Original Article

Systematic review and meta-analysis of the effect of continuous cerebrospinal fluid drainage on keyhole surgery during the perioperative period

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Background: Lumbar continuous drainage of fluid (LCDF) has become more widely used in the diagnosis and treatment of neurological diseases in recent years. The use of LCDF can enable a better understanding of the patient's condition and reduce the incidence of related complications. LCDF can also affect complications of perforation surgery, including mortality during hospitalization, cerebral vasospasm (CVS), bleeding, and aneurysmal subarachnoid hemorrhage (aSAH).

Methods: Articles published from library construction to April 2021 were searched for in the English-language databases PubMed, Cochrane Library, and Embase. All randomized controlled trials (RCTs) with LCDF and hole locking surgery were meta-analyzed using the Cochrane Collaboration's RevMan 5.3 software.

Results: Ten RCTs involving 1,092 patients (continuous drainage group, n=585; control group, n=507) were included in the meta-analysis. For the statistical different in incidence of perioperative cerebral infarction in the two groups, the odds ratio (OR) was 5.42 [95% confidence interval (CI): (2.71, 10.83); P<0.00001], and for the statistical difference in the incidence of cerebral hemorrhage, the OR was 4.76 [95% CI: (2.11, 10.76); P=0.0002]. Perioperative complications were fewer in the LCDF-treated drainage group than in the conventional group.

Discussion: This meta-analysis of 10 RCTs confirmed that LCDF compared with other treatments is associated with a lower incidence of perioperative complications, such as cerebral hemorrhage, hydrocephalus, and cerebral infarction, as well as increased Glasgow Outcome Scale (GOS).

Keywords: Continuous lumbar large-pool cerebrospinal fluid drainage (continuous lumbar large-pool CSF drainage); locking surgery; neurosurgery; perioperative period; mate analysis

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Introduction

Lumbar continuous drainage of fluid (LCDF) is a mature clinical technology used in the diagnosis and treatment of neurological diseases. The many advantages of LCDF include its simplicity, economy, and minimal trauma (1). This technique was first used to treat or prevent cerebrospinal fluid (CSF) leakage after craniocerebral and spinal surgery in patients at risk for CSF leakage after surgery (2). However, Ringel *et al.* (3) reported that while continuous CSF drainage could induce dural decompression and facilitate frontal lobe operation, it was associated with the occurrence of serious complications, including CSF leakage and meningitis, after surgery. Aneurysmal subarachnoid hemorrhage (aSAH) is a common cerebrovascular disease. Cerebral vasospasm (CVS) and rebleeding are all serious complications in the early stage after aSAH and can cause high mortality. In their study of 211 patients, Bakhshi *et al.* (4) observed the adverse effects of LCDF, and found iatrogenic spinal fluid leakage and Jiaxing meningocele to be the most common complications. Pathogens of meningitis include *E. coli* and *Pseudomonas aeruginosa*. Although lumbar large pool drainage technology has gradually matured, excessive drainage can lead to epidural hematoma and even brain hernia, retrograde infection, and symptoms of nerve root stimulation at the puncture site. Foreign scholars have explored methods to prevent complications of LCDF, which have included connecting an intravenous infusion pump to an external device to achieve a continuous and controlled flow rate (5). Although LCDF is a mature technology, its relationship with complications of locking surgery is still a topic of concern.

Keyhole surgery is an important minimally invasive neurosurgical approach. Wilson first proposed this concept in 1971, stating that locking holes can meet the needs of microscopic neurosurgery and this method improves the traditional craniotomy and limits the size of the surgical approach (6). The approach is simple and is widely used to treat hypertension, cerebral hemorrhage, intracranial aneurysm, and other intracranial diseases. However, various complications can still occur during perforation surgery, including cerebral hemorrhage, cerebral infarction, hydrocephalus, and infection. Researchers have attempted to reduce the incidence of complications during locking prior to surgery via various means, among which persistent drainage of CSF has received broad attention (7).

The aim of this meta-analysis was to summarize randomized controlled trials (RCTs) studying the effects of continuous lumbar large pool CSF drainage on perioperative complications in neurology patients undergoing locking surgery. We screened and meta-analyzed 8 RCTs, and reviewed case comparison results from China and overseas. Our findings will provide a scientific basis and theoretical reference for the application of continuous lumbar large-pool CSF drainage in neurology patients. Compared with the previous literatures, this study not only included perioperative complications, but also analyzed the mortality, CVS, rebleeding, and aSAH, which can better study the therapeutic effect of continuous lumbar cisternal CSF drainage. We present the following article in accordance with the PRISMA reporting checklist (available at https://dx.doi.org/10.21037/apm-21-2728).

Methods

Strategy for article retrieval

The PubMed, Cochrane Library, and Embase databases were searched for relevant RCTs. Keywords were searched for related keywords, and Medical Subject Headings (MeSH terms) for continuous lumbar drainage of fluid, keyhole surgery, and perioperative following the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0) combined with subject search bar to "subarachnoid hemorrhage, lumbar drain". The search was restricted to RCTs published up to April 2021, and the start date was selected to overlap with the last systematic review of the prevention strategy, literature was searched using the following descriptive terms, such as LCDF, CVS, aSAH, infection, bleeding, history of chronic disease, paralysis, infection, hypotension, hyponatremia, smoking, small vessel disease infarction, risk factors for death, cerebrovascular disease, cerebral infarction, and the descriptive term of stroke. According to pre-formulated inclusion and exclusion criteria, obtain the full text of the literature included in the study.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (I) RCTs, with either hidden or blind allocation; (II) study participants over 18 years old; (III) study participants undergoing neurosurgical perforation procedures for hydrocephalus, subarachnoid hemorrhage, intracranial infection, or rupture of aneurysm; (IV) intervention measures: control

group treatment included routine treatment to restore the automatic cerebrovascular regulation mechanism, maintain effective blood volume and effective cerebral perfusion, control intracranial pressure, and prevent cerebral edema, and the drainage group underwent continuous drainage with a lumbar puncture; (V) main outcome indexes included hospitalization mortality, and the incidence of CVS, hemorrhage, and hydrocephalus; (VI) secondary outcome indexes included short-term clinical efficacy, 6-month prognosis, and adverse reactions.

The exclusion criteria were as follows: (I) studies with unclear data; (II) studies in Chinese; (III) does not contain the required disease data; (IV) non-controlled studies or non-RCTs; (V) studies with unreliable results; (VI) studies involving intermittent lumbar puncture discharge of spinal fluid or lateral ventricular flushing.

Literature extraction

Two independent researchers independently extracted data from the eligible articles. Differences which arose during data extraction were resolved through discussion or the opinion of a third researcher was sought. Data extracted from the articles included basic information (document topic, first author, author year, author information, and literature source), basic characteristics of the study participants (sex, age, study sample size, and baseline comparability), literature research methods, research scheme design, intervention measures in the experimental and control groups, outcome evaluation indicators, and outcome data.

Quality assessment

To determine the quality of the articles, a quality evaluation was conducted according to the bias risk assessment recommended by the RevMan (version 5.3). The evaluation considered the following seven elements, such as sequence generation and allocation concealment (selection bias or allocation bias), blinding of participants and personnel (performance bias), blinding of outcome assessors (detection bias), etc. Regarding these seven items, "Yes" meant that an article had a small risk of bias, and "No" meant that an article had a high degree of bias. If the study had not been fully reported in detail, the risk was unknown. The modified Jadad scale review was used to evaluate the quality of the attached research and literature. The evaluation included random sequence generation, allocation concealment, blinding, and tracking/exit; a score of 1 to 3 points indicated low quality, and a score of 4 to 7 points indicated high quality.

Data extraction

The results of the mate-analysis were expressed in forest maps, accompanied by the corresponding confidence intervals (CIs). If there was no overlap between the CIs of the individual results, statistical inhomogeneity was considered to exist between the studies. Combined stochastic and fixed models with acceptable inhomogeneity required further subgroup analysis. Studies were divided into subgroups according to design. When the inhomogeneity between different studies could not be ignored, the effect size for each subgroup was ignored to cope with inhomogeneity, and a combined statistical model was selected. A sensitivity analysis of the results was conducted to investigate whether the overall combined results were being influenced by a single study. Research of this paper can impact the mate-analysis results in this way. First, if a study is deleted, the constructive value of the size of the integrated composite effect is other than 95% of the integrated synthetic effect, and the results yield significantly different results.

Sensitivity analysis

Sensitivity analysis was used to evaluate whether the meta-analysis results were stable and reliable. Specifically, the change of meta-analysis results was observed by excluding some controversial studies, low-quality studies or analyzing the same group of data with different statistical methods/effect models. If the sensitivity analysis does not substantially change the results, the results are reliable. On the contrary, it should be careful in interpreting the results and drawing conclusions.

Statistical analysis

The Cochrane Collaboration's RevMan 5.3 software was used for the meta-analysis. The calculation method used the ratio [odds ratio (OR)] as the effect size with 95% CI. The heterogeneity threshold for the included studies was α=0.1. When no heterogeneity existed between the studies ($P>0.1$; $I^2<50\%$), the fixed-effects model was selected for meta-analysis; when heterogeneity existed ($I^2>50\%$), the stochastic effect model was used for meta-analysis. $P<0.05$ indicated a statistically significant difference. For single risk

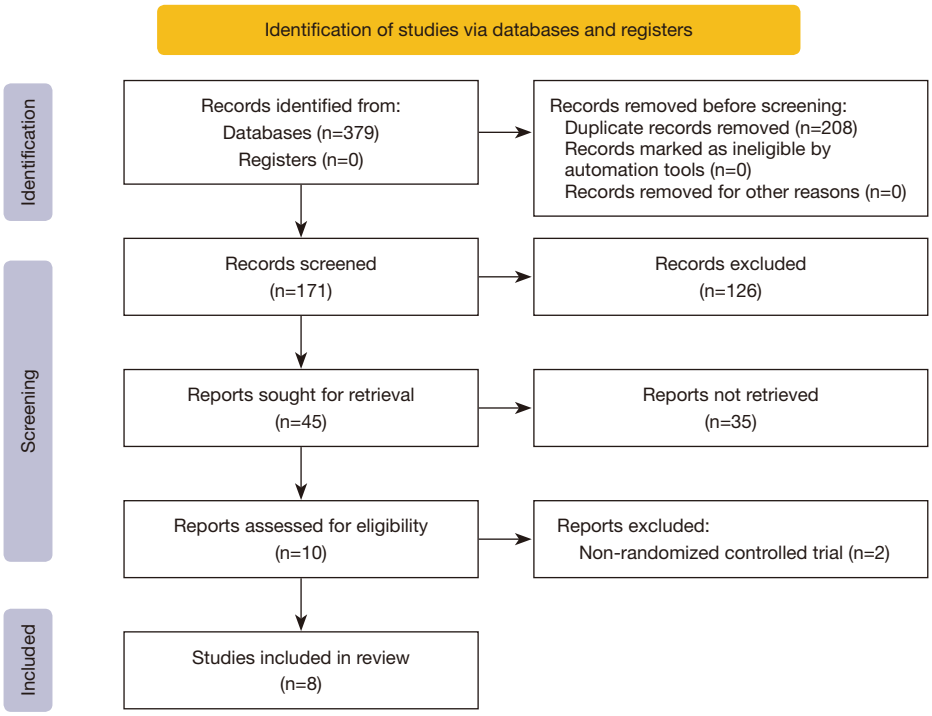

Figure 1 Flow chart for the article retrieval process.

factor analysis of more than 8 studies, funnel plots were used to analyze publication bias of risk factors.

Results

Results of article retrieval

A total of 379 relevant articles were retrieved, including 137 from PubMed, 129 from Embase, and 113 from Ovid-Medline. Of these articles, 208 duplicates were excluded, as were 126 articles that did not meet the inclusion criteria based on the reading of their text titles and abstracts. The full texts of the remaining articles were read, and 35 documents were subsequently excluded. Finally, 8 articles which met the inclusion criteria were included (8-15). The literature retrieval process is shown in *Figure 1*, and the basic information of the included articles is shown in *Table 1*.

Bias risk assessment of the included articles

The Cochrane Handbook (version 5.1) of the systematic review writing manual was adopted for assessment of the risk of bias in the 8 included articles. The results of the bias risk assessment are shown in *Figures 2,3*.

Hydrocephalus

Four articles reported the incidence of hydrocephalus during hospitalization. Hydrocephalus was experienced by 72 of 404 patients in the drainage group, and 24 of 315 patients in the conventional group. The results of heterogeneity analysis showed I^2=67% and P=0.03, which indicated significant heterogeneity in the literature; consequently, a random-effects model was used. The meta-analysis results showed OR =2.30, 95% CI: (0.90, 5.89), Z=1.74, and P=0.08; therefore, these results showed a no significant difference in the incidence of persistent drainage of CSF drainage between the drainage and conventional groups (P>0.05) (*Figure 4*). The funnel diagram was symmetrical (*Figure 5*), with most of the data corresponding to points within the 95% CI. This suggested that an incidence of hydrocephalus above 5k+10=95 indicated that publication bias.

Hematencephalon

Eight studies reported the incidence of cerebral hemorrhage during hospitalization. In the analysis, 585 patients in the drainage group and 507 patients in the conventional group experienced cerebral hemorrhage. The results of heterogeneity analysis showed I^2=68% and P=0.003,

Table 1 Basic characteristics of the included articles

Author	Publication year	Drainage group (case)	Control group (case)	Ending indicator	Stochastic method	Age (years old)	Follow-up time (months)
Al-Tamimi (8)	2012	105	105	Delayed neurofunctional defects, cerebral infarction, complications, and clinical prognosis	Computer random	45–62	6
Kwon (9)	2008	47	60	CVS, fatality rate, clinical prognosis, and hospitalization time	Computer random	Less than 70	6
Park (10)	2015	126	108	Clinical vasospasm, cerebral infarction, GOS at discharge, and mortality	Computer random	Unclear	6
Sun (11)	2014	76	72	Intracerebral hemorrhage, vasospasm, chronic hydrocephalus incidence, tube timing, infection, and GOS	Random	Average of 56.8	2
Hänggi (12)	2008	20	20	GOS, neurological defects, and vasospasm	Random	18–70	3
Otawara (13)	2007	38	40	Hydrocephalus, meningitis, and vasospasm	Random	17–73 (average of 51.2)	Unclear
Klimo (14)	2004	81	86	Anascular spasm, cerebral infarction, and GOS	Random	18–68	3
Kasuya (15)	1991	92	16	Brain infarction and hydrocephalus	Random	Unclear	Unclear

CVS, cerebral vasospasm; GOS, Glasgow Outcome Scale.

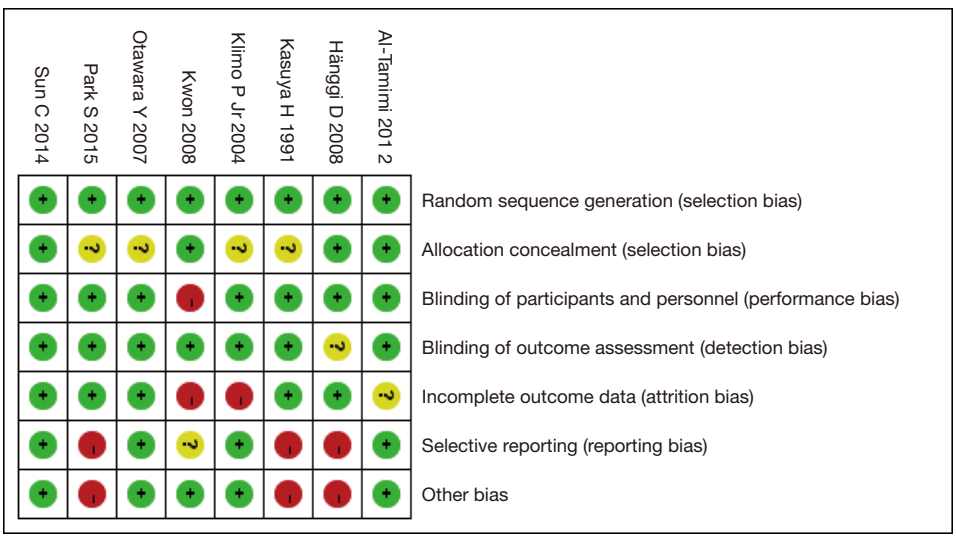

Figure 2 Assessment of bias risk for the included articles.

which indicated significant heterogeneity in the literature; consequently, a random-effects model was used. The meta-analysis results showed OR =4.76, 95% CI: (2.11, 10.76), Z=3.75, and P=0.0002, these results showed a significant difference in the incidence of continuous lumbar CSF drainage between the drainage and conventional groups (P<0.05). A forest map is shown in *Figure 6*. The funnel diagram was symmetrical (*Figure 7*), with most of the data corresponding to points within the 95% CI. The non-safety number was 186, this suggested that an incidence of cerebral hemorrhage above 5k+10=95 indicated that publication bias.

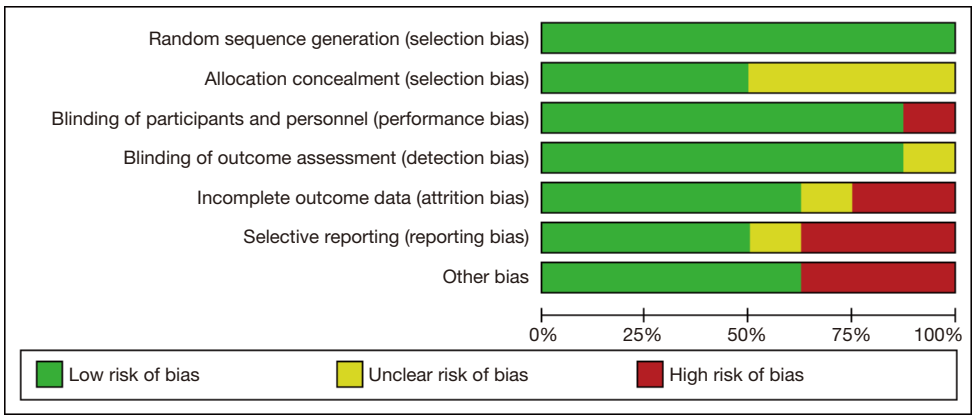

Figure 3 Multiple studies in the articles correspond to the results of risk of bias assessment for the included articles.

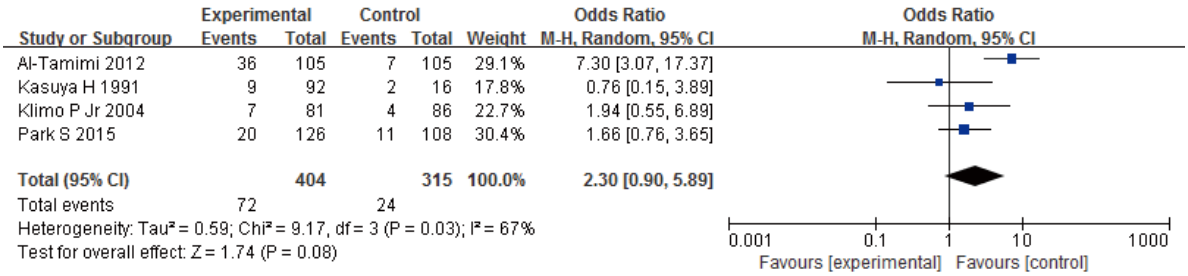

Figure 4 Forest map comparing the incidence of hydrocephalus in the experimental and control groups.

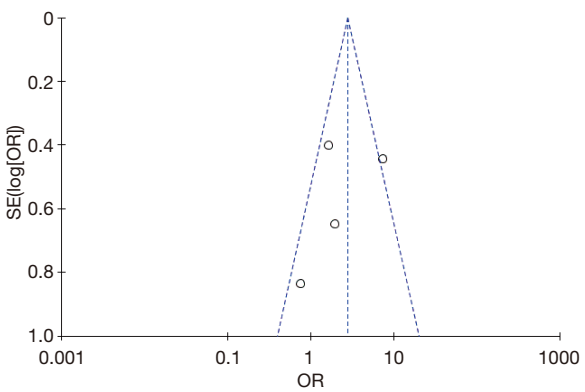

Figure 5 Funnel plot for the incidence of hydrocephalus in the experimental and control groups.

showed I^2=64% and P=0.006, which indicated significant heterogeneity in the literature; consequently, a random-effects model was used. The meta-analysis results showed OR =5.42, 95% CI: (2.71, 10.83), Z=4.78, and P<0.00001, these results showed a significant difference in the incidence of continuous lumbar CSF drainage between the drainage and conventional groups (P<0.05). A forest map is shown in *Figure 8*. The funnel diagram was symmetrical (*Figure 9*), with most of the data corresponding to points within the 95% CI. The non-safety number was 213, which indicated that at least 213 non-positive controls were required for to bring hypertension and cerebrovascular disease-related outcomes above 5k+10=95, suggesting that an incidence of cerebral infarction above 5k+10=95 indicated that publication bias.

Cerebral infarction

All 8 studies reported the incidence of cerebral infarction during hospitalization. Cerebral infarction occurred 585 patients in the drainage group and 507 patients in the conventional group. The results of heterogeneity testing

Late-onset nerve injury

All 8 studies reported the incidence of delayed nerve injury during hospitalization or follow-up. Delayed nerve injury occurred in 585 patients in the drainage group and 507 patients in the conventional group. The results

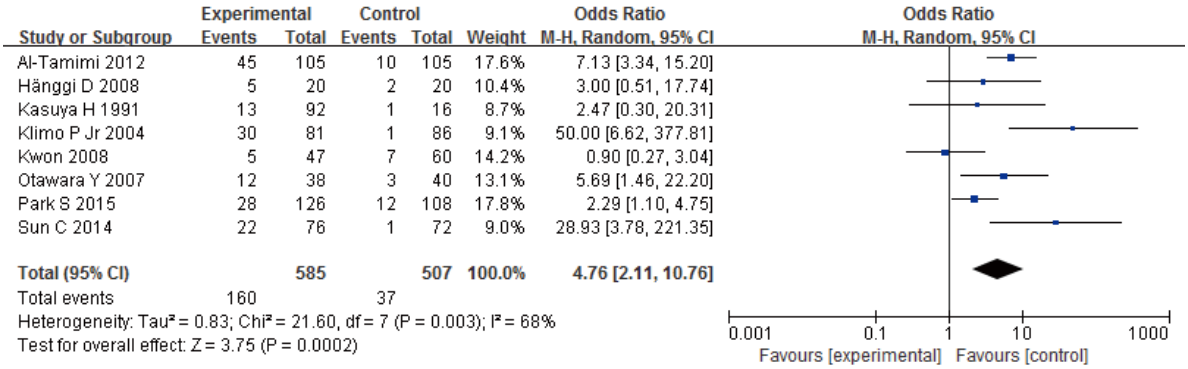

Figure 6 Forest map comparing the incidence of perioperative cerebral hemorrhage in the experimental and control groups.

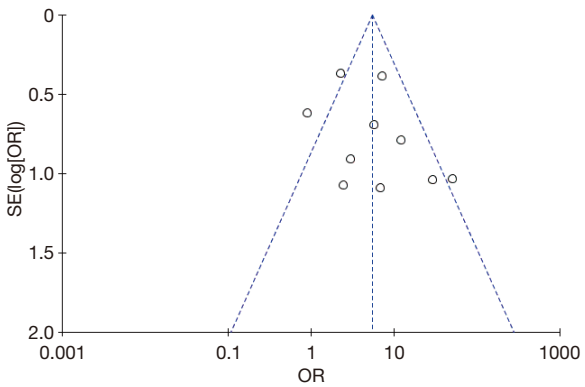

Figure 7 Funnel plot for the incidence of perioperative cerebral hemorrhage in the experimental and control groups.

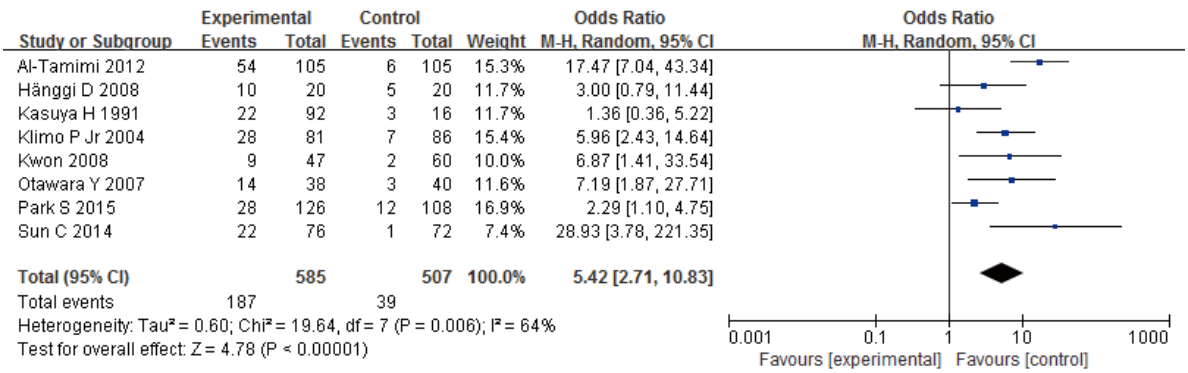

Figure 8 Forest map comparing the incidence of perioperative cerebral infarction in the experimental and control groups.

of heterogeneity testing showed I^2=0% and P=0.58, which indicated obvious heterogeneity in the literature; consequently, a fixed-effects model was used. The results of the meta-analysis showed OR =3.62, 95% CI: (2.10, 6.22), Z=4.65, and P<0.00001; therefore, significant differences in the incidence of delayed nerve injury caused by persistent CSF drainage existed between the two groups (P<0.05). A forest map is shown in *Figure 10*. The funnel diagram was symmetrical (*Figure 11*), with most of the data corresponding to the 95% CI points. The non-safety number was 92,

which indicated that at least 92 non-positive controls were required to produce hypertension and cerebrovascular disease-related outcomes above 5k+10=95, suggesting that an incidence of delayed nerve injury above 5k+10=95 indicated that publication bias.

Infection

All 8 studies reported the incidence of infection during hospitalization or follow-up. Infection occurred in 585 patients in the drainage group and 507 patients in the conventional group. The results of heterogeneity testing showed I^2=15% and P=0.31, which indicated obvious heterogeneity in the literature; consequently, a fixed-effects model was used. The meta-analysis results showed OR =4.12, 95% CI: (2.75, 6.18), Z=6.83, and P<0.00001. Therefore, there was a significant difference in the incidence of perioperative infection between the two groups of patients (P<0.05). A forest map is shown in *Figure 12*. The funnel diagram was symmetric (*Figure 13*), with most of the data corresponding to points within the 95% CI. The non-safety number was 148, which indicated that at least 148 non-positive controls were needed to bring hypertension and cerebrovascular disease-related outcomes above 5k+10=95, suggesting that an incidence of delayed nerve injury above 5k+10=95 indicated that publication bias.

Glasgow Outcome Scale (GOS)

Five studies reported patients' Glasgow Prognostic Score (GPS) during hospitalization or follow-up. The GOS was reported for 345 patients in the drainage group and 287 patients in the conventional group. Heterogeneity test results showed I^2=0% and P=0.76, which indicated significant heterogeneity in the literature; consequently, a fixed-effects model was used. The results of the meta-analysis showed

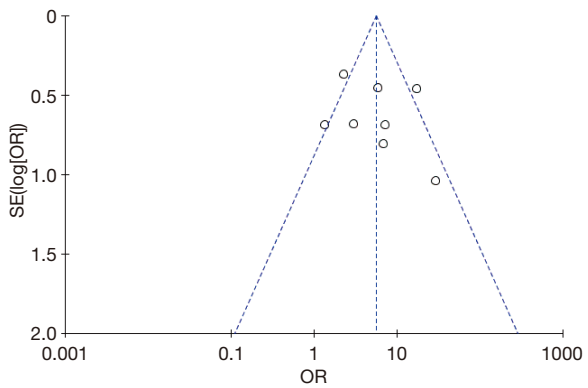

Figure 9 Funnel plot for the incidence of perioperative cerebral infarction in the experimental and control groups.

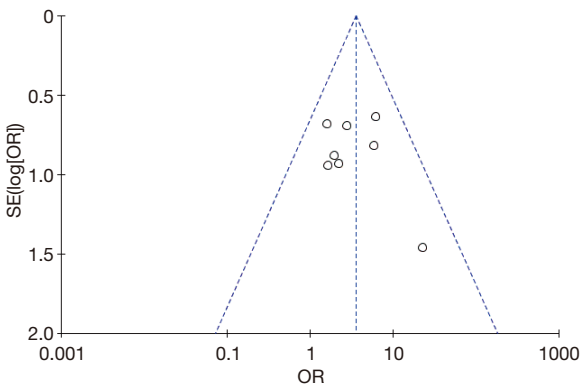

Figure 11 Funnel plot for the incidence of delayed nerve injury in the experimental and control groups.

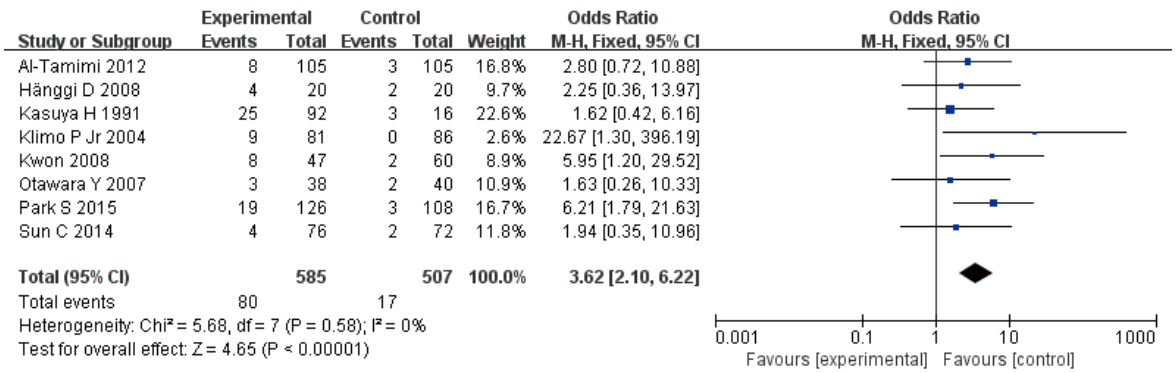

Figure 10 Forest map comparing the incidence of delayed perioperative nerve injury in the experimental and control groups.

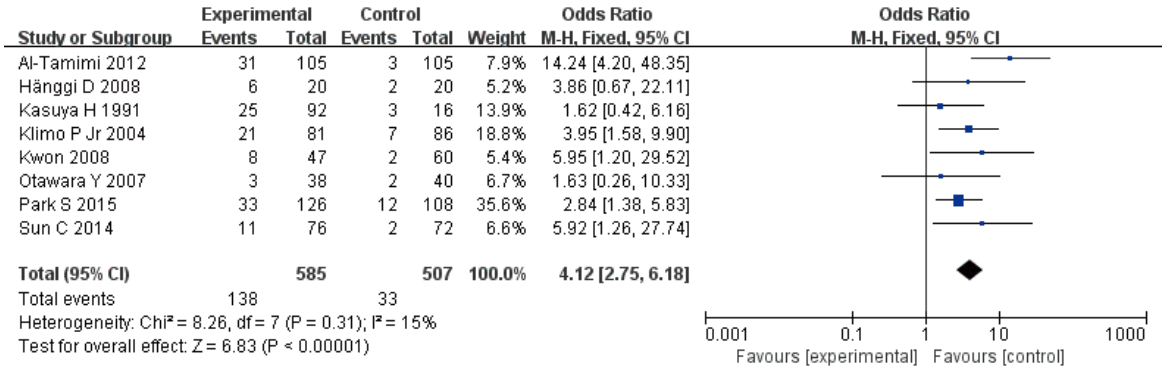

Figure 12 Forest map comparing the perioperative incidence of perforation infection the experimental and control groups.

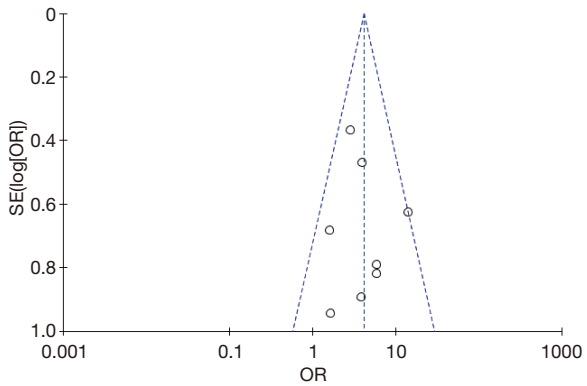

Figure 13 Funnel plot for the incidence of perioperative infection in the experimental and control groups.

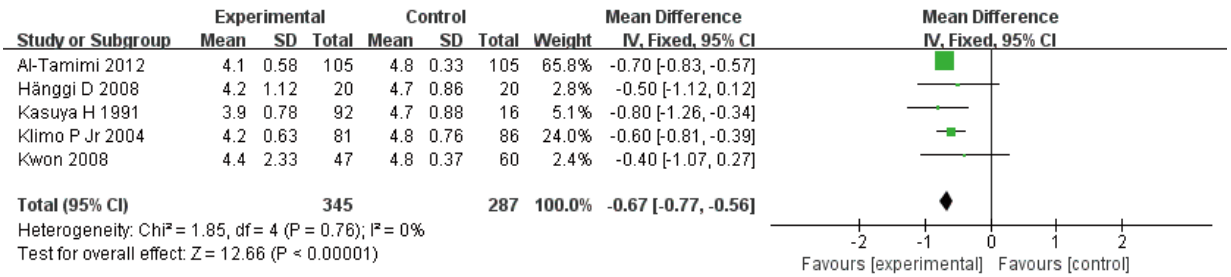

Figure 14 Forest plot comparing GPS during the perioperative period of keyhole surgery in the experimental and control groups. GPS, Glasgow Prognostic Score.

mean ratio (MR) =–0.67, 95% CI: (–0.77, –0.56), Z=12.66, and P<0.00001; therefore, significant differences in GPS existed between the two groups (P<0.05). A forest map is shown in *Figure 14*. The funnel diagram was symmetrical (*Figure 15*), with most of the data corresponding to points within the 95% CI. The non-safety number was 32, which indicated that at least 32 non-positive controls were required to produce hypertension and cerebrovascular disease-related outcomes above 5k+10=95, suggesting that an incidence of GOS above 5k+10=95 indicated that publication bias.

Discussion

The effect of CSF drainage of lumbar cistern on the

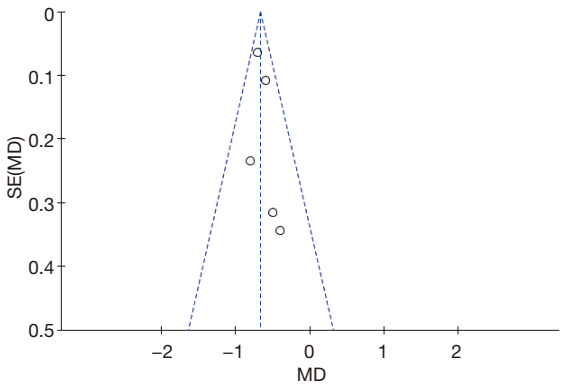

Figure 15 Funnel plot for the perioperative GPS in the experimental and control groups. GPS, Glasgow Prognostic Score.

prognosis of patients, especially on the mortality rate, remains to be studied. Therefore, according to the Cochrane systematic evaluation method, this study searched RCTs on improving the prognosis of patients with CSF drainage of lumbar cistern to verify the effectiveness and safety of drainage. This meta-analysis included 8 RCTs of continuous lumbar pool drainage (8-15). Of the 8 selected studies, seven reported the age, sex, prognostic indicators, and follow-up time of patients, with no statistically significant differences between the drainage and control groups (P>0.05). All 8 studies randomly divided patients into drainage and control groups, but none of them reported blindness, and none of the articles reported the number of deaths during the study. The limitations of the interventions in this study indicated that measurement deviations could exist between drainage and control patients. To further the research reliability and reference ability, research methods and designs should be improved in the future.

Continuous lumbar pool CSF drainage is routinely used to treat aSAH, and can reduce mortality and complications among patients with this condition (16,17). Locking neurosurgery is suitable for patients with intracranial aneurysm, hypertension, cerebral hemorrhage, and other diseases. Continuous lumbar pool CSF drainage significantly influences the perioperative period of locking surgery (18,19). The preliminary results of our meta-analysis of 8 original RCTs suggest that continuous drainage of CSF can reduce a number of perioperative complications in patients undergoing locking surgery, including hydrocephalus, cerebral hemorrhage, cerebral infarction, and delayed nerve damage, while improving the GPS; thus, it has a critical impact on patient prognosis. Early craniotomy of aneurysm neck clipping or endovascular intervention after onset can well control rebleeding. There are many treatments for CVS, including nimodipine, nicardipine, fasudil, endothelin receptor antagonist, magnesium, statins, and endovascular balloon angioplasty. However, the control of CVS is still an important part in the prevention of high mortality of aSAH (20). To date, there have been few reports on the impact of continuous drainage of CSF on the perioperative period of perforation surgery, intracranial or puncture site infection, low intracranial pressure, and cerebral hernia nerve root damage or stimulation. These indicators need to be closely observed in future studies (21,22), such as intracranial or puncture site infection, low cranial pressure, hernia nerve root damage or irritation. Some scholars believe that continuous lumbar pool drainage can improve clinical symptoms but does not reduce permanent nerve damage caused by CVS (23). Decline of intracranial pressure increases the possibility of aneurysmal re-rupture and bleeding, which suggests that the advantages and disadvantages should be considered before continuous drainage (24). Even with the blinding of patients and researchers, the use of both invasive and noninvasive procedures could lead to a high risk of incomplete implementation of the blinding method, which may produce information bias and thus affect the reliability of the meta-analysis.

Conclusions

Our results confirm that continuous lumbar pool drainage can reduce the incidence of some complications in the perioperative period of keyhole surgery, including cerebral hemorrhage, hydrocephalus, cerebral infarction, infection, and delayed nerve injury, while increasing the GPS. However, current studies do not provide sufficient evidence for the clinical promotion and application of continuous lumbar pool drainage, and more high-quality, large-sample, and multicenter RCTs should be conducted to obtain more reliable evidence.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://dx.doi.

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-2728). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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