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META-ANALYSIS

Efficacy and safety of gastroscopic hemostasis in the treatment of acute gastric hemorrhage: A meta-analysis

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Abstract

BACKGROUND

Gastric cancer (GC) is a malignant tumor with a high incidence and mortality rate worldwide for which acute bleeding is a common clinical complication. Gastroscopic hemostasis is an important method for treating acute bleeding in GC; however, its efficacy and safety remain controversial.

AIM

To systematically analyze the efficacy and safety of gastroscopic hemostasis for the treatment of acute gastric hemorrhage.

METHODS

The PUBMED, Web of Science, Wiley Library, EMBASE, Wanfang, CNKI, and VIP databases were searched for studies related to gastroscopic hemostatic treatment for acute GC published through February 20, 2023. The literature was screened according to the inclusion and exclusion criteria, data were extracted, and literature quality was evaluated. The meta-analysis was performed using RevMan software (version 5.3), while Begg's test for publication bias was performed using Stata 13.0 software.

RESULTS

Six randomized controlled trials and two retrospective analyses were retrieved.

Five studies had a low, two had an uncertain, and one had a high risk of bias. Compared with the control group, the hemostatic rate of gastroscopic hemostasis was increased [relative risk (RR) = 1.24; 95% confidence interval (CI): 1.08 to 1.43; P = 0.003]; the rate of rebleeding (RR = 0.27; 95%CI: 0.09 to 0.80; P = 0.02), rate of surgery transfer (RR = 0.16; 95%CI: 0.06 to 0.43; P = 0.0003), serum C-reactive protein level [mean difference (MD) = -5.16; 95%CI: -6.11 to 4.21; P < 0.00001], interleukin-6 level (MD = -6.37; 95%CI: -10.33 to -2.42; P = 0.002), and tumor necrosis factor-α level (MD = -2.29; 95%CI: -4.06 to -0.52; P = 0.01) were decreased; and the quality of life improvement rate was increased (RR = 1.95; 95%C I= 1.41-2.71; P < 0.0001). Begg's test revealed no significant publication bias.

CONCLUSION

The efficacy and safety of endoscopic hemostasis were higher than those of the control group, suggesting that it is an effective treatment for acute GC hemorrhage.

Key Words: Gastroscope; Gastric cancer; Acute bleeding; Curative effect; Security; Meta-analysis

Core Tip: This meta-analysis provides a wealth of evidence emphasizing the effectiveness and safety of endoscopic hemostasis for treating acute gastrointestinal bleeding in patients with gastric cancer (GC). Compared with the control group, endoscopic hemostasis effectively controlled acute gastric bleeding in GC while significantly reducing the bleeding and transfer rates, indicating its efficacy at treating patients with acute gastric bleeding in GC. Nevertheless, further high-quality clinical research is required to confirm the safety and efficacy of endoscopic hemostasis in the treatment of acute GC bleeding.

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INTRODUCTION

Gastric cancer (GC) is a malignant tumor with one of the highest prevalence and mortality rates among all cancers worldwide. Acute hemorrhage from GC is a serious life-threatening complication[1-3]. GC-related bleeding accounts for an estimated 1%-8% of acute upper gastrointestinal bleeding cases[4,5]. Effective hemostatic treatment is crucial for patients with acute hemorrhage due to GC, as it can reduce the risk of mortality. Emergency gastroscopy can be used for rapid intervention, bleeding assessment, the identification of bleeding sources, and hemostatic treatment[6,7]. Thus, gastroscopic hemostasis is the preferred treatment for acute GC bleeding[8], although little evidence supports the use of endoscopic hemostatic treatment for acute GC bleeding.

The 30 d mortality rate of gastrointestinal bleeding in advanced GC after endoscopic hemostatic treatment is approximately 15.9%-43% higher than that of other causes of gastrointestinal bleeding[9-11]. However, some studies have shown that emergency gastroscopy can improve the detection rate of bleeding causes and aid the assessment of the risk of rebleeding and hemostatic effects[12,13]. The efficacy and safety of endoscopic hemostasis for the treatment of acute bleeding from GC remain controversial. Siau *et al*[14] reported that early gastroscopy could increase the risk of rebleeding. However, a recent study that included a large number of patients with GC (n = 45) reported a fairly low success rate for endoscopic hemostasis (31%). In the remaining 69% of GC bleeding cases, transarterial embolization was used to save patients after gastroscopy failed[15]. Therefore, this study aimed to systematically evaluate the efficacy and safety of gastroscopic hemostasis in the treatment of acute GC hemorrhage using a meta-analysis to objectively and accurately investigate this question.

MATERIALS AND METHODS

Search strategy

The PUBMED, Web of Science, Wiley Library, EMBASE, Wanfang, China National Knowledge Network, and VIP databases were searched for studies published from the inception of each database through February 20, 2023. The reference lists of all retrieved articles were manually searched to identify any other relevant studies.

The search used a combination of subjects and free words. The following English keywords and their Chinese counterparts were used in the search: Gastroscopy, emergency gastroscopy, hemostasis, gastric cancer, GC, acute bleeding, bleeding, and curative effects.

Literature inclusion criteria

The study inclusion criteria were as follows: (1) Randomized controlled study or retrospective analysis of gastroscopic hemostasis for the treatment of acute GC bleeding; (2) subjects including GC patients with acute gastric bleeding; (3) patients in the experimental group were treated with gastroscopy hemostasis, while patients in the control group were treated with conventional drugs; and (4) outcome indexes were successful hemostasis, rebleeding rate, transfer rate, serum C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and quality of life improvement, including at least one outcome measure.

Literature exclusion criteria

The study exclusion criteria were as follows: (1) Study subjects included individuals with GC accompanied by acute hemorrhage; (2) experimental group underwent endoscopic hemostasis treatment for managing bleeding, while the control group received conventional medication for hemostasis; (3) publication language not Chinese or English; (4) incomplete or missing data; and (5) duplicate publication.

Literature screening and data extraction

The literature was searched according to the specified search strategy and screened using the preferred reporting items for systematic reviews and meta-analyses flow chart. The literature was screened separately by two researchers and then crosschecked. In cases of disagreement, a third researcher was invited to participate in the discussions. Two researchers independently extracted the data in accordance with the designated data extraction table, including authors, publication date, country, sample size of the experimental and control groups, patient age, intervention measures, and original outcome data. After the study extraction process, both researchers performed cross-checking and a third researcher ruled out dispute cases.

Literature quality evaluation

This randomized controlled study evaluated the quality of the bias risk assessment tools recommended by the Cochrane Handbook and made judgments on the random allocation method, allocation hiding, blinding method, data integrity, selective reporting, and six other items. If all six items were answered "yes," the study was classified as having a low risk of bias; if all six items were answered "no" or "unclear," the study was classified as having an uncertain risk of bias; if all items were "no" or "unclear," the study was classified as having a high risk of bias. The Newcastle-Ottawa Scale (NOS) was used for the retrospective analysis. An NOS score < 5 was classified as a high risk of bias, while a score ≥ 5 was classified as a low risk of bias.

Statistical methods

RevMan 5.4 software was used to process the data for the meta-analysis. Risk ratios (RR) and 95% confidence intervals (CI) were used to count the data, and the mean difference (MD) and 95%CI were used for measurement data. The Q test was used for the heterogeneity analysis. Values of $P < 0.1$ and $I^2 > 50\%$ indicated interstudy heterogeneity. The random-effects model was used for the meta-analysis in these cases; otherwise, the fixed-effects model was used. Stata 13.0 software was used to perform Begg's test for the publication bias analysis. Statistical significance was set at $P < 0.05$.

RESULTS

Literature screening results

A total of 1998 papers were preliminarily retrieved from the databases; of them, 253 duplicates were removed using Endnote and NoteExpress, and 1745 papers remained. The title and abstract screening removed 1429 unqualified papers, leaving 316 papers. The full-text review eliminated 273 papers, leaving six randomized controlled trials (RCTs) and two retrospective studies[12,16-22] (Figure 1).

Basic information and quality evaluation of the included literature

Six RCTs and two retrospective studies were included in this study, including 672 patients (328 in the experimental group, 344 in the control group). General information about the included studies is presented in Table 1. The risk of bias in the included studies was evaluated using the Cochrane Handbook and NOS scale. Five studies had a low risk of bias, two had an uncertain risk of bias, and only one had a high risk of bias (Table 1).

Statistical analysis results

Analysis of hemostasis rate after gastroscopic hemostasis: Analyses of the hemostatic rates of gastroscopic hemostatic treatment were reported in seven studies (267 and 215 patients in the experimental and control groups, respectively). Due to moderate heterogeneity among the included studies ($P = 0.0008$, $I^2 = 74\%$), a random-effects analytical model was adopted. The meta-analysis results showed that the hemostasis rate of the experimental group was significantly higher than that of the control group (RR = 1.24; 95%CI: 1.08 to 1.43; $P = 0.003$) (Figure 2). Begg's test found no publication bias among the included studies ($P > 0.05$).

Analysis of rebleeding rate after gastroscopic hemostasis: Five studies reported analyses of rebleeding rates for gastroscopic hemostatic treatment (207 and 221 patients in the experimental and control groups, respectively). Due to moderate

Table 1 General information of the included studies

Ref.	Year of publication	Country	Study type	Experimental group				Control group				Study dates	Risk of bias	Outcomes
				Sample size	Age (yr)	Male/female	Intervention methods	Sample size	Age (yr)	Male/female	Intervention methods			
Sheibani *et al*[16]	2013	United States	Retrospective analysis	14	57 ± 12	/	Gastroscopy hemostasis	18	57 ± 12	/	Drug hemostasis	2005.1-2012.1	Low	1, 2, 3
Zheng[17]	2017	China	Retrospective analysis	30	55.1 ± 9.8	19/11	Emergency gastroscopy hemostasis	47	56.2 ± 11.0	31/16	Drug hemostasis	2011.3-2016.1	High	1, 2, 3, 7
Zhang[18]	2018	China	RCT	32	55.47 ± 12.31	18/14	Emergency gastroscopy hemostasis	32	56.17 ± 11.62	19/13	Drug hemostasis	2015.1-2017.3	Low	1, 2, 3, 4, 5, 6, 7
Long[19]	2019	China	RCT	36	58.95 ± 5.21	20/16	Emergency gastroscopy hemostasis	36	58.75 ± 5.62	21/15	Drug hemostasis	/	Unclear	1, 2
Qi *et al*[20]	2019	China	RCT	40	56.45 ± 3.23	/	Emergency gastroscopy hemostasis	40	56.45 ± 3.23	/	Drug hemostasis	2017.12-2018.12	Low	1
Ren *et al*[12]	2021	China	RCT	93	49 ± 3.01	54/38	Emergency gastroscopy hemostasis	88	47 ± 3.83	47/41	Drug hemostasis	2018.9-2020.9	Low	1, 2
Xiang[21]	2021	China	RCT	34	54.45 ± 2.15	19/15	Gastroscopy hemostasis	34	54.63 ± 2.26	18/16	Drug hemostasis	2019.8-2020.12	Unclear	1, 5, 6
Zhang *et al*[22]	2021	China	RCT	49	56.6 ± 4.76	31/18	Gastroscopy hemostasis	49	56.55 ± 4.71	29/20	Drug hemostasis	2018.10-2019.10	Low	3, 4, 5, 6, 7

1: Hemostasis success rate; 2: Rebleeding rate; 3: Operational transfer rate; 4: Patient's serum C-reactive protein level; 5: Serum interleukin-6 level; 6: Serum tumor necrosis factor-α level; 7: Quality of life improvement rate. RCT: Randomized controlled trial.

heterogeneity among the included studies (P = 0.004, I^2 = 74%), a random-effects model of analysis was adopted. The meta-analysis results showed that the rebleeding rate in the experimental group was significantly lower than that in the control group (RR = 0.27; 95%CI: 0.09 to 0.80; P = 0.02) (Figure 3). Begg's test found no publication bias among the included studies (P > 0.05).

Transfer rate of hemostatic treatment under gastroscopy: Four studies analyzed the transfer rate for gastroscopic hemostatic treatment. A total of 125 and 146 patients were included in the experimental and control groups, respectively. There was no heterogeneity among the included studies (P = 0.19, I^2 = 37%); therefore, a fixed-effects analytical model was adopted. The conversion rate of treatment was significantly lower in the experimental than control groups (RR = 0.16; 95%CI: 0.06 to 0.43; P = 0.0003) (Figure 4). Begg's test found no publication bias among the included studies (P > 0.05).

Analysis of serum CRP after gastroscopic hemostasis: Two studies reported analyses of serum CRP levels after gastroscopic hemostatic treatment (81 and 81 patients in the experimental and control groups, respectively). There was no

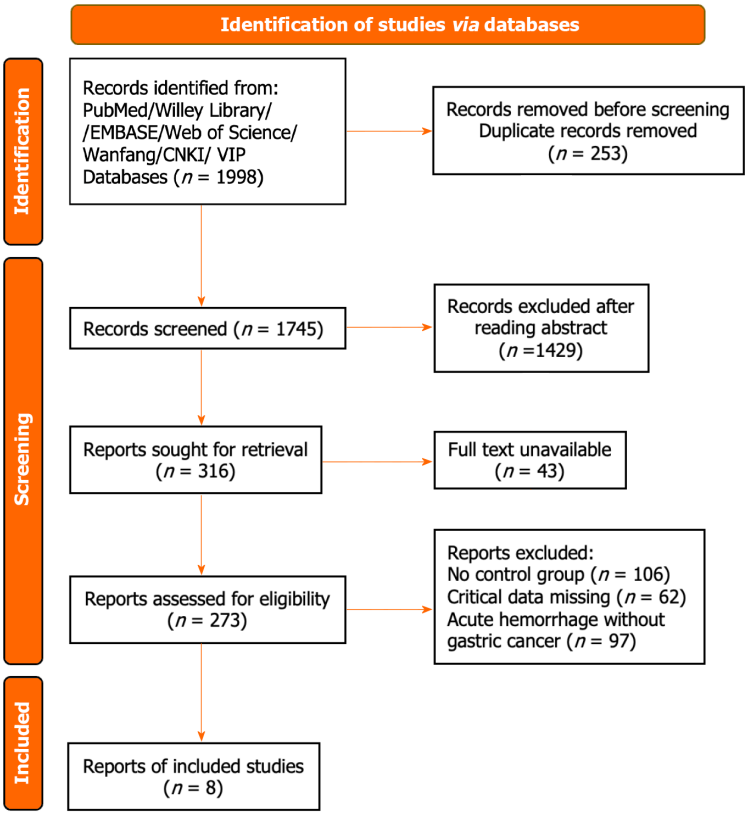

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Figure 1 Literature screening flow chart and results.

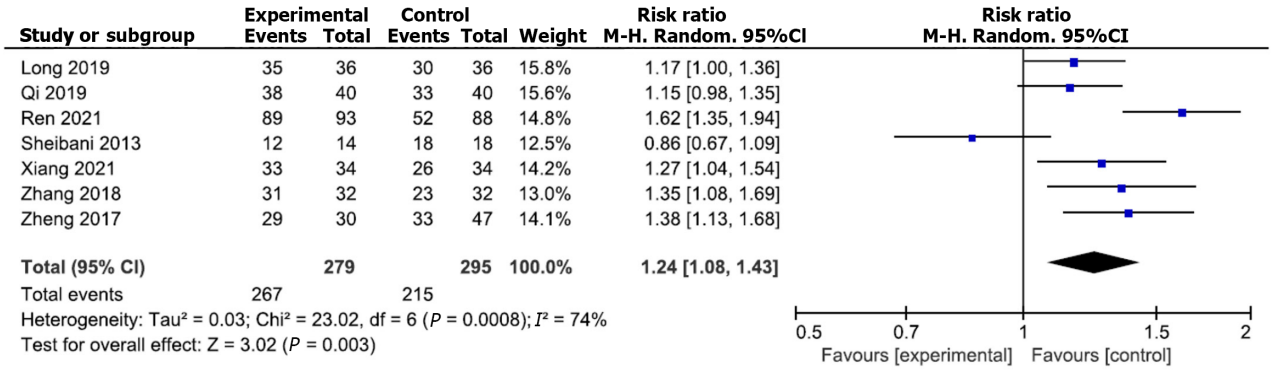

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Figure 2 Forest map comparing hemostatic rates of experimental and control groups after hemostatic treatment. CI: Confidence interval.

heterogeneity among the included studies (P = 0.68, I^2 = 0%); therefore, a fixed-effects analytical model was used. The meta-analysis results showed that mean serum CRP level was significantly lower in the experimental versus control group (MD = -5.16; 95%CI: -6.11 to -4.21; P < 0.00001) (Figure 5). Begg's test found no publication bias among the included studies (P > 0.05).

Analysis of serum IL-6 level for hemostatic treatment under gastroscopy: Three studies analyzed serum IL-6 levels after gastroscopic hemostatic treatment (115 and 115 patients in the experimental and control groups, respectively). Heterogeneity was detected among the included studies (P < 0.00001, I^2 = 94%); therefore, a random-effects model of analysis was adopted. The meta-analysis results showed that the mean serum IL-6 level after treatment was significantly lower in the experimental versus control group (MD = -6.37; 95%CI: -10.33 to -2.42; P = 0.002) (Figure 6). Begg's test found no publication bias among the included studies (P > 0.05).

Analysis of serum TNF-α after gastroscopic hemostasis: An analysis of serum TNF-α after gastroscopic hemostasis was reported in three studies (115 and 115 patients in the experimental and control groups, respectively). Heterogeneity existed among the included studies (P < 0.00001, I^2 = 98%); therefore, a random-effects analytical model was adopted. The

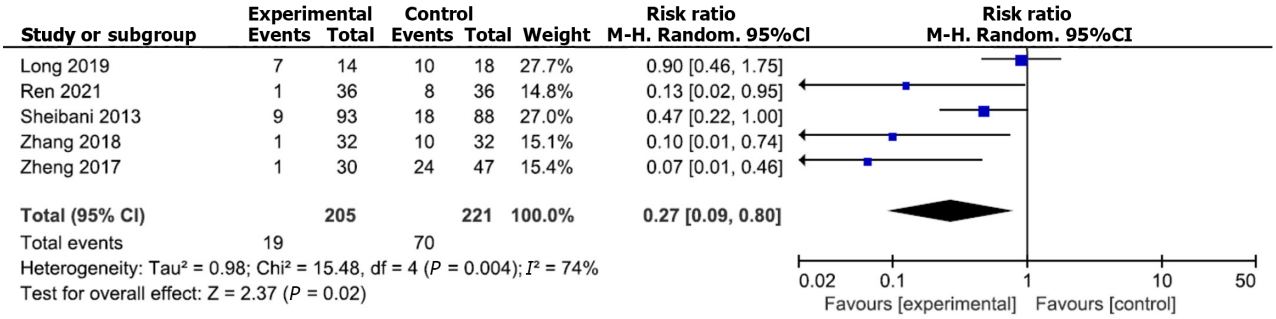

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Figure 3 Forest map comparing rebleeding rates of experimental and control groups after hemostatic treatment. CI: Confidence interval.

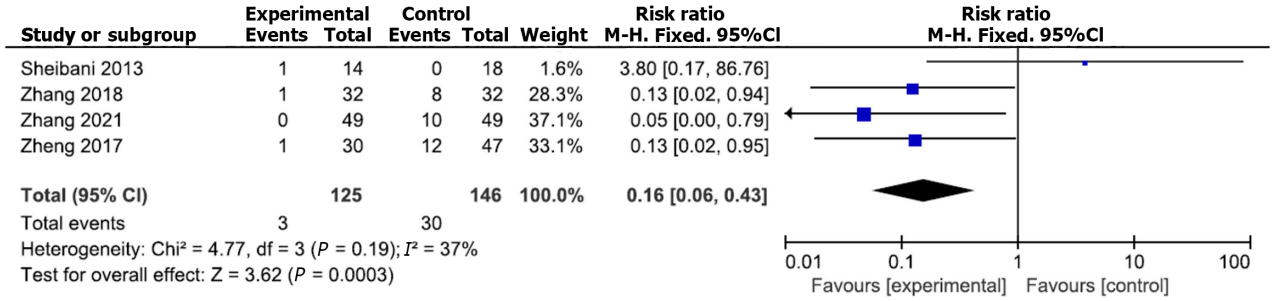

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Figure 4 Forest map comparing conversion rates of experimental and control groups after hemostatic treatment. CI: Confidence interval.

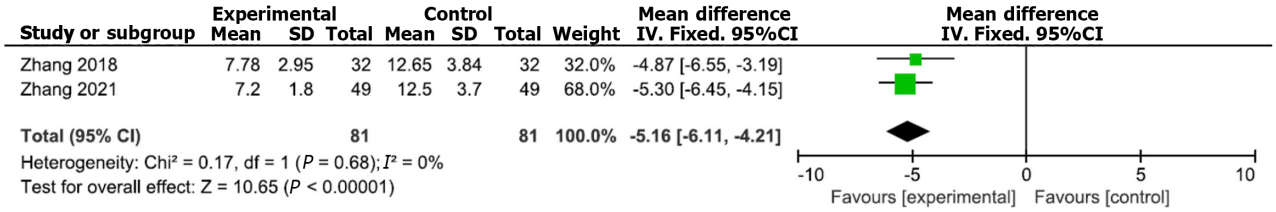

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Figure 5 Forest map comparing serum C-reactive protein levels of experimental and control groups after hemostatic treatment. CI: Confidence interval.

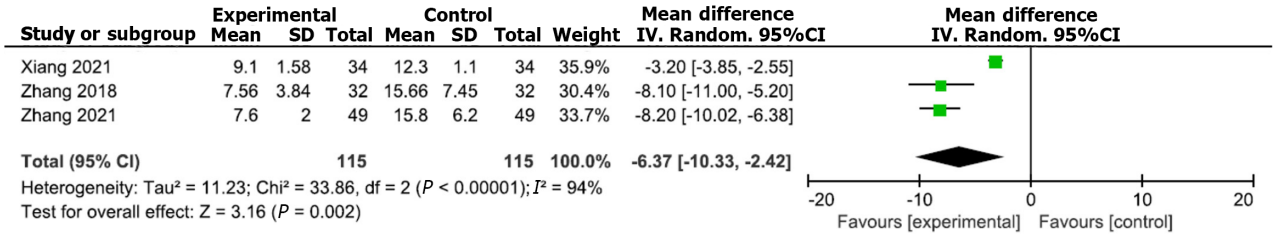

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Figure 6 Forest map comparing serum interleukin-6 Levels of experimental and control groups after hemostatic treatment. CI: Confidence interval.

mean serum TNF-α level after treatment was significantly lower in the experimental vs control group (MD = -2.29; 95%CI: -4.06 to 0.52; P = 0.01) (Figure 7). Begg's test found no publication bias in the included studies (P > 0.05).

Improvement of quality of life after gastroscopic hemostasis: Three studies analyzed the quality of life improvement rate after gastroscopic hemostasis (111 and 128 patients in the experimental and control groups, respectively). No heterogeneity was noted among the included studies (P = 0.97, I^2 = 0%); therefore, a fixed-effects analytical model was adopted.

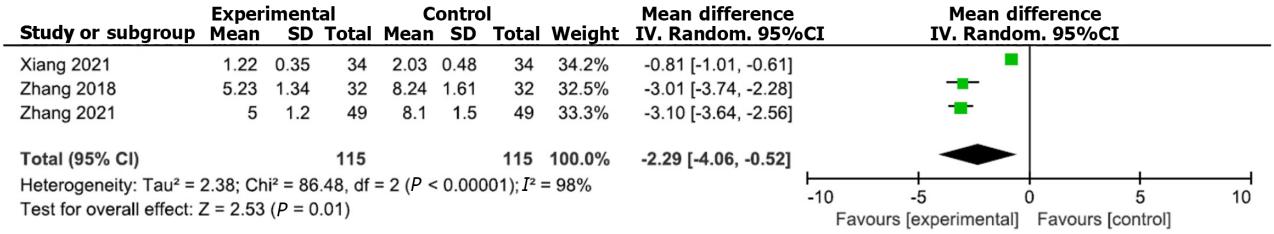

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Figure 7 Forest map comparing serum tumor necrosis factor-α levels of experimental and control groups after hemostatic treatment. CI: Confidence interval.

The quality of life improvement rate after treatment was higher in the experimental versus control group (RR = 1.95; 95%CI: 1.41 to 2.71; $P < 0.0001$) (Figure 8). Begg's test found no publication bias among the included studies ($P > 0.05$).

DISCUSSION

Acute hemorrhage in GC is a common form of gastrointestinal hemorrhage. In response to the high recurrence and malignancy rates of GC[1,6,23-25], great progress has been made in recent years toward improving the diagnostic process and multidisciplinary treatment strategy for resectable GC. However, owing to the high recurrence rate, the patient survival rate is still not ideal[26-28]. Gastroscopic hemostatic treatment can effectively prevent acute bleeding and reduce patient fatality rates, thus aiding the treatment of these patients[12,16]. However, published literature related to the efficacy and safety of endoscopic hemostasis in the treatment of acute GC bleeding is controversial and shows strong differences[14,15]. Therefore, this meta-analysis aimed to evaluate the efficacy and safety of endoscopic hemostasis for the treatment of acute GC-related bleeding by summarizing various studies.

Our results showed that gastroscopic hemostasis could effectively control acute bleeding in GC and that the hemostasis rate was much higher in the treatment vs control group. In addition, the rebleeding and surgical transfer rates were significantly reduced. Thus, endoscopic hemostasis for the treatment of acute bleeding in patients with GC has a relatively high success rate, consistent with previous findings[12,16,29]. In the context of acute bleeding in GC, this meta-analysis particularly emphasizes the elevation of CRP, IL-6, and TNF-α levels[9,12,16,20]. These inflammatory factors play multiple roles in the development of GC. They can promote the proliferation and survival of cancer cells by activating specific signaling pathways such as phosphoinositide 3-kinase/protein kinase B and mitogen-activated protein kinase[30, 31]. Moreover, high levels of inflammatory factors promote angiogenesis by providing abundant nutrients to cancer cells [32]. Additionally, the inflammatory microenvironment may locally alter the composition and stiffness of the extracellular matrix locally, thereby facilitating cancer cell invasion and migration[33].

Several studies demonstrated that inflammatory factors play an important role in GC patients with acute bleeding. Serum levels of CRP, IL-6, and TNF-α gradually increase in patients with acute bleeding in GC[18,22,34]. Therefore, when bleeding is controlled, the levels of CRP, IL-6, and TNF-α tend to decrease. Consistent with these findings, our study reached the same conclusion: Serum levels of CRP, IL-6, and TNF-α were significantly lower in the experimental vs control group, indicating that endoscopic hemostasis treatment had better hemostatic control than the control treatment. Moreover, the quality of life of the patients in the endoscopic treatment group improved significantly.

The GC microenvironment is a highly complex biological system that includes tumor cells, immune cells, fibroblasts, various cytokines, and chemical factors[19]. In this environment, immune cells such as tumor-associated macrophages and T cells may further influence the tumor growth dynamics and the risk of bleeding in patients by releasing pro- and anti-inflammatory factors[35]. Some studies found a correlation between high levels of transforming growth factor-β and low levels of interferon-γ with an increased risk of bleeding[9,12]. Although endoscopic hemostasis is widely used to control acute bleeding in GC, the specific molecular mechanisms are not fully understood. In contrast, endoscopic treatment may achieve hemostasis by activating the coagulation cascade, promoting platelet aggregation, and regulating certain inflammatory and coagulation factors[36]. Evidence suggests that these treatment modalities may reduce local inflammatory reactions, thereby improving patient quality of life and prognosis[10,22]. It is worth noting that similar inflammatory and immune responses have been observed in other gastrointestinal cancers such as esophageal and colorectal cancer[37,38]. These observations not only provide valuable perspectives for comparing different types of gastrointestinal cancers, but they also have the potential to reveal common therapeutic strategies for this class of cancer.

The limitations of this study are as follows: (1) Because meta-analyses summarize only published studies, they were limited by the quality of the original studies, and the overall quality of the studies included here was low; (2) this meta-analysis included only published studies, while unpublished studies were not considered; and (3) the number of studies and sample size included here were small. These factors may have affected the accuracy and reliability of the results.

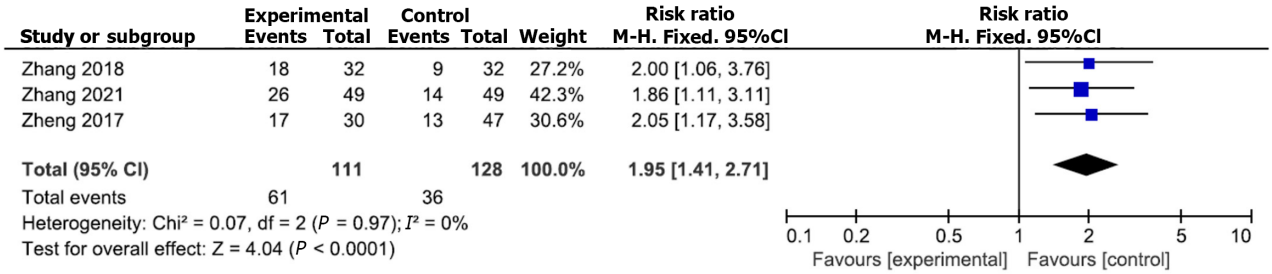

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Figure 8 Forest map comparing quality of life improvement rates of experimental and control groups after hemostatic treatment. CI: Confidence interval.

CONCLUSION

In conclusion, RCTs with larger sample sizes and better quality standards should be conducted to further clarify the safety and effectiveness of gastroscopic hemostasis for the treatment of acute GC bleeding.

ARTICLE HIGHLIGHTS

Research background

Gastric cancer (GC) is a malignant tumor with a high incidence and mortality rate worldwide for which acute bleeding is a common clinical complication.

Research motivation

Gastroscopic hemostasis is an important method for treating acute bleeding in GC; however, its efficacy and safety remain controversial.

Research objectives

This meta-analysis provides a wealth of evidence emphasizing the effectiveness and safety of endoscopic hemostasis for treating acute gastrointestinal bleeding in patients with GC.

Research methods

Several databases was searched for related to gastroscopic hemostatic treatment for acute GC. The literature was screened according to the inclusion and exclusion criteria, data were extracted, and literature quality was evaluated. The meta-analysis was performed using RevMan software (version 5.3), while Begg's test for publication bias was performed using Stata 13.0 software.

Research results

Compared with the control group, the hemostatic rate of gastroscopic hemostasis was increased [relative risk (RR) = 1.24; 95% confidence interval (CI) = 1.08-1.43; P = 0.003]; the rate of rebleeding (RR = 0.27; 95%CI: 0.09 to 0.80; P = 0.02), rate of surgery transfer (RR = 0.16; 95%CI: 0.06 to 0.43; P = 0.0003), serum C-reactive protein level [mean difference (MD) = -5.16; 95%CI: -6.11 to 4.21; P < 0.00001], interleukin-6 level (MD = -6.37; 95%CI: -10.33 to -2.42; P = 0.002), and tumor necrosis factor-α level (MD=-2.29; 95%CI: -4.06 to -0.52; P = 0.01) were decreased; and the quality of life improvement rate was increased (RR = 1.95; 95%CI: 1.41 to 2.71; P < 0.0001).

Research conclusions

The efficacy and safety of endoscopic hemostasis were higher than those of the control group.

Research perspectives

Endoscopic hemostasis is an effective treatment for acute GC hemorrhage.

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FOOTNOTES

Author contributions: Lin B and Pan HY contributed to conception and design; Lin B contributed to administrative support; Lin B and Pan HY contributed to provision of study materials or patients; Pan HY, Wang XW, He QX, Lu YD; Zhang WY, Jin JW and Lin B contributed to collection and assembly of data; Lin B and Pan HY contributed to data analysis and interpretation; All authors contributed to manuscript writing, final approval of manuscript.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

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