Review Article

DOI:

Duration of vasoconstrictors after endoscopic variceal ligation in acute variceal bleeding: A systematic review and network meta-analysis

Running head: Duration of vasoconstrictors after EVL

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How to cite this article: Giri S, Panda S, Singh A, Varghese A, Ingawale S, Tapper EB, et al. Duration of vasoconstrictors after endoscopic variceal ligation in acute variceal bleeding: A systematic review and network meta-analysis. Hepatology Forum 2025; 6(4):XX–XX.

Received: April 08, 2025; **Revised:** July 24, 2025; **Accepted:** August 05, 2025;

Authors Contributions: Concept – SG, AC; Design – SG, SI, AC; Supervision – SG, EBT, DCR, AC; Materials – SG, SP, AS, JV, SI; Data Collection and/or Processing – SG, SP, AS, JV, SI; Analysis and/or Interpretation – SG, AS; Literature Search – SG, SP, AS, JV, SI; Writing – SG, AS; Critical Reviews – SG, SP, AS, JV, SI, EBT, DCR, AC.

Conflict of Interest: There are no conflicts of interest to declare.

Use of AI for Writing Assistance: The authors declare that they have not used any AI tools or technologies to prepare this manuscript.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

Abstract

Background and Aim: Studies on the duration of vasoconstrictors after endoscopic variceal ligation (EVL) for acute variceal bleeding (AVB) have shown varying results. The present network meta-analysis compared the effectiveness of vasoconstrictors after EVL based on the therapy duration.

Materials and Methods: The electronic databases of MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and Scopus were searched from inception to March 2024 for randomized studies comparing the duration of vasoconstrictors in AVB after EVL (Group 1: ≤ 24 hours, Group 2: >24 to ≤72 hours, Group 3: >72 to ≤120 hours). Rebleeding and mortality risk were analyzed using pair-wise and network meta-analyses.

Results: Eleven studies (n=1,066) met the inclusion criteria. Rebleeding rates varied from 0–38% in Group 1, 2–12% in Group 2, and 0–26% in Group 3. There was no difference in the risk of rebleeding in Group 1 (risk ratio [RR]: 1.36, 95% confidence interval [CI]: 0.48–3.52) or Group 2 (RR: 1.34, 95% CI: 0.42–4.54), compared to Group 3. Similarly, there was no difference either in 5-day mortality risk among the groups (RR: 0.66, 95% CI: 0.09–2.52 and 1.08, 95% CI: 0.15–6.43 for Groups 1 and 2, respectively, vs. Group 3) or 30-day mortality risk (RR: 1.18, 95% CI: 0.51–2.51 and 0.98, 95% CI: 0.36–2.52 for Groups 1 and 2, respectively, vs. Group 3).

Conclusion: The current network meta-analysis provides no evidence to support the use of vasoconstrictors following EVL. These data suggest that vasoconstrictors can be stopped early after EVL, facilitating early discharge from the hospital.

Keywords: Banding; endoscopy; esophagogastroduodenoscopy; octreotide; terlipressin; varices.

Introduction

Acute variceal bleeding (AVB) associated with cirrhosis and portal hypertension is a devastating clinical complication associated with substantial morbidity and mortality.[1,2] Each bleeding episode is associated with a mortality risk of approximately 15–25%.[3,4] Best practice for management includes a combination of vasoconstrictor and endoscopic therapy,[5] which includes sclerotherapy or endoscopic variceal ligation (EVL). EVL is preferred and is more widely used due to lower rates of rebleeding and fewer endoscopic complications.[6,7] Traditionally, vasoconstrictor therapy has been continued for up to 5 days post-procedure to prevent rebleeding, and current guidelines suggest using vasoconstrictors for 3 to 5 days in AVB.[5]

There is considerable controversy surrounding the appropriate duration of use of vasoconstrictors in AVB. On the one hand, patients with high MELD scores or hepatic venous pressure gradient > 20 mmHg, where early transjugular intrahepatic portosystemic shunt (TIPS) is recommended,[5] are at significant risk of rebleeding after primary hemostasis, thereby potentially justifying continued vasoconstrictor therapy (typically for at least five days or until TIPS or transplant is undertaken). On the other hand, the rationale for continuing vasoconstrictors post-endoscopic therapy is to reduce portal pressure and the risk of variceal rebleeding. However, previous data supporting this recommendation were developed when endoscopic sclerotherapy was the main treatment modality. Studies have shown the superiority of a combination of endoscopic sclerotherapy with vasoconstrictors over endoscopic sclerotherapy alone in preventing 5-day rebleeding rates,[8,9] but the same results have not been duplicated with EVL. Indeed, EVL alone has a primary hemostasis rate of some 95% and a low rebleeding rate.[7,10] Additionally, some vasoconstrictors, including octreotide, have a very rapid onset of tachyphylaxis,[11] raising pathophysiologically based questions about the role of prolonged vasoconstrictor therapy. Thus, guidelines may need to be reevaluated using data currently available from studies on EVL.

It is also notable that prolonged vasoconstrictor treatment not only lengthens hospital stay but may carry a significant risk of major adverse events (AE), including cardiac arrhythmias, pulmonary edema, respiratory failure, hyponatremia, and ischemic events.[12] One meta-analysis reported treatment-related AEs with terlipressin in 22% of cases, with serious AEs being 5%, with higher rates in those having hepatorenal syndrome and bilirubin > 4.3 mg/dL.[12] Thus, the appropriate duration of vasoconstrictor treatment post-EVL requires further evaluation. Therefore, in this study, we aimed to help clarify this issue by analyzing the effect of treatment duration of vasoconstrictor therapy on the risk of rebleeding after AVB and mortality.

Materials and Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-Analyses (PRISMA-NMA) guideline was used to report the current meta-analysis.[13]

Information sources and search strategy

The following databases were searched for relevant studies using the keywords: (Varices OR Variceal bleeding OR Variceal hemorrhage) and (Variceal ligation OR Band ligation OR Hemostasis) and (Vasoconstrictor OR Octreotide OR Somatostatin OR Terlipressin): MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and Scopus. Searches were from inception to March 2024. Additionally, the bibliography of all identified studies, guidelines, and reviews on the topic was searched for relevant trials.

Study selection

Two reviewers independently screened titles and abstracts of retrieved search records for inclusion and exclusion criteria. Any differences were settled through discussion. Randomized controlled trials (RCTs) fulfilling the following PICO criteria were included: (a) Patients – Cirrhosis with AVB undergoing EVL; (b) Intervention – short duration of vasoconstrictors after EVL; (c) Comparison – standard duration of vasoconstrictors after EVL; (d) Outcomes – rebleeding and mortality. Single-arm studies, conference abstracts, and studies involving pediatric patients were excluded. Differences of opinion with regard to suitability for inclusion were settled through discussion.

Data extraction

Two investigators extracted data independently, while a third reviewer resolved disagreement as to which data would be included. The following information was collected: study author and year, country, number of

patients, demographic profiles of patients, clinical features of patients, endoscopic findings and treatment, dose and duration of vasoconstrictor, and outcomes including rebleeding and mortality.

Risk of bias in individual studies and confidence in cumulative evidence
Two independent reviewers evaluated the risk of bias using the Cochrane risk-of-bias tool for randomized trials (RoB 2).[14] The certainty of the evidence for all outcomes was assessed using the grading of recommendations assessment, development and evaluation (GRADE) approach for network meta-analysis.[15]

Statistical analysis
A pair-wise meta-analysis was carried out using RevMan software (version 5.4.1, Cochrane Collaboration) and a random effects model. Dichotomous variables were assessed utilizing the Mantel-Haenszel test, and estimates were reported as risk ratio (RR) with their 95% confidence interval (CI). The study utilized Stata 17.0 software and MetaInsight (CRSU NMA web-based app) to conduct a network meta-analysis with a Bayesian random effects model.[16] For comparison in network meta-analysis, studies were divided into three groups based on the duration – very short/group 1 (≤ 24 hours), short/group 2 (> 24 and ≤ 72 hours), and standard/group 3 (> 72 to 120 hours). Global inconsistency was assessed using the Wald test.[17] Interventions were ranked relative to different outcomes using their surface under the cumulative ranking (SUCRA) score.[18] Publication bias was evaluated by analyzing the asymmetry of the funnel plot.[19]

Results

Baseline characteristics of the studies and risk of bias
The search strategy, as summarized in *Methods*, yielded 1,830 records, out of which 11 were included in the final analysis (Fig. 1). All studies were from Asia (Table 1).[20–30] The type and approach to dosing of vasoconstrictors varied: two studies used octreotide (100 μg bolus followed by 25 μg/h),[20,21] two used somatostatin (250-μg IV bolus followed by 250-μg/h infusion),[24,25] six studies used terlipressin (a bolus dose of 2 mg in five studies [22,26–28,30] or 2 mg/4 h for the first 24 hours in one study,[29] followed by 1 mg/6 h in five studies [22,26,27,29,30] or 1 mg/4 h in one study [28]), and one used either somatostatin or terlipressin.[23] The majority of patients included in the studies were males, and ethanol was the most common etiology of cirrhosis in most of the studies. The majority of the patients had Child-Pugh B or C cirrhosis classification. The definitions of rebleeding used in various studies are summarized in Supplementary Table 1. Risk of bias analysis using RoB 2 showed low evidence of bias in six studies,[22–25,29,30] some concern in four studies [20,21,26,28], and a high risk of bias in one study [27] (Supplementary Fig. 1).

Pair-wise meta-analysis
Five studies compared vasoconstrictor therapy that was stopped after EVL (0 hours) vs. vasoconstrictor therapy continued for 120 hours;[20,21,23,25,28] three compared 24 hours vs. 72 hours [22,27,29]; two compared 48 hours vs. 120 hours;[28,30] and one study each compared 12 hours vs. 72 hours [26] and 72 hours vs. 120 hours.[24] There was no difference in the risk of rebleeding at 5 days between the shorter duration (0–72 hours) and standard (72–120 hours) duration of vasoconstrictor therapy (RR 1.13, 95% CI: 0.67–1.91; I^2=16%) (Fig. 2). On subgroup analysis, there was no difference in the risk of rebleeding between vasoconstrictors for 0 vs. 120 hours (five studies) (RR 1.48, 95% CI: 0.55–3.97; I^2=53%) and 24 hours vs. 72 hours (three studies) (RR 0.84, 95% CI: 0.28–2.51; I^2 = 0%). Similarly, there was no difference in the risk of mortality between short-duration and standard-duration vasoconstrictors at 5 days (RR 0.91, 95% CI: 0.46–1.77; I^2=0%) (Supplementary Fig. 2) or 30 days (RR 1.05, 95% CI: 0.67–1.65; I^2=0%) (Supplementary Fig. 3). Subgroup analysis also showed no difference in mortality at 5 or 30 days.

Subgroup analysis based on the type of vasoconstrictor showed a higher risk of rebleeding with a short duration of octreotide (RR 4.45, 95% CI: 1.72–11.54; I^2=0%). However, there was no difference in the risk of rebleeding between short duration and standard duration for somatostatin and terlipressin (Supplementary Fig. 4). Comparison of AEs showed no difference between the shorter and standard duration in six studies,[22,24,26,27,28,31] while three studies showed a higher incidence of AEs with the standard duration of vasoconstrictors.[25,30-32] Comparative analysis could not be performed due to the non-uniform definition of AEs in the included studies.

Network meta-analysis

5-day rebleeding
All 11 studies reported on the rate of rebleeding at 5 days after EVL. There was no difference among vasoconstrictor groups (Group 1: ≤ 24 hours, Group 2: > 24 to ≤ 72 hours, Group 3: > 72 to ≤ 120 hours) on network estimate (Supplementary Table 2), with the very short duration and short duration having RR 1.36 (95% CI: 0.48–3.52) and RR 1.34 (95% CI: 0.42–4.54), respectively, compared to the standard duration group (Fig. 3). The SUCRA plot was generated from the ranking plot. Ranking based on SUCRAs accounts better for the uncertainty in the estimated treatment effects. Based on the SUCRA plot analysis for rebleeding, Group 3 was the best treatment for prevention of rebleeding at 5 days, with a SUCRA of 72.6, followed by Group 2 (40.5) and Group 1 (36.8) (Fig. 4) (certainty of evidence: very low).

5-day mortality
A total of 10 studies reported on mortality rates at 5 days after EVL. There was no difference among vasoconstrictor groups (as above) on network estimate (Supplementary Table 3), with the very short duration and short duration having RR 0.66 (95% CI: 0.09–2.52) and RR 1.08 (95% CI: 0.15–6.43), respectively, compared to the standard duration group (Fig. 3). Based on the SUCRA plot analysis for rebleeding, Group 1 was the best treatment for prevention of mortality at 5 days, with a SUCRA of 71.3, followed by Group 3 (41.1) and Group 2 (37.5) (Fig. 4). The certainty of evidence for the SUCRA ranking was moderate.

30-day mortality
A total of 10 studies reported data on the incidence of mortality at 30 days after EVL. There was no difference between the groups on network estimate (Supplementary Table 4), with the very short duration and short duration having RR 1.18 (95% CI: 0.51–2.51) and RR 0.98 (95% CI: 0.36–2.52), respectively, compared to the standard duration group (Fig. 3). Based on the SUCRA plot analysis for rebleeding, Group 2 was the best treatment for prevention of mortality at 30 days, with a SUCRA of 60.4, followed by Group 3 (57.9) and Group 1 (31.7) (Fig. 4). The certainty of evidence for the SUCRA ranking was moderate.

Publication bias, heterogeneity, network coherence, and quality of evidence
Funnel plot visual assessment did not show any evidence of significant publication bias (Supplementary Fig. 5). The estimated value of between-study variance for the network meta-analysis is 0.147 for the primary outcome, suggestive of no heterogeneity. The evaluation of inconsistency between the direct and indirect estimates for the primary outcome did not show any evidence of the same (Supplementary Table 5). The global test based on a random-effects design-by-treatment interaction model showed no evidence of inconsistency for any of the outcomes (p-value: 0.469 for the primary outcome). On analysis of individual durations (Supplementary Fig. 6), there was no difference in the risk of rebleeding compared to 120 hours. SUCRA analysis showed that a duration of 24 hours was the best treatment for the prevention of rebleeding at 5 days (86.3), followed by 72 hours (67.6), 12 hours (55.9), 120 hours (41.8), 48 hours (27.5), and 0 hours (20.8) (Supplementary Fig. 7). Sensitivity analysis using leave-one-out analysis showed no difference in the effect. Table 2 displays the outcomes of treatment comparisons along with the quality of evidence.

Discussion

Current guidelines for the treatment of patients with AVB vary. The British guideline recommends giving terlipressin or somatostatin at presentation and continuing it for up to 5 days after successful hemostasis (the level of evidence reported in the guideline is 1a).[31] The most recent AASLD guideline recommends that treatment with vasoactive agents should then be stopped concurrently with the start of non-selective beta-blockers and not later than day 5.[32] The present network meta-analysis of 11 studies revealed no difference in the risk of rebleeding in patients who received vasoconstrictors for 0–24 hours (RR: 1.36, 95% CI: 0.48–3.52) and 24–72 hours (RR: 1.34, 95% CI: 0.42–4.54), compared to those receiving them for 72–120 hours. Similarly, there was no difference in mortality between the groups at either 5 or 30 days after EVL. Pair-wise analysis also did not show significant differences in various outcomes between short- and standard-duration vasoconstrictors. These findings are similar to the results of a recent individual patient data meta-analysis, which showed no difference in the rebleeding and mortality between the standard and shorter duration groups at 5 and 42 days.[33]

Bacterial infections are frequently associated with AVB in patients with cirrhosis. One study reported that bacterial infection was a significant and independent predictor of failure to achieve acute hemostasis in patients with cirrhosis and AVB.[34] Another study found that most infections occurred within the first 5 days of admission, with half occurring within the first 48 hours. Bacterial infection was associated with a higher requirement for blood transfusion and a higher incidence of rebleeding (43.5% vs. 9.8% in those without

infection).[35] A previous meta-analysis reported a higher pooled incidence of bacteremia after sclerotherapy compared to EVL (17% vs. 6%). Again, the frequency of bacteremia after emergency sclerotherapy was significantly higher than after elective sclerotherapy (22% vs. 14%).[36] This could be responsible for the higher incidence of rebleeding after sclerotherapy in AVB, requiring continuation of vasoconstrictors, but not in patients undergoing EVL.

A previous study reported AEs in 50% of patients receiving terlipressin for variceal bleeding, the most common being electrolyte disturbances and hyponatremia. Other AEs included abdominal pain and cardiac dysrhythmia, requiring discontinuation of the drug. However, most of these AEs were either self-limited or improved after drug discontinuation.[37] One RCT included in the present analysis, using terlipressin, reported a significantly higher incidence of AE in the treatment group, with the most common AE being diarrhea, followed by hypokalemia and bradycardia.[28] The reported AEs with octreotide include gastrointestinal abnormalities, bradycardia, hypoglycemia, and hyperglycemia.[38] Thus, vasoconstrictors are associated with multiple different AEs, which not only limit their effectiveness but have the potential to cause harm. With the epidemiology shifting towards an increasing prevalence of metabolic dysfunction-associated steatotic liver disease-related cirrhosis,[39–41] more patients with variceal bleeding are likely to have cardiometabolic comorbidities, increasing the risk of AEs with vasoconstrictors, especially terlipressin.[42] We speculate that reducing the duration of vasoconstrictors will reduce the incidence of associated AEs and reduce cost. However, comparative analysis of the AEs could not be performed due to the absence of a uniform definition of AEs, requiring further studies.

It should be noted that in the studies included in this meta-analysis, patients in whom AVB could not be controlled endoscopically were excluded. Thus, it is possible that prolonged vasoconstrictor therapy, particularly terlipressin, could play a role in these patients. Multiple risk factors can contribute to the failure to control bleeding.[43] One study reported, in a predictive model of failure to control bleeding after sclerotherapy for AVB, that active bleeding at endoscopy was the strongest predictor of failure to control bleeding, as well as 30-day mortality.[44] Another study analyzed risk factors for failure to control bleeding after EVL for AVB and found that portal vein thrombosis and Child-Pugh C status with active bleeding on endoscopy were independent predictors of failure of emergency EVL.[45] Similarly, active bleeding on endoscopy, hypovolemic shock at presentation, and previous history of EVL (scars leading to insufficient suction) were found to be independent risk factors for failure to control bleeding after EVL.[46] Thus, patients at risk for failure to control bleeding may be best served by the continuation of vasoconstrictors, though further studies are required in this small subgroup of patients.

The strength of the present analysis is that it included only RCTs. Also, we conducted both pair-wise as well as network meta-analyses to increase the robustness of the results. Despite this, there are limitations that should be kept in mind. First, there was a significant variation in the duration of vasoconstrictors administered, which forced us to define the duration of therapy as “short” vs. “standard.” Second, there were differences in the type of vasoconstrictor used in various studies, along with variation in the dosage and timing (Table 1). Although this is a concern, it should be noted that a previous meta-analysis reported no difference between the vasoconstrictors (terlipressin vs. somatostatin vs. octreotide) in terms of rebleeding after initial hemostasis for AVB.[47] Third, there was variation in the proportion of patients with Child-Pugh B or C status among studies. However, given that patients in all of the studies included were randomized, it is unlikely that there were imbalances within individual studies. Fourth, all of the studies included were from Asian medical centers, which, in theory, could limit generalizability to Western medical centers. It is notable, however, that a recent, small, multicenter U.S. study found no difference in rebleeding or mortality in trials of 24 vs. 72 hours of octreotide, suggesting that the data here are more widely generalizable [48]. Fifth, there was some heterogeneity in the definition of rebleeding, which could impact the validity of pooled estimates (Supplementary Table 1). Sixth, since the studies included in this meta-analysis did not report on hospital length of stay, we could not comment on this outcome. Nonetheless, we speculate that shorter treatment duration with vasoconstrictors in patients with AVB is likely to reduce hospital length of stay, consistent with a recent study that found that patients receiving 24 hours of octreotide therapy in AVB had shorter hospital length of stay than patients receiving 72 hours of octreotide therapy.[48] Seventh, many SUCRA rankings are based on low to moderate certainty of evidence, requiring cautious interpretation of the results. Lastly, a cost-effectiveness analysis could not be performed due to the unavailability of data regarding the same in the included studies.

CONCLUSION

In conclusion, the present network meta-analysis showed that rebleeding and mortality were similar for short or longer durations of vasoconstrictor therapy in patients with cirrhosis and AVB. The study further emphasized that there is a lack of quality evidence to support the prolonged use of vasoconstrictors after EVL. Given these data, clinical practice should evolve to discontinuing vasoconstrictors early after EVL, facilitating early discharge from the hospital and reducing the cost and burden on healthcare facilities. The most appropriate time for early discontinuation requires further study, and additional studies are required to identify the subset of patients at risk for failure to control bleeding who might benefit from the continuation of vasoconstrictors.

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TABLES

Table 1. Baseline characteristics and study populations of the included studies

Author (year)	Country	Drug and dose	Duration	No. of patients	Age, years	Sex (male %)	Alcoh Cirrhosi
Sung (1995)[20]	Hong Kong	**Octreotide** 100 μg bolus and 25 μg/h	0	47	56 (32-78)	76.6%	31.9
			120 hours	47	58 (17-77)	65.9%	36.2
Lee (1999)[21]	South Korea	**Octreotide** 100 μg bolus and 25 μg/h	0	30	50±10	93.3%	50
			120 hours	24	47±9	91.7%	62.5
Azam (2012)[22]	Pakistan	**Terlipressin** 2 mg bolus and 1 mg/6 h	24 hours	65	49.8±11.2	73.8%	6.2
			72 hours	65	49.7±12.1	75.4%	16.9
Lo (2013)[23]	Taiwan	**Somatostatin** 250-μg/h or **terlipressin** 1 mg/6 h	0	58	54.2±9.7	84.5%	38
			120 hours	60	52.5±14.4	81.7%	40
Chitapanarux (2015)[24]	Thailand	**Somatostatin** 250-μg IV bolus and 250-μg/h infusion	72 hours	50	45.1±12.4	92.0%	62.0
			120 hours	45	49.5±11.0	92.1%	42.2
Kumar (2015)[25]	India	**Somatostatin** 250-μg IV bolus and 250-μg/h infusion	0	30	42 (12-65)	80%	33
			120 hours	31	45 (26-73)	77%	39
Salim (2017)[26]	Pakistan	**Terlipressin** 2 mg bolus and 1 mg/6 h	12 hours	65	51.3±11.5	57%	-
			72 hours	25	53.6±11.1		-
Zaman (2019)[27]	Pakistan	**Terlipressin** 2 mg bolus and 1 mg/6 h	24 hours	50	55.2±5.6	58%	-
			72 hours	50			-
Poudel (2022)[28]	India	**Terlipressin** 2 mg bolus and 1 mg/4 h	0	25	48.3±12.0	80%	68
			48 hours	25	48.1±10.2	80%	68
			120 hours	24	48.0±11.6	87.5%	83.3
Vaishnav (2024)[29]	India	**Terlipressin** 2 mg/4 h for the first 24 hours and 1 mg/6 h	24 hours	75	44 (36–51)	85.1%	48.6
			72 hours	75	40 (37–48)	89.3%	42.7
Lo (2024)[30]	Taiwan	**Terlipressin** 2 mg bolus and 1 mg/6 h	48 hours	52	55.2±11.1	86.5%	42.3
			120 hours	48	58.9±12.3	81.2%	47.9

Table 2. Summary of findings table for the primary outcome comparing the duration of vasoconstrictors after endoscopic variceal ligation

Population: Patients with cirrhosis and acute variceal bleeding undergoing endoscopic variceal ligation **Intervention:** very short (≤ 24 hours) and short (> 24 and ≤ 72 hours) duration of vasoconstrictors **Comparator (reference):** standard duration (> 72 to 120 hours) of vasoconstrictors **Primary outcome:** Rebleeding within five days **Setting**: Inpatient							
Total studies: 11 RCTs **Total participants**: 1066	**Relative effect (95% CI)**	**Anticipated absolute effect**			**Certainty of evidence**	**Ranking (SUCRA)**	**Interpretation**
		***Without* intervention**	***With* intervention**	**Difference**			
Very short (≤ 24 hours) (5 RCTs; 363 patients)	1.36 (0.48-3.52)	75 per 1,000	102 per 1,000	27 more per 1,000 (39 fewer to 189 more)	●●○○ Low*¶	3 (36.8)	Probably inferior
Short (> 24 to ≤ 72 hours) (3 RCTs; 244 patients)	1.34 (0.42-4.54)	75 per 1,000	100 per 1,000	25 more per 1,000 (44 fewer to 265 more)	●●○○ Low*¶	2 (40.5)	Probably inferior

Standard (> 72 to 120 hours)	Reference comparator	Not estimable	Not estimable	Not estimable	Reference comparator	1 (72.6)	Reference comparator

Downgraded due to *Risk of bias ¶Imprecision

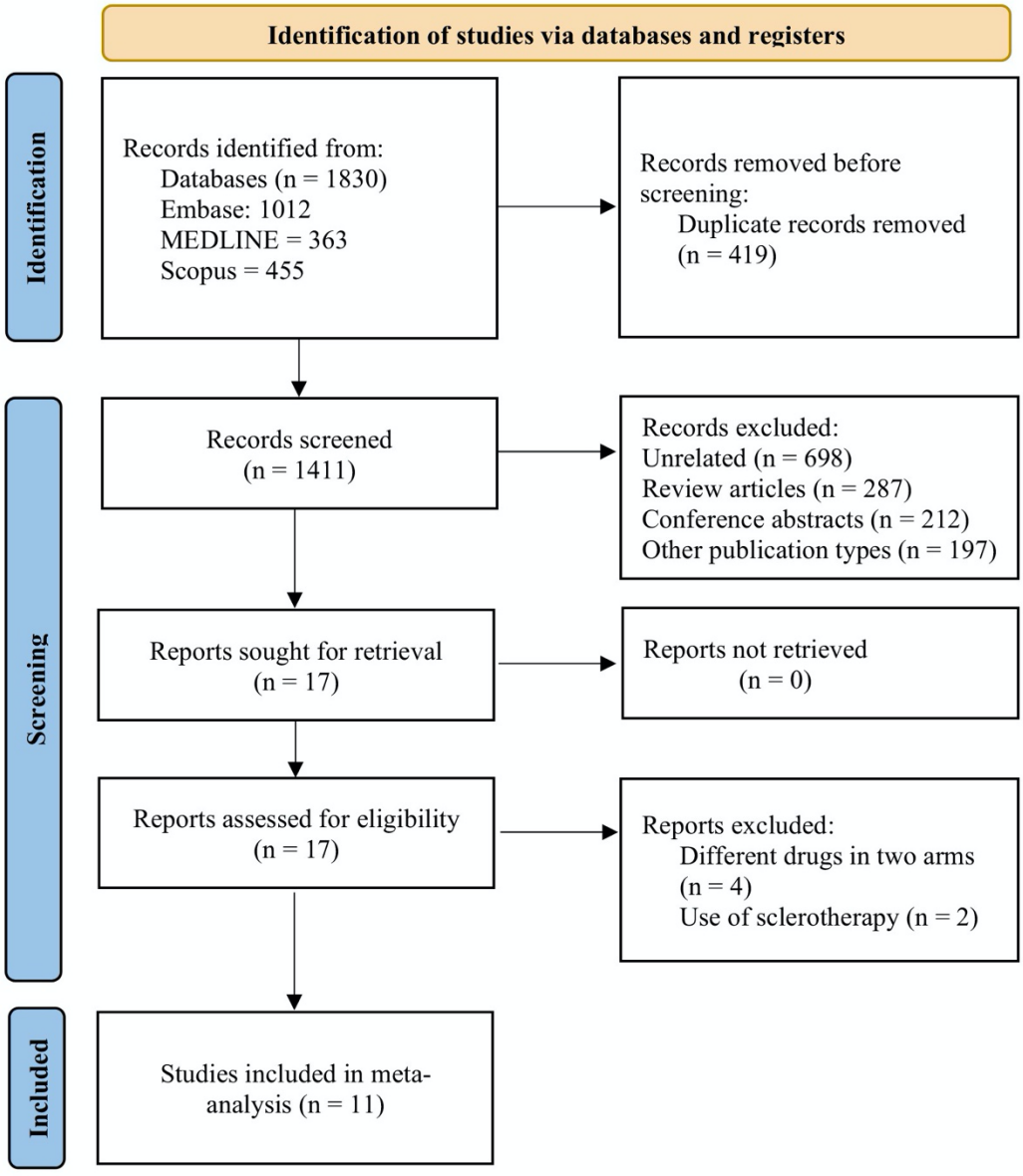

Figure 1. PRISMA flowchart for study identification, selection, and inclusion process. Shown is the process used to identify studies included in the analysis

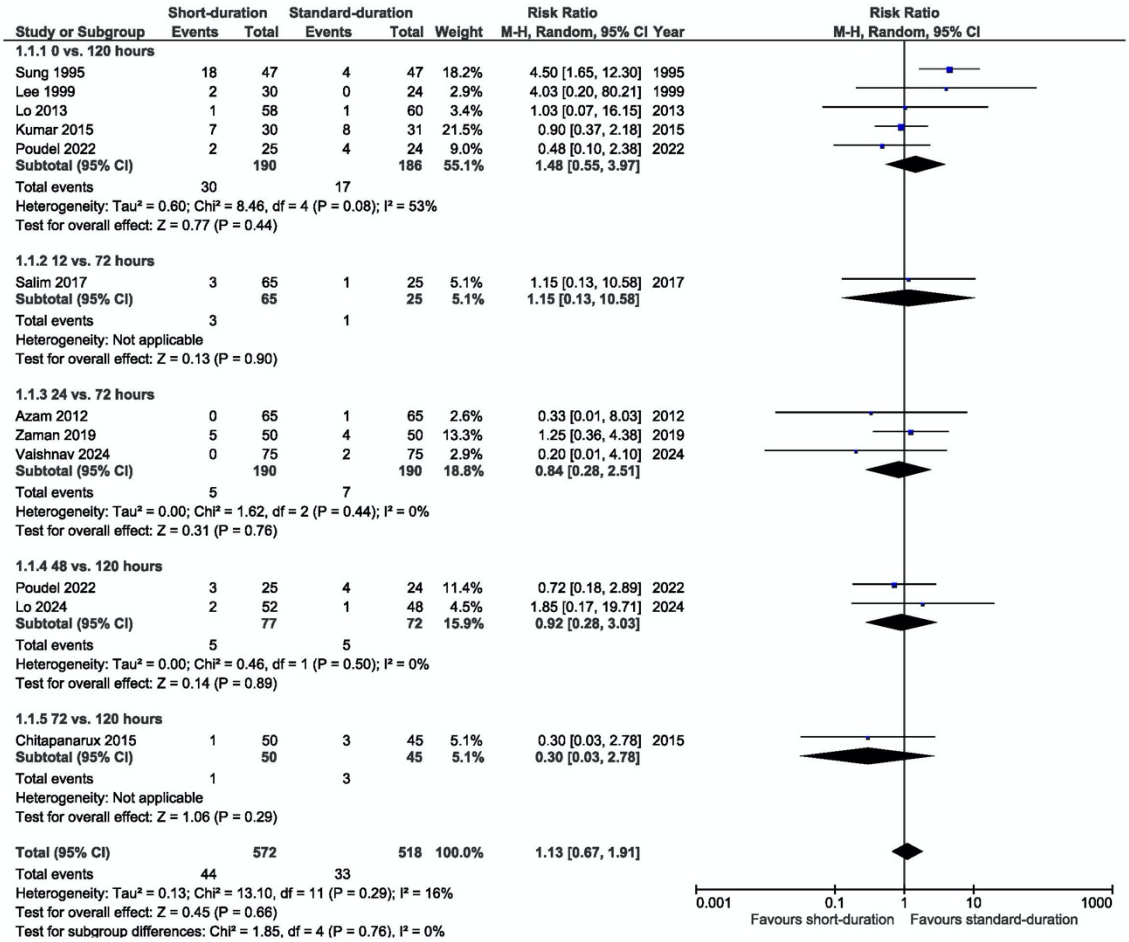

Figure 2. Forest plot comparing the risk of rebleeding at 5 days between short-duration vs. standard duration of vasoconstrictors with sub-group analysis

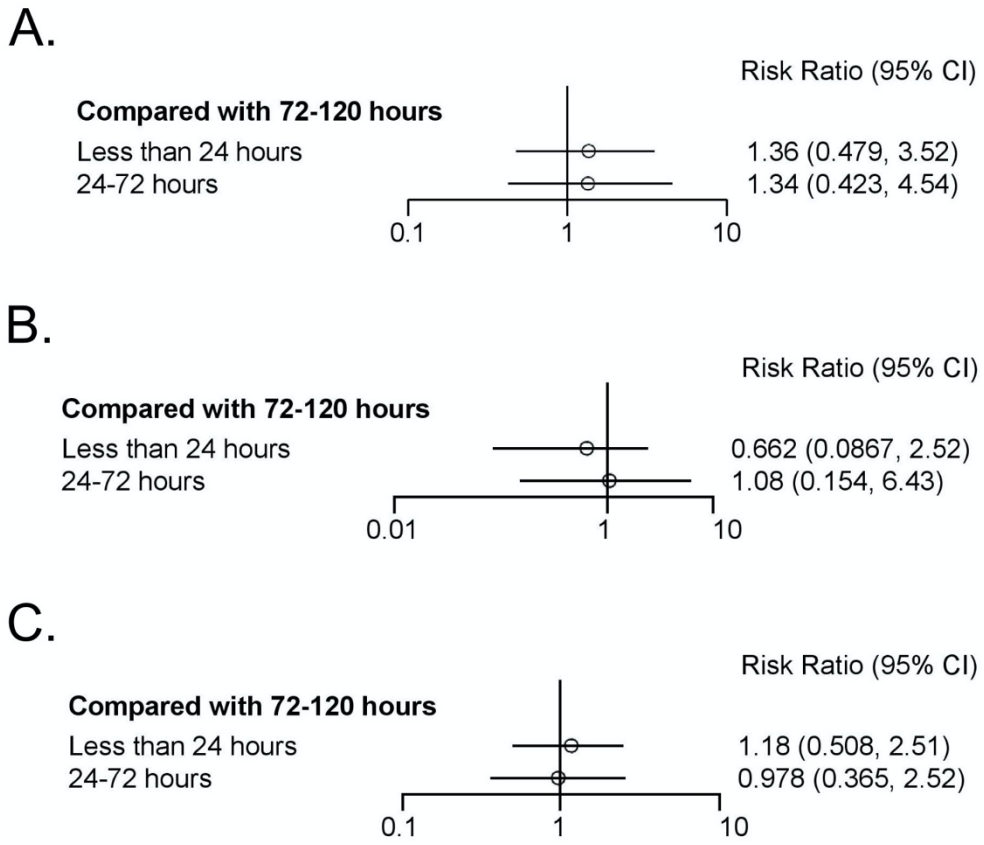

Figure 3. Bayesian Forest plots depicting the risk of different outcomes. (A) rebleeding, (B) mortality at 5 days, and (C) mortality at 30 days in different groups is shown [the duration of vasoconstrictor therapy is as follows: group 1 (≤ 24 hours) and group 2 (> 24 and ≤ 72 hours)] and control group [group 3 (> 72 to 120 hours)]

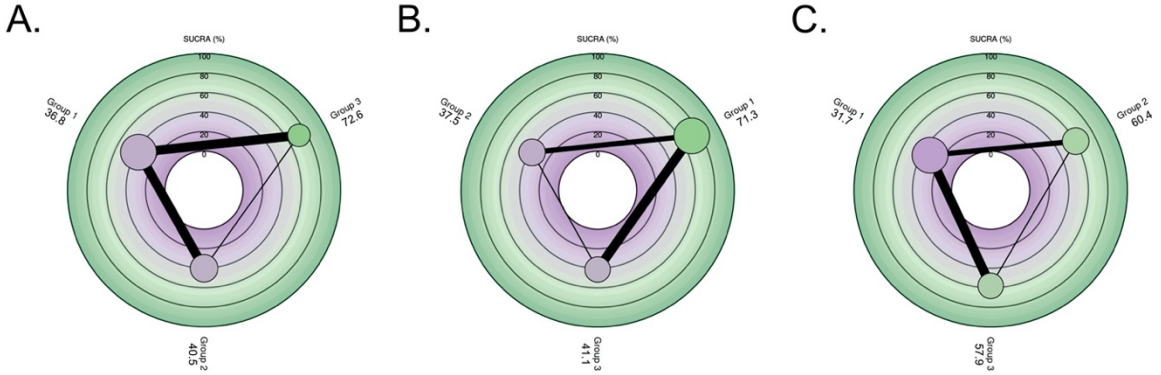

Figure 4. Radial surface under the cumulative ranking analysis (SUCRA) and network plots. Shown are plots for (A) rebleeding, (B) mortality at 5 days, and (C) mortality at 30 days. The number beside the suction techniques indicates SUCRA values. The duration of vasoconstrictor therapy is as follows: Group 1 (≤ 24 hours), group 2 (>

24 and ≤ 72 hours), and group 3 (> 72 to 120 hours). (The node size is in relation to the number of participants analyzed, while the lines connecting nodes indicate the network plot. The treatments are ranked radially based on their ranking score varying from 0-100.)