8 (16.3)	1.92 (.42-8.86)	.402		
Comorbidity						
Cirrhosis	0	6 (12.2)	0	.999		
Use of antiplatelet/anticoagulant	3 (27.3)	18 (36.7)	.65 (.15-2.75)	.554		
NSAID use	2 (18.2)	17 (34.7)	.42 (.08-2.16)	.298		
Helicobacter pylori status	0	3 (6.1)	0	.999		
TXA spray (+)	2 (18.2)	28 (57.1)	.17 (.03-.85)	.032	.10 (.01-.87)	.037
Standard treatment						
Coagulation	6 (54.5)	33 (67.3)	Reference			
Hemostatic clips	4 (36.4)	13 (26.5)	1.69 (.41-6.99)	.467		
Band ligation	0 (0)	1 (2.0)	0	1.000		
Combination*	1 (9.1)	2 (4.1)	2.75 (.21-35.33)	.437		

RR, Relative risk; *CI*, confidence interval; *AKI*, acute kidney injury; *NSAID*, nonsteroidal anti-inflammatory drug; *TXA*, tranexamic acid.
*Combination indicate coagulation plus hemostatic clips.

active ingredient, along with cornstarch and magnesium stearate as excipients. Although TXA is the major component of the powder, the excipients may have some hemostatic effects. Cornstarch is commonly used in the pharmaceutical industry to improve flowability, disintegration, and hardness, whereas magnesium stearate is used as a lubricant. However, the proportion of these excipients is <10% of the total weight of the powder. We therefore assumed the hemostatic effect from the excipients could be negligible. Finally, although our study excluded patients with uremic and tumor bleeding, these are important unresolved clinical problems. Thus, the efficacy of local TXA treatment for these types of bleeding could not be answered by the current study. Further investigation is warranted to determine the potential of local TXA treatment for uremic bleeding and tumor ulcer bleeding.

In conclusion, the results of this study showed that the precise delivery of topical TXA combined with standard endoscopic hemostasis reduced the early treatment failure rate of patients with bleeding peptic ulcers and downgraded the Forrest classification in such patients. A single dose of 1.25 g of TXA delivered by EGD was safe and caused no significant adverse events in patients with serum creatinine levels ≤2.9 mg/dL. Future multicenter studies with larger sample sizes are required to validate these findings.

DISCLOSURE

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Abbreviations: CI, confidence interval; PPI, proton pump inhibitor; UGI, upper GI; RR, relative risk; SRH, stigmata of recent hemorrhage; TAE, transarterial embolization; TXA, tranexamic acid.

DIVERSITY, EQUITY, AND INCLUSION: We worked to ensure gender balance in the recruitment of human subjects. We worked to ensure ethnic or other types of diversity in the recruitment of human subjects. We worked to ensure that the language of the study questionnaires reflected inclusion. We worked to ensure sex balance in the selection of non-human subjects. The author list of this paper includes contributors from the location where the research was conducted who participated in the data collection, design, analysis, and/or interpretation of the work.

All data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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