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Intra-arterial Thrombolysis Following Successful Thrombectomy in Patients with Acute Large Vessel Occlusion: A systematic review and meta-analysis of Randomized Control Trials

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - J.Kaesmacher reported grants from Swiss Academy of Medical Sciences/Bangerter Foundation, Swiss Stroke Society, Clinical Trials Unit Bern; Dr Saver reported receiving personal fees from Roche, Medtronic, and Genentech; and owning stock options in Rapid Mdical outside the submitted work.

INPLASY registration number: INPLASY202510042

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 January 2025 and was last updated on 13 January 2025.

INTRODUCTION

Review question / Objective We aimed to evaluate the efficacy and safety of intra-arterial thrombolysis among large vessel occlusion patients with successful reperfusion by endovascular treatment (EVT) though a study-level meta-analysis of randomized controlled trials (RCTs).

Condition being studied Endovascular treatment (EVT) has emerged as the standard of care for patients with acute ischemic stroke due to large vessel occlusion (LVO). Despite achieving successful angiographic reperfusion (expanded Thrombolysis In Cerebral Infarction [eTICI] scale 2b50-3, indicating 50-100% reperfusion of visible vessels) by EVT, less than half of stroke patients are disability-free at 90 days. Even if eTICI higher than 2b50 is achieved, visible distal emboli and microcirculatory failure (i.e. no-reflow) may impair cerebral tissue reperfusion, promote infarct growth and reduce the likelihood of functional outcome. The optimal management of acute ischemic stroke patients with large vessel occlusion (LVO) after successful angiographic reperfusion (expanded Thrombolysis in Cerebral Infarction, eTICI2b50-3) by endovascular thrombectomy (EVT) remains uncertain.

METHODS

Participant or population Patients with large vessel occlusion achieving successful reperfusion by endovascular treatment.

Intervention Intra-arterial administration of an adjunctive thrombolytic agent after EVT.

Comparator Without intra-arterial thrombolysis after EVT.

Study designs to be included Randomized Clinical Trials.

Eligibility criteria The inclusion criteria for our systematic review and meta-analysis were as follows: (1) randomized clinical trials in the English language, (2) performed a direct comparison between intra-arterial thrombolysis and standard management in patients successfully treated with EVT, (3) reporting of the modified Rankin Scale (mRS) score of 0–1 at 3 months and symptomatic intracranial hemorrhage (sICH) rates. In a second step, two investigators accessed clinicaltrials.gov and forward and backward literature searching of all articles retrieved by the systematic search to gather information on all ongoing but not finished randomized clinical trials.

Information sources MEDLINE, PubMed, Scopus, and Embase.

Main outcome(s) The modified Rankin Scale (mRS) score of 0–1 at 3 months.

Quality assessment / Risk of bias analysis The methodological quality of the clinical trials was evaluated using the Cochrane Collaboration tool (RoB 2), which considers the intended intervention, missing outcome data, measurement of the outcome, and selection of reported results.

Strategy of data synthesis All results were presented as the effect estimate appropriate to the type of outcome with 95% confidence intervals (CI) using a random-effects model based on the Mantel–Hansel method. Differences between included studies were accounted with mixed-effects model with a term for random intercept and random slope. Summations of point estimates derived from the random-effects model were used to evaluate the association between the intervention (intra-arterial thrombolytics vs control) and all primary, secondary and safety outcomes.We expect variability in patient selection among the RCTs. Therefore, we plan on using a random-effect model with restricted maximum-likelihood estimation to perform. We plan on using an inconsistency index (12) to assess for heterogeneity.

Subgroup analysis For the subgroup analysis, pooled estimates for each subgroup were calculated using a random-effects model. These pooled estimates provided summary measures of treatment effect within each subgroup. Afterward, Cochran's Q-test was used to assess treatment effect heterogeneity between the pooled strata.
• These subgroups will include: Age, gender, baseline NIHSS, Prestroke mRS, baseline ASPECTS, TOAST, and eTICI.

Sensitivity analysis To assess heterogeneity in effect size between the studies and subgroup differences, the I^2 statistic was used. An I^2value of ≥50%, or higher was considered heterogeneous. Funnel plots were used to visually assess publication bias for the primary endpoint. The Luis Furuya-Kanamori (LFK) index was used to quantify the presence of publication bias, where values from -1 to +1 indicate the absence of bias.

Country(ies) involved China, Spain.

Keywords Large vessel occlusion, Endovascular treatment, Intra-arterial thrombolysis, Successful reperfusion.

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