

Efficacy and Safety of High-Dose Omeprazole Combined with Octreotide in the Treatment of Peptic Ulcer Bleeding: A Systematic Review and Meta-Analysis

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Abstract

Objective: To systematically evaluate the efficacy and safety of high-dose omeprazole combined with octreotide in treating bleeding peptic ulcers.

Methods: A computerized search was conducted across China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), VIP, Wanfang Data, PubMed, Embase, The Cochrane Library, and Web of Science, up to September 1, 2026. Randomized controlled trials (RCTs) were included based on the PICOS principle. In the high-dose group, patients received octreotide combined with high-dose omeprazole (single dose of 50 - 120 mg administered via intravenous infusion or continuous infusion via micro-pump); in the standard-dose group, patients received octreotide combined with standard-dose omeprazole (single dose of 30 - 40 mg administered via intravenous infusion). Octreotide administration was identical between groups. Meta-analysis was performed using RevMan 5.4; odds ratios (OR) were used for dichotomous variables and mean differences (MD) for continuous variables, both reported with 95% confidence intervals (CI). Fixed- or random-effects models were selected according to heterogeneity, and funnel plots were used to assess publication bias. **Results:** The initial search yielded 190 relevant articles, which reduced to 122 after removing duplicates. After screening titles and abstracts according to inclusion and exclusion criteria, 30 articles remained. Full-text review confirmed the inclusion of 20 RCTs involving a total of 1800 patients. Subgroup analyses were conducted based on two predefined efficacy evaluation criteria: Standard 1 (based on 9 studies) showed that the high-dose group significantly outperformed the

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standard-dose group in terms of marked efficacy (OR = 2.77, 95% CI 2.08 - 3.70), inefficacy (OR = 0.17, 95% CI 0.10 - 0.28), and overall efficacy (OR = 5.83, 95% CI 3.55 - 9.56) ($P < 0.01$), while no significant difference was observed in response rate (OR = 0.81, 95% CI 0.59 - 1.10, $P = 0.18$). Standard 2 (based on 5 studies) yielded consistent results: the high-dose group also demonstrated significantly better performance in marked efficacy (OR = 2.32, 95% CI 1.53 - 3.51), inefficacy (OR = 0.21, 95% CI 0.10 - 0.42), and overall efficacy (OR = 4.78, 95% CI 2.37 - 9.60) ($P < 0.01$), although response rate still showed no significant difference (OR = 0.84, 95% CI 0.54 - 1.30, $P = 0.43$). Regarding continuous outcomes, the high-dose group showed significantly shorter hemostasis time (15 studies, MD = -12.06 h, 95% CI -16.64 to -7.48, $P < 0.01$), reduced blood transfusion volume (12 studies, MD = -1.17 U, 95% CI -1.62 to -0.73, $P < 0.01$), and shorter hospital stay (10 studies, MD = -2.31 d, 95% CI -3.01 to -1.61, $P < 0.01$). No statistically significant difference was found in adverse event rates between the two groups (9 studies, OR = 1.30, 95% CI 0.73 - 2.32, $P = 0.38$). Subgroup analysis suggested a potential trend toward improved efficacy with an 80 mg dosage regimen and a 3-day treatment course; however, high heterogeneity ($I^2 = 91\% \sim 100\%$) among these continuous outcomes limited the robustness of the findings. Publication bias assessment revealed funnel plots for dichotomous outcomes (including all efficacy measures and adverse events) were generally symmetrical, indicating low risk of bias. Funnel plots for the two continuous outcomes—hemostasis time and blood transfusion volume—showed asymmetric distributions, suggesting possible publication bias due to unpublished negative results or small-study effects. **Conclusion:** Current evidence indicates that high-dose omeprazole added to octreotide may improve hemostatic efficacy in peptic ulcer bleeding, shorten hemostasis time and hospital stay, reduce the need for blood transfusion, and does not significantly increase adverse events. However, most included studies were conducted in Chinese populations, with inadequate reporting of randomization, allocation concealment, and blinding; heterogeneity in intervention protocols; short follow-up periods; and lack of assessment of hard endpoints such as rebleeding, surgery, and mortality. Therefore, these findings require further validation through multicenter, large-scale, standardized randomized controlled trials (RCTs). This study has been registered with PROSPERO (CRD420261491716) and reported according to PRISMA guidelines.

Keywords

Omeprazole, Octreotide, Peptic Ulcer Hemorrhage, Randomized Controlled Trial, Meta-Analysis

1. Background

Peptic ulcer bleeding is a prevalent and potentially life-threatening gastrointestinal emergency, marked by abrupt onset and rapid clinical deterioration. Failure

to achieve prompt and effective hemostasis may precipitate hemorrhagic shock, contributing to persistently elevated mortality—underscoring its substantial burden on patient morbidity and survival [1]. Gastric acid critically contributes to both the initiation and perpetuation of ulcer hemorrhage: an acidic intragastric milieu ($\text{pH} < 4$) promotes fibrinolysis, impairs platelet adhesion and aggregation, and destabilizes nascent thrombi, thereby compromising primary and secondary hemostasis [2]. Proton pump inhibitors (PPIs), exemplified by omeprazole, exert potent and sustained inhibition of gastric $\text{H}^+ - \text{K}^+ - \text{ATPase}$ in parietal cells, thereby elevating intragastric pH to ≥ 6 —a threshold associated with enhanced platelet function, stable clot formation, and accelerated mucosal repair. Robust evidence from landmark randomized controlled trials (RCTs) confirms that high-dose intravenous omeprazole administered following endoscopic hemostasis significantly reduces rebleeding rates and all-cause mortality compared with placebo or standard-dose regimens [3].

Octreotide, a synthetic somatostatin analog, mediates multifaceted hemostatic effects—including selective splanchnic vasoconstriction, reduction of portal venous pressure and gastric mucosal blood flow, and suppression of gastric acid and pepsin secretion—thereby targeting both hemodynamic and biochemical determinants of bleeding [4]. Prior RCTs have established octreotide monotherapy as superior to histamine-2 receptor antagonists in achieving initial hemostasis and preventing early rebleeding in peptic ulcer bleeding, with a favorable safety profile [5]. Mechanistically, the combination of high-dose omeprazole and octreotide offers complementary pathways—acid suppression coupled with visceral vasoconstriction—potentially yielding synergistic hemostatic efficacy. Nevertheless, existing clinical evidence remains fragmented: individual studies are underpowered, heterogeneous in design and outcome definitions, and insufficiently powered to assess the comparative efficacy and safety of high-dose combination therapy. To address this evidence gap, the present study undertakes a rigorous systematic review and meta-analysis to quantitatively synthesize current evidence on the efficacy and safety of high-dose omeprazole plus octreotide in patients with acute peptic ulcer bleeding. Consistent with the outcomes reported in the eligible RCTs, the efficacy outcomes assessed in this review are the marked efficacy rate, effective rate, ineffective rate, overall effective rate, hemostasis time, blood transfusion volume, and length of hospital stay; the safety outcome is adverse drug reactions. Although rebleeding, surgical intervention, and mortality are important clinical endpoints, they were not reported in the included studies and therefore are not pooled in this meta-analysis. The findings are intended to inform evidence-based, risk-stratified therapeutic decision-making in clinical practice.

2. Materials and Methods

2.1. Literature Search

A computer-based search was conducted across various Chinese and English databases, including China National Knowledge Infrastructure (CNKI), China Biol-

ogy Medicine Database (CBM), VIP Chinese Science and Technology Journal Full-text Database, Wanfang Data, PubMed, Embase, The Cochrane Library, and Web of Science, to retrieve data published up to September 1, 2026. A combined approach using subject headings and free-text keywords was employed. The corresponding English keywords included: omeprazole, omeprazole sodium, Losec, Prilosec, Sandostatin, SMS 201-995, octreotide, peptic ulcer hemorrhage, Peptic Ulcer, Gastrointestinal Hemorrhage, peptic ulcer bleeding, upper gastrointestinal bleeding, gastric ulcer bleeding, duodenal ulcer bleeding. The English database, using PubMed as an example, has a search strategy shown in **Table 1**.

Table 1. PubMed search strategy.

Steps	Search query	Results
#1	((omeprazole[Title/Abstract]) OR (omeprazole sodium[Title/Abstract])) OR (Losec[Title/Abstract]) OR (Prilosec[Title/Abstract])	9848
#2	(omeprazole[MeSH Terms]) OR (((omeprazole[Title/Abstract]) OR (omeprazole sodium[Title/Abstract])) OR (Losec[Title/Abstract]) OR (Prilosec[Title/Abstract]))	14,113
#3	((octreotide[Title/Abstract]) OR (Sandostatin[Title/Abstract])) OR (SMS 201-995[Title/Abstract])	10,198
#4	(octreotide[MeSH Terms]) OR (((octreotide[Title/Abstract]) OR (Sandostatin[Title/Abstract])) OR (SMS 201-995[Title/Abstract]))	12,895
#5	(((((Peptic Ulcer[Title/Abstract]) OR (Gastrointestinal Hemorrhage[Title/Abstract])) OR (peptic ulcer bleeding[Title/Abstract])) OR (upper gastrointestinal bleeding[Title/Abstract])) OR (gastric ulcer bleeding[Title/Abstract])) OR (duodenal ulcer bleeding[Title/Abstract])) OR (peptic ulcer haemorrhage[Title/Abstract])	45,069
#6	(Peptic Ulcer Hemorrhage[MeSH Terms]) OR ((((((Peptic Ulcer[Title/Abstract]) OR (Gastrointestinal Hemorrhage[Title/Abstract])) OR (peptic ulcer bleeding[Title/Abstract])) OR (upper gastrointestinal bleeding[Title/Abstract])) OR (gastric ulcer bleeding[Title/Abstract])) OR (duodenal ulcer bleeding[Title/Abstract])) OR (peptic ulcer haemorrhage[Title/Abstract]))	49,113
#7	#2 AND #4 AND #6	13

2.2. Inclusion and Exclusion Criteria

2.2.1. Inclusion Criteria

Based on the PICOS principles of evidence-based medicine (population, intervention and control, outcome, and study design), the following inclusion criteria for studies were established: 1) Study population: Patients with symptoms of acute upper gastrointestinal bleeding, such as hematemesis or melena, who were diagnosed by physicians as having peptic ulcer with bleeding upon admission; patients with bleeding caused by varices, or those with comorbidities including stroke, acute heart failure, severe infection, or renal disease were excluded. 2) Intervention and control measures: The high-dose group received octreotide combined with high-dose omeprazole, with a single dose of omeprazole ranging from 50 to 120 mg administered either by intravenous infusion or continuous intravenous infusion via a micro-infusion pump. The standard-dose group received octreotide combined with standard-dose omeprazole, with a single dose of omeprazole rang-

ing from 30 to 40 mg administered by intravenous infusion. Both groups received identical dosing regimens, routes of administration, and treatment durations for octreotide; the duration of omeprazole therapy was also the same, ranging from 47 hours to 14 days. Additionally, all patients received standardized basic supportive care, including fluid resuscitation, infection prevention, and nutritional support. 3) Outcome measures: The therapeutic effect of high-dose omeprazole combined with octreotide in peptic ulcer with bleeding was comprehensively evaluated based on five indicators: hemostatic efficacy (excellent response, effective response, ineffective response, and overall effective rate), time to hemostasis (hours), length of hospital stay (days), blood transfusion volume (units), and drug adverse reactions. For efficacy assessment, multiple criteria were used across the included studies. Due to the limited number of available publications, this meta-analysis adopted two commonly used efficacy evaluation standards for comprehensive analysis: Standard 1 (based on 9 studies [6]-[14]): Effective was defined as cessation of bleeding within 48 hours after treatment; moderately effective as cessation within 48 - 72 hours; and ineffective as persistent bleeding beyond 72 hours. Standard 2 (based on 5 studies [15]-[19]): Effective was defined as cessation of bleeding within 24 hours after treatment; moderately effective as cessation within 24 - 72 hours; and ineffective as persistent bleeding beyond 72 hours. Overall effective rate (%) = (number of excellent responders + number of effective responders)/total number of cases × 100%. 4) Types of studies included: Randomized controlled trials (RCTs).

2.2.2. Exclusion Criteria

Exclusion criteria: 1) Retrospective studies. 2) Non-clinical trials. 3) Duplicated publications or studies with methodological flaws and poor quality. 4) Patients who received concomitant treatment with other acid-suppressing, hemostatic, or growth-inhibiting drugs. 5) Patients who underwent mechanical compression, endoscopic hemostasis, or surgical hemostasis. 6) Studies that did not specify whether randomization was used.

2.3. Data Extraction from Literature

The retrieved articles from the database were imported into EndNote X9, a reference management software. After removing duplicates, two researchers independently conducted literature screening and assessment (including title, abstract, and full text) to determine eligibility for inclusion in the study. Disagreements were resolved through discussion with a third party. The collected information included: first author details, publication year, sample size of participants, gender and age distribution, intervention details, study design methods, and outcome measures.

2.4. Assessment of Study Quality

The quality of included studies was assessed using the Cochrane Collaboration's recommended tool for bias risk assessment. Each study was evaluated based on

seven criteria: 1) randomization method, 2) allocation concealment, 3) blinding (participants and researchers), 4) blinding (outcome assessment), 5) data completeness, 6) selective reporting, and 7) other biases. Risk levels were categorized as low, unclear, or high.

2.5. Data Analysis Methods

Statistical analysis of the screened literature was performed using Review Manager 5.4 software. For dichotomous variables, odds ratios (OR) were used; for continuous variables, mean differences (MD) were applied. All effect sizes were reported with 95% confidence intervals (CI). Heterogeneity among studies was assessed using the χ^2 test and I^2 statistic. If no significant heterogeneity was found ($P > 0.10$, $I^2 < 50\%$), a fixed-effects model was used for meta-analysis; otherwise, a random-effects model was applied, followed by subgroup or sensitivity analyses to explore sources of heterogeneity. Funnel plots were used to assess publication bias, with asymmetry in the funnel plot indicating potential publication bias.

3. Results

3.1. Literature Search Results

The systematic search yielded a total of 190 articles, including 134 from Chinese databases (29 from CNKI, 56 from Wanfang Medicine, 11 from VIP, and 38 from the China Biomedical Literature Database (CBM)) and 56 from English databases (13 from PubMed, 5 from Web of Science, 34 from Embase, and 4 from the Cochrane Library). Duplicate records were removed using EndNote X9 software, resulting in 122 unique articles. An initial screening based on titles and abstracts identified 30 potentially relevant studies. After full-text review and systematic evaluation considering study design, risk of bias assessment, and pre-determined inclusion and exclusion criteria, 20 high methodological quality and clinically relevant studies were rigorously selected, involving a total of 1800 patients. See **Figure 1**.

3.2. Characteristics of Included Studies

A total of 20 studies were included. Their basic characteristics, including sample size, age, etiology type, interventions, treatment duration, and outcome measures, are summarized in **Table 2** and **Table 3**.

3.3. Risk of Bias Assessment in Included Studies

All 20 included studies were randomized controlled trials. Three studies used random number tables and one used computer-generated randomization, all of which were judged to have a low risk of bias. The remaining studies were categorized as having an unclear risk of bias due to lack of detailed methodological descriptions. Allocation concealment was not clearly reported in any study, thus classified as unclear risk of bias. Blinding was not mentioned in any study, also resulting in an unclear risk of bias. All studies provided complete data with no

evidence of selective reporting, so the risk of bias for this domain was considered low. For other potential sources of bias, information was insufficient, leading to an overall judgment of unclear risk of bias. See **Figure 2**.

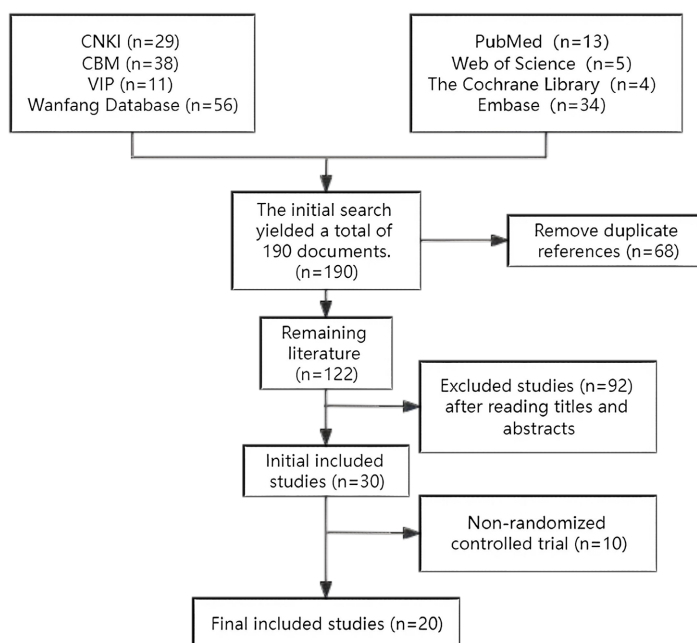


Figure 1. Flowchart of literature screening process.

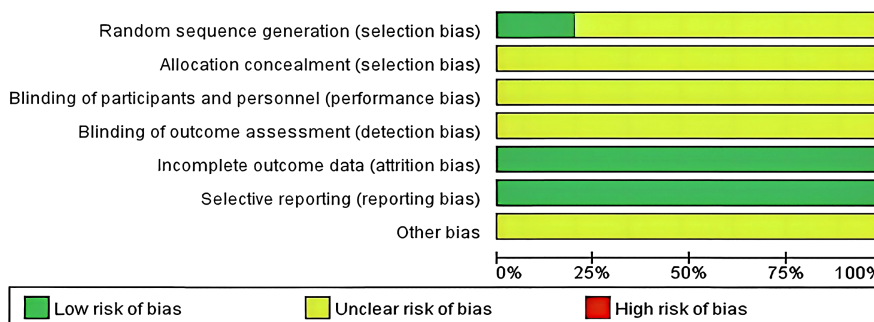


Figure 2. Summary of included studies' bias.

Table 2. Basic characteristics of included studies.

Included Studies	Average age (years)		Sample size (male/female)		Type of etiology	
	High-dose group	Standard-dose group	High-dose group	Standard-dose group	High-dose group	Standard-dose group
Ye QR 2018 [6]	49.2 ± 9.4	48.7 ± 9.6	40 (27/13)	40 (26/14)	22 cases of duodenal ulcer, 14 cases of gastric ulcer, and 4 cases of compound ulcer	20 cases of duodenal ulcer, 15 cases of gastric ulcer, and 5 cases of compound ulcer
Zhou YT 2014 [7]	44.42 ± 5.64	46.45 ± 5.78	100 (67/33)	100 (70/30)	33 cases of gastric ulcer, 60 cases of duodenal bulb ulcer, and 7 cases of compound ulcer	24 cases of gastric ulcer, 62 cases of duodenal bulb ulcer, and 14 cases of compound ulcer

Continued

Wang HT 2019 [8]	37.9 ± 4.6	40.0 ± 3.2	39 (28/11)	39 (25/14)	18 cases of gastric ulcer, 21 cases of duodenal ulcer	20 cases of gastric ulcer, 19 cases of duodenal ulcer
Wen M 2017 [9]	40.0 ± 1.2	47.0 ± 2.1	40 (17/23)	40 (26/14)	-	-
Wang Y 2017 [10]	41.13 ± 3.1	48.02 ± 3.5	30 (16/14)	30 (18/12)	Among all patients, 35 had gastric ulcers and 25 had duodenal ulcers ^①	
Hu SY 2017 [11]	49.34 ± 5.13	49.18 ± 5.26	41 (27/14)	41 (28/13)	23 cases of duodenal bulb ulcer, 14 cases of gastric ulcer, and 4 cases of compound ulcers	23 cases of duodenal bulb ulcer, 15 cases of gastric ulcer, and 3 cases of compound ulcer
Xu GQ 2020 [12]	41.3 ± 7.5	42.5 ± 7.6	40 (18/22)	40 (19/21)	24 cases of duodenal bulb ulcer, 13 cases of gastric ulcer, and 3 cases of compound ulcer	23 cases of duodenal bulb ulcer, 12 cases of gastric ulcer, and 5 cases of compound ulcer
Chen K 2018 [13]	48.9 ± 4.2	48.8 ± 4.3	42 (29/13)	42 (30/12)	24 cases of duodenal bulb ulcer, 13 cases of gastric ulcer, and 5 cases of compound ulcer	25 cases of duodenal bulb ulcer, 12 cases of gastric ulcer, and 5 cases of compound ulcer
Wei HJ 2022 [14]	38.68 ± 4.36	39.46 ± 5.23	46 (26/20)	46 (25/21)	15 cases of gastric ulcer, 27 cases of duodenal bulb ulcer, and 4 cases of compound ulcer	14 cases of gastric ulcer, 26 cases of duodenal bulb ulcer, and 6 cases of compound ulcer
Sun R 2021 [15]	42.0 ± 4.5	43.5 ± 2.5	34 (19/15)	34 (20/14)	17 cases of duodenal ulcer, 13 cases of gastric ulcer, and 4 cases of compound ulcer	16 cases of duodenal ulcer, 14 cases of gastric ulcer, and 4 cases of compound ulcers
Yue ZK 2017 [16]	45.23 ± 3.10	46.43 ± 4.29	50 (28/22)	50 (26/24)	15 cases of gastric ulcer, 30 cases of duodenal ulcer, and 5 cases of compound ulcer	18 cases of gastric ulcer, 30 cases of duodenal ulcer, and 2 cases of compound ulcer
Gong XP 2017 [17]	46.22 ± 2.89	45.78 ± 3.28	45 (24/21)	45 (26/19)	29 cases of gastric ulcer, 11 cases of duodenal ulcer, and 5 cases of compound ulcer	25 cases of gastric ulcer, 4 cases of compound ulcer, and 16 cases of duodenal ulcer
Li XQ 2019 [18]	45.3 ± 2.7	46.7 ± 3.1	10 (4/6)	10 (5/5)	-	-
Zhai WT 2020 [19]	55.4 ± 8.2	49.8 ± 9.5	57 (37/20)	57 (40/17)	15 cases of duodenal ulcer, 10 cases of compound ulcer, and 32 cases of gastric ulcer	17 cases of duodenal ulcer, 6 cases of compound ulcer, and 34 cases of gastric ulcer
Liu JJ 2020 [20]	50.09 ± 4.32	50.17 ± 4.28	40 (28/12)	40 (27/13)	-	-
Liu H 2017 [21]	47.65 ± 3.78	46.12 ± 4.12	55 (29/26)	55 (27/28)	32 cases of gastric ulcer, 17 cases of duodenal bulb ulcer, and 6 cases of compound ulcer	31 cases of gastric ulcer, 19 cases of duodenal bulb ulcer, and 5 cases of compound ulcer
Luo ZX 2024 [22]	46.42 ± 5.44	46.31 ± 5.58	40 (28/12)	40 (30/10)	14 cases of gastric ulcer, 7 cases of compound ulcer, and 19 cases of duodenal ulcer	13 cases of gastric ulcer, 6 cases of compound ulcer, and 21 cases of duodenal ulcer

Continued

Guo S 2018 [23]	43.12 ± 3.14	43.27 ± 3.27	32 (18/14)	32 (17/15)	-	-
Jiao PL 2017 [24]	47.04 ± 5.37	46.83 ± 5.54	74 (47/27)	74 (46/28)	-	-
Zheng XL 2020 [25]	50.6 ± 10.2	50.3 ± 10.6	45 (22/23)	45 (27/18)	-	-

Note: “-” indicates unknown etiology; ① denotes that the individual values for the combined group and the single group were not provided in the literature.

Table 3. Treatment characteristics and outcome measures of included studies.

Included Studies	High-dose group	Standard-dose group	Outcome measures
Ye QR 2018 [6]	Octreotide was administered in combination with omeprazole 80 mg plus 0.9% NS 100 ml, given by intravenous infusion at an unspecified rate, every 12 hours for a 3-day course, based on the control group regimen.	Octreotide 0.1 mg dissolved in 10 mL of 0.9% sodium chloride injection was administered slowly by intravenous bolus (recommended infusion time ≥5 minutes), followed by continuous intravenous infusion at a rate of 12.5 µg/h. This was combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection, administered intravenously every 12 hours for a total treatment duration of 3 days.	①②③④ ⑤⑥⑦
Zhou YT 2014 [7]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml by intravenous infusion at a rate of 8 mg/h for a duration of 3 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥5 minutes), followed by continuous intravenous infusion at 25 µg/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total treatment duration of 3 days.	①②③④ ⑤⑥
Wang HT 2019 [8]	Octreotide was administered in combination with omeprazole 80 mg plus 0.9% NS 100 ml, given by intravenous infusion at an unspecified rate, every 12 hours for a 3-day course, based on the control group regimen.	Octreotide 0.1 mg dissolved in 10 mL of 0.9% sodium chloride injection solution is administered slowly by intravenous bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at a rate of 12.5 µg/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered by intravenous infusion every 12 hours for a total treatment duration of 3 days.	①②③④
Wen M 2017 [9]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml by intravenous infusion at a rate of 8 mg/h for a duration of 3 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 0.9% sodium chloride injection should be administered slowly by intravenous push (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at a rate of 25 µg/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection, administered intravenously every 12 hours for a total treatment duration of 3 days.	①②③④ ⑤⑥⑧
Wang Y 2017 [10]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml by intravenous infusion at a rate of 8 mg/h for a duration of 3 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 0.9% sodium chloride injection should be administered slowly by intravenous push (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at a rate of 25 µg/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection, administered intravenously every 12 hours for a total treatment duration of 3 days.	①②③④ ⑤⑥

Continued

Hu SY 2017 [11]	Octreotide was administered in combination with omeprazole 80 mg plus 0.9% NS 100 ml, given by intravenous infusion at an unspecified rate, every 12 hours for a 3-day course, based on the control group regimen.	Octreotide 0.1 mg dissolved in 10 mL of 0.9% sodium chloride injection should be administered slowly by intravenous bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at a rate of 12.5 $\mu\text{g}/\text{h}$. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection, administered by intravenous drip every 12 hours for a total treatment duration of 3 days.	①②③④ ⑤⑥⑦
Xu GQ 2020 [12]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml by intravenous infusion at a rate of 8 mg/h, for a duration of 6 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 20% glucose injection solution is administered slowly by intravenous bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at a rate of 25 $\mu\text{g}/\text{h}$. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total course of 6 days.	①②③④ ⑤⑥⑧
Chen K 2018 [13]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml by intravenous infusion at a rate of 8 mg/h, for a duration of 3 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered slowly by intravenous bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at a rate of 25 $\mu\text{g}/\text{h}$. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total treatment duration of 3 days.	①②③④ ⑤⑥⑧
Wei HJ 2022 [14]	Octreotide was administered in combination with omeprazole 80 mg plus 0.9% NS 100 ml, given by intravenous infusion at an unspecified rate, every 12 hours for a 3-day course, based on the control group regimen.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at 25 $\mu\text{g}/\text{h}$. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total treatment duration of 3 days.	①②③④ ⑤⑥⑦⑧
Sun R 2021 [15]	Octreotide was administered in combination with omeprazole 50 mg plus 0.9% NS 100 ml, infused intravenously at a rate of 8 mg/h for a duration of 3 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at 25 $\mu\text{g}/\text{h}$. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total course of 3 days.	①②③④ ⑤⑥⑦
Yue ZK 2017 [16]	Octreotide was administered in combination with omeprazole 50 mg plus 0.9% NS 100 ml by intravenous infusion at a rate of 6 mg/h, for a total duration of 48 hours, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at 25 $\mu\text{g}/\text{h}$ for 72 hours. This is combined with omeprazole 30 mg dissolved in 90 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours, for a total treatment duration of 48 hours.	①②③④ ⑧
Gong XP 2017 [17]	Octreotide was administered in combination with omeprazole 50 mg plus 0.9% NS 100 ml by intravenous infusion at a rate of 6 mg/h, for a total duration of 48 hours, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at 25 $\mu\text{g}/\text{h}$ for 72 hours. This is combined with omeprazole 30 mg dissolved in 90 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours, for a total treatment duration of 48 hours.	①②③④ ⑤⑦⑧

Continued

Li XQ 2019 [18]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml by intravenous infusion at a rate of 8 mg/h, for a duration of 3 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered slowly by intravenous bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at a rate of 25 μ g/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered by intravenous drip every 12 hours for a total treatment duration of 3 days.	①②③④
Zhai WT 2020 [19]	Octreotide was administered in combination with omeprazole 120 mg + 0.9% NS 100 ml intravenous infusion, at an unspecified rate, once every 12 hours, for a course of 5 days, based on the control group regimen.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at 25 μ g/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total course of 5 days.	①②③④ ⑤⑦
Liu JJ 2020 [20]	Octreotide was administered in combination with omeprazole 80 mg plus 0.9% NS 100 ml, given by intravenous infusion at an unspecified rate, every 12 hours, for a treatment duration of 14 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 10 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at 25 μ g/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total treatment duration of 14 days.	①②③④ ⑤⑥⑦
Liu H 2017 [21]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml by intravenous infusion at a rate of 8 mg/h for a duration of 3 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at 25 μ g/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total course of 3 days.	①②③④ ⑤⑦
Luo ZX 2024 [22]	Octreotide was administered in combination with omeprazole 80 mg plus 0.9% NS 100 ml by intravenous infusion, at an unspecified rate, every 12 hours for a 14-day course, based on the control group regimen.	Octreotide 0.1 mg dissolved in 10 mL of 5% glucose injection solution is administered slowly by intravenous bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at a rate of 25 μ g/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total treatment duration of 14 days.	①②③④ ⑤⑥⑦⑧
Guo S 2018 [23]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml, given intravenously via infusion at an unspecified rate, once daily for a course of 2 days, based on the control group regimen.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at 25 μ g/h. This is combined with omeprazole 40 mg dissolved in 250 mL of 0.9% sodium chloride injection solution, administered once daily via intravenous drip for a total duration of 2 days.	⑤⑥⑦⑧
Jiao PL 2017 [24]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml by intravenous infusion at a rate of 8 mg/h for a duration of 3 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 0.9% sodium chloride injection should be administered slowly by intravenous push (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at a rate of 25 μ g/h. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection, administered intravenously every 12 hours for a total treatment duration of 3 days.	①②③④ ⑧

Continued

Zheng XL 2020 [25]	Octreotide was administered in combination with omeprazole 80 mg + 0.9% NS 100 ml by intravenous infusion, with unspecified infusion rate and frequency, for a treatment duration of 7 days, based on the control group protocol.	Octreotide 0.1 mg dissolved in 20 mL of 5% glucose injection solution is administered intravenously as a slow bolus (recommended infusion time ≥ 5 minutes), followed by continuous intravenous infusion at 25 $\mu\text{g/h}$. This is combined with omeprazole 40 mg dissolved in 100 mL of 0.9% sodium chloride injection solution, administered intravenously every 12 hours for a total course of 7 days.	①②③④

Note: In all studies, the high-dose group received high-dose omeprazole combined with octreotide, while the standard-dose group received standard-dose omeprazole combined with octreotide. The dosage and administration of octreotide were identical between the two groups. ① Efficacy rate, ② effective rate, ③ inefficacy rate, ④ total effective rate, ⑤ hemostasis time, ⑥ blood transfusion volume, ⑦ hospitalization duration, ⑧ adverse reactions; NS: normal saline; GS: glucose solution.

3.4. Meta-Analysis Results

3.4.1. Evaluation of Treatment Efficacy

Nine studies [6]-[14] reported on the outcomes of cure, effective response, inefficacy, and overall effectiveness. The statistical heterogeneity tests yielded results of ($P = 0.98$, $I^2 = 0\%$), ($P = 0.96$, $I^2 = 0\%$), ($P = 0.99$, $I^2 = 0\%$), and ($P = 0.99$, $I^2 = 0\%$), respectively, indicating no significant statistical heterogeneity among the groups for these treatment outcome measures; thus, a fixed-effects model was adopted. The model analysis showed that the high-dose group differed significantly from the conventional-dose group in terms of cure rate [OR = 2.77, 95% CI (2.08, 3.70)], inefficacy [OR = 0.17, 95% CI (0.10, 0.28)], and overall effectiveness [OR = 5.83, 95% CI (3.55, 9.56)] (all $P < 0.05$), but there was no statistically significant difference in effective response [OR = 0.81, 95% CI (0.59, 1.10)] ($P > 0.05$). (See Figures 3-6)

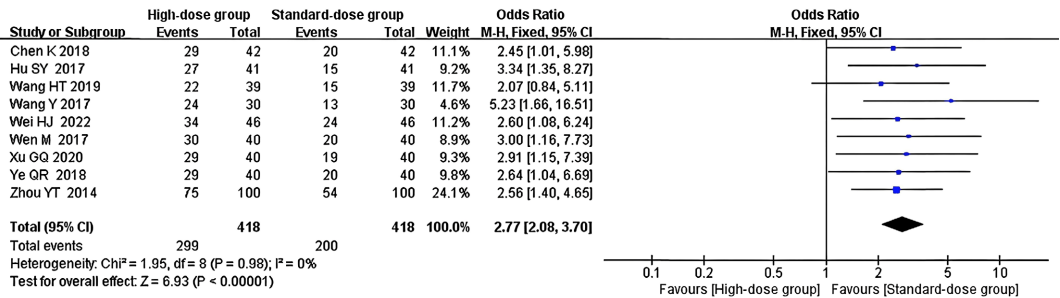


Figure 3. Forest plot of the significant efficacy comparison based on Standard 1.

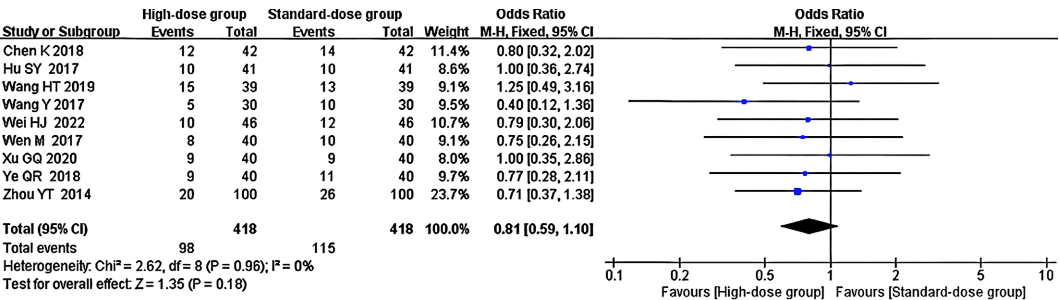


Figure 4. Forest plot of the effective rate for Standard 1.

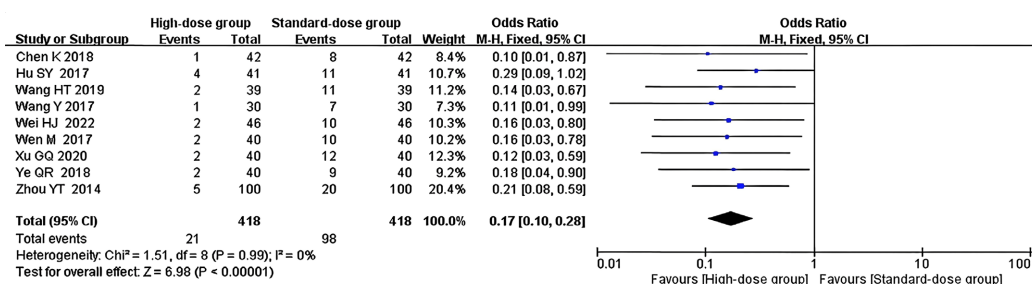


Figure 5. Inefficient forest plot for Standard 1.

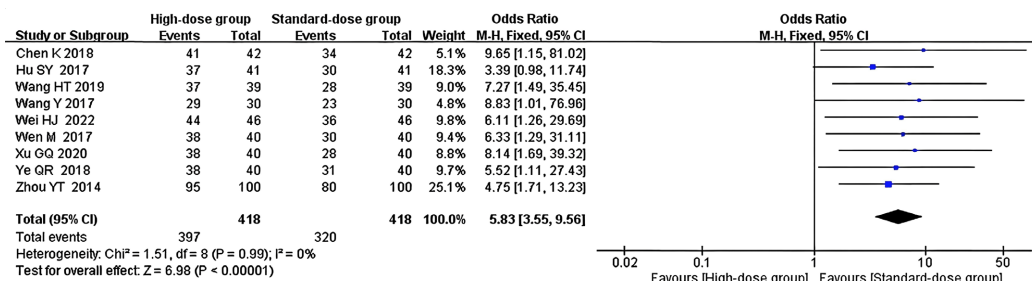


Figure 6. Forest plot of the overall effective rate for Standard 1.

Standard 2 included five studies [15]-[19] reporting on the outcomes of cure, effective response, inefficacy, and overall effectiveness. The statistical heterogeneity tests yielded results of ($P = 0.68$, $I^2 = 0\%$), ($P = 0.58$, $I^2 = 0\%$), ($P = 0.97$, $I^2 = 0\%$), and ($P = 0.97$, $I^2 = 0\%$), indicating no significant statistical heterogeneity among the groups regarding treatment efficacy indicators, thus warranting the use of a fixed-effects model. The model analysis revealed that the high-dose group showed statistically significant differences compared to the conventional-dose group in terms of cure rate [OR = 2.32, 95% CI (1.53, 3.51)], inefficacy [OR = 0.21, 95% CI (0.10, 0.42)], and overall effectiveness [OR = 4.78, 95% CI (2.37, 9.60)] (all $P < 0.05$), but no significant difference was observed in effective response [OR = 0.84, 95% CI (0.54, 1.30)] ($P > 0.05$). (See Figures 7-10)

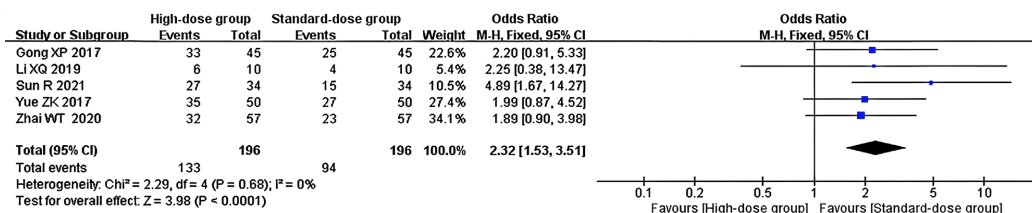


Figure 7. Forest plot of the significant efficacy comparison based on Standard 2.

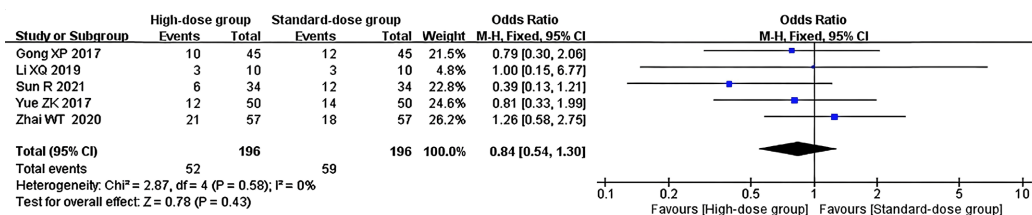


Figure 8. Forest plot of the effective rate for Standard 2.

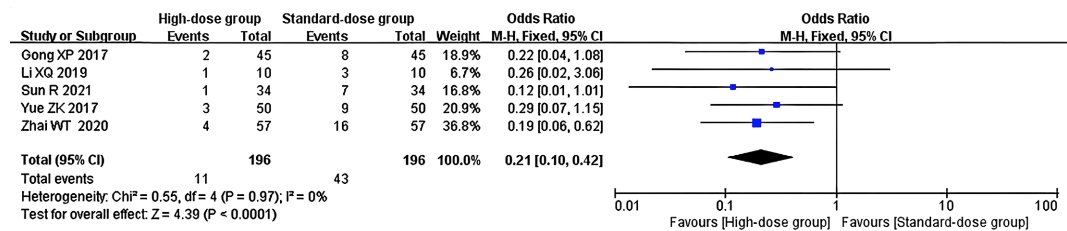


Figure 9. Inefficient forest plot for Standard 2.

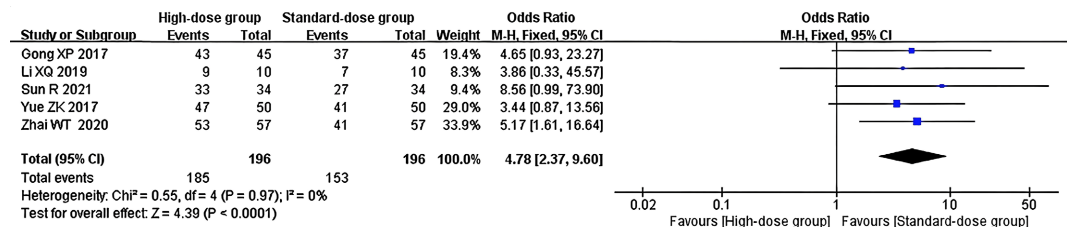


Figure 10. Forest plot of the overall effective rate for Standard 2.

3.4.2. Comparison of Hemostasis Time

Fifteen studies [6] [7] [9]–[15] [17] [19]–[23] reported hemostasis time. Heterogeneity testing revealed substantial statistical heterogeneity ($P < 0.00001$, $I^2 = 100\%$), warranting the use of a random-effects model. Pooled analysis showed that the high-dose group achieved significantly shorter hemostasis time compared with the conventional-dose group (MD = -12.06 hours, 95% CI: -16.64 to -7.48 ; $P < 0.00001$). Sensitivity analysis was conducted by sequentially excluding each individual randomized controlled trial (RCT). The results showed that the I^2 value remained at 100% regardless of which study was removed, indicating that heterogeneity was not driven by any single study but rather stemmed from systematic differences among studies (such as administration route, dosage, duration of treatment, etc.). See **Figure 11**.

Subgroup analysis by omeprazole dosage: The 50 mg subgroup included two studies (158 patients in total, 79 in each group), with a pooled MD of -7.79 hours (95% CI: -23.03 to 7.44), $P = 0.32$, $I^2 = 99\%$, showing no significant inter-group difference; the 80 mg subgroup included 12 studies (1092 patients in total, 546 in each group), with a pooled MD of -12.52 hours (95% CI: -15.46 to -9.58), $P < 0.00001$, $I^2 = 97\%$, demonstrating a significant reduction in hemostatic time in the high-dose group at this dosage; the 120 mg subgroup included only one study, which lacked independent replication, making it insufficient to support dose-response inference. See **Figure 12**.

Subgroup analysis by treatment duration: The 2-day subgroup included two studies (154 patients in total, 77 in the intervention group vs. 77 in the control group), with a pooled mean difference (MD) of -6.43 hours (95% CI: -18.83 to 5.97), $P = 0.31$, $I^2 = 100\%$, indicating no statistically significant difference in hemostatic time between the high-dose and standard-dose groups; the 3-day subgroup included nine studies (856 patients in total, 428 in each group), with a pooled MD of -13.74 hours (95% CI: -15.35 to -12.13), $P < 0.00001$, $I^2 = 75\%$,

showing that the high-dose group had significantly shorter hemostatic time than the standard-dose group; the 14-day subgroup included two studies (160 patients in total, 80 in each group), with a pooled MD of -8.37 hours (95% CI: -29.36 to 12.62), $P = 0.43$, $I^2 = 99\%$, indicating no statistically significant difference. Subgroups for 5 days and 6 days each included only one study; due to insufficient sample size and lack of replicative evidence, effective pooling analysis could not be performed, nor could efficacy differences under these durations be assessed. See **Figure 13**.

Subgroup analysis by infusion rate: The 6 mg/h subgroup included only one study (90 patients in total, 45 in each group); limited by single-center, single-study design, heterogeneity measures could not be calculated, and robust effect estimation was not feasible. See **Figure 14**.

In summary, inconsistencies in treatment duration (particularly 3 days vs. non-3 days), dosage (especially 80 mg vs. other doses), and infusion rate may represent important potential sources of heterogeneity in the overall effect observed in this study.

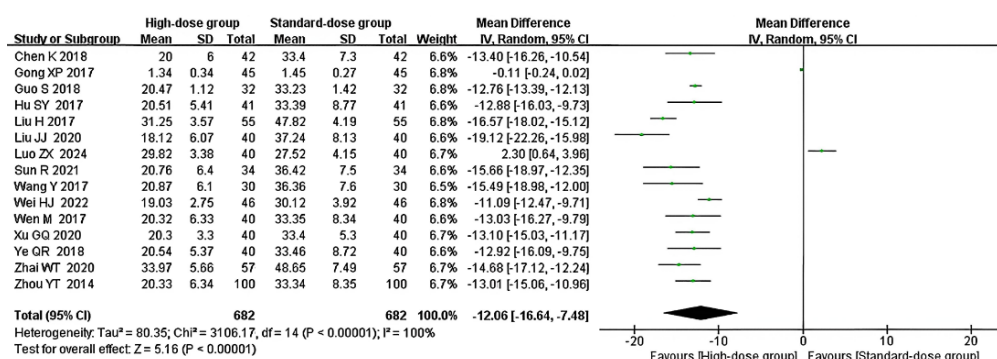


Figure 11. Hemostasis time.

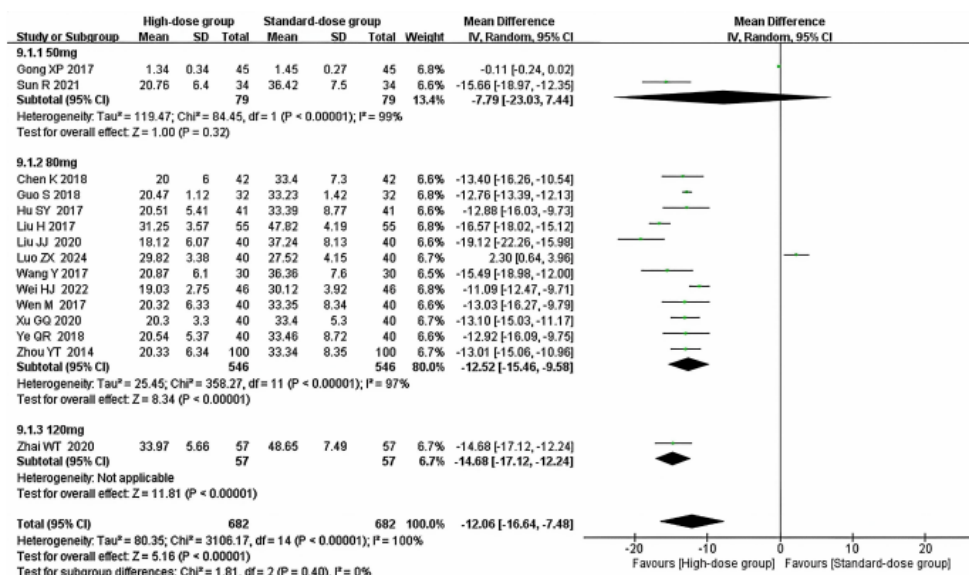


Figure 12. Forest plot of subgroup analysis on hemostasis time based on different doses of omeprazole.

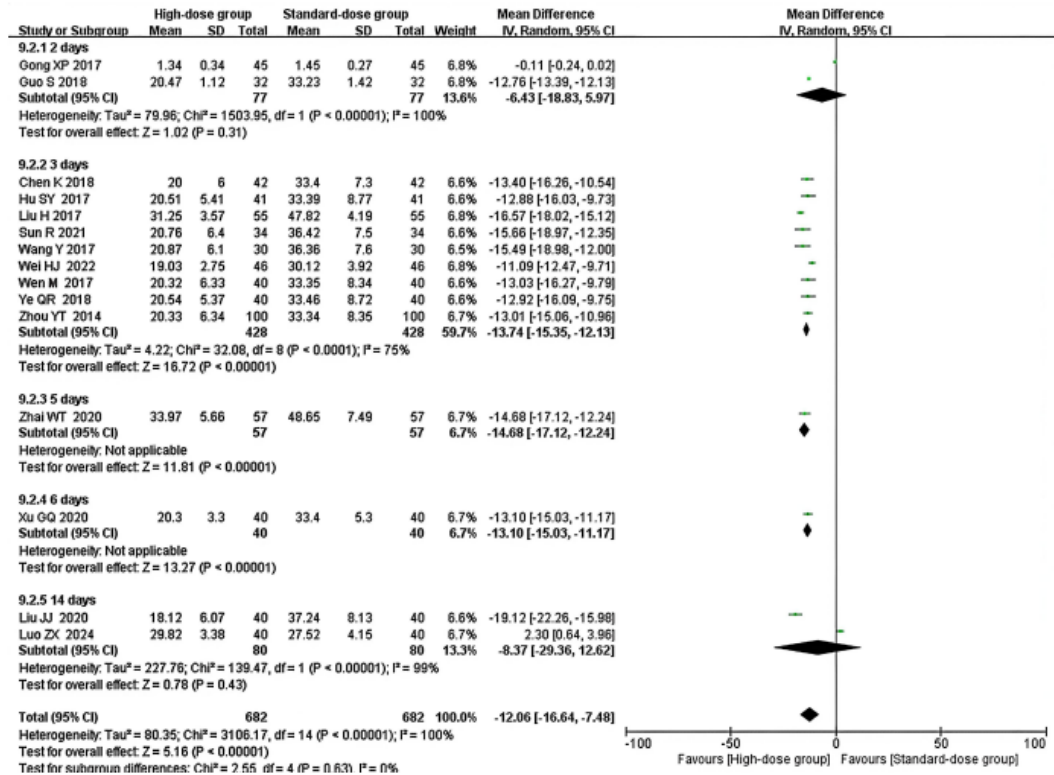


Figure 13. Forest plot of subgroup analysis on hemostasis time according to omeprazole treatment duration.

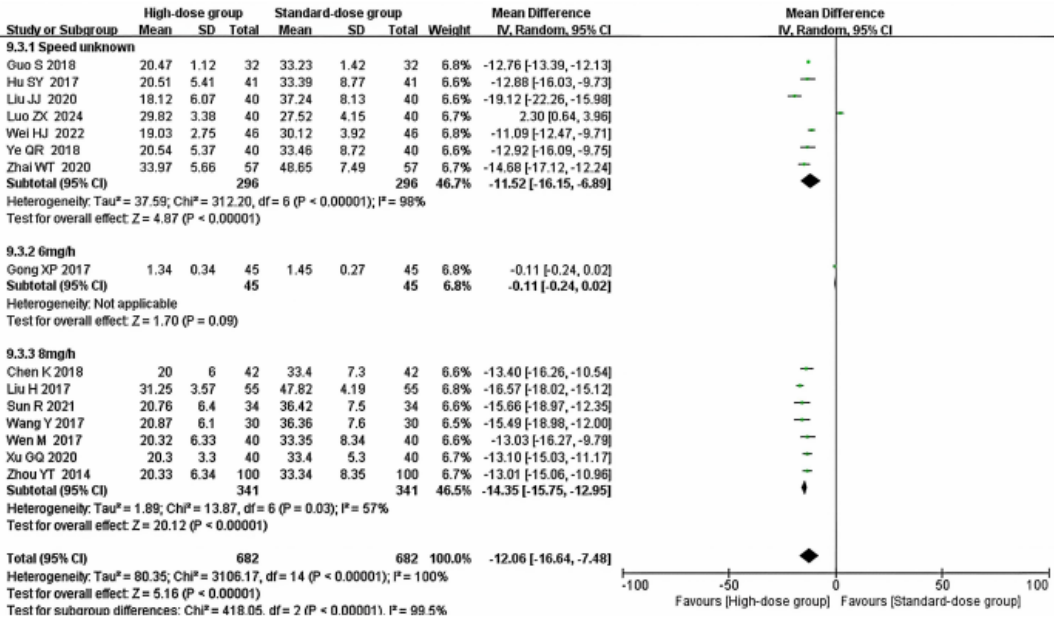


Figure 14. Forest plot of subgroup analysis on hemostasis time according to omeprazole infusion rate.

3.4.3. Comparison of Blood Transfusion Volume

Twelve studies [6] [7] [9]-[15] [20] [22] [23] reported blood transfusion volume. Significant statistical heterogeneity was observed ($P < 0.00001$, $I^2 = 99\%$), justify-

ing the use of a random-effects model. Pooled analysis demonstrated that the high-dose group required significantly less blood transfusion than the conventional-dose group (MD = -1.17 units, 95% CI: -1.62 to -0.73; $P < 0.00001$). Sensitivity analysis was conducted by sequentially excluding each individual randomized controlled trial (RCT). The results showed that the I^2 value remained at 99% regardless of which study was removed, indicating that heterogeneity was not driven by any single study but rather stemmed from systematic differences among studies (such as administration route, dosage, duration of treatment, etc.). See **Figure 15**.

Subgroup analysis by infusion rate showed that in subgroups where infusion rate was not clearly reported (6 studies, $n = 239$ per group), blood transfusion decreased by 1.02 units (MD = -1.02, 95% CI: -1.28 to -0.76; $I^2 = 89\%$). In contrast, the subgroup with a fixed infusion rate of 8 mg/h (6 studies, $n = 286$ per group) demonstrated a larger effect size (MD = -1.33, 95% CI: -2.12 to -0.54; $I^2 = 99\%$). See **Figure 16**.

Stratification by single dose revealed that the 80 mg subgroup included 11 studies ($n = 491$ per group), showing a reduction in blood transfusion by 1.05 units (MD = -1.05, 95% CI: -1.47 to -0.62; $I^2 = 98\%$). The 50 mg dose was only represented in one study, and due to insufficient sample size and lack of replication, reliable assessment of its effect or heterogeneity could not be performed. See **Figure 17**.

Analysis by treatment duration showed significant benefit in both the 3-day subgroup (MD = -1.24, 95% CI: -1.91 to -0.57; $I^2 = 99\%$) and the 14-day subgroup (MD = -1.21, 95% CI: -2.08 to -0.34; $I^2 = 97\%$; $P = 0.006$). However, the 2-day and 6-day regimens were each represented by only one study, and due to limited data availability, no robust conclusions could be drawn regarding differences in efficacy or heterogeneity. See **Figure 18**.

Overall, all analyzable subgroups showed consistent effect directions, supporting the notion that high-dose omeprazole reduces blood transfusion requirements. However, due to the very limited number of studies in certain subgroups (e.g., 50 mg dose, 2-day/6-day regimens), current evidence is insufficient to definitively establish the relative superiority of different dosing parameters.

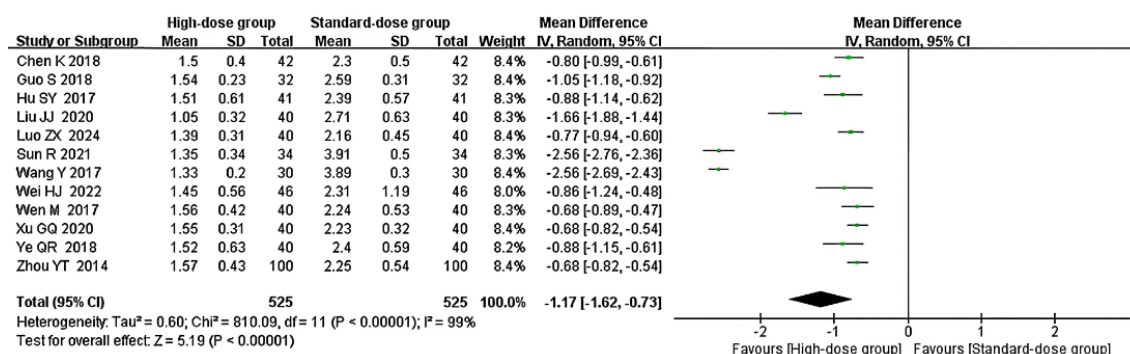


Figure 15. Blood transfusion volume.

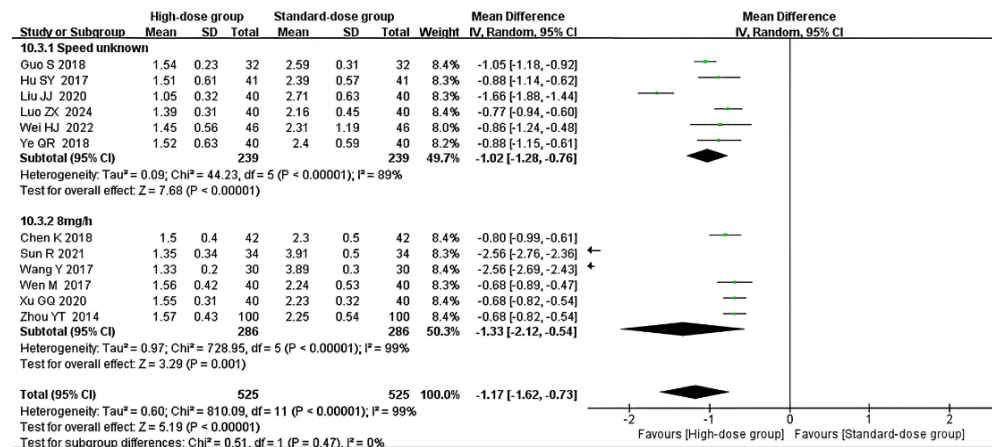


Figure 16. Forest plot of subgroup analysis on transfusion volume according to omeprazole infusion rate.

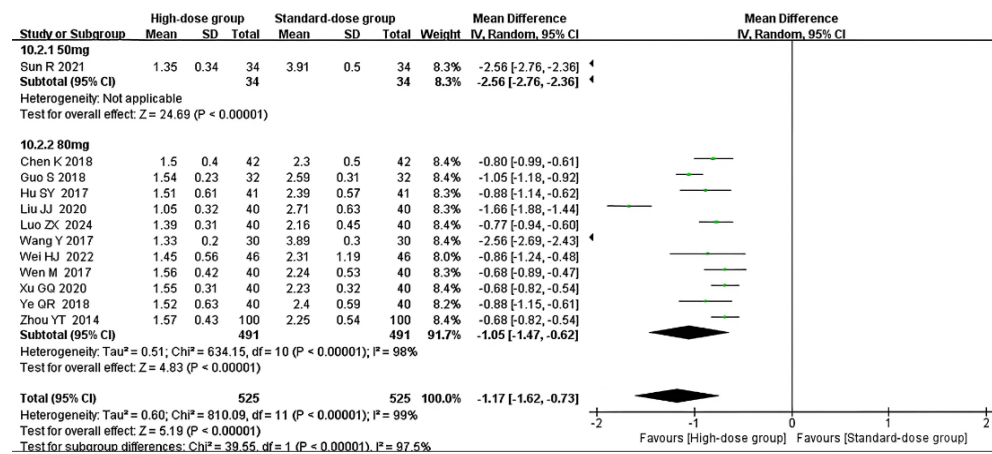


Figure 17. Forest plot of subgroup analysis on transfusion volume according to omeprazole dose.

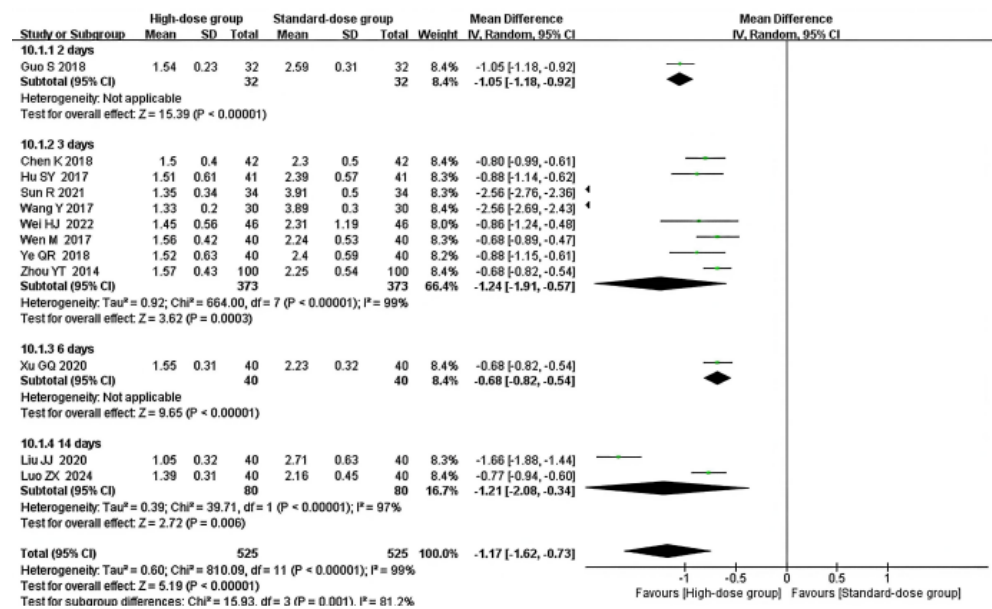


Figure 18. Forest plot of subgroup analysis on transfusion volume according to omeprazole treatment duration.

3.4.4. Comparison of Length of Hospital Stay

Ten studies [6] [11] [14] [15] [17] [19]–[23] reported length of hospital stay. Substantial heterogeneity was observed ($P < 0.00001$, $I^2 = 91\%$), supporting the use of a random-effects model. Meta-analysis showed that the high-dose group had a significantly shorter length of hospital stay than the conventional-dose group (MD = -2.31 days, 95% CI: -3.01 to -1.61 ; $P < 0.00001$). Sensitivity analysis was conducted by sequentially excluding each individual randomized controlled trial (RCT). The results showed that the I^2 value remained at 91% regardless of which study was removed, indicating that heterogeneity was not driven by any single study but rather stemmed from systematic differences among studies (such as administration route, dosage, duration of treatment, etc.). See **Figure 19**.

Subgroup analysis by omeprazole infusion rate: The “unknown rate” group included 7 studies, with a weighted mean difference (MD) of -2.22 days (95% CI: -3.14 to -1.30), showing high heterogeneity ($I^2 = 93\%$); the 8 mg/h group included 2 studies, with an MD of -2.55 days (95% CI: -3.84 to -1.25), $I^2 = 78\%$; and the 6 mg/h group consisted of only one study, precluding meta-analysis and heterogeneity assessment. Due to imbalanced sample sizes across infusion rate subgroups and insufficient replication evidence, current data are inadequate for reliable evaluation of clinical differences among different infusion rates. Notably, all analyzable subgroups consistently showed that higher infusion rates were associated with shorter hospital stays. See **Figure 20**.

Subgroup analysis by treatment duration: The 2-day group included 2 studies, with an MD of -2.34 days (95% CI: -2.73 to -1.95), $I^2 = 0\%$, indicating robust results; the 3-day group included 5 studies, with an MD of -2.58 days (95% CI: -3.32 to -1.83), $I^2 = 74\%$, showing moderate heterogeneity; the 14-day group included 2 studies, with an MD of -2.49 days (95% CI: -4.57 to -0.41), $I^2 = 93\%$, exhibiting very high heterogeneity; and the 5-day group included only one study, making statistical inference impossible. Limited by uneven distribution of study numbers across duration subgroups—particularly due to sparse evidence for longer durations—the current data do not support meaningful comparisons of efficacy between different treatment regimens. See **Figure 21**.

Additionally, the 120 mg dose subgroup also included only one study, lacking sufficient basis for heterogeneity assessment and preventing conclusions about specific effects at this dosage level. See **Figure 22**.

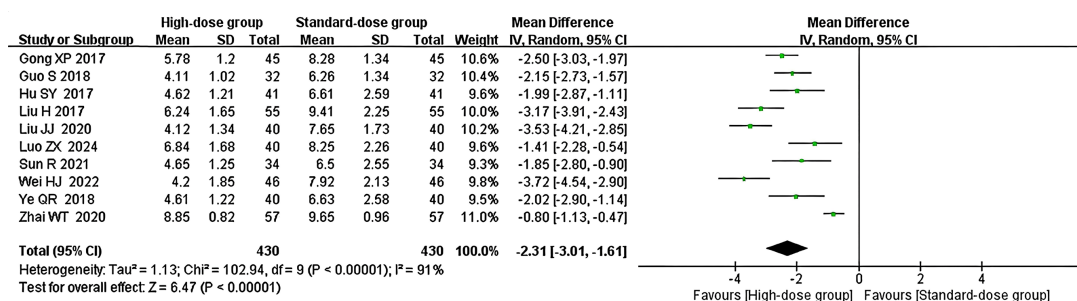


Figure 19. Length of hospital stay.

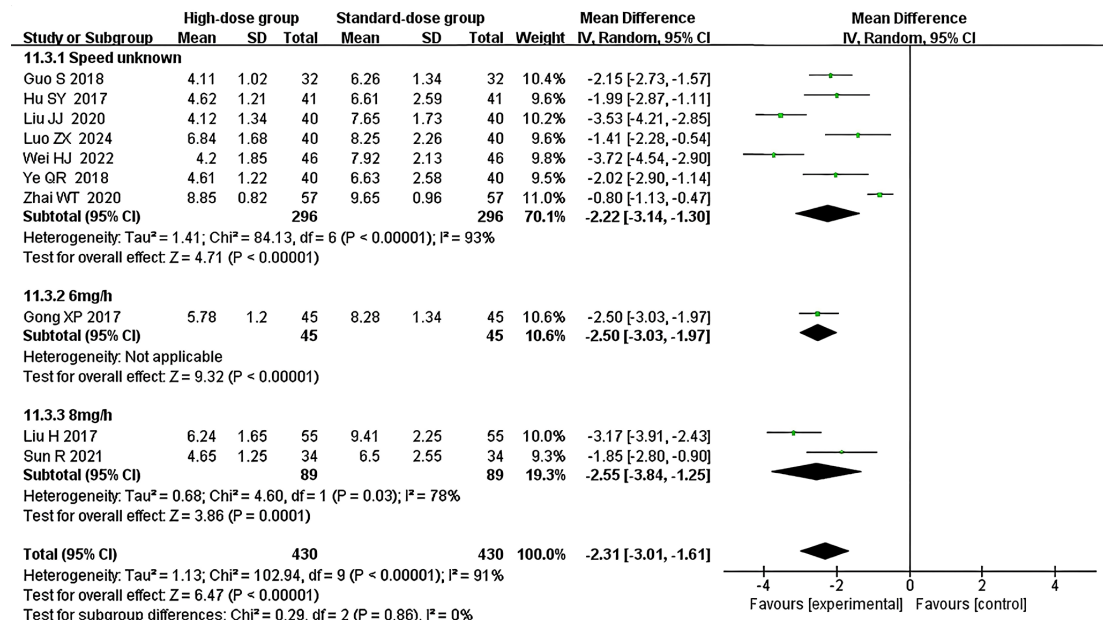


Figure 20. Forest plot of subgroup analysis of length of hospital stay based on different infusion rates of omeprazole.

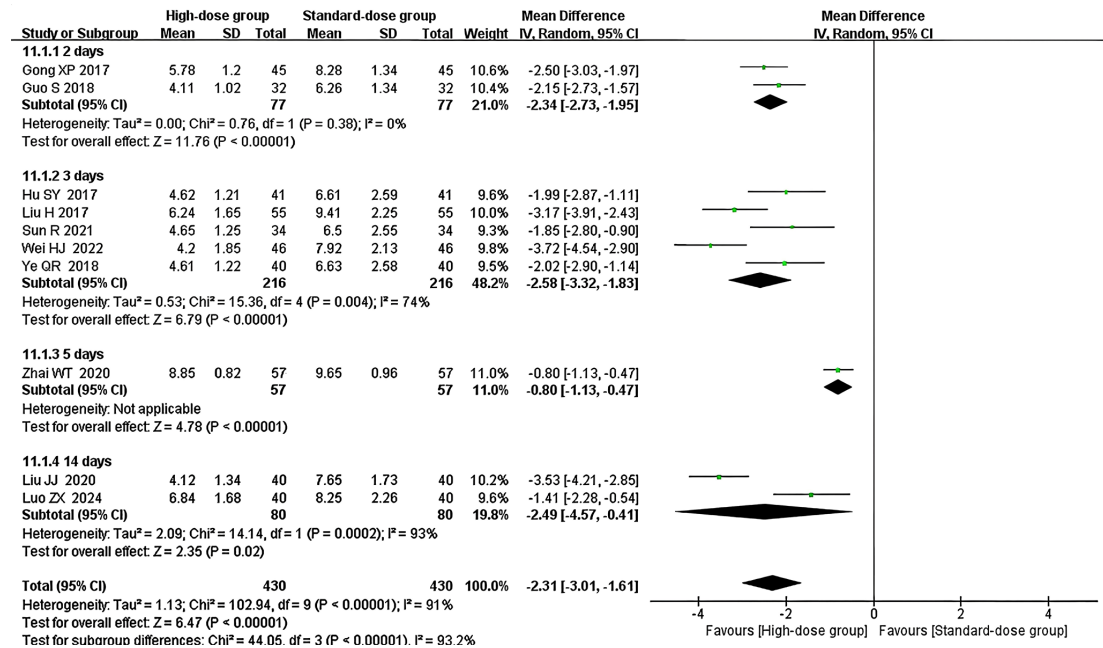


Figure 21. Forest plot of subgroup analysis on length of hospital stay based on different durations of omeprazole treatment.

In summary, existing evidence suggests that high-dose omeprazole combined with octreotide significantly reduces hospitalization duration in patients with peptic ulcer bleeding. However, the observed overall heterogeneity ($I^2 > 75\%$) likely stems primarily from systematic differences in intervention parameters such as treatment duration, dosage, and infusion rate, highlighting the need for future studies to standardize these variables and report findings accordingly.

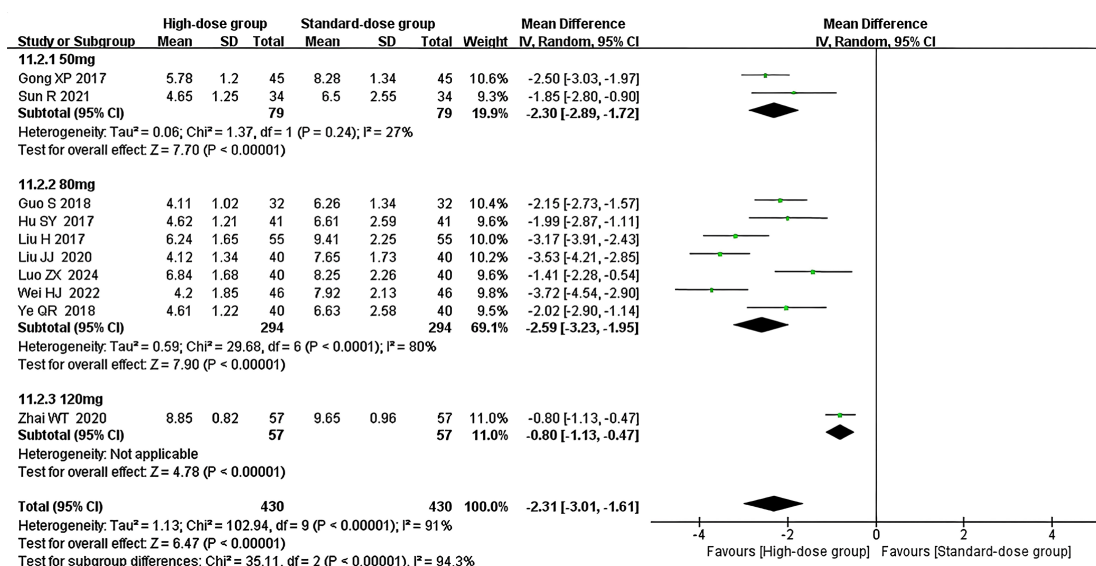


Figure 22. Forest plot of subgroup analysis of length of hospital stay based on different doses of omeprazole.

3.4.5. Comparison of Adverse Events

Nine studies [9] [12]-[14] [16] [17] [22]-[24] reported adverse events. Homogeneity was confirmed ($P = 1.00$, $I^2 = 0\%$), supporting the use of a fixed-effects model. Meta-analysis revealed no statistically significant difference in adverse event incidence between the high-dose and conventional-dose omeprazole groups ($OR = 1.30$, 95% CI: 0.73 to 2.32; $P = 0.38$). The above results indicate that the reported adverse reactions did not differ significantly between groups; See **Figure 23**.

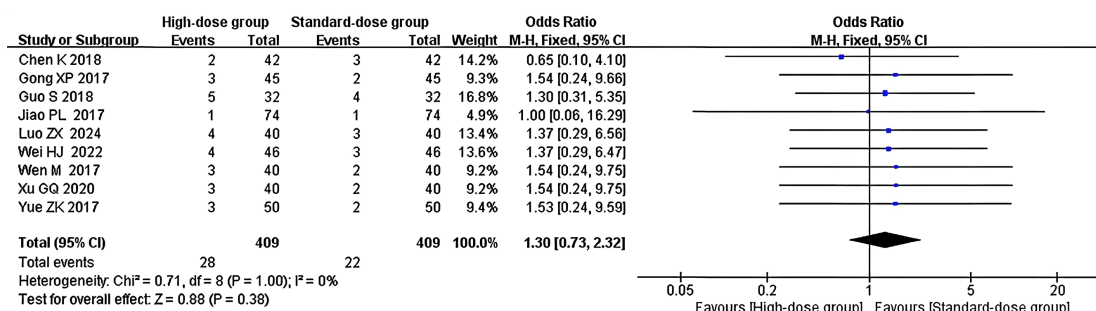


Figure 23. Adverse events.

3.4.6. Assessment of Publication Bias

Publication bias was assessed by visual inspection of funnel plots (**Figure 24**). For the dichotomous efficacy outcomes under both Standard 1 and Standard 2—overall effective rate, marked efficacy rate, effective rate, and ineffective rate—the funnel plots were approximately symmetrical around the pooled effect estimates, with no obvious concentration of studies on one side. The funnel plots for length of hospital stay and adverse events also showed no marked asymmetry. These observations suggest that substantial publication bias was unlikely for these outcomes.

In contrast, the funnel plots for hemostasis time and blood transfusion volume

displayed marked asymmetry, with a relative lack of small studies reporting favorable results (*i.e.*, shorter hemostasis time or lower transfusion volume) in the lower left quadrant. This pattern is consistent with potential small-study effects, which may reflect publication bias, selective outcome reporting, or methodological and clinical differences among smaller trials. Because both outcomes also showed high heterogeneity ($I^2 = 100\%$ and 99% , respectively), the asymmetry should not be interpreted as definitive evidence of publication bias alone. Therefore, the pooled estimates for hemostasis time and blood transfusion volume should be interpreted with caution.

Overall, the efficacy and safety estimates for the dichotomous outcomes and adverse events appeared relatively robust to publication bias, whereas the continuous outcomes of hemostasis time and blood transfusion volume require confirmation in larger, multicenter, high-quality RCTs with standardized intervention protocols. As funnel plot inspection is subjective and the number of studies per outcome was limited, these findings should be regarded as exploratory.

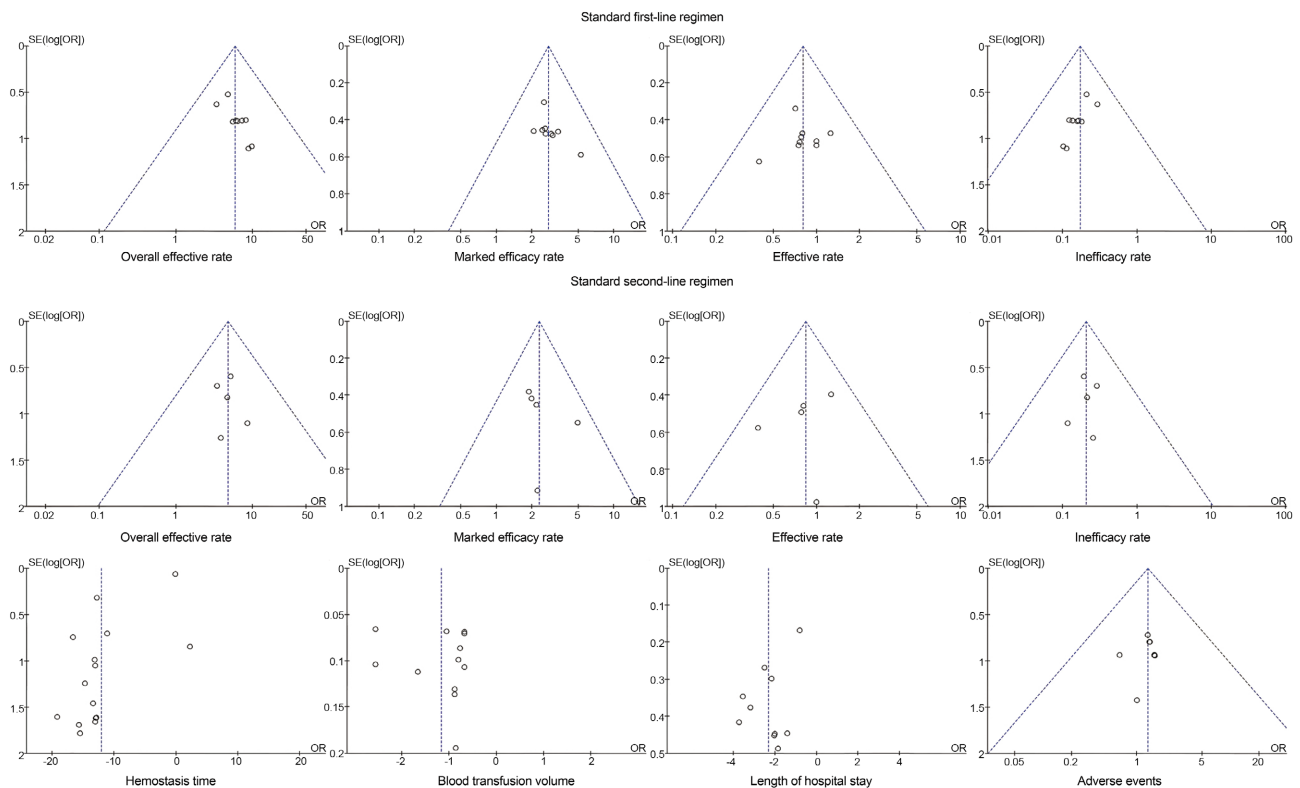


Figure 24. Funnel plots for assessment of publication bias.

4. Discussion

4.1. Main Findings

This study is the first to use a systematic review and meta-analysis approach to compare the efficacy and safety of high-dose omeprazole combined with octreotide versus standard-dose omeprazole combined with octreotide in treating

peptic ulcers with bleeding. The results showed that the high-dose group demonstrated significantly higher rates of clinical effectiveness and overall response, along with a notably lower rate of treatment failure. Additionally, the high-dose group achieved significantly shorter hemostatic time, reduced blood transfusion requirements, and shorter hospital stays. There was no statistically significant difference in adverse event rates between the two groups, suggesting that increasing the omeprazole dose on top of octreotide can achieve better hemostatic outcomes without increasing safety risks.

4.2. Pharmacological Mechanism Analysis

From a pharmacological perspective, the findings of this study are well supported by theoretical mechanisms. Gastric acid plays a critical role in maintaining and recurring ulcer bleeding: when gastric pH falls below 6, platelet aggregation and clot formation are significantly impaired, and newly formed clots are easily dissolved by gastric acid and pepsin. High-dose intravenous omeprazole rapidly and sustainably elevates gastric pH toward neutrality, thereby stabilizing clots and promoting platelet aggregation, which facilitates hemostasis at the ulcer site. A randomized double-blind controlled trial by Khuroo *et al.* [26] confirmed that high-dose omeprazole significantly reduces rebleeding rates and surgical requirements in patients with peptic ulcer bleeding. Lau *et al.*'s [1] landmark study further demonstrated that continuous intravenous infusion of high-dose omeprazole after endoscopic hemostasis significantly lowers the 30-day rebleeding rate (6.7% vs. 22.5%). Meanwhile, octreotide, as a somatostatin analog, selectively constricts visceral blood vessels, reducing portal and gastric mucosal blood flow, while also suppressing gastric acid and pepsin secretion. Its hemostatic mechanism complements that of omeprazole. The combination of both drugs produces a synergistic effect, providing a mechanistic explanation for the superior efficacy observed in the high-dose group.

4.3. Heterogeneity, Sensitivity Analysis, and Blood Transfusion Volume

Notably, the heterogeneity among studies for the three continuous outcome measures—hemostatic time, blood transfusion volume, and hospital stay—was high (I^2 values of 100%, 99%, and 91%, respectively). Possible reasons include variations in high-dose omeprazole regimens across studies (doses ranging from 50 to 120 mg, differing infusion rates, and treatment durations), differences in patient populations regarding ulcer types, discrepancies in units used to measure blood transfusion volumes and transfusion criteria, and variations in clinical protocols and discharge standards across centers. Sensitivity analysis using one-study-at-a-time exclusion showed no substantial changes in pooled effect sizes or heterogeneity, indicating robustness of the meta-analysis results and minimal influence from any single study. Nevertheless, the high heterogeneity underscores the importance of individualized treatment and standardized clinical procedures

in practice. The meta-analysis also revealed that the high-dose group required significantly less blood transfusion than the standard-dose group, consistent with Leontiadis *et al.*'s [27] finding that proton pump inhibitors reduce transfusion needs in ulcer bleeding patients. Reduced transfusion volume not only lowers the risk of transfusion-related complications but also helps conserve blood resources and alleviate healthcare burdens.

4.4. Safety Analysis

Regarding safety, nine included studies reported adverse events in both groups. The above study showed no statistically significant difference in the incidence of adverse events between the two groups ($P > 0.05$), but this result does not support the conclusion that “increasing the dose of omeprazole on top of octreotide can improve hemostatic efficacy without increasing safety risks.” The reason is that the 95% confidence interval is wide, failing to rule out potentially clinically meaningful harms. Moreover, most included studies had methodological limitations regarding allocation concealment and blinding—such as inadequate description or poor implementation—which reduced their internal validity and weakened the reliability of causal inference. Common adverse effects were mild symptoms such as nausea, dizziness, and bloating, with no serious adverse events leading to treatment discontinuation or life-threatening conditions. This suggests that high-dose omeprazole is well tolerated and safe during short-term use (typically ≤ 7 days). However, it should be noted that the observation period of this study is relatively short, and potential long-term risks associated with high-dose proton pump inhibitor (PPI) use—such as intestinal infections, hypomagnesemia, and increased fracture risk—cannot be ruled out. Therefore, the principle of “short duration, adequate dosage, and timely de-escalation” should still be followed. The 2021 American Gastroenterological Association guidelines also recommend short-term high-dose PPI therapy for high-risk ulcer bleeding patients after endoscopic hemostasis, rather than long-term maintenance [28].

4.5. Publication Bias Analysis

Publication bias analysis revealed that funnel plots for overall efficacy rate, marked efficacy rate, effective rate, inefficacy rate, hospitalization duration, and adverse reactions were generally symmetric, suggesting a low likelihood of publication bias for these outcomes. In contrast, funnel plots for hemostatic time and blood transfusion volume showed poor symmetry, which may be related to the generally small sample sizes across included studies and the tendency for positive results to be more likely published. This could also be compounded by clinical heterogeneity mentioned above, indicating caution in interpreting results for these two outcomes.

4.6. Study Limitations

This study has several limitations: First, most of the 20 included RCTs did not

clearly describe specific methods for random sequence generation, allocation concealment, or blinding implementation, and many studies were rated as having “unclear” risk of bias, potentially affecting the quality of evidence. Second, all included studies were conducted in Chinese populations, and there were differences among studies in intervention protocols (dose, infusion rate, treatment duration), limiting the generalizability of conclusions. Third, high clinical heterogeneity was observed in outcomes such as hemostatic time and blood transfusion volume; although sensitivity analysis confirmed robust results, this heterogeneity might obscure the true dose-response relationship. Fourth, follow-up periods in the included studies were relatively short, precluding assessment of long-term hard endpoints such as rebleeding rate and mortality.

4.7. Conclusion and Future Directions

In summary, current evidence indicates that adding high-dose omeprazole to octreotide therapy significantly improves hemostatic efficacy, reduces hemostatic time and hospital stay, decreases blood transfusion requirements, and does not increase adverse events, demonstrating favorable effectiveness and safety. These findings are consistent with recommendations from both domestic and international guidelines [4]. However, due to limitations in methodological quality and clinical heterogeneity of the included studies, further validation is needed through well-designed, rigorously reported multicenter RCTs with larger sample sizes. Future research should focus on long-term prognostic outcomes and comparative optimization of different dosing regimens to better define the optimal treatment strategy.

This study is registered on the PROSPERO website and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, with registration ID CRD420261491716.

Author Contributions

Conceptualization, Wan Li and Chuanxin Zou; methodology, Wan Li; software, Wan Li; validation, Wan Li and Zixiong Zheng; formal analysis, Wan Li; investigation, Wan Li; resources, Wan Li; data curation, Wan Li; writing—original draft preparation, Wan Li; writing—review and editing, Wan Li, Zixiong Zheng, and Chuanxin Zou; visualization, Wan Li; supervision, Chuanxin Zou; project administration, Chuanxin Zou; funding acquisition, Chuanxin Zou. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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