

# INPLASY

INPLASY2023100076

doi: 10.37766/inplasy2023.10.0076

Received: 23 October 2023

Published: 23 October 2023

## Corresponding author:

Zhongming Qiu

qiuzhongmingdoctor@163.com

## Author Affiliation:

Department of Neurology, The 903rd Hospital of The Chinese People's Liberation Army, Hangzhou, China.

## Mechanical thrombectomy for large-core ischemic stroke: a systematic review and meta-analysis of randomized controlled trials with trial sequential analysis

Qiu, ZM<sup>1</sup>; Liu, C<sup>2</sup>.

## ADMINISTRATIVE INFORMATION

**Support** - This work was supported by National Natural Science Foundation of China (Nos. 82001264) and Chongqing Technology Innovation and Application Development Project (No. 2022TIAD-KPX0017).

**Review Stage at time of this submission** - Completed but not published.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY2023100076

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 October 2023 and was last updated on 13 December 2024.

## INTRODUCTION

**Review question / Objective** The objective of this study was to compare the efficacy and safety of endovascular thrombectomy (EVT) vs Medical treatment (BMT) using a systematic review and meta-analysis of randomized controlled trials.

**Condition being studied** Endovascular treatment (EVT) for acute ischemic stroke (AIS) with large ischemic core infarct did not obtain routine recommendation in current clinical guidelines.

## METHODS

**Participant or population** AIS patients with ASPECTS  $\leq 5$  or infarct core volume  $\geq 50$  mL receiving EVT or receiving best medical treatment (BMT).

**Intervention** Endovascular thrombectomy (EVT) could effectively rescue at-risk brain tissue by restoring blood flow among patients with large vessel occlusion caused acute ischemic stroke (AIS), and therefore was regarded as the first-line therapeutic strategy for these patients.

**Comparator** We conducted a systematic review and meta-analysis including all available RCTs that compared EVT in addition to best medical treatment (BMT) versus BMT alone for large-core AIS.

**Study designs to be included** Hence, based on the results of preceding retrospective research, six RCTs across different countries, namely, LAESTE, TENSION, TESLA, RESCUE-Japan LIMIT, SELECT2, and ANGEL-ASPECT, investigating the efficacy and safety of EVT among patients with large-core AIS were continuously designed and carried out. We conducted a systematic review and

meta-analysis including all available RCTs that compared EVT in addition to best medical treatment (BMT) versus BMT alone for large-core AIS.

**Eligibility criteria** The inclusion criteria for this large ischemic core systematic review and meta-analysis were as follows: (1) the study design was a randomized clinical trial; (2) patients with ASPECTS  $\leq 5$  or infarct core volume  $\geq 50$  mL, (3) interventional arm receiving EVT, and control arm receiving BMT, and (4) reporting of mRS score of 0–3 at 3 months, 90-day mortality, and sICH. Randomized trials with less than 100 patients were excluded.

**Information sources** We searched PubMed, Embase, the Cochrane Central Register of Controlled Trials, and the clinical trial registry maintained at ClinicalTrials.gov from January 1, 1980 until June 30, 2024, using the following terms: “Stroke or cerebrovascular accident or brain vascular accident OR cerebrovascular stroke OR cerebral infarct OR cerebrovascular disorder OR intracranial vascular disease OR cerebrovascular disease OR brain vascular disorder OR cerebrovascular occlusion OR cerebrovascular insufficiency OR cerebrovascular accident” and “thrombectomy OR endovascular treatment OR endovascular therapy OR aspiration thrombectomy” and “large ischemic core OR large core OR large infarct core OR large infarct region OR 50cc OR 50ml OR 70cc OR 70ml”. We limited search results to human studies and randomized clinical trials.

**Main outcome(s)** This systematic review and meta-analysis indicated that in patients with LVO stroke with a large ischemic core, EVT was associated with improved functional outcomes over MM without increasing sICH risk. The results of ongoing RCTs may provide further insight in this patient population.

**Quality assessment / Risk of bias analysis** On account of that all included studies were randomized clinical trials, these risk of bias due to randomization process, deviations from intended intervention, missing outcome data, measurement of the outcome and selection of reported results were assessed by the Cochrane Collaboration tool (RoB 2).

**Strategy of data synthesis** The analysis plan was performed on an intention-to-treat basis. The  $\chi^2$  test was used to analyze the heterogeneity of the results in each study. It was considered that an  $I^2 < 50\%$  and  $p > 0.1$  indicated that the combined

results were homogeneous, and hence, the fixed effect model was used for analysis. When  $I^2$  was  $\geq 50\%$  or  $p \leq 0.1$ , this indicated that the combination result had heterogeneity, and therefore, the random-effect model was applied to analyze the data. Risk ratio (RR) with 95% CI was used as a measure of the association of intervention strategies with outcomes.

**Subgroup analysis** Subgroup analyses based on the primary outcome were conducted according to different study characteristics: baseline onset to randomization time ( $\geq 360$  vs  $< 360$  min), the use of IVT (IVT vs not receiving IVT), the occlusion site (MCA vs ICA), different population (Asians vs non-Asians) and different etiologies (atherothrombotic vs cardioembolic vs other or unknown). We also conducted a subgroup analysis for sICH stratified by the different definitions in each study. To explore the effects of advanced perfusion imaging, association of EVT with outcomes compared to BMT were investigated in two trials of ANGEL-ASPECT and RESCUE-JAPAN LIMIT and the other trials, respectively. We connected with Principal Investigator to obtain the number of different outcomes among patients with ASPECTS 0-2 in all enrolled RCTs. The effects of EVT on outcomes were subsequently investigated among AIS with ASPECTS 0-2.

**Sensitivity analysis** Sensitivity test was conducted to identify any trial that might have exerted a disproportionate influence on the summary treatment effect on outcomes by removing each individual trial from the meta-analysis one at a time.

**Country(ies) involved** China.

**Keywords** Acute ischemic stroke, Randomized controlled trials, Endovascular treatment, best medical treatment.

#### **Contributions of each author**

Author 1 - Zhongming Qiu.

Author 2 - Chang Liu.