INTRODUCTION

Condition being studied: Watershed stroke, butylphthalide, and hemodynamics.

METHODS

Participant or population: This study will include patients who were diagnosed as WS regardless their race, gender, and age.
**Intervention:** In the intervention group, all eligible WS patients received butylphthalide on hemodynamics.

**Comparator:** In the control group, all included WS participants underwent any other managements, except butylphthalide.

**Study designs to be included:** This study will include randomized controlled trials (RCTs) that focus on exploring the effect of butylphthalide on hemodynamics in patients with WS.

**Eligibility criteria:** This study will include all RCTs that compared the effect of butylphthalide vs. other treatments on hemodynamics in patients with WS, irrespective all other studies, race, gender, and age.

**Information sources:** MEDLINE, EMBASE, Cochrane Library, PsycINFO, Web of Science, Cumulative Index to Nursing and Allied Health Literature, and China National Knowledge Infrastructure will be searched from database inception to the March 1, 2020. We will not impose any language and publication status limitations. In addition, we will perform searches in conference abstracts, and from reference lists of eligible studies.

**Main outcome(s):** The primary outcomes are hemodynamic indices, as measured by mean velocity of blood flow, flow velocity, mean blood flow, cardiac output, and blood pressure.

**Additional outcome(s):** The secondary outcomes include cerebral blood flow, cerebral blood volume, mean transit time, quality of life, and any adverse events.

**Data management:** Two investigators will independently extract data from included studies based on the predefined standardized form of data collection. Any discrepancies between two investigators in extracted data will be solved by a third expert investigator through discussion. Extracted information includes study basic characteristics (including title, first author, et al), patient characteristics (including age, race, gender, et al), study setting, sample size, study methods (including details of randomization, blind, et al), intervention and comparators (including types, dosage, mode of delivery, et al), outcomes (any outcome measurements, safety, et al), and funding information.

**Quality assessment / Risk of bias analysis:** Study methodological quality will be measured using Cochrane risk of bias through selection, performance, detection, attrition, reporting and other biases. Each item is further assessed as high, unclear or low risk of bias. Two independent reviewers will assess the methodological quality for all included studies, respectively. A third expert investigator will help to solve all disagreements occur between two investigators.

**Strategy of data synthesis:** In this study, we will use RevMan 5.3 software for statistical analysis. We will calculate all binary data using risk ratio and 95% confidence intervals (CIs), and all continuity data using mean difference, or standardized mean difference and 95% CIs. Heterogeneity among studies will be checked by $I^2$ test. The value of $I^2 \leq 50\%$ exerts minor heterogeneity, while the value of $I^2 > 50\%$ shows obvious heterogeneity. If $I^2 \leq 50\%$, we will use a fixed-effect model, and will also consider to conduct meta-analysis is sufficient data on the same outcomes are collected. If $I^2 > 50\%$, we will utilize a random-effect model, and will carry out subgroup analysis or meta-regression test to check any potentials factors for the obvious heterogeneity. Where pooling was inappropriate, the results of the trials will be reported as a narrative description using detailed written commentary on the study findings, different interventions and controls (e.g butylphthalide vs. physical therapy), and outcome measurements (e.g. mean velocity of blood flow, flow velocity, mean blood flow, cardiac output, and blood pressure).

**Subgroup analysis:** Data permitting, we will perform subgroup analysis considering different study characteristics, patient characteristics, interventions, controls, and outcome measurements.
Sensitivity analysis: If sufficient available data are extracted, we will plan to conduct sensitivity analysis to check the stability for the outcome results by excluding low methodological quality studies.

Language: English.

Countries involved: China.

Other relevant information: Not applicable.

Keywords: Watershed stroke; butylphthalide; hemodynamics; effect.

Dissemination plans: We will submit this study to a peer-reviewed journal for publication.