Shunting outcomes in post-hemorrhagic hydrocephalus

A protocol for systematic review and meta-analysis

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Abstract

Background: The best treatment option for patients with post-hemorrhagic hydrocephalus (PHH) remains controversial. The objective of the current meta-analysis is to systematically evaluate the long-term outcomes of patients with PHH treated by ventriculoperitoneal shunt (VPS) and lumboperitoneal shunt (LPS).

Methods: We search literatures through PubMed, Web of Science, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), the Chinese Science and Technology Periodical Database (VIP) and Wan fang databases, and Chinese Biomedical Literature Database (CBM) from its beginning to June 15, 2020. Randomized controlled trials (RCTs) and non-RCTs in English or Chinese studies will be considered. The primary outcome is the rate of shunt failure after shunt implantation.

Results and conclusion: The study will compare the two types of shunt surgery in the treatment of PHH, providing evidence for the treatment option for the patients with PHH.

Study registration number: The study is priorly registered through International Platform of Registered Systematic Review and Meta-analysis Protocols on June 17, 2020 (INPLASY202060063).

Abbreviations: CSF = cerebrospinal fluid, ETV = endoscopic third ventriculostomy, GCS = Glasgow coma scale, INPH = idiopathic normal pressure hydrocephalus, IVH = intraventricular hemorrhage, LPS = lumboperitoneal shunt, mRS = modified Rankin Scale, NIHSS = National Institute of Health stroke scale, PHH = post-hemorrhagic hydrocephalus, SAEs = serious adverse events, SAH = subarachnoid hemorrhage, VPS = ventriculoperitoneal shunt.

Keywords: post-hemorrhagic hydrocephalus, ventriculoperitoneal shunt, lumboperitoneal shunt, treatment outcomes

1. Introduction

Traumatic or non-traumatic intraventricular hemorrhage (IVH) frequently leads to post-hemorrhagic hydrocephalus (PHH) as a result of obstruction of cerebrospinal fluid (CSF) outflow, dysfunction of CSF absorption, or CSF hypersecretion.\textsuperscript{1,2} The majority of patients with PHH are shunt-dependent since conservative treatments or temporary CSF drainage always fail to divert the accumulated CSF.\textsuperscript{3} The most commonly used option is ventriculoperitoneal shunt (VPS).\textsuperscript{4,5} Lumboperitoneal shunt (LPS), as an alternative option, has become the first-line treatment for patients with idiopathic normal pressure hydrocephalus (INPH) in Japan.\textsuperscript{5} The indications for performing LPS have recently broadened to other types of communicating hydrocephalus, including communication PHH.\textsuperscript{4,6} Increasing number of studies reported that LPS had some advantages over VPS, including avoidance of access to lateral ventricles, minimal brain injury, and low incidence of postoperative infection.\textsuperscript{7} Although shunt implantation could effectively alleviate the symptoms and improve the neurological function, the long-term shunt failure is an unacceptably common outcome.\textsuperscript{8,9} The best treatment option for patients with PHH still remains unknown.
2. Objective

The objective of the current meta-analysis is to systematically evaluate the long-term outcomes of patients with PHH treated by VPS and LPS.

3. Methods

3.1. Study registration

The study is priorly registered through International Platform of Registered Systematic Review and Meta-analysis Protocols on June 17, 2020 (INPLASY202060063). This study protocol was prepared according to the guidelines of preferred reporting items for systematic review and meta-analysis protocols statement.10]

3.2. Eligible criteria

3.2.1. Types of studies. Randomized controlled trials (RCTs) and non-RCTs that simultaneously evaluated the clinical outcomes of patients with PHH treated by VPS and LPS will be included. Other studies, including retrospective studies, case reports, case series, research letters, reviews, noncomparative studies, and meeting abstracts, will be excluded.

3.2.2. Interventions

3.2.2.1. Study group. Patients with PHH treated by VPS.

3.2.2.2. Control group. Patients with PHH treated by LPS.

3.2.2.3. Participants. Adult patients (age ≥18 years) who were diagnosed as PHH according to medical history, clinical manifestations, brain imaging, and supplemental tests regardless of gender, racial, and region, will be included.

3.2.2.4. Language. English and Chinese studies will be considered.

3.2.2.5. Search strategy. We search literatures through PubMed, Web of Science, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), the Chinese Science and Technology Periodical Database (VIP) and Wan fang databases, and Chinese Biomedical Literature Database (CBM) from its beginning to June 15, 2020. The search strategy is (“clinical outcomes” OR “efficacy” OR “safety” OR “follow-up” OR “shunting outcomes”) AND (“post hemorrhagic” OR “intracranial hemorrhage” OR “intraventricular hemorrhage” OR “subarachnoid hemorrhage”) AND (“hydrocephalus” OR “ventriculomegaly” OR “accumulation of cerebrospinal fluid”) AND (“shunts” OR “ventriculoperitoneal shunt” OR “lumboperitoneal shunt”). An example of search strategy in PubMed database is shown in Table 1.

3.3. Outcomes

3.3.1. Primary outcomes. The primary outcome is the rate of shunt failure after shunt implantation. According to the previous studies, shunt failure is defined as the occurrence of clinical or radiological signs of shunt obstruction, breakage, tubing exposure, malfunction, or infection requiring shunt revision, or shunt-related morbidity and mortality.

3.3.2. Secondary outcomes. The secondary outcome is the rate of complications that are associated with shunt surgery.

3.4. Data collection and analysis

3.4.1. Study selection. All eligible studies will be input into Endnote X7 software after 2 experienced and practiced evaluators review the title, abstract, and full text of each study according to the inclusion and exclusion criteria. Re-evaluation by a third reviewer is required while there are different judgments on study selection. Duplicative records will also be removed. The reasons of all removed trials will be listed in a flowchart of study selection.

3.4.2. Data extraction. Once the studies are included, 2 independent assessors will collect data including corresponding author, date of publication, study design, country of study, study period, participants (numbers, age, gender, race, clinical features, intervention, types of shunt system, postoperative outcomes, follow-up period), shunt outcomes, and complications. Re-evaluation by a third reviewer is required while there are any debates on data extraction.

| Number | Description |
|--------|-------------|
| #1     | “post hemorrhagic” OR “intracranial hemorrhage” OR “intraventricular hemorrhage” OR “subarachnoid hemorrhage” [Title/Abstract] |
| #2     | “traumatic intracranial hemorrhage” OR “intracranial hemorrhage” [MeSH] |
| #3     | #1 or #2 |
| #4     | “hydrocephalus” OR “ventriculomegaly” OR “accumulation of cerebrospinal fluid” [Title/Abstract] |
| #5     | “hydrocephalus” [MeSH] |
| #6     | #4 or #5 |
| #7     | “shunt” OR “ventriculoperitoneal shunt” OR “lumboperitoneal shunt” [Title/Abstract] |
| #8     | “cerebrospinal fluid shunts” [MeSH] |
| #9     | #7 or #8 |
| #10    | “clinical outcomes” OR “efficacy” OR “safety” OR “follow-up” [Title/Abstract] |
| #11    | “treatment outcomes” OR “patient outcome assessment” [MeSH] |
| #12    | #10 or #11 |
| #13    | #3 and #6 and #9 and #12 |
| #14    | Limit #13 to human |
| #15    | Limit #14 to “comparative study” or “randomized controlled clinical trial” or “non-randomized controlled clinical trial” [Publication type] |
| #16    | Limit #15 to yr = “June 15, 2020” |
3.4.3. Dealing with missing data. We will contact the corresponding author on reasonable request if there is missing or unclear data. Finally, the studies will be removed if the data is not available despite our conscientious attempts.

3.4.4. Quality assessment. The quality of included studies will be independently evaluated according to the Cochrane risk-of-bias tool containing 7 aspects. The evaluation of bias will be classified into 3 categories: high risk, low risk, and unclear risk. The bothersome question is that there are any debates.

3.4.5. Publication bias. We will check the publication bias using funnel plots if at least 10 studies are included. Specifically, Begg and Egger regression is used to determine the funnel plot asymmetry.[11] An independent monitoring committee, including statisticians, and data analysts, will assess the quality. We use Cochrane risk-of-bias tool to evaluate the randomized controlled trials.

3.5. Sensitivity analysis

The sensitivity analysis will be performed by removing 1 study each time from pooled analysis followed by reporting the results in a summary table.[12]

3.6. Data synthesis

All data are analyzed using the statistical software program Review Manager 5.3 (Nordic Cochran Centre, Copenhagen, Denmark). A 2-tailed probability values (P) less than .05 is considered to have statistical difference. The outcomes are mainly described as percent (%) with its 95% confidence intervals. Heterogeneity among included studies will be tested using I² statistics. A fixed-effect model will be used if the value of I² under 50%, and a random-effect model will be used if the value of I² beyond 50%. The reasons of heterogeneity will be fully understood regarding the study design and patients characteristics.

4. Discussion

With the advent of shunt systems, CSF shunts that divert the accumulated CSF to the peritoneal cavity have long been used as the first-line treatment for patients with hydrocephalus.[9] While offering some advantages over VPS, the long-term outcomes of LPS implantation, sometimes, is not as expected and the majority of patients choose VPS rather than LPS.[13,14] A prospective, multicenter trial that analyze the long-term outcomes of patients with INPH treated by LPS and compare with a historical VPS control from a previous conducted trial suggested LPS presented higher risk of shunt revisions at 1 year after surgery.[13] Despite of growing number of researches focusing on the benefits of LPS surgery in the treatment of INPH, no completed systematic review has compared LPS and VPS for the treatment of PHH. In this regard, our work will provide evidence for the treatment options for patients with PHH.

Author contributions

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References

[1] Chen Q, Feng Z, Tan Q, et al. Post-hemorrhagic hydrocephalus: recent advances and new therapeutic insights. J Neurol Sci 2017;375:220–30.
[2] Karimy JK, Zhang J, Kurland DB, et al. Inflammation-dependent cerebrospinal fluid hypersecretion by the choroid plexus epithelium in posthaemorrhagic hydrocephalus. Nat Med 2017;23:997–1003.
[3] Wells J, Chen X, Holubkov R, et al. Shunting outcomes in posthaemorrhagic hydrocephalus: results of a Hydrocephalus Clinical Research Network prospective cohort study. J Neurol Neurosurg Psychiatry 2017;90:19–29.
[4] Wang Z, Wang K, Qian Z, et al. Lumboperitoneal and ventriculoperitoneal shunt surgery for posthaemorrhagic communicating hydrocephalus: a comparison. World Neurosurg 2019;127:e638–43.
[5] Kazui H, Miyajima M, Mori E, et al. Lumboperitoneal shunt surgery for idiopathic normal pressure hydrocephalus (SINPHONI-2): an open-label randomised trial. Lancet Neurol 2015;14:585–94.
[6] Sun T, Yuan Y, Zhang Q, et al. One-year outcome of patients with posttraumatic hydrocephalus treated by lumboperitoneal shunt: an observational study from China. Acta Neurochir (Wien) 2018;160:2031–8.
[7] Wang YY, Barbaro NM, Lawton MT, et al. Complications of lumboperitoneal shunts. Neurosurgery 2007;60:1045–8, discussion 1049.
[8] Toma AK, Papadopoulos MC, Stapleton S, et al. Systematic review of the outcome of shunt surgery in idiopathic normal-pressure hydrocephalus. Acta Neurochir (Wien) 2013;155:1977–80.
[9] Kahle KT, Kulkarni AV, Limbrick DD, et al. Hydroceplalus in children. Lancet 2016;387:788–99.
[10] Shamsi R, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement [J]. Syst Rev 2015;4:1–9.
[11] Zhang YW, Jiang C, Li XH, et al. Effect and safety of Huangqi-Guizhi-Wuwu Decoction and Exzian Decoction in the treatment of frozen shoulder: a protocol for systematic review and meta-analysis. Medicine (Baltimore) 2020;99:e20540.
[12] Ju M, Cheng H, Qu K, et al. Efficacy and safety of ramucirumab treatment in patients with advanced colorectal cancer. Medicine 2020;99:e20618.
[13] Karabatsou K, Quigley G, Buxton N, et al. Lumboperitoneal shunts: are the complications acceptable? Acta Neurochir (Wien) 2004;146:1193–7.
[14] Sun T, Yuan Y, Zhang Q, et al. Establishing a Preoperative Evaluation System for Lumboperitoneal Shunt: approach to attenuate the risk of shunt failure. World Neurosurg 2018;117:e308–15.
[15] Miyajima M, Kazui H, Mori E, et al. One-year outcome in patients with idiopathic normal-pressure hydrocephalus: comparison of lumboperitoneal shunt to ventriculoperitoneal shunt. J Neurol Surg 2016;125:1483–92.