Endovascular Mechanical Thrombectomy in Large-Vessel Occlusion Ischemic Stroke Presenting with Low National Institutes of Health Stroke Scale: Systematic Review and Meta-Analysis

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Key words
- Intravenous tissue plasminogen activator
- Large vessel occlusion
- Mechanical thrombectomy
- Stroke

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INTRODUCTION: **Mechanical thrombectomy has become the standard of care for management of most large vessel occlusion (LVO) strokes. When patients with LVO present with minor stroke symptomatology, no consensus on the role of mechanical thrombectomy exists.**

METHODS: **A systematic review and meta-analysis were performed to identify studies that focused on mechanical thrombectomy, either as a standalone treatment or with intravenous tissue plasminogen activator (IV tPA), in patients with mild strokes with LVO, defined as a baseline National Institutes of Health Stroke Scale score ≤5 at presentation. Data on methodology, quality criteria, and outcome measures were extracted, and outcomes were compared using odds ratio as a summary statistic.**

RESULTS: **Five studies met the selection criteria and were included. When compared with medical therapy without IV tPA, mechanical thrombectomy and medical therapy with IV tPA were associated with improved 90-day modified Rankin Scale (mRS) score. Among medical patients who were not eligible for IV tPA, those who underwent mechanical thrombectomy were more likely to experience good 90-day mRS than those who were not. There was no significant difference in functional outcome between mechanical thrombectomy and medical therapy with IV tPA, and no treatment subgroup was associated with intracranial hemorrhage or death.**

CONCLUSIONS: **In patients with mild strokes due to LVO, mechanical thrombectomy and medical therapy with IV tPA led to better 90-day functional outcome. Mechanical thrombectomy plays an important role in the management of these patients, particularly in those not eligible for IV tPA.**

INTRODUCTION

Mechanical thrombectomy has recently been adopted as the standard of care for patients with acute large-vessel occlusion (LVO) and National Institutes of Health Stroke Scale (NIHSS) scores ≥6.[1] However, patients with LVO may present with minor stroke symptomatology (defined as NIHSS score ≤5), and there is evidence from nonrandomized studies to support the presence of LVO as a stronger predictor of outcome than severity of symptomatology in these patients.[2-5] With mean NIHSS scores of 16.8 in both the mechanical thrombectomy and medical groups, the 5 landmark randomized trials on thrombectomy for acute ischemic stroke published in 2015 were geared toward severe stroke symptomatology.[1] Three of the 5 trials excluded patients with NIHSS of <6[2,3] or <8[4], respectively. In recent years, multiple studies have investigated the safety and utility of mechanical thrombectomy as an efficacious alternative or supplement to medical therapy in this patient population.[6-9] We therefore sought to conduct a systematic review and meta-analysis of the existing literature to determine if mechanical thrombectomy can benefit patients with LVO who present with mild stroke symptomatology.

METHODS

Literature Search Strategy

A systematic review of studies comparing mechanical thrombectomy, either as standalone management or with intravenous tissue plasminogen activator (IV tPA), in patients with mild strokes with LVO was performed. Five electronic

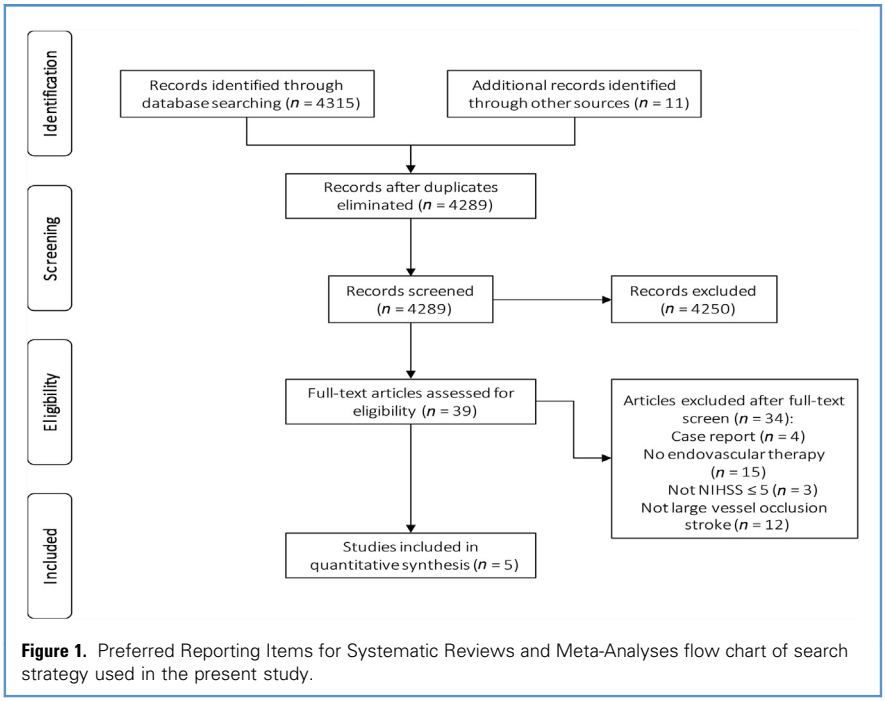

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart of search strategy used in the present study.

databases including MEDLINE, PubMed, Embase, Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews were searched from database inception to September 2017. Appropriate free text and MeSH terms were used to identify all studies: "stroke," "mild stroke," "minimal stroke," "NIHSS ≤5," "endovascular," "thrombectomy," "stent-retriever," and "thrombolysis." Reference lists of all articles found were searched to further identify potentially relevant studies.

Selection Criteria and Outcome Measures

Studies eligible for this systematic review were those that specifically included patients with mild stroke with large-vessel occlusion (intracranial internal carotid artery, middle cerebral artery M1 and M2, anterior cerebral artery, posterior circulation), defined as baseline NIHSS ≤5 at presentation. All studies selected included mechanical thrombectomy for mild stroke, either as a standalone treatment or with IV tPA. Case reports, abstracts, editorials, and expert opinions were excluded. All studies selected were human trials and in English. If more than 1 article had been published from the same center with the same dataset, only the article with the most complete dataset published was used. Functional outcomes at 90 days were assessed using the modified Rankin Score (mRS) and further classified as good (mRS score 0–2) or excellent (mRS score 0–1). Complications included 90-day mortality and symptomatic intracerebral hemorrhage, defined as an intracranial bleed resulting in clinical deterioration with an increase in the NIHSS score of ≥4 points, a 1-point deterioration in the level of consciousness, or any intracranial hemorrhage leading to death.

Data Extraction

Two reviewers (K. P., W. N.) independently appraised studies, using a standard form and extracted data on methodology, quality criteria, and outcome measures. All extracted and tabulated data were checked by an additional reviewer (C. G.). The quality of studies was assessed using assessment criteria recommended by the Centre for Evidence-Based Medicine (University of Oxford). Discrepancies between reviewers were resolved by discussion, and consensus was reached.

Statistical Analysis

The odds ratio (OR) was used as a summary statistic. In the present study, random-effect models were tested. In a random-effects model, it was assumed that there were variations between studies. χ^2 tests were used to study heterogeneity between trials. I^2 statistic was used to estimate the percentage of total variation across studies, owing to heterogeneity rather than chance, with values >50% considered as substantial heterogeneity. I^2 can be calculated as: $I^2 = 100\% \times (Q-df)/Q$, with Q defined as Cochrane's heterogeneity statistics and df defined as degree of freedom. If there was substantial heterogeneity, the possible clinical and methodologic reasons for this were explored qualitatively. In the present meta-analysis, the results using the random-effects model were presented to take into account the possible clinical diversity and methodologic variation between studies. All P values were 2-sided. All statistical analysis was conducted with Review Manager Version 5.3.3 (Cochrane Collaboration, Software Update, Oxford, United Kingdom).

Subgroup Analysis

In order to account for heterogeneity, subgroup analysis was conducted to compare mechanical thrombectomy and medical therapy with and without IV tPA. For the purposes of this meta-analysis, medical therapy populations with <10% of patients receiving IV tPA were defined as medical therapy without IV tPA.

RESULTS

Of the 4326 records identified through database searching and other sources, 5 studies met criteria for inclusion in the analysis (Figure 1).[6-10] The studies included a total of 413 cases, 52 of which were composed of 26 matched pairs. Subgroup analysis was conducted to compare mechanical thrombectomy and medical therapy with and without IV tPA (Table 1).

Mechanical Thrombectomy and Medical Therapy with IV tPA Versus Medical Therapy without IV tPA

Three studies were included in this subgroup analysis.[6,7,9] When compared with patients who received medical therapy without IV tPA, patients treated with IV tPA or mechanical thrombectomy were more likely to experience both good (OR 4.37, 95% confidence interval [CI] 1.82–10.48, $P = 0.001$) and excellent (OR 1.96, 95% CI 1.04–3.68, $P = 0.04$) mRS scores at 90 days. Testing for subgroup difference found substantial heterogeneity (I^2 =