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Thrombectomy for patients with a large infarct core: a study-level meta-analysis with trial sequential analysis

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Hong-Jie Jhou, Li-Yu Yang, Po-Huang Chen and Cho-Hao Lee

Abstract

Background: The effectiveness and safety of endovascular treatment compared with medical management alone regarding outcomes for patients with a large infarct core remain uncertain.

Objectives: To juxtapose the clinical outcomes of thrombectomy versus the best medical care in patients with a large infarct core.

Design: Systematic review and meta-analysis.

Data sources and methods: We conducted searches in PubMed, Cochrane, and Embase for articles published up until November 8, 2023. Randomized trials were selected for inclusion if they encompassed patients with large vessel occlusion and sizable strokes receiving thrombectomy. The primary outcome was functional outcomes at 3 months after pooling data using random-effects modeling. Safety outcomes included mortality at 3 months, symptomatic intracranial hemorrhage (SICH), and decompressive craniectomy. We performed a trial sequential analysis to balance type I and II errors.

Results: From 904 citations, we identified six randomized trials, involving a cohort of 1897 patients with a large ischemic region. Of these, 953 individuals underwent endovascular thrombectomy. At 3 months, thrombectomy was significantly correlated with better neurological prognosis, as evidenced by the increased odds of good functional outcomes (odds ratio (OR), 2.90; 95% confidence interval (CI), 2.08–4.05) and favorable functional outcomes (OR, 2.40; 95% CI, 1.86–3.09). Mortality rates did not demonstrably diminish as a consequence of the endovascular management (OR, 0.78; 95% CI, 0.58–1.06). However, the incidence of SICH was greater in the thrombectomy group compared to those with only medical treatment (5.5% vs 3.2%; OR, 1.77; 95% CI, 1.11–2.83). The application of trial sequential analysis yielded definitive evidence regarding favorable function outcomes and a shift in the distribution of modified Rankin scale scores at 3 months; however, others remained inconclusive.

Conclusion: The results from most of the included trials display consistency. Meta-analysis of these six randomized trials offers high-quality evidence that thrombectomy significantly mitigates disability in patients with a large infarction, while also increasing the risk of SICH.

Trial registration: PROSPERO, CRD42023480359.

Keywords: acute ischemic stroke, a large infarct core, meta-analysis, thrombectomy

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Correspondence to:
Po-Huang Chen
Cho-Hao Lee
Division of Hematology and Oncology Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, No. 325, Section 2, Cheng-gong Road, Neihu 114, Taipei, Taiwan
chenpohuang@hotmail.com
drleechohao@gmail.com

Hong-Jie Jhou
Department of Neurology, Changhua Christian Hospital, Changhua, Taiwan

School of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Li-Yu Yang
School of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Department of Neurology, Chang Bing Show Chwan Memorial Hospital, Changhua, Taiwan

Introduction

Stroke holds the position of the fifth leading cause of mortality and is a predominant contributor to disability within the United States, annually affecting nearly 800,000 individuals.[1] In 2015, a meta-analysis[2] of five randomized control trials

(RCTs) substantiated the clinical benefit of thrombectomy for patients with large vessel occlusion in anterior circulation stroke. Yet, the eligibility criteria were stringent, leading to the exclusion of many patients, such as those presenting with delayed onset of stroke or a large infarct core. Subsequent research gradually confirmed that, under specific imaging criteria, the treatment window for thrombectomy can be protracted up to 24 h.[3–5] Despite these advancements, the management of patients with a large ischemic region remains a challenging issue.

In the RESCUE-Japan LIMIT study,[6] while thrombectomy was associated with an augmented incidence of symptomatic intracranial hemorrhage (SICH), it facilitated a reduction in the proportion of disability among patients with a large infarct core. Unfortunately, due to the concentration of the trial's exclusive conduct within Japan, small number of patients, and the majority of patients being selected using magnetic resonance imaging (MRI), the research lacks broad representativeness. As a result, it may not change current clinical practices. In the subsequent RCTs,[7–11] the use of more readily accessible computed tomography (CT) imaging as selection criteria has been adopted. These trials have yielded similar findings, further extending the application of thrombectomy for large infarct core strokes. However, the number of patients included in these studies is limited, and most of the studies were prematurely terminated according to the results of a planned interim analysis. Therefore, our research aims to confirm the benefits and risks of thrombectomy for large infarct volumes through a meta-analysis.

Methods

This systematic review and meta-analysis were conducted in strict accordance with a protocol that was pre-registered (PROSPERO, CRD42 023480359). Our reporting aligns with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines,[12] which were detailed in Supplemental Table 1. Given the nature of a meta-analysis, which synthesizes data from previously published studies, ethical approval was not required for this research.

Search strategy

Our comprehensive literature search covered three databases, including Medline, Embase, and the Cochrane Central Register of Controlled Trials. The search timeframe spanned from the inception of each database to November 8, 2023 and was conducted without language restrictions. We employed a combination of keywords relating to large infarct core, thrombectomy, and optimal medical management, alongside filters to pinpoint RCTs (Supplemental Table 2). Supplemental sources included conference abstracts, trial registries (e.g., ClinicalTrials.gov), and conference presentations for unpublished data.

Study selection

RCTs investigating the effectiveness of thrombectomy on adult patients (aged ⩾18 years) with a significant infarct core, compared with those reviving best medical management (BMM), were included. Non-RCTs, case series, and studies without a control arm were excluded. When participant samples were overlapped, we only used the newest studies to avoid double counting.

Outcome measurement

Our primary outcomes were set as a good functional outcome (modified Rankin Scale (mRS) score of 0–2), a favorable functional outcome (mRS score of 0–3) at 3 months, an excellent functional outcome (mRS score of 0–1), and a shift in the distribution of mRS scores at 3 months. The safety outcomes included mortality at 3 months, SICH, and decompressive craniectomy among patients with a large infarct core following thrombectomy.

Data extraction

Titles and abstracts retrieved from the search were independently screened by two authors (H.-J.J. and L.-Y.Y.) to exclude irrelevant articles. Full-text articles that potentially met the inclusion criteria were independently evaluated by at least two reviewers. Any disputes arising throughout the selection process were resolved by discussion or with the input of the third author (P.-H.C. or C.-H.L.), if necessary. We adhered to an intention-to-treat approach, despite the suggestion that a per-protocol design might reveal larger effect sizes.

Risk of bias assessment

Two authors (H.-J.J. and L.-Y.Y.) independently assessed the methodological quality using the Cochrane risk of bias tool.[13] Disagreements were resolved through discussion or the third author. Studies were categorized as "low," "unclear," or "high" risk across several bias domains. Due to the nature of the interventions, blinding was not possible, which was factored into the bias assessment.

Handling of missing data

Efforts were made to contact trial authors to retrieve any missing data. When these attempts did not yield the missing information, analyses were conducted using only the available data. No imputation methods were employed to estimate missing data, acknowledging the potential impact this could have on the analysis results.

Statistical analysis

Our data were analyzed using fixed-effect and random-effects models as per the Cochrane Handbook for Systematic Reviews of Interventions. The fixed-effect model assumed homogeneity of effect sizes, whereas the random-effects model, using the DerSimonian and Laird methods, accounted for potential variability across studies.[14,15] Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for categorical outcomes. Statistical heterogeneity was assessed using the I^2 statistic and the Cochrane Q test, with I^2 values over 50% and a Cochrane Q p-value of less than 0.10 considered indicative of substantial heterogeneity. We also conducted subgroup analyses to explore the effect of the time from stroke onset to thrombectomy. Sensitivity analysis resulted in the exclusion of the LASTE trial,[11] published exclusively through an international conference. Small-study effects were assessed by using the regression-based Egger's test. Publication bias was determined from funnel plots for any outcome. We managed and analyzed the data using the "metafor" and "meta" packages in R software.[16–18] Significance for all two-tailed tests was set at $p < 0.05$.

Trial sequential analysis

In our meta-analysis, trial sequential analysis (TSA) was implemented with a predefined relative risk reduction of 20% to address the heightened risk of type I errors arising from limited data and repetitive testing. The TSA software (version 0.9.5.10 Beta; Copenhagen Trial Unit, Copenhagen, Denmark, www.ctu.dk/tsa), following the O'Brien–Fleming alpha-spending function, was set to a two-sided α of 0.05 and a power of 80%.[19,20] This robust statistical method recalculates sample size requirements, controls for the potential of random errors, and establishes both trial sequential monitoring boundaries and futility boundaries. By determining event rates for dichotomous outcomes and employing a fixed relative risk reduction, TSA ensures that our results are both statistically and clinically significant, safeguarding against premature estimations of effect.

Quality assessment

The quality of evidence for each outcome was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach (GRADEpro, version 20; McMaster University, 2014).[21] This assessment considered risk of bias, inconsistency, indirectness, imprecision, and publication bias. Outcomes were classified as having high, moderate, low, or very low certainty. The GRADE handbook provided guidance, and any discrepancies were settled through consensus.[22]

Results

The systematic search identified 904 citations and 37 records were excluded due to duplicates (Figure 1). After title and abstract review and full-text assessment, 858 were excluded, leaving 6 articles[6–11] that met eligibility criteria with 1 trial providing results prior to publication[10] and 1 conference data.[11] The trial characteristics were summarized in Table 1. All studies were RCTs involving 1897 participants and were included in the quantitative synthesis. In total, 953 patients

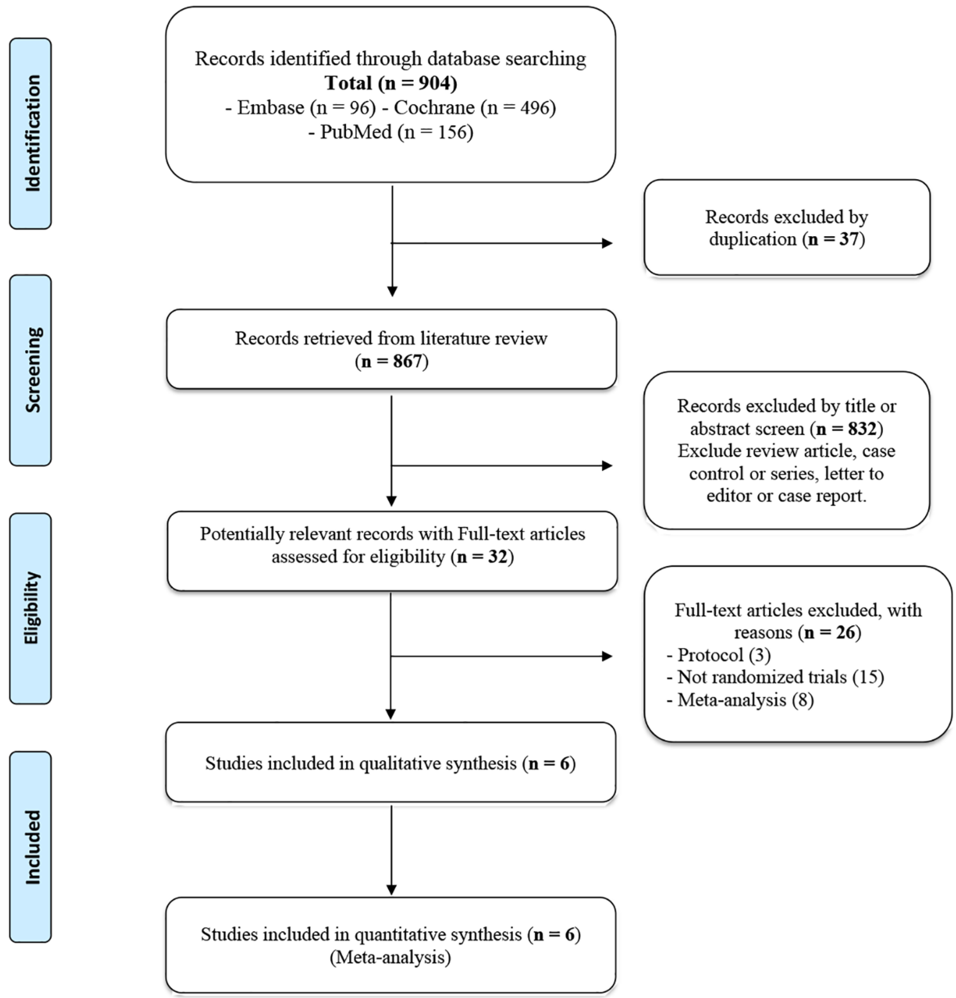

Figure 1. Flow diagram of study selection.

underwent endovascular thrombectomy, while the remainder received BMM. Table 2 outlines the characteristics of all included trials.

Primary outcomes: Good functional outcomes

Six trials[6–11] analyzing 1897 subjects provided data regarding good functional outcomes. Patients with thrombectomy had an 11.8% increase in the rate of achieving functional independence by 11.8% with a number needed to treat (NNT) of 8.3 (19.2% vs 7.4%; OR, 2.90; 95% CI, 2.08–4.05; $I^2 = 16\%$; p-value for heterogeneity = 0.31; Figure 2(a)). In subgroup analysis, thrombectomy reduced disability in all-time window and the heterogeneity was reduced (Supplemental Figure 1(A)). Similarly, the result using sensitivity analysis aligned with the antecedent analysis (Supplemental Figure 2(A)). In the findings of TSA, the z-statistic line crossed the conventional boundary in favor of patients with thrombectomy, but not pass the trial sequential monitoring boundary, suggesting inconclusive results (Supplemental Figure 3(A)).

Primary outcomes: Favorable functional outcomes

Among the six studies[6–11] analyzed for favorable functional outcomes, a significant improvement was observed in thrombectomy group, with a NNT of 6.1 (36.0% vs 19.6%; OR, 2.40; 95% CI, 1.86–3.09; $I^2 = 27\%$; p-value for heterogeneity = 0.23; Figure 2(b)). In subgroup analysis, similar results were noted in all-time window, and the heterogeneity was decreased (Supplemental Figure 1(B)). We noted similar outcomes in sensitivity analysis (Supplemental Figure 2(B)).

Table 1. Inclusion criteria of six randomized trials.

Author, year	Years of age (years)	Time window, hour	NIHSS	Pre-stroke mRS score	Occlusion site specified in protocol	Inclusion criteria
Yoshimura et al., 2022[6]	⩾18	0–24	⩾6	0–1	ICA, MCA M1	1. NCCT ASPECTS 3–5 2. DWI-MRI ASPECTS 3–5
Huo et al., 2023[7]	18–80	0–24	6–30	0–1	Terminal ICA, MCA M1	1. NCCT ASPECTS 3–5 2. NCCT ASPECTS >5 (>6 h) and core 70–100 mL 3. NCCT ASPECTS 0–2 and core 70–100 mL
Sarraj et al., 2023[8]	18–85	0–24	⩾6	0–1	Distal ICA, MCA M1	1. NCCT ASPECTS 3–5 2. Core >50 mL
Bendszus et al., 2023[9]	⩾18	0–12	<26	0–2	ICA (intracranial segment), MCA M1	1. NCCT ASPECTS 3–5 2. DWI-MRI ASPECTS 3–5
Yoo, 2023[10]	18–85	0–24	⩾6	0–1	Terminal ICA, MCA M1	1. NCCT ASPECTS 2–5
Costalat et al., 2023[11]	⩾18	0–7	NA	0–1	ICA, MCA M1, MCA M1–M2± cervical lesion (tandem)	1. NCCT ASPECTS 0–5 2. DWI-MRI ASPECTS 0–5 3. ASPECTS 4–5 in ⩾80-year-old patients

ASPECTS, Alberta Stroke Program Early Computed Tomography Score; CT, computed tomography; DWI, diffusion-weighted imaging; ICA, internal carotid artery; MCA, middle cerebral artery; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; NA, not available; NCCT, noncontrast computed tomography; NIHSS, National Institutes of Health Stroke Scale.

From the TSA results, the cumulative *z*-statistic line both crossed the conventional boundary and the trial sequential monitoring boundary in favor of patients with thrombectomy, which confirmed conclusive evidence with statistical significance (Supplemental Figure 3(B)).

Primary outcomes: Excellent functional outcomes

We pooled data from six trials[6–11] and found that the proportion of excellent function outcomes was higher in patients with thrombectomy than control group and a NNT was 19.6 (7.9% versus 4.8%; OR, 1.84; 95% CI, 1.12–3.02; $I^2 = 24\%$; *p*-value for heterogeneity = 0.25; Figure 2(c)). In subgroup analysis, the heterogeneity was reduced and only TENSION trials indicated a trend toward excellent functional outcomes in patients receiving thrombectomy (Supplemental Figure 1(C)). In sensitivity analysis, the result was no difference with antecedent analysis (Supplemental Figure 2(C)). From the TSA results, the cumulative *z*-statistic line crossed the conventional boundary in favor of patients with thrombectomy but did not reach the trial sequential monitoring boundary, leaving the meta-analysis inconclusive (Supplemental Figure 3(C)).

Primary outcomes: A shift in the distribution of modified Rankin scale scores at 3 months

Figure 3 shows the distribution of mRS scores at 3 months for overall population. The OR for a shift in the distribution of modified Rankin scale scores toward better outcomes in favor of thrombectomy was 1.63 (95% CI, 1.38–1.93; $I^2 = 45\%$; *p*-value for heterogeneity = 0.11; Figure 2(d)).[6–11] In subgroup analysis, the heterogeneity was decreased and patients with thrombectomy had a shift toward better functional status in all-time window (Supplemental Figure 1(D)). In sensitivity analysis, the result was consistent with prior analyses (Supplemental Figure 2(D)). In the TSA graph, the cumulative *z*-statistic line crossed the trial sequential monitoring boundary for significance, demonstrating conclusive evidence (Supplemental Figure 3(D)).

Table 2. Characteristics of included studies.

Author, year	Study design	Country	No. of patients	Age (year)	Female (%)	NIHSS	ASPECTS 0–2 (%)	HTN (%)	DM (%)	AF (%)	Previous Stroke (%)	tPA (%)	Occlusion site, ICA (%)	Occlusion site, M1 (%)	Occlusion site, M2 (%)	Successful recanalization (%)	Procedure-related complications (%)	Overall RoB
Yoshimura et al., 2022[6]	RCT	Japan	EVT: 101 MM: 102	76.6 ± 10.0 75.7 ± 10.2	44.0 43.0	22 (18–26) 22 (17–26)	3.9	70.3 68.6	22.8 19.6	59.4 58.8	24.8 25.5	26.7 28.4	46.5 48.0	73.3 68.6	0 3.9	86.0	8.9	Low
Huo et al., 2023[7]	RCT	China	EVT: 231 MM: 225	68 (61–73) 67 (59–73)	41.3 36.0	16 (13–20) 15 (12–19)	13.6	59.1 60.4	18.7 17.8	24.8 20.9	16.1 16.0	28.7 28.0	36.1 36.0	63.0 63.1	0.9 0.9	81.3	7.8	Low
Sarraj et al., 2023[8]	RCT	North America, Europe, Australia, New Zealand	EVT: 178 MM: 174	66 (58–75) 67 (58–75)	39.3 42.5	19 (15–23) 29 (15–22)	5.7	76.4 71.3	29.8 31.6	26.4 21.8	10.7 7.5	20.8 17.3	44.9 37.9	51.1 57.5	3.9 4.6	79.8	18.5	Low
Bendszus et al., 2023[9]	RCT	Europe, Canada	EVT: 125 MM: 128	73 (65–81) 74 (64–80)	45.0 52.0	19 (16–22) 18 (15–22)	15.1	80.0 81.0	23.0 24.0	26.0 41.0	10.0 15.0	39.0 34.0	33.0 29.0	66.0 69.0	0 1.0	83.0	7.0	Low
Yoo, 2023[10]	RCT	United States	EVT: 152 MM: 148	66 (54–74) 76.5 (57.5–73.5)	50.0 43.2	19 (15–23) 18 (14.5–21)	NA	72.1 80.9	29.5 17.7	32.9 30.9	10.8 12.2	20.4 20.3	21.7 16.2	78.3 83.8	NA	73.3	7.9	Low
Costalat et al., 2023[11]	RCT	France	EVT: 166 MM: 167	73 (66–79) 74 (65–80)	48.6 46.7	21 (18–24) 21 (18–24)	55.9	64.8 67.9	17.6 25.5	NA	NA	34.6 35.2	NA	NA	NA	86.1	6.3	Low

AF, atrial fibrillation; ASPECTS, Alberta Stroke Program Early Computed Tomography Score; DM, diabetes mellitus; EVT, endovascular thrombectomy; HTN, hypertension; ICA, internal carotid artery; M1, horizontal segment of middle cerebral artery; M2, insular segment of middle cerebral artery; MM, medical management; NA, not available, NIHSS, National Institutes of Health Stroke Scale; RCT, randomized controlled trial; RoB, risk of bias; tPA, tissue plasminogen activator.

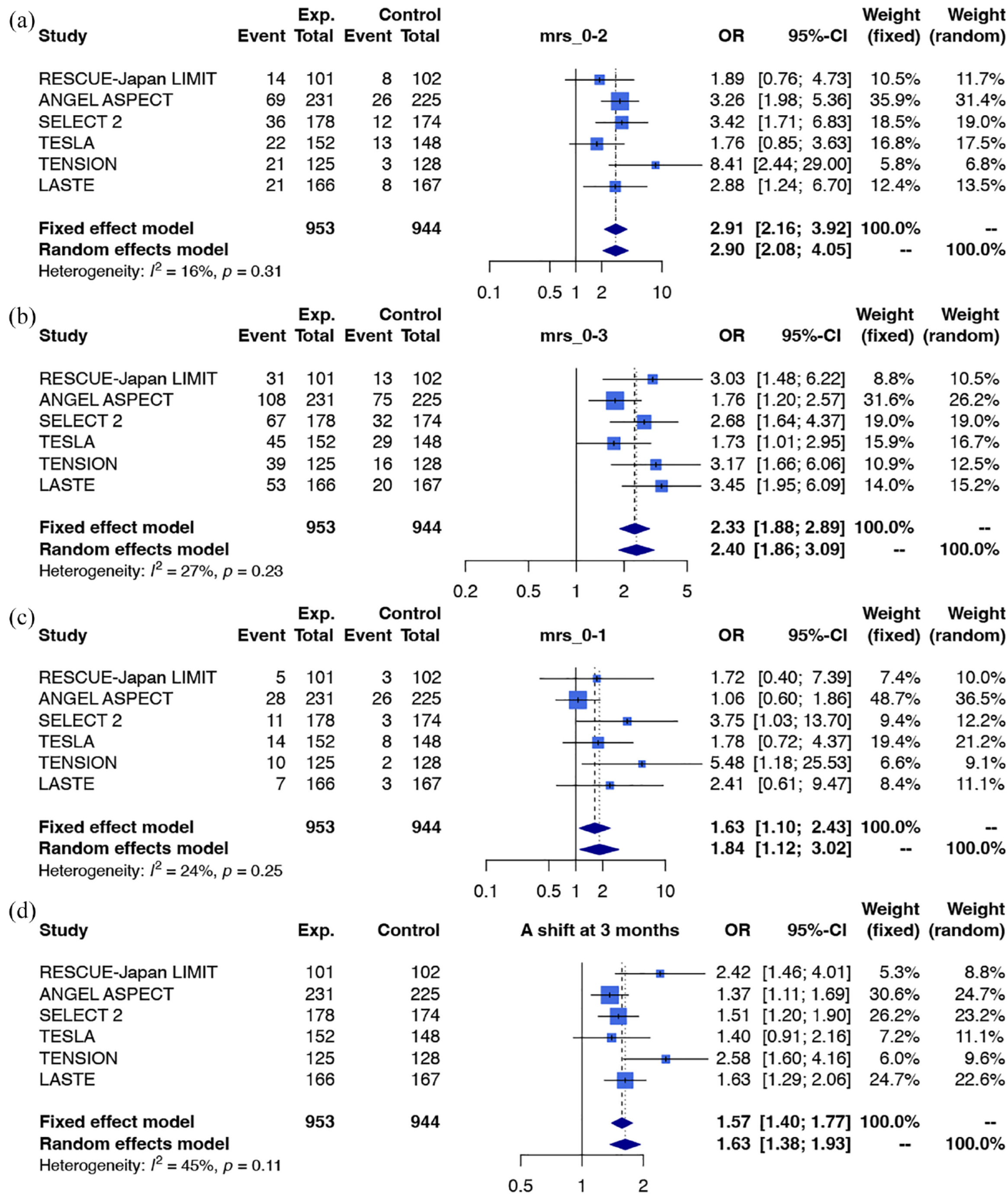

Figure 2. Forest plots showing the treatment effect for primary outcomes at 3 months. (a) Good functional outcome. (b) Favorable function outcome. (c) Excellent functional outcome. (d) A shift in the distribution of modified Rankin scale scores.

Safety outcomes: Mortality at 3 months

No significant difference was found in the risk of mortality at 3 months between patients with and without thrombectomy (31.1% vs 36.3%; OR, 0.78; 95% CI, 0.58–1.06; $I^2 = 57\%$; p-value for heterogeneity = 0.04; Figure 4(a)).[6–11] In subgroup analysis, the heterogeneity was reduced and only LASTE trials showed thrombectomy could decrease mortality (Supplemental Figure 1(E)). In sensitivity analysis, increased ORs were

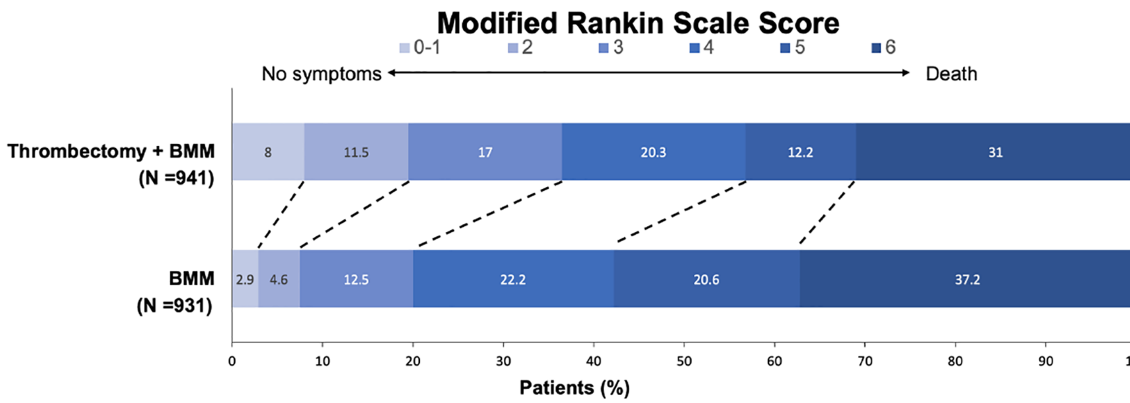

Figure 3. Distribution of scores on the modified Rankin Scale at 3 months in the intervention and control groups in the overall trial population.

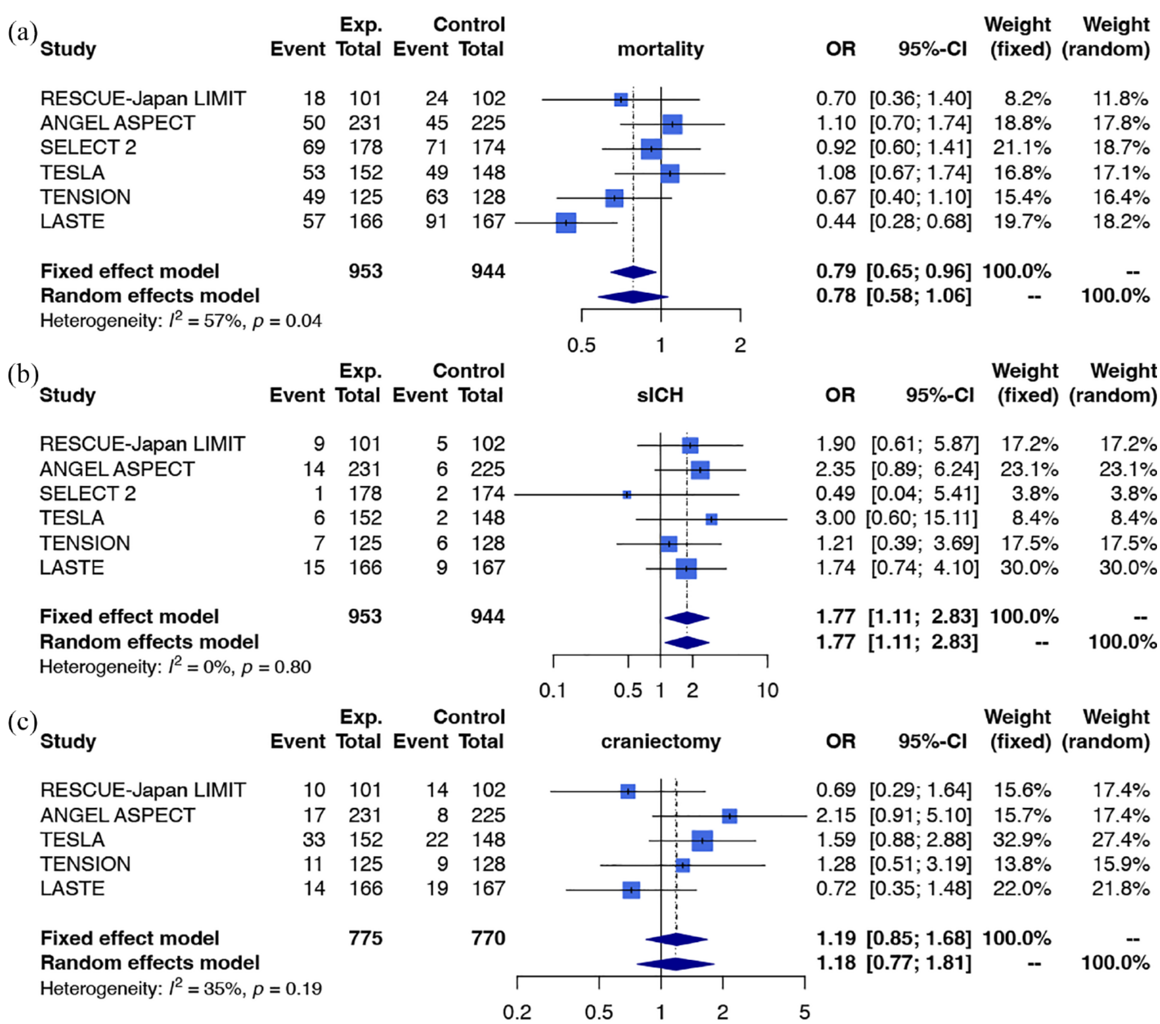

Figure 4. Forest plots demonstrating the treatment effect for safety outcomes. (a) Mortality at 3 months. (b) Symptomatic intracranial hemorrhage. (c) Decompressive craniectomy.

not observed in the thrombectomy group compared to BMM (Supplemental Figure 2(E)). From the TSA graph, the cumulative *z*-statistic line did not cross any boundary, demonstrating inconclusive evidence (Supplemental Figure 3(E)).

Safety outcomes: SICH

The proportion of patients with SICH (5.5% vs 3.2%; OR, 1.77; 95% CI, 1.11–2.83; $I^2 = 0\%$; *p*-value for heterogeneity = 0.80; Figure 4(b))[6–11] was significantly higher in patients receiving thrombectomy than in those with BMM. The number needed to harm was 43.5. In subgroup analysis, there was a higher risk of SICH in patients with thrombectomy when time window was between 0 and 24 h (Supplemental Figure 1(F)). In sensitivity analysis, thrombectomy was associated with an increased risk of SICH compared to BMM, consistent with previous analyses (Supplemental Figure 2(F)). The graph of TSA regarding SICH showed inconclusive evidence due to the *z*-curve not passing any monitoring boundary (Supplemental Figure 3(F)).

Safety outcomes: Decompressive craniectomy

The proportion of patients with decompressive craniectomy (11.0% vs 9.4%; OR, 1.18; 95% CI, 0.77–1.81; $I^2 = 35\%$; *p*-value for heterogeneity = 0.19; Figure 4(c))[6,7,9–11] was not significantly between patients receiving thrombectomy and those with BMM. In subgroup analysis, the rate of decompressive craniectomy was no difference among all-time window and the heterogeneity remained mild (Supplemental Figure 1(G)). Sensitivity analysis showed that thrombectomy did not elevate the risk of decompressive craniectomy compared to BMM (Supplemental Figure 2(G)). The graph of TSA regarding SICH showed inconclusive evidence due to the *z*-curve not passing any monitoring boundary (Supplemental Figure 3(G)).

Grading the quality of evidence

Supplemental Table 3 summarizes the risk of bias for all studies. While all studies exhibited a low overall risk of bias, there were some concerns regarding the blinding of participants and personnel in each of them. Publication bias was not observed for any of the outcomes (Supplemental Figure 4). A summary of GRADE assessments is in Supplemental Table 4. The certainty of the evidence regarding good functional outcomes, favorable functional outcomes, and a shift in the distribution of mRS scores was deemed high. The certainty of the evidence concerning an excellent functional outcome at 3 months, SICH, and decompressive craniectomy was considered moderate. In contrast, the certainty of the evidence regarding mortality at 3 months was rated as low.

Discussion

This up-to-date systematic review and meta-analysis finds that the implementation of thrombectomy over BMM for patients with a large infarct core results in the recovery of functional independence, with a NNT for a good functional outcome of 8.3. While patients undergoing endovascular management have an elevated risk of SICH, this side effect has not translated into notable differences in terms of mortality rates or the incidence of craniectomy. The findings of TSA demonstrated a favorable functional outcome and a shift in the distribution of mRS scores were conclusive, but others remain inconclusive.

Currently, the efficacy and safety of endovascular thrombectomy to rebuild cerebral circulation are established in patients with minimal ischemic area (The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) $\geqslant 6$).[2] While it seems rational to consider thrombectomy for treating patients with large infarct areas (ASPECTS <6), most studies exclude those patients due to concerns about the risk of reperfusion injury and the potential for intracranial hemorrhage. Consequently, the class of recommendation for the treatment of patients with large infarct areas remains at 2B.[23] In a prospective study,[24] one of half patients receiving thrombectomy with ASPECTS <6 achieved a good functional outcome. Therefore, thrombectomy in low ASPECTS patients might be considered until RCTs provide evidence. Despite variations in inclusion and exclusion criteria, the majority of the six recently published RCTs exhibit positive outcomes.

Our review highlights a lack of uniformity in defining large infarct areas across studies. Most involved studies rely on ASPECTS value obtained from non-contract computed tomography, sometimes complemented by perfusion imaging for assessment. Notably, the RESCUE-Japan LIMIT trial[6] mainly employs brain MRI to determine the ASPECTS score. Evidence suggests that DWI-ASPECTS scores are approximately 1 point lower than CT-ASPECTS in hyperacute stroke patients, a crucial consideration for interpreting RCT outcomes.[25] Despite the inconsistencies in image interpretation, our study affirms the role of thrombectomy in mitigating disability in stroke patients. Specifically, in stroke patients with ASPECTS 3 or less, those undergoing thrombectomy tend to demonstrate more favorable outcomes, though without statistically significant differences.[26] Regarding quantitative imaging for core volume, a treatable upper core limit is approximately 120mL in selected patients with ischemic core of 70–300m.[27] The HERMES Collaboration's analysis suggests benefits for cores up to 150mL, especially in younger patients treated swiftly.[28] Based on a post hoc analysis from SELECT-2 conducted by Sarraj et al.,[29] it is apparent that as the infarct core size, patient age, and time from imaging to reperfusion or end of procedure increase, the prognosis worsens. Therefore, a comprehensive evaluation considering both clinical and imaging data is advisable when making decisions regarding patient management.

The primary clinical trial endpoints extend beyond assessing good functional outcomes to encompass the distribution of mRS scores, median mRS scores, and utility-weighted mRS, highlighting the lack of consensus on evaluating thrombectomy's efficacy in large ischemic core patients.[30] Our findings indicate that thrombectomy significantly reduces disability across various assessment tools compared to medical management in patients with a large infarct core. In comparison to the HERMES[2] and AURORA[31] studies, our research yields results in which only half of the patients are able to regain good functional independence after thrombectomy (our study: 19.5%; HERMES study: 46%; AURORA study: 45.9%). In contrast, the rate of achieving good functional independence in the control group of our study (7.5%) is lower than that of the control group in the HERMES study (26.5%) and the AURORA study (19.3%). This discrepancy can be partially ascribed to the reduced utilization of thrombolysis and patients with a large infarction core in our study, compared to the HERMES study and AURORA studies.

When managing patients with extensive stroke, anticipating outcomes akin to those with high ASPECTS scores is impractical. To provide a more nuanced assessment of the clinical efficacy of thrombectomy, we compile the distribution of scores at 3months for both intervention and control groups across the overall trials. Our results indicate a positive shift in the mRS scale toward better outcomes, favoring endovascular therapy over medical management alone. In our analysis, we have found that the proportion of patients experiencing severe disability (43%) in our study is relatively higher when compared to the HERMES (22%) and AURORA (25%) studies, approximately twice as much. However, in comparison to medical treatment, thrombectomy results in an 8.4% reduction in the rate of mRS 5 outcomes, indicating a significant decrease in the number of patients who were bedridden. This effect not only holds clinical significance but also carries a disproportionately positive impact on both society and financial aspects.

The definition of SICH differs across studies in this analysis; three studies[7,9,11] applied the Heidelberg Bleeding Classification for SICH, while the others[6,8,10] used the SITS-MOST (Safe Implementation of Thrombolysis in Stroke-Monitoring Study) definition, with incidence rates of 6.9% and 3.7%, respectively, in thrombectomy group. This contrasts with earlier rates reported in HERMES (4.4%) and AURORA (5.3%), making the incidence rates of SICH used by SITS-MOST appear optimistic. During the thrombolysis era, the SITS-MOST definition of SICH accurately predicted poor prognosis yet remained conservative in identifying bleeding events.[32] Now, in the thrombectomy era, with the heightened risk of device-related subarachnoid hemorrhage, adopting a standardized ICH definition such as the Heidelberg Bleeding Classification becomes imperative.[33] This classification offers a thorough ICH-type assessment, meeting the requirements for post-thrombectomy evaluations.

In the meta-analysis, Abdollahifard et al.[34] analyzed 47 articles, indicating thrombectomy might enhance functional independence and reduce mortality in patients with large core infarctions compared to BMM, despite the risk of selection bias from mainly cohort studies. Wei et al.[35] focused on high-quality studies, including three RCTs and a secondary analysis of the HERMES trials,[36] and found comparable results. While prior meta-analyses[34,35] have examined the effectiveness of thrombectomy in patients with a large infarct core, our research seeks to delve into any variances between our findings and those from earlier studies. A key strength of our meta-analysis is the inclusion of six RCTs enrolling 1894 patients utilizing an intention-to-treat approach. This broader scope and updated review surpass previous meta-analyses, which relied on no more than three RCTs, improving our study's statistical robustness. Although our results align with prior analyses, we use TSA to manage the risk of type I and type II errors, offering a more conservative effect size estimation. Additionally, we incorporate an assessment of the risks of craniotomy post-thrombectomy. Finally, we appraise the certainty of the evidence using the GRADE approach, providing valuable insight for clinicians and patients in informed decision-making.

Limitation

The results of our study should be interpreted in light of its limitations. Subgroups of patients may exhibit varied responses to thrombectomy, and many of these could be adequately examined using study-level meta-analysis. Our results are in congruent with MAGNA trials,[37] an individual patient data meta-analysis, incorporating data from three published trials. Additionally, most studies do not include patients with ASPECTS 0–2 except LASTE trial. In the subgroup analysis of the LASTE trial, there is no difference of a shift in the distribution of mRS scale between two groups. Moreover, data extraction for the TESLA trial[10] is sourced from a preprint, and information for the LASTE trials[11] is obtained from conference presentations. Hence, caution is warranted, as potential minimal variations from future peer-reviewed publications could not be ruled out. Furthermore, the diverse selection criteria among trials might affect the generalizability of reported findings. Despite these differences, the analysis of outcomes does not reveal significant heterogeneity. Besides, this study was limited to thrombectomy in the internal carotid artery or M1 segment of the middle cerebral artery, restricting its generalizability to other occlusion sites. Lastly, the consideration of different core estimates and imaging modalities within the trials highlights the need for a nuanced interpretation and acknowledgment of potential variations in study outcomes.

Conclusion

Our findings indicate that thrombectomy for patients with a large infarction core has a NNT of 8.3 for the achievement of functional independence. Further trials are necessary to confirm the benefits and risks of thrombectomy for patients with ASPECTS 0–2.

Declarations

Ethics approval and consent to participate

Not applicable for this study type.

Consent for publication

Not applicable.

Author contributions

Hong-Jie Jhou: Conceptualization; Data curation; Writing – original draft.

Li-Yu Yang: Conceptualization; Writing – original draft.

Po-Huang Chen: Methodology; Writing – review & editing.

Cho-Hao Lee: Methodology; Writing – review & editing.

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Competing interests

P.-H.C. is a doctor in Tri-Service General Hospital. P.-H.C. has received grants from Tri-Service General Hospital (Fund number: TSGH-D-112157).

Availability of data and materials

The data that support the findings of this study are available from the corresponding author (P.-H.C. and C.-H.L.) on reasonable.

Protocol registration

The protocol of this systematic review and meta-analysis has been registered to PROSPERO (CRD42023480359).

ORCID iDs

Hong-Jie Jhou https://orcid.org/0000-0003-3304-4643

Li-Yu Yang https://orcid.org/0000-0003-0530-812X

Po-Huang Chen https://orcid.org/0000-0002-0280-6417

Cho-Hao Lee https://orcid.org/0000-0002-6061-5168

Supplemental material

Supplemental material for this article is available online.

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