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Cisternal and intraventricular irrigation in subarachnoid and intraventricular haemorrhage

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ABSTRACT

Background Subarachnoid haemorrhage (SAH) and intraventricular haemorrhage (IVH) are associated with poor patient outcomes. Intraventricular fibrinolysis is effective in clearing IVH and improving patient survival and neurological outcome. By similar rationale, cisternal irrigation has been proposed as a potential method to accelerate haematoma clearance in SAH. We aimed to provide a comprehensive review and meta-analysis evaluating the effect of intraventricular and cisternal irrigation on clinical outcomes in patients with SAH and IVH.

Methods The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed preparing this systematic review and study selection was performed by multiple investigators. We extracted ORs from the individual studies and aggregated these using a random effects model. The quality of evidence was evaluated using Grading of Recommendations, Assessment, Development and Evaluations assessment and ROBINS-I or RoB-2.

Results 24 articles were included. In SAH, we found that cisternal irrigation with fibrinolytic agents was associated with reduced mortality (OR: 0.68, 95% CI 0.46 to 1.00), higher probability of favourable functional outcome (OR: 1.80, 95% CI 1.30 to 2.51), and reduced risks of DCI (OR: 0.28, 95% CI 0.18 to 0.42) and cerebral vasospasm (OR: 0.28, 95% CI 0.18 to 0.42), compared with conventional therapy. Cisternal irrigation with vasodilatory agents was associated with lower mortality (OR: 0.32, 95% CI 0.13 to 0.79) and reduced risk of cerebral vasospasm (OR: 0.37, 95% CI 0.17 to 0.79). The evidence for irrigation therapy of IVH was sparse and insufficient to show any significant effect.

Conclusion In this study, we found that cisternal irrigation could improve the prognosis in patients with SAH compared with conventional therapy. There is no evidence to support cisternal irrigation treatment of IVH.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Subarachnoid haemorrhage (SAH) and intraventricular haemorrhage are associated with poor patient outcomes, however, cisternal and intraventricular irrigation have been proposed to accelerate haematoma clearance and improve patient outcomes.

WHAT THIS STUDY ADDS

⇒ We found that in patients with SAH, cisternal irrigation with fibrinolytic agents was associated with reduced mortality, improved functional outcome, and lower risk of delayed cerebral ischaemia and vasospasms, compared with conventional therapy. Cisternal irrigation with vasodilatory agents was associated with lower mortality and decreased risk of cerebral vasospasms.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Fibrinolytic and vasodilatory cisternal irrigation may be warranted in the treatment of SAH. Larger prospective studies are needed to verify these results.

INTRODUCTION

Aneurysmal subarachnoid haemorrhage (SAH) and intraventricular haemorrhage (IVH) are catastrophic cerebrovascular events associated with high mortality and severe morbidity.[1–3] Direct exposure of cerebral vessels to the neuroinflammatory effects of haemoglobin degradation products is considered to play a major role in the pathogenesis of cerebral vasospasm and delayed cerebral ischaemia (DCI), being a complicating cause of morbidity in approximately one in four SAH survivors.[4] Likewise, in IVH, haematoma formation and blood degradation products are associated with secondary neurological injuries due to obstructive hydrocephalus, mass effect and elevated intracranial pressure.[2] Conventional treatment typically includes supportive care and cerebrospinal fluid drainage to decompress the intracranial space and facilitate passive haematoma evacuation.[1 5]

A recent meta-analysis documented significant benefits from accelerated haematoma clearance using intraventricular fibrinolysis therapy, showing significant improvements in survival rate and functional outcome,[6] compared with passive drainage in patients with IVH. Based on a similar rationale, intraventricular and cisternal irrigation using

physiological saline combined with fibrinolytic or vasoactive agents, has been proposed as a potential method to further accelerate haematoma and toxin clearance and thereby improve outcomes in both SAH and IVH.

In this study, we provide a systematic review and meta-analysis of the current literature on intraventricular or cisternal irrigation for SAH and IVH compared with conventional therapy. We evaluate the efficacy of both fibrinolytic and vasodilatory cisternal irrigation treatments with respect to clinical endpoints; including mortality, functional outcome, DCI and cerebral vasospasm.

METHODS

Search strategy

The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses criteria[7] (online supplemental tables S1 and S2). We searched the PubMed, Embase and Cochrane databases for full-text articles published in English until 11 October 2023, using the search strategy: ("lavage" or "irrigation" or "IRRAflow") AND ("hemorrhage" or "bleeding" or "hemorrhagic stroke") AND ("intraventricular" or "IVH" or "SAH" or "subarachnoid" or "intracerebral" or "ICH") NOT ("subdural" or "CSDH" or "SPECT" or "chronic subdural" or "abscess" or "pediatric" or "scalp" or "liver" or "infants" or "children" or "child" or "neonatal" or "natal" or "preterm") AND intracranial hemorrhages [MeSH Terms], without filters or limits. The search was repeated without MeSH Terms, limited to studies published within 1 year to include the newest research. If the full text was inaccessible, the article was requested from the corresponding author or publisher.

Eligibility criteria and study selection

We included studies that evaluated the effect of cisternal or intraventricular irrigation therapy in adult patients (>18 years) with either SAH or IVH (primary or secondary). Studies were excluded if they did not report clinical outcomes (mortality, functional outcome, DCI or cerebral vasospasm) or technical details of the irrigation intervention, such as irrigation rate, duration, saline solution and catheter placement. We also excluded in vitro studies, animal studies, reviews, meta-analyses and studies that were unavailable as full text. If the same cohort was included in multiple reports, the most recent eligible report was included. Articles were managed using Covidence.[8] Duplicates were removed. All articles were initially assessed for eligibility by one investigator (MGK) based on abstract and title. The selected articles were then full text screened for eligibility by two investigators (MGK, MH). Disagreements were resolved by the principal investigator (ARK).

Outcomes and data extraction

We assessed the clinical outcomes mortality, functional outcome, DCI and cerebral vasospasm. All outcomes were dichotomised. A favourable functional outcome was defined as a modified Rankin Scale score of 0–2 (ie, independent in daily living), or a Glasgow Outcome Scale score of either 4–5 or 'good recovery' or 'moderate disability'. DCI was defined as the appearance of new ischaemic lesions detected on CT or MRI at least 48 hours after initial treatment. As cerebral vasospasm is an angiographic phenomenon that may or may not manifest clinically but is predictive of DCI, cerebral vasospasm was defined as either angiographically verified narrowing of cerebral arteries or an increase in mean flow velocity ≥160 cm/s on transcranial Doppler. If neither of these measures were reported, symptomatic vasospasm (neurological deterioration without other explanation) was considered a valid measure for cerebral vasospasm. Data were extracted by one investigator (ANRL).

Intervention subgroups

To increase homogeneity, the included studies were grouped by diagnosis (SAH or IVH). In studies investigating SAH, the study populations were further grouped into four categories based on the tested intervention: (1) conventional treatment, covering medical management, standard intensive care and in some cases external ventricular drain (see online supplemental tables S3 and S4 for details); (2) simple cisternal irrigation, with no active substances; (3) fibrinolytic cisternal irrigation using either tissue plasminogen activator or urokinase; (4) vasodilatory cisternal irrigation using calcium channel blockers, corticosteroids, phosphodiesterase inhibitors or magnesium sulfate. Furthermore, we included a meta-analysis of all studies comparing either fibrinolytic irrigation, vasodilatory irrigation or simple irrigation to conventional therapy, to assess the overall effect of cisternal irrigation.

Most studies investigated a combination of vasodilatory and fibrinolytic irrigation, thus complicating the grouping of the studies. To accommodate this, the analysis of fibrinolytic irrigation includes both studies using only fibrinolytic irrigation, and studies using fibrinolytic irrigation as the primary intervention and vasodilatory irrigation as a rescue therapy in patients showing signs of cerebral vasospasm. The analysis of vasodilatory irrigation includes both studies using only vasodilatory irrigation and studies using vasodilatory irrigation and fibrinolytic irrigation simultaneously as preventive therapy.

Quality assessment

The evidence quality was assessed using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.[9] Detailed GRADE guidance was used to assess the overall risk of bias, inconsistency, imprecision, indirectness and publication bias of the pooled estimates and reported in a summary of findings table. Each individual study was assessed for risk of bias with either ROBINS-I for observational studies[10] or RoB-2 for randomised

studies.[11] Publication bias was investigated by means of a visual inspection of the funnel plots for each outcome (online supplemental figures S1–S3).

Statistical analysis

The meta-analysis was stratified by patient diagnosis (IVH or SAH) and the type of irrigation investigated. Treatment effects were represented by ORs and pooled using a Mantel-Haenszel random-effects model. Results were reported as forest plots with 95% CIs. In addition, we pooled prevalence proportions of each outcome across all studies, including studies with no or non-comparable control groups, to further evaluate the effect between intervention groups. The statistical significance of differences in prevalence between groups was determined based on the 95% CIs. All analyses were conducted using RevMan V.5.4 software.[12]

RESULTS

Study selection and quality assessment

We identified 135 studies, and 4 duplicates were removed. The remaining 131 studies were screened by title and abstract and 60 studies were selected for full-text review. 22 articles were excluded due to the unavailability of the full-text study. In total, 24 studies were included in the review and meta-analysis (figure 1), including 7 randomised controlled trials, 14 cohort studies, 2 case reports and 1 case–control study. The included articles evaluated a variety of irrigation interventions for both SAH and IVH with differences in irrigation solutions, catheter placements, irrigation durations and most importantly the

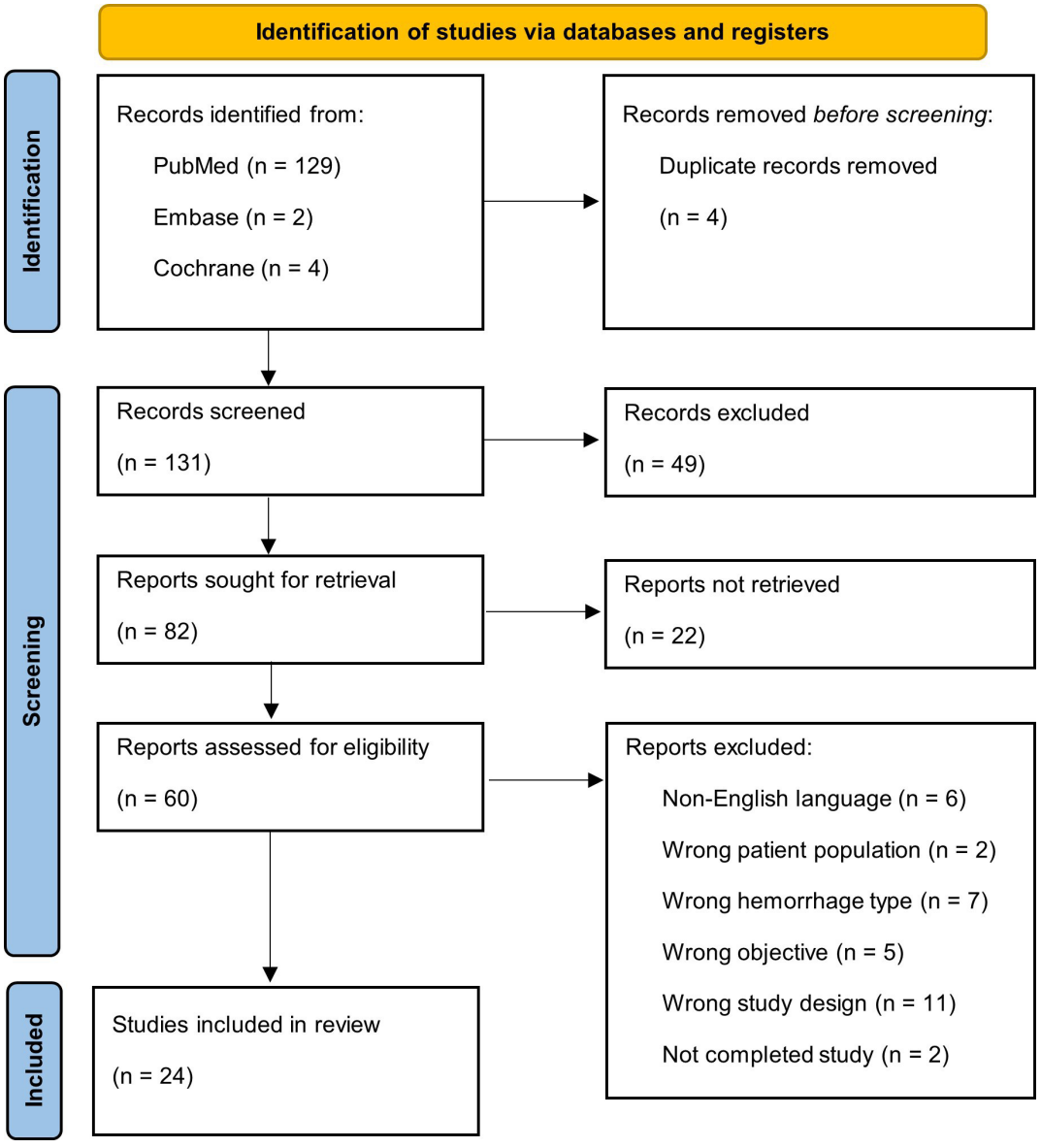


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart showing the study selection process.

presence of active substances in the irrigation fluid (see online supplemental table S4 for details). The GRADE summary findings for selected outcomes and interventions are shown in table 1 and online supplemental table S5 and the risk of bias of the included studies can be found in online supplemental tables S6 and S7. Based on visual inspection of funnel plots, the risk of publication bias was low for all comparisons (online supplemental figures S5–S7).

Irrigation therapy in SAH

A total of 22 studies evaluated irrigation treatments for SAH, including intraoperative and postoperative methods. Intraoperative irrigation (5 of 22 studies) was conducted to blood collections in the subarachnoid space through the open cisternal access after clipping the aneurysm. Irrigation duration was approximately 30 min. Methods for postoperative irrigation (16 of 22 studies) included continuous saline infusion into the cerebrospinal fluid compartment through a ventricular or cisternal catheter and simultaneous drainage through a second ventricular or cisternal catheter. The duration of irrigation and irrigation rate were reported with substantial inconsistency across studies. The duration ranged between 2 and 18 days and the irrigation rate ranged between 20 and 180 mL/hour for postoperative irrigation. A detailed description of intervention methods can be found in online supplemental table S4.

Overall cisternal irrigation in SAH

The mean mortality rate in patients treated with conventional therapy was 0.18 (95% CI 0.14 to 0.23)[13–22] (online supplemental figure S4). Our meta-analysis showed a significant reduction in mortality in patients treated with any kind of irrigation therapy versus conventional therapy (OR: 0.65, 95% CI 0.45 to 0.94, p=0.02, GRADE: high) (figure 2A, table 1, online supplemental table S5) when comparing 10 studies.[13–22]

In seven studies, the mean proportion of patients with favourable outcome after SAH was 0.46 (95% CI 0.32 to 0.61)[13 16 18–22] after conventional therapy (online supplemental figure S5). Our meta-analysis showed significantly increased odds for a favourable outcome in patients treated with irrigation of any kind versus conventional therapy (OR: 1.83, 95% CI 1.35 to 2.48, p<0.001, GRADE: high) (figure 2B, table 1, online supplemental table S5).[13 16 18–22] The mean rate of DCI following SAH in patients treated with conventional therapy was 0.31 (95% CI 0.22 to 0.39)[14 15 17 19–22] (online supplemental figure S6). Our meta-analysis showed a significantly reduced rate of DCI in patients treated with any cisternal irrigation versus conventional therapy (OR: 0.33, 95% CI 0.19 to 0.58, p<0.001, GRADE: low) (figure 2C, table 1, online supplemental table S5).[14 15 17 19–22]

The mean rate of cerebral vasospasm following SAH in patients treated with conventional therapy was 0.47 (95% CI 0.29 to 0.66)[15 17–20 22] (online supplemental figure S7). Our meta-analysis showed a significantly reduced rate of cerebral vasospasm in patients treated with any cisternal irrigation versus conventional therapy (OR: 0.32, 95% CI 0.20 to 0.51, p<0.001, GRADE: low) (figure 2D, table 1, online supplemental table S5).[15 17–20 22]

Only two studies included simple irrigation treatment.[17 23] Mean prevalences for all outcomes can be found in online supplemental figures S4–S7.

Fibrinolytic cisternal irrigation in SAH

The mean mortality rate was significantly lower in patients treated with fibrinolytic irrigation (0.09, 95% CI 0.04 to 0.13)[14–16 18–22 24 25] compared with conventional treatment (0.18, 95% CI 0.14 to 0.23)[13–22] (online supplemental figure S4). Our meta-analysis showed significantly reduced mortality rate in patients treated with fibrinolytic irrigation versus conventional therapy (OR: 0.68, 95% CI 0.46 to 1.00, p=0.05, GRADE: high) (figure 3A, table 1, online supplemental table S5).[14–16 18–22]

The mean rate of favourable outcome was significantly higher in patients treated with fibrinolytic irrigation (0.75, 95% CI 0.69 to 0.81)[16 18–22 24–29] compared with conventional treatment (0.46, 95% CI 0.32 to 0.61)[13 16 18–22] (online supplemental figure S5). Our meta-analysis showed significantly higher odds for favourable outcome for fibrinolytic irrigation versus conventional treatment (OR: 1.80, 95% CI 1.30 to 2.51, p<0.001, GRADE: high) (figure 3B, table 1, online supplemental table S5).[16 18–22]

The mean rate of DCI was significantly lower in patients with SAH treated with fibrinolytic irrigation (0.13, 95% CI 0.07 to 0.19)[19–22 24 27 30 31] than in patients treated with conventional treatment (0.31, 95% CI 0.22 to 0.39)[14 15 17 19–22] (online supplemental figure S6). Our meta-analysis showed significantly reduced risk of DCI in patients with SAH treated with fibrinolytic irrigation versus conventional therapy (OR: 0.28, 95% CI 0.18 to 0.42, p<0.001, GRADE: high) (figure 3C, table 1, online supplemental table S5).[14 15 19–22]

The mean rate of cerebral vasospasm was significantly lower in patients treated with fibrinolytic irrigation (0.21, 95% CI 0.14 to 0.28)[15 18–20 22 24–27 29 30] than in patients treated with conventional treatment (0.47, 95% CI 0.29 to 0.66)[15 17–20 22] (online supplemental figure S7). Our meta-analysis showed significantly lower risk of cerebral vasospasm in patients treated with fibrinolytic irrigation versus conventional therapy (OR: 0.28, 95% CI 0.18 to 0.42, p<0.001, GRADE: high) (figure 3D, table 1, online supplemental table S5).[15 18–20 22]

Vasodilatory cisternal irrigation in SAH

The mean mortality in patients treated with vasodilatory irrigation was 0.05 (95% CI 0.01 to 0.08).[13 18 23 24 32 33] This was significantly lower than for conventional treatment, however, there was no statistically significant difference between patients treated with fibrinolytic irrigation and vasodilatory irrigation (online supplemental figure S4). Comparing four studies, we observed a significantly lower mortality rate in patients treated with vasodilatory

Table 1 Summary of findings and GRADE assessment

Cisternal irrigation overall compared with conventional treatment for subarachnoid haemorrhage[13–22]					
Outcomes	**Participants (studies) (n)**	**Certainty of the evidence (GRADE)**	**Relative effect OR (95% CI)**	**Anticipated absolute effects**	
				Risk with conventional treatment per 1000	**Risk difference with combined irrigation per 1000 (95% CI) ref. Conventional**
Favourable outcome	1113 (2 RCTs, 5 observational)	⊕⊕⊕⊕ High	1.83 (1.35 to 2.48)	523	144 (74 to 208)
Mortality	1858 (2 RCTs, 8 observational)	⊕⊕⊕⊕ High	0.65 (0.45 to 0.94)	189	–57 (–94 to –9)
DCI	1237 (1 RCT, 6 observational)	⊕⊕◯◯ Low	0.33 (0.19 to 0.58)	251	–152 (–191 to –88)
Cerebral vasospasm	1075 (1 RCT, 5 observational)	⊕⊕◯◯ Low	0.32 (0.20 to 0.51)	403	–225 (–284 to –147)
Fibrinolytic cisternal irrigation vs conventional treatment for subarachnoid haemorrhage[14–16 18–22]					
Outcomes	**Participants (studies) (n)**	**Certainty of the evidence (GRADE)**	**Relative effect OR (95% CI)**	**Anticipated absolute effects**	
				Risk with conventional treatment per 1000	**Risk difference with fibrinolytic irrigation per 1000 (95% CI) ref. Conventional**
Favourable outcome	1031 (2 RCTs, 4 observational)	⊕⊕⊕⊕ High	1.80 (1.30 to 2.51)	536	139 (64 to 207)
Mortality	1715 (2 RCTs, 6 observational)	⊕⊕⊕⊕ High	0.68 (0.46 to 1.00)	182	–51 (–89 to 0)
DCI	1176 (1 RCT, 5 observational)	⊕⊕⊕⊕ High	0.28 (0.18 to 0.42)	248	–163 (–192 to –126)
Cerebral vasospasm	974 (1 RCT, 4 observational)	⊕⊕⊕⊕ High	0.28 (0.18 to 0.42)	381	–234 (–281 to –175)
Vasodilatory cisternal irrigation vs no vasodilatory cisternal irrigation for subarachnoid haemorrhage13 18 23 24					
Outcomes	**Participants (studies) (n)**	**Certainty of the evidence (GRADE)**	**Relative effect OR (95% CI)**	**Anticipated absolute effects**	
				Risk with no vasodilatory irrigation per 1000	**Risk difference with vasodilatory irrigation per 1000 (95% CI) ref. No vasodilatory irrigation**
Favourable outcome	317 (3 RCTs, 1 observational)	⊕⊕◯◯ Low	2.03 (0.97 to 4.26)	651	140 (–7 to 237)

Continued

Table 1 Continued

Cisternal irrigation overall compared with conventional treatment for subarachnoid haemorrhage[13–22]					
Mortality	317 (3 RCTs, 1 observational)	⊕⊕⊕◯ Moderate	0.32 (0.13 to 0.79)	171	−109 (−145 to −31)
DCI	70 (1 RCT)	⊕◯◯◯ Very low	0.48 (0.14 to 1.62)	257	−115 (−211 to 102)
Cerebral vasospasm	275 (3 RCTs)	⊕◯◯◯ Very low	0.37 (0.17 to 0.79)	338	−179 (−258 to −51)

DCI, delayed cerebral ischaemia; GRADE, Grading of Recommendations, Assessment, Development and Evaluations; RCT, randomised controlled trial.

irrigation (OR: 0.32, 95% CI 0.13 to 0.79, p=0.01, GRADE: moderate) (figure 4A, table 1, online supplemental table S5).[13 18 23 24]

The mean rate of favourable outcome following SAH in vasodilatory irrigation was 0.70 (95% CI 0.60 to 0.79).[13 18 23 24 32–34] This was significantly higher than for conventional treatment; however, there was no statistically significant difference between patients treated with fibrinolytic irrigation and vasodilatory irrigation (online supplemental figure S5). Four studies evaluated the rate of favourable outcome in patients with SAH treated with vasodilatory irrigation. We found no statistically significant evidence in our meta-analysis that vasodilatory irrigation treatment was associated with increased odds for favourable functional outcome in patients with SAH (OR: 2.03, 95% CI 0.97 to 4.26, p=0.06, GRADE: low) (figure 4B, table 1, online supplemental table S5).[13 18 23 24]

The mean rate of DCI following SAH in vasodilatory irrigation was 0.25 (95% CI 0.09 to 0.41).[24 31–33] This was significantly higher than for fibrinolytic irrigation; however, there was no statistically significant difference between vasodilatory irrigation and conventional treatment (online supplemental figure S6). One study evaluated the rate of DCI in patients treated with vasodilatory irrigation versus fibrinolysis and found no statistically significant effect on the risk of DCI in patients with SAH (OR: 0.48, 95%CI 0.14 to 1.62, p=0.24, GRADE: very low) (table 1, online supplemental table S5).[24]

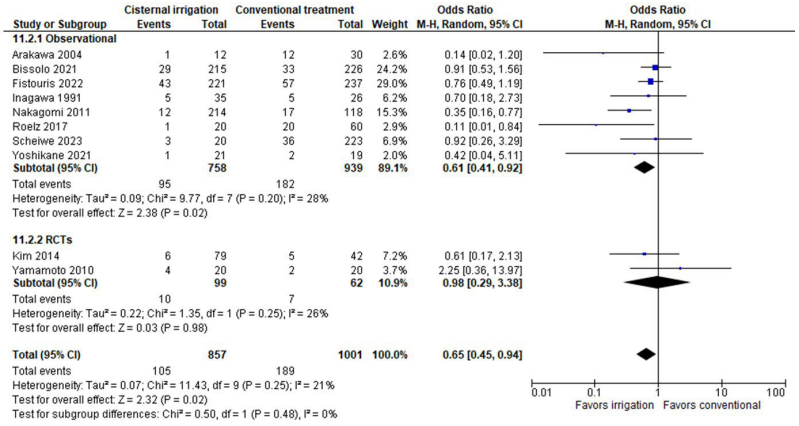
The mean rate of cerebral vasospasm was significantly lower in patients treated with vasodilatory irrigation (0.15, 95% CI 0.09 to 0.21)[13 18 23 24] than in patients treated with conventional treatment; however, there was no statistically significant difference between fibrinolytic irrigation and vasodilatory irrigation (online supplemental figure S7). Three studies evaluated the effect of vasodilatory irrigation versus no vasodilatory irrigation on the rate of cerebral vasospasm in SAH patients. Our meta-analysis showed a significant reduction in the rate of cerebral vasospasm in patients treated with vasodilatory irrigation (OR: 0.37, 95% CI 0.17 to 0.79, p=0.01, GRADE: very low) (figure 4D, table 1, online supplemental table S5).[18 23 24]

Irrigation therapy in IVH

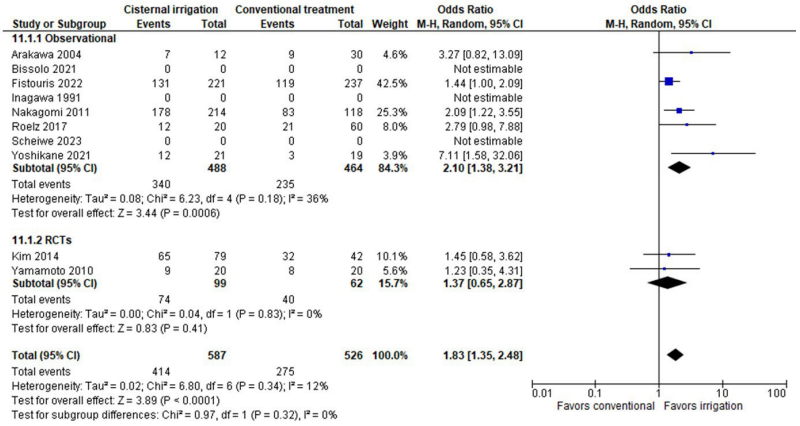
For IVH, only two studies evaluated simple irrigation treatment.

One RCT with 81 patients suffering from IVH, evaluated cisternal irrigation with saline and gentamicin during surgery versus trepanation drainage and found a significantly increased rate of favourable outcome (ADL=good/excellent) in patients treated with cisternal irrigation at 3 months after surgery (92.1% vs 82.5%, p<0.01).[35] Another RCT with 21 patients[36] evaluated the effect of intraventricular irrigation using the irrigation system IRRAflow,[37] using a dual-lumen catheter for automatised fluid exchange based on periodic irrigation and aspiration.[38] The study was terminated early, due to safety concerns,[36] as they found that the intervention group had a higher rate of catheter occlusion

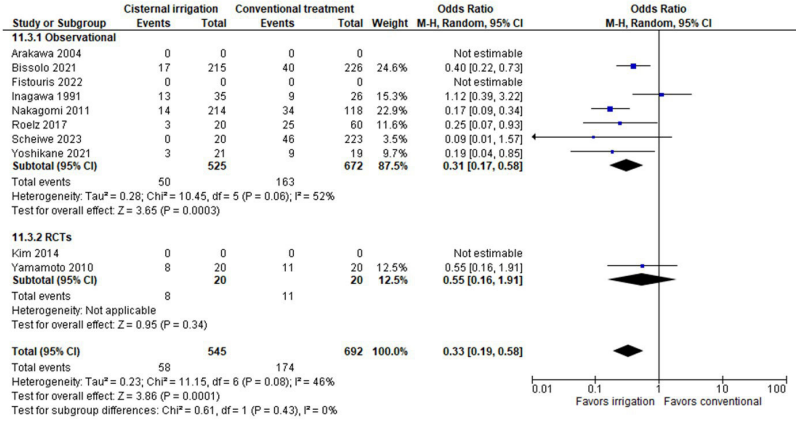
A – Mortality



B – Functional Outcome



C – Delayed Cerebral Ischemia



D – Cerebral Vasospasm

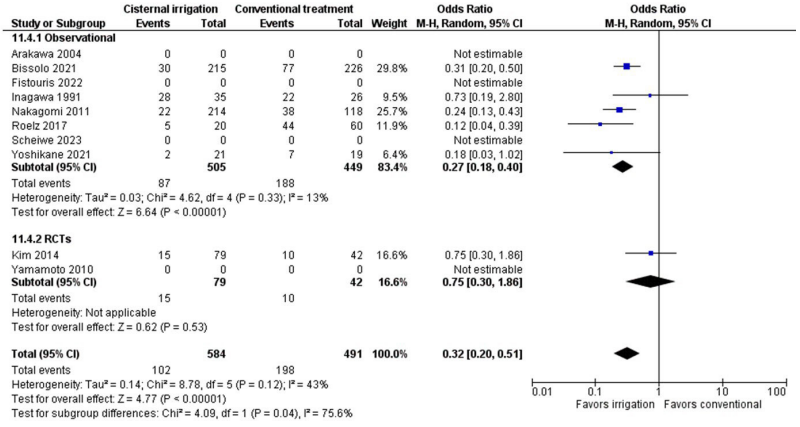
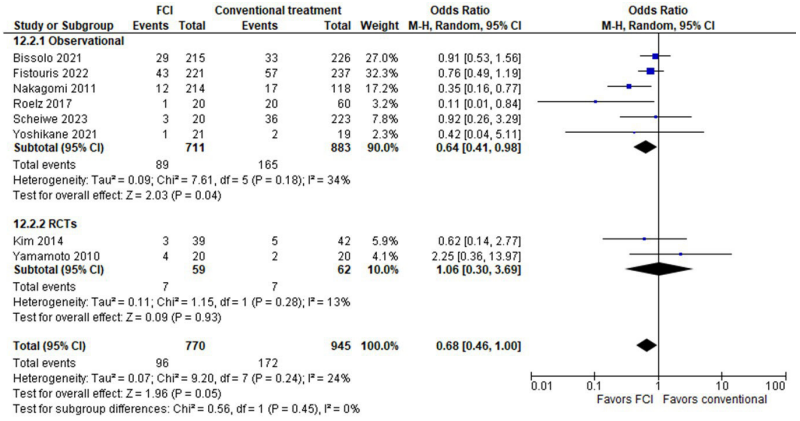
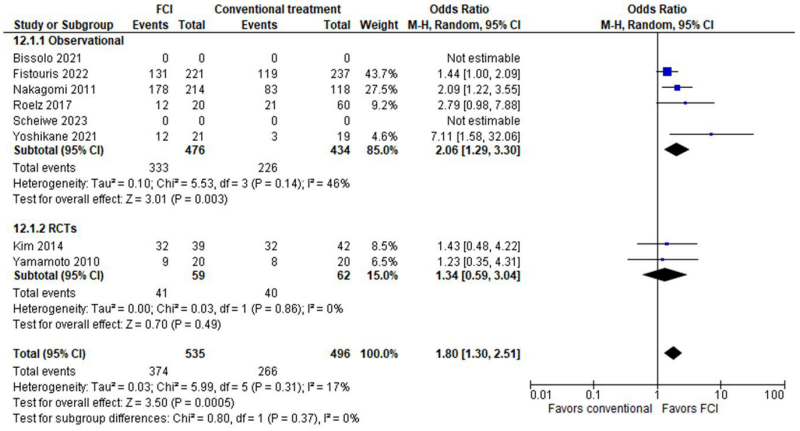


Figure 2 Pooled ORs comparing combined cisternal irrigation to conventional therapy. (A) Mortality, (B) functional outcome, (C) delayed cerebral ischaemia and (D) cerebral vasospasm. RCT, randomised controlled trial.

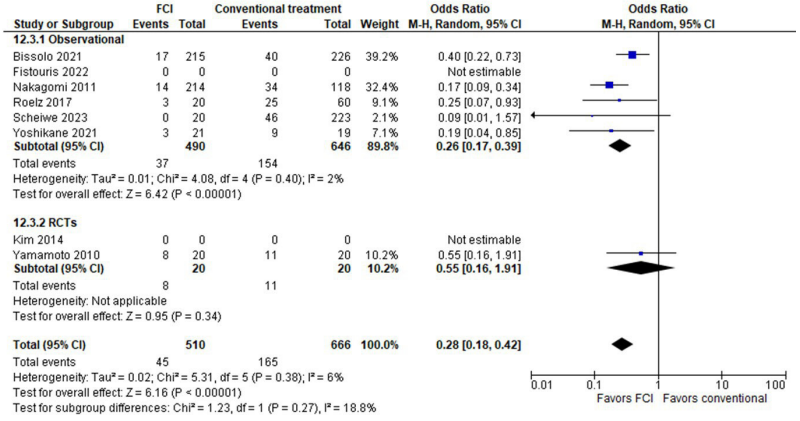
A – Mortality



B – Functional Outcome



C – Delayed Cerebral ischemia



D - Cerebral Vasospasm

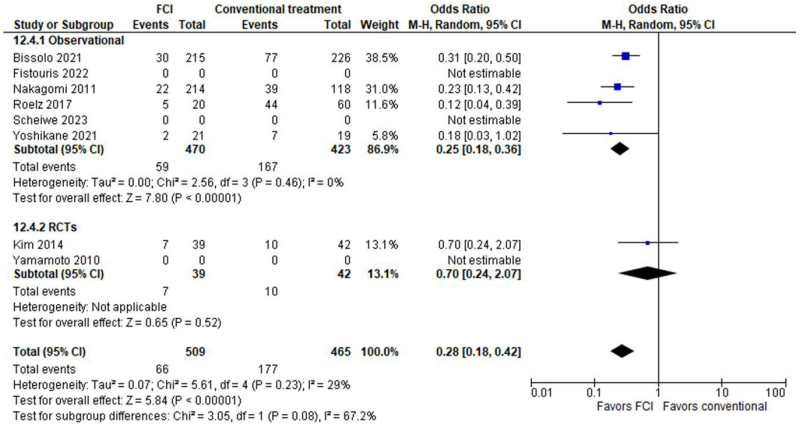


Figure 3 Pooled ORs comparing fibrinolytic cisternal irrigation to conventional therapy. (A) Mortality, (B) functional outcome, (C) delayed cerebral ischaemia and (D) cerebral vasospasm. FCI, fibrinolytic cisternal irrigation; RCT, randomised controlled trial.

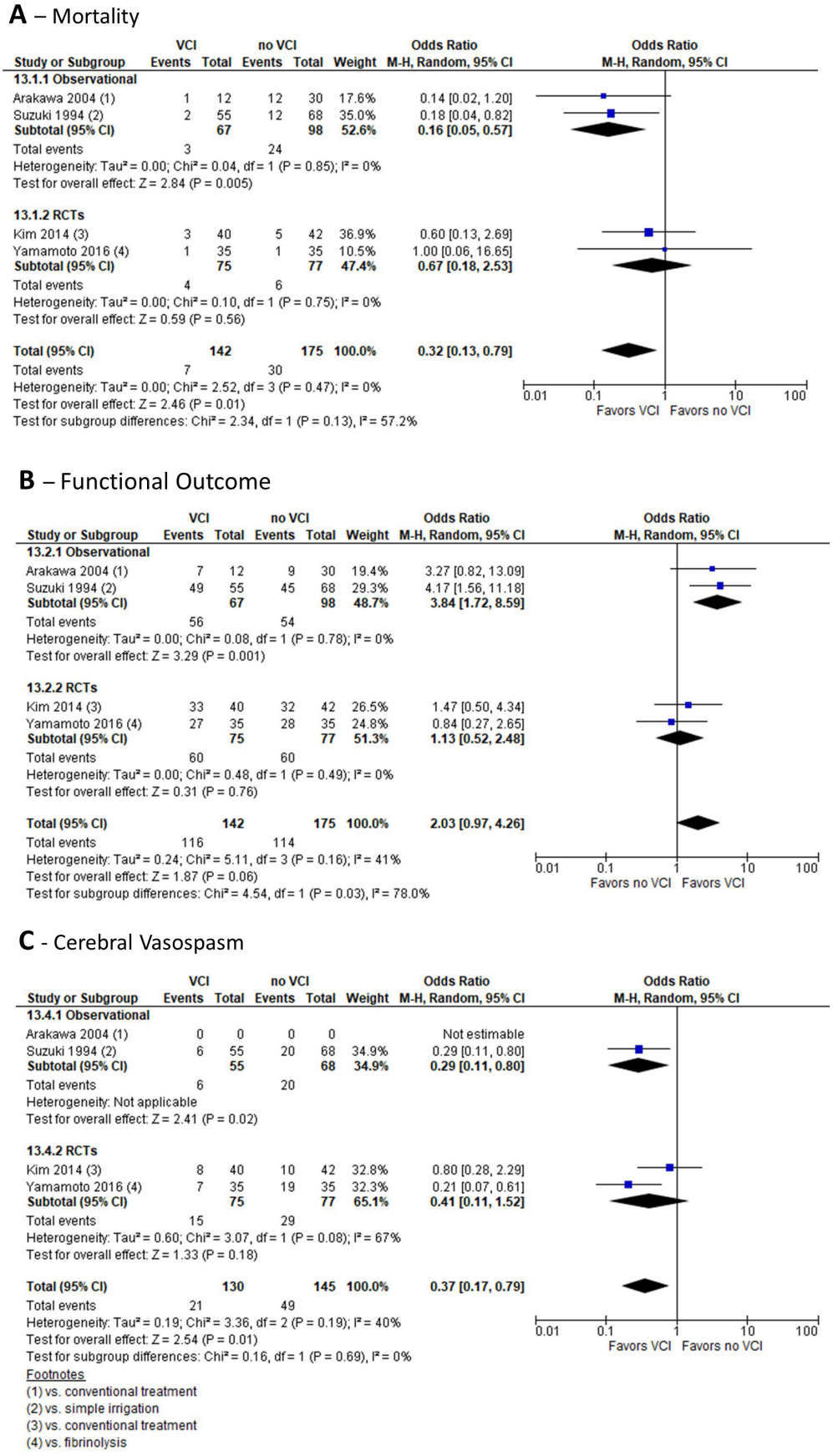


Figure 4 Pooled ORs comparing vasodilatory cisternal irrigation to treatment without vasodilatory cisternal irrigation. (A) Mortality, (B) functional outcome, (C) cerebral vasospasm. RCT, randomised controlled trial; VCI, vasodilatory cisternal irrigation.

(HR: 4.4, 95% CI 0.6 to 31.2, p=0.14). They did not find any statistically significant difference in mortality or functional outcome between the intervention and control group.

DISCUSSION

In this review and meta-analysis, we evaluated the existing evidence on cisternal irrigation treatment for SAH and IVH. Concerning irrigation treatment in SAH, we found that fibrinolytic irrigation significantly reduced the mortality rate and improved functional outcome compared with conventional treatment. These findings could be mediated by the reduced risks of radiographic DCI and cerebral vasospasm. Our meta-analysis showed that vasodilatory irrigation also resulted in a significant reduction in mortality and a reduced risk of cerebral vasospasm in SAH patients, compared with no vasodilatory irrigation. However, the analyses did not support improvements in functional outcome or the rate of DCI in patients for this intervention. The evidence on irrigation in patients with IVH was very limited and one study raised safety concerns with the methodology, although the majority of adverse events were related to design features of the irrigation technology.[36] While another study pointed to beneficial outcomes in IVH patients treated with irrigation, it is important to consider the safety of the methods and technology used and thus the potential of the treatment remains unclarified.

When comparing any kind of cisternal irrigation to conventional therapy in SAH, our meta-analysis showed significant positive results for all outcomes. However, due to the sparse and heterogenic evidence of both vasodilatory irrigation and irrigation with only electrolyte solution, these results may be driven primarily by the effects of fibrinolytic irrigation.

Obstructive hydrocephalus, DCI and cerebral vasospasm are major contributors to the high morbidity and mortality in patients with SAH and IVH and are caused in part by blood coagulation and blood degradation products.[4] Fibrinolytic irrigation represents a rational treatment option that could prevent secondary injuries by accelerating clot clearance and washing out blood degradation products.[39 40]

Despite promising indications, the current evidence on irrigation therapy for SAH and IVH is sparse, and most of the existing studies are observational retrospective studies or case reports. While some studies included in this systematic review and meta-analysis found no statistically significant difference between treatments, none of the included studies reported worse outcomes in patients treated with irrigation therapy compared with no irrigation, suggesting that irrigation therapy overall is safe and feasible; however, we did not investigate safety outcomes in this study. To conclusively verify the effect of fibrinolytic or vasodilatory cisternal irrigation, it seems justified to perform a large, randomised trial.

Limitations

There was substantial heterogeneity in the surgical methodologies and irrigation interventions used in the included studies, which complicated study stratification. A high heterogeneity score is expected with the number of observational studies included, however, pooling studies may have resulted in substantial increase in heterogeneity, since including different combinations of fibrinolytic irrigation and vasodilatory irrigation treatment may be a significant driver for the high heterogeneity. Furthermore, the evidence quality was compromised for some outcomes, due to sparse literature, inclusion of observational studies without control groups, and substantial variations in the time points of outcome registration. For IVH, the evidence quality was compromised by few studies and low sample size. Finally, the funnel plots did not raise concern regarding publication bias, however, publication bias could result in non-publication of data showing neutral or negative results of irrigation therapy and cannot be ruled out. Moreover, the results for vasodilatory cisternal irrigation compared with other treatments revealed a discrepancy between randomised controlled trial and observational studies.

CONCLUSION

Cisternal irrigation may be associated with improved prognosis in patients with SAH when compared with conventional therapy. Fibrinolytic irrigation reduced mortality and improved functional outcome; effects that were also reflected in reduced risks of DCI and cerebral vasospasm. Vasodilatory cisternal irrigation may be a safe and feasible treatment for cerebral vasospasm; however, the current evidence is sparse, and future randomised studies are required to assess the treatment efficacy. We found no evidence to support irrigation therapy in patients with IVH.

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