

Efficacy of microsurgery for patients with cerebral hemorrhage secondary to gestational hypertension

A systematic review protocol of randomized controlled trial

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Abstract

Background: Microsurgery is widely utilized for patients with cerebral hemorrhage (CH). The purpose of this study is to assess the efficacy and safety of microsurgery for the treatment of patients with CH secondary to gestational hypertension (GH).

Methods: Relevant randomized controlled trials in eight electronic databases of Cochrane Library, PUBMED, EMBASE, Web of Science, VIP, WANFANG, Chinese Biomedical Literature Database, and China National Knowledge Infrastructure will be included. All electronic databases will be searched from inceptions to the present without language restriction. RevMan 5.3 software will be applied for statistical analysis.

Results: This study will summarize a high-quality synthesis of maternal mortality, severe maternal complications, maternal quality of life, limbs function, muscle strength, and muscle tone to evaluate the efficacy and safety of microsurgery for patients with CH secondary to GH.

Conclusions: This study will provide evidence that microsurgery is an effective intervention in patients with CH secondary to GH.

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Abbreviations: CH = cerebral hemorrhage, GH = gestational hypertension, RCTs = randomized controlled trials.

Keywords: cerebral hemorrhage, efficacy, gestational hypertension, microsurgery, randomized controlled trial, safety

1. Introduction

Cerebral hemorrhage (CH) is a very common cerebrovascular disorder in clinical practice.^[1–3] Patients who experience such disorder often have difficulty in walking, speaking, and understanding, and paralysis or numbness of the face, arm, or leg, which significantly affect their health-related quality of life.^[4–6] Furthermore, it also causes high morbidity and mortality in patients with CH.^[7–9] It has been estimated that the mortality rate in such patients can reach 40% to 50%, and 75% of those survivors cannot live independently 1 year post stroke.^[10]

Many factors can cause CH, especially for pregnant women, such as gestational hypertension (GH).^[5,11,12] GH is a major predictor of pregnancy-associated CH.^[13,14] Several

managements are responsible for patients with CH secondary to the GH, including microsurgery, medication, acupuncture, moxibustion, and Tuina, especially for microsurgery.^[15–22] A variety of studies have reported that microsurgery is an effective management for patients with CH secondary to the GH.^[4,22–24] However, convinced evidence-based level is still needed to support this therapy. Therefore, this study aims to summarize and critically assess the evidence from current clinical studies that have investigated the efficacy of microsurgery as a treatment for patients with CH secondary to the GH.

2. Methods

2.1. Study selection criteria

2.1.1. Types of studies. We will consider randomized controlled trials (RCTs) comparing microsurgery with other treatment. However, case studies, case-control studies, reviews, and non-RCTs will be excluded.

2.1.2. Types of interventions. The participants in the experimental group must receive microsurgery for CH secondary to GH.

The participants in the control group can receive any treatments, except microsurgery.

2.1.3. Types of participants. Pregnant participants of any age with clinically diagnosed as CH secondary to GH will be considered for inclusion.

2.1.4. Types of outcome measurements. The outcomes comprise of maternal mortality, severe maternal complications (such as number of participants with pre-eclampsia, pre-term

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labor, and pregnancy loss), maternal quality of life (as measured by Maternal Perceived Quality of Life, or relevant scales), limbs function, muscle strength, and muscle tone.

2.2. Search strategy

The electronic databases of Cochrane Library, PUBMED, EMBASE, Web of Science, VIP, WANFANG, Chinese Biomedical Literature Database, and China National Knowledge Infrastructure will be searched from inception to the present without language limitation. The detailed strategy for searching the Cochrane Library will be shown in Table 1. Similar detailed search strategies will be modified and adapted to other electronic databases.

In addition, clinical trials registry, conference proceedings, dissertations, and reference lists of included studies will be searched.

2.3. Data collection and analysis

2.3.1. Study selection. Two authors will independently scan the titles and abstracts of all literature identified, and all irrelevant records and duplicated studies will be excluded. The remaining studies will be subsequently screened by reading full-text. In the event of divergences between two authors that they can not solve via discussion, and a third author will be consulted, who can help make the decision. The whole process of study selection will be presented in flowchart.

2.3.2. Data extraction. Data from the eligible studies will be extracted and collected by two authors independently according to the previous designed data extraction sheet. Any disagreements will be resolved by consensus with the help of a third author. We will collect information, such as title, first author, publication year, characteristics of study and patients, study methods, treatment details, outcome indicators, adverse events, and follow-up details. We will contact primary authors of trials for further information when necessary.

2.3.3. Missing data dealing with. We will try to require information by contacting corresponding author of the primary studies for the missing, unclear or insufficient data. If we cannot

obtain these data, only available data will be analyzed based on the intent-to-treat principle.

2.3.4. Risk of bias assessment. The risk of bias will be assessed by two independent authors using Cochrane risk of bias tool. It has 7 dimensions, and each one is further classified as high, unclear and low risk of bias. Any different opinions between two authors will be resolved by discussion with the help of a third author.

2.3.5. Measures of treatment effect. Enumeration outcome data will be evaluated as risk ratio and 95% confidence intervals, and continuous outcome data will be calculated as mean difference or standardized mean difference and 95% confidence intervals.

2.3.6. Assessment of heterogeneity. The heterogeneity among eligible studies will be identified using I^2 statistics. $I^2 \leq 50\%$ indicates minor heterogeneity, while $I^2 > 50\%$ means substantial heterogeneity.

2.3.7. Assessment of reporting bias. When more than 10 eligible RCTs are included, funnel plot and Egger's regression test will be conducted for reporting bias identification.^[25,26]

2.3.8. Subgroup analysis. We will carry out subgroup analysis to investigate the potential factors of significant heterogeneity based on the different study characteristics, treatments and controls, and outcome measurements.

2.3.9. Sensitivity analysis. When sufficient studies are available, we will conduct sensitivity analysis to check the stability of outcome results by removing low quality studies.

2.3.10. Ethics and dissemination. Ethical approval will not be required because this study will not use individual patient data. The results of this study are expected to disseminate by the publication in a peer-reviewed journal or conference proceedings.

2.4. Data synthesis

RevMan 5.3 software will be adopted for statistical analysis. Meta-analysis will be performed if more than two or above

Table 1
Search strategy for Cochrane Library.

Number	Search terms
1	Mesh descriptor: (stroke) explode all trees
2	Mesh descriptor: (cerebral hemorrhage) explode all trees
3	((cerebral hemorrhage*) or [cerebral*] or [cerebral next hemorrhage*] or [hemorrhage*] or [hemorrhagic stroke*] or [hemorrhagic apoplexy*]):ti, ab, kw
4	Or 1–3
5	Mesh descriptor: (hypertension, pregnancy-induced) explode all trees
6	((pregnancy induced hypertension*) or [gestational hypertension*] or [hypertensive disorder*] or [pregnancy*] or [hypertension*] or [proteinuria*]):ti, ab, kw
7	Or 5–6
8	Mesh descriptor: (microsurgery) explode all trees
9	Mesh descriptor: (general surgery) explode all trees
10	Mesh descriptor: (surgical procedures, operative) explode all trees
11	(([surgical*] or [surgery*] or [procedures*] or [operative*] or [operative surgical procedures*] or [general surgery*]):ti, ab, kw
12	Or 8–11
13	MeSH descriptor: (randomized controlled trials) explode all trees
14	MeSH descriptor: (clinical trials as topic) explode all trees
15	(([random*] or [randomly*] or [control*] or [placebo*] or [allocation*] or [blind*] or [trial*] or [RCT*] or [clinical study*] or [controlled study*]):ti, ab, kw
16	Or 8–9
17	4 and 7 and 12 and 16

eligible studies with minor heterogeneity at same outcome measurements will be included. If there is minor heterogeneity among sufficient studies ($I^2 \leq 50\%$), a fixed-effect model will be used for data synthesizing, and meta-analysis will be employed. If there is significant heterogeneity among enough studies ($I^2 > 50\%$), the source of such substantial heterogeneity will be further analyzed, a random-effect model will be used for data pooling, and subgroup analysis will be carried out. If there is still substantial heterogeneity after subgroup analysis, we will not conduct data pooling and meta-analysis. At the same time, outcome results will be reported as narrative summary.

3. Discussion

Although previous studies have reported that microsurgery is utilized for the treatment of patients with CH secondary to GH, its efficacy and safety has not been assessed systematically. Thus, it is crucial to make sure whether microsurgery is a good option for the patients with CH secondary to GH. The objective of this study is to systematically assess the efficacy and safety of microsurgery for the treatment of patients with CH secondary to GH. We hope this review will provide most recent information on the credibility current evidence and research directions for both clinical practice and future studies.

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References

- [1] Suzuki K, Sakamoto T. Clinical epidemiology of cerebral hemorrhage. *Nihon Rinsho* 2006;64:315–9.
- [2] Ueno M. Hypertensive cerebral hemorrhage. *Nihon Rinsho* 2004;62:363–8.
- [3] Wilterdink JL, Feldmann E. Cerebral hemorrhage. *Adv Neurol* 1994;64:13–23.
- [4] Nakase H, Motoyama Y, Yamada S. Cerebral hemorrhage. *Nihon Rinsho* 2016;74:671–6.
- [5] Zubkov AY, Wijdicks EF. Deep venous thrombosis prophylaxis in cerebral hemorrhage. *Rev Neurol Dis* 2009;6:21–5.
- [6] González-Duarte A, Cantú C, Ruíz-Sandoval JL, et al. Recurrent primary cerebral hemorrhage: frequency, mechanisms, and prognosis. *Stroke* 1998;29:1802–5.
- [7] Escudero Augusto D, Marqués Alvarez L, Taboada Costa F. Up-date in spontaneous cerebral hemorrhage. *Med Intensiva* 2008;32:282–95.
- [8] Ye L, Gao L, Cheng H. Inflammatory profiles of the interleukin family and network in cerebral hemorrhage. *Cell Mol Neurobiol* 2018;38:1321–33.
- [9] Proust F, Leveque S, Derrey S, et al. Spontaneous supratentorial cerebral hemorrhage: role of surgical treatment. *Neurochirurgie* 2007;53(2-3 Pt 1):58–65.
- [10] Klebe D, McBride D, Flores JJ, et al. Modulating the immune response towards a neuroregenerative Peri-injury Milieu after cerebral hemorrhage. *J Neuroimmune Pharmacol* 2015;10:576–86.
- [11] Zou Y, Zhang W, Huang C, et al. Clinical significance of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in acute cerebral hemorrhage with gastrointestinal hemorrhage, and logistic regression analysis of risk factors. *Exp Ther Med* 2019;18:1533–8.
- [12] Tzourio C, Arima H, Harrap S, et al. APOE genotype, ethnicity, and the risk of cerebral hemorrhage. *Neurology* 2008;70:1322–8.
- [13] Say L, Chou D, Gemmill A, et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Global Health* 2014;2:e323–33.
- [14] Khan KS, Wojdyla D, Say L, et al. WHO analysis of causes of maternal death: a systematic review. *Lancet (London, England)* 2006;367:1066–74.
- [15] Yuan P, Bao CL, Dong GR. Clinical safety research of penetrating acupuncture at the head points for cerebral hemorrhage at the acute stage. *Zhongguo Zhen Jiu* 2012;32:577–81.
- [16] Song GF, Wu CJ, Dong SX, et al. Rehabilitation training combined acupuncture for limb hemiplegia caused by cerebral hemorrhage: a protocol for a systematic review of randomized controlled trial. *Medicine (Baltimore)* 2019;98:e14726.
- [17] Dong XS, Song GF, Wu CJ, et al. Effectiveness of rehabilitation training combined with acupuncture on aphasia after cerebral hemorrhage: a systematic review protocol of randomized controlled trial. *Medicine (Baltimore)* 2019;98:e16006.
- [18] Xia ZY, Wang J, Guo JW, et al. Effect of Chinese drugs for breaking blood expelling stasis on acute cerebral hemorrhage: a prospective randomized double-blind controlled study. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2016;36:821–6.
- [19] Hu W, Xin Y, Chen X, et al. Tranexamic acid in cerebral hemorrhage: a meta-analysis and systematic review. *CNS Drugs* 2019;33:327–36.
- [20] Mizutani T, Kojima H, Miki Y. Arterial dissections of penetrating cerebral arteries causing hypertension-induced cerebral hemorrhage. *J Neurosurg* 2000;93:859–62.
- [21] Mao Y, Nan GX, Zhang L, et al. Contrast extravasation mimics cerebral hemorrhage in acute ischemic stroke after Solitaire FR clot retrieval and intraarterial thrombolysis: a case report. *Acta Neurol Belg* 2015;115:723–5.
- [22] Negură Marderos A, Aldea MJ, Buzea T, et al. Cerebral hemorrhage occurring in pregnancy. *Rev Med Chir Soc Med Nat Iasi* 1976;80:39–43.
- [23] Guo R, Blacker DJ, Wang X, et al. Practice patterns for neurosurgical utilization and outcome in acute intracerebral hemorrhage: intensive blood pressure reduction in acute cerebral hemorrhage trials 1 and 2 Studies. *Neurosurgery* 2017;81:980–5.
- [24] Jia Y, Zhong X, Liu J. Clinical study on Zhuyu Xiaozhong mixture combined with stereotaxic drainage in treating hypertensive cerebral hemorrhage. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2000;20:498–500.
- [25] Sutton AJ, Duval SJ, Tweedie RL, et al. Empirical assessment of effect of publication bias on meta-analyses. *BMJ* 2000;320:1574–7.
- [26] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.