ORIGINAL ARTICLE

Endovascular Treatment of Medium-Vessel-Occlusion Strokes

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ABSTRACT

BACKGROUND

Endovascular thrombectomy for acute ischemic stroke due to medium-vessel occlusion has had varying results across trials. Whether thrombectomy improves functional outcomes in patients with medium-vessel occlusion and moderate-to-severe deficits is unclear.

METHODS

We conducted an open-label, randomized trial with blinded outcome assessment at 48 centers in China. Eligible patients were adults who presented within 24 hours after the onset of a moderate-to-severe stroke (National Institutes of Health Stroke Scale [NIHSS] score, ≥6; scale, 0 to 42, with higher scores indicating greater neurologic deficits) due to occlusion of a medium vessel. Patients were assigned in a 1:1 ratio to thrombectomy plus medical management (thrombectomy group) or medical management alone (control group). The primary outcome was functional disability as measured by the shift in the modified Rankin scale score (scale, 0 [no disability] to 6 [death]) at 90 days. Violation of the proportional-odds assumption precluded the use of shift in the modified Rankin scale score, so as prespecified, functional independence (modified Rankin scale score of 0, 1, or 2) at 90 days was used as the primary outcome. Safety outcomes were symptomatic intracranial hemorrhage and 90-day mortality.

RESULTS

Among 280 patients in the thrombectomy group and 283 in the control group, the median age was 71 years, the median NIHSS score was 10 (range, 3 to 36), and 42.8% were women; 36.6% received intravenous thrombolysis. Functional independence at 90 days was seen in 58.6% of the patients in the thrombectomy group and in 46.6% of those in the control group (adjusted rate ratio, 1.24; 95% confidence interval, 1.07 to 1.44; P=0.004). The incidence of symptomatic intracranial hemorrhage was 4.7% in the thrombectomy group and 2.2% in the control group; 90-day mortality was 11.1% and 10.2%, respectively.

CONCLUSIONS

Among patients with acute ischemic stroke due to medium-vessel occlusion and moderate-to-severe deficits, thrombectomy led to a greater likelihood of functional independence than medical management alone but also to a higher risk of symptomatic intracranial hemorrhage. (Funded by the National Natural Science Foundation of China and the Noncommunicable Chronic Diseases–National Science and Technology Major Project; ORIENTAL-MeVO ClinicalTrials.gov number, NCT06146790.)

Medium-vessel occlusions account for 25 to 40% of ischemic strokes and represent an important clinical challenge.[1,2] Although endovascular thrombectomy has improved outcomes in patients with large-vessel occlusions, its benefit in patients with medium-vessel occlusions remains contentious. Recent randomized trials — ESCAPE-MeVO (Endovascular Treatment to Improve Outcomes for Medium Vessel Occlusions), DISTAL (Endovascular Therapy plus Best Medical Treatment [BMT] versus BMT Alone for Medium Vessel Occlusion Stroke — A Pragmatic, International, Multicenter, Randomized Trial), and DISCOUNT (Evaluation of Mechanical Thrombectomy in Acute Ischemic Stroke Related to a Distal Arterial Occlusion) — have shown neutral or unfavorable results, a situation that challenges the extrapolation of data regarding large vessels to medium arteries.[3-5]

Earlier observational studies suggested that thrombectomy for medium-vessel occlusion was technically feasible and potentially effective,[6-8] but data from recent randomized trials did not reproduce these observations. In the ESCAPE-MeVO trial, which involved 530 patients, thrombectomy showed no functional benefit as compared with usual care but did lead to higher mortality and a higher incidence of symptomatic intracranial hemorrhage.[3] Similarly, the DISTAL trial, which involved 543 patients, did not result in a lower level of disability or a lower mortality than best medical treatment alone.[4] The DISCOUNT trial, which involved 161 patients, was halted early for futility and safety, with worse functional outcomes after thrombectomy and higher rates of symptomatic intracranial hemorrhage than were seen with control.[5] Current guidelines recommended caution when considering endovascular therapy for medium-vessel occlusions.[9,10]

These previous trials, however, enrolled a patient population that was largely characterized by mild clinical deficits, older age, and high eligibility for intravenous thrombolysis — factors that potentially limited generalizability.[11] We conducted the ORIENTAL-MeVO trial to address these gaps in order to better define the role of thrombectomy in medium-vessel occlusions.

Methods

Trial Design and Oversight

We conducted this investigator-initiated, prospective, open-label, multicenter, randomized, controlled trial with blinded outcome assessment at 48 centers in China. The trial protocol (available with the full text of this article at NEJM.org) was approved by the medical ethics committee at each participating center, and the design of the trial has been published previously.[12] Written informed consent was obtained before randomization from all the patients or their legal representatives. The trial was performed in accordance with the principles of the Declaration of Helsinki and is reported according to CONSORT (Consolidated Standards of Reporting Trials) guidelines.[13,14]

The steering committee designed and oversaw the trial. The institutional review board at each participating center approved the trial. An independent data and safety monitoring board reviewed safety and conduct. An independent clinical research organization (Hope Medical Technology) monitored quality. An independent clinical-event adjudication committee, whose members were unaware of the treatment assignments, adjudicated the primary and secondary efficacy outcomes. An independent adverse-events committee assessed adverse events, procedure-related complications, and serious adverse events. All images were assessed in a blinded manner by a central imaging laboratory. An independent statistician performed the analyses. The authors vouch for the accuracy and completeness of the data and for the adherence of the trial to the protocol.

Patient Population

Adults (≥18 years of age) who had a modified Rankin scale score of 0, 1, or 2 (indicating functional independence on a scale from 0 [no disability] to 6 [death]) before the stroke and who presented with moderate-to-severe clinical deficits (defined as a National Institutes of Health Stroke Scale [NIHSS] score of ≥6, on a scale from 0 to 42, with higher scores indicating greater neurologic deficits) within 24 hours after the time that they were last known to be well were eligible. Patients had to have occlusion of the codominant or nondominant M2 or M3 segment of the middle cerebral artery (MCA); the A1, A2, or A3 segment of the anterior cerebral artery; or the P1, P2, or P3 segment of the posterior cerebral artery. The diameter of the codominant or nondominant M2 segment vessel could not exceed 2.0 mm. A codominant M2 segment supplies 50% of the MCA territory, whereas a nondominant M2 segment supplies less than 50% of the MCA territory.

A Quick Take is available at NEJM.org

The site of arterial occlusion was determined on the basis of baseline computed tomographic (CT) angiography or magnetic resonance angiography (MRA), according to the local practice at each participating center. All the vascular imaging was submitted in Digital Imaging and Communications in Medicine (DICOM) format to the central imaging core laboratory for blinded adjudication of the location of the occluded segment. Imaging had to show less than 50% ischemic involvement of the clinically estimated at-risk territory on noncontrast CT or diffusion magnetic resonance imaging (MRI) or show a penumbra-to-core mismatch ratio (the ratio of critically hypoperfused tissue to the ischemic-core estimate) of more than 1.4 with a volume of at least 10 ml on CT perfusion or MR perfusion imaging. Key exclusion criteria were multiterritory occlusions, intracranial hemorrhage, or contraindications to MRI or CT angiography.

RANDOMIZATION AND TREATMENTS

After eligibility was confirmed and written informed consent was obtained, patients were randomly assigned, in a 1:1 ratio, by a Web-based system to receive endovascular thrombectomy plus medical management (thrombectomy group) or medical management alone (control group). Randomization was stratified according to trial center and occlusion site. Endovascular approaches (stent retrievers, aspiration, angioplasty, stents, or intraarterial thrombolysis) were used at the operator's discretion. Endovascular procedures were performed by neurointerventionalists who met prespecified credentialing criteria (>5 years' experience and >80 previous thrombectomy procedures), at centers that performed more than 100 thrombectomy procedures per year. Standard medical treatment was provided according to current guidelines and included antiplatelet therapy (one or two antiplatelet agents, at the discretion of the treating physician) and intravenous thrombolysis with alteplase or tenecteplase when patients met established eligibility criteria.[10,15]

OUTCOMES

The primary outcome was functional disability at 90 days (within a window of ±14 days) in the intention-to-treat population. Functional disability was determined on the basis of the modified Rankin scale score by means of structured telephone interviews conducted with patients or caregivers by evaluators who were unaware of the treatment assignments. The planned primary analysis was assessment of an ordinal shift in the distribution of modified Rankin scale scores. In the event of violation of the proportional-odds assumption, functional independence (a modified Rankin scale score of 0, 1, or 2) was prespecified to serve as the primary outcome.

Secondary outcomes included functional independence (if not elevated to the primary outcome); excellent outcome (modified Rankin scale score, 0 or 1); independent ambulation (modified Rankin scale score, ≤3); shift in the full 7-level distribution of modified Rankin scale scores; the NIHSS score at 24 hours (within a window of ±6 hours) and at 5 to 7 days after randomization or at discharge, whichever occurred first; and quality of life as measured by means of the EuroQoL Group 5-Dimension 5-Level (EQ-5D-5L) questionnaire.[16] Safety outcomes included symptomatic intracranial hemorrhage, assessed according to the modified SITS-MOST (Safe Implementation of Thrombolysis in Stroke-Monitoring Study) criteria,[17] and 90-day mortality. Imaging outcomes included intracranial hemorrhage, assessed according to the Heidelberg classification,[18] and recanalization on CT angiography or MRA at 24 to 72 hours.

STATISTICAL ANALYSIS

The sample-size calculation was based on a dichotomized modified Rankin scale outcome (a score of 0, 1, or 2 vs. a score of 3 to 6). We assumed that 46% of the patients in the control group and 58% of those in the thrombectomy group would have a modified Rankin scale score of 0, 1, or 2 at 90 days. This difference is equivalent to a common odds ratio of 1.62 for functional improvement across the modified Rankin scale, a value within the range that was reported in a meta-analysis comparing intravenous thrombolysis with standard care in a subgroup of patients with non–large-vessel occlusion (odds ratio, 1.65).[19] Allowing for 5% of the patients to withdraw, we calculated that the enrollment of 564 patients would provide the trial with 80% power for the planned analysis.

In the intention-to-treat analysis, patients with protocol deviations (including crossover) were retained in the randomized group; only patients who withdrew consent were excluded from the intention-to-treat population. The proportional-odds assumption was evaluated with the use of the Brant test. Analyses of binary

outcomes were performed with generalized linear models with a Poisson distribution, a log link, and robust standard errors to estimate rate ratios and risk ratios directly.[20] For the comparison of the NIHSS and EQ-5D-5L questionnaire scores at 90 days (modeled as continuous variables), a gaussian distribution with an identity link function was used to estimate the mean difference.

Missing data for the modified Rankin scale score at 90 days were addressed with the use of multiple imputation by chained equations. Ten imputed datasets were generated with predictive mean matching (five nearest neighbors) to preserve the observed distributions. The imputation model included patient age, the baseline NIHSS score, the modified Rankin scale score before the stroke, and occlusion site. Derived categorical outcomes (e.g., modified Rankin scale score of 0, 1, or 2: yes or no) were computed from the imputed continuous modified Rankin scale values in each dataset.

Subgroup analyses were prespecified for the primary outcome and were defined according to patient age (<70 or ≥70 years), sex (male or female), baseline stroke severity (NIHSS score of <8 or ≥8; and NIHSS score of <10 or ≥10), the presumed cause (large-artery atherosclerosis, cardioembolism, undetermined cause, or other determined cause), time from onset to randomization (≤4.5 hours, >4.5 to <8 hours, or ≥8 hours), occlusion site (M2 segment, M3 segment, anterior cerebral artery, or posterior cerebral artery), and intravenous thrombolysis (no or yes). Because confidence intervals were not adjusted for multiple comparisons, causal inferences should not be drawn from secondary and subgroup analyses.

Analyses were performed with the use of Stata software, version 17.0 (StataCorp). Additional details are provided in the statistical analysis plan, which was finalized before the database lock and is provided with the protocol. A cost-effectiveness analysis was specified in the protocol but is not reported here.

RESULTS

PATIENTS

From December 2023 through April 2025, a total of 564 patients were enrolled at 48 sites (Fig. S1 in the Supplementary Appendix, available at NEJM.org) and randomly assigned to receive either endovascular thrombectomy plus standard medical management (281 patients) or standard medical management alone (283 patients). One patient in the thrombectomy group withdrew shortly after randomization and was excluded from the intention-to-treat analysis, which left 563 patients in the primary analysis (Fig. S2).

Twelve patients (2.1%) crossed over to the other treatment (9 patients from control to thrombectomy, and 3 from thrombectomy to control). A total of 14 patients had protocol violations, including 8 (3 in the thrombectomy group and 5 in the control group) with a baseline NIHSS score of less than 6 (Table S4). Primary-outcome data were missing for 11 patients (for 7 in the thrombectomy group and for 4 in the control group).

The demographic and clinical characteristics of the patients at baseline were well balanced between the two groups (Table 1 and Table S1). The representativeness of the trial population is shown in Table S2. The median age of the patients was 71 years (interquartile range, 62 to 77 in the thrombectomy group and 62 to 78 in the control group); 42.8% of the patients were women. Overall, the median baseline NIHSS score was 10 (interquartile range, 7 to 15; range, 3 to 36).

Occlusion of the M2 segment of the MCA was present in 38.9% of the patients, and occlusion of the M3 segment in 18.5%. Intravenous thrombolysis was administered in 206 patients (36.6%). Among patients who presented within 4.5 hours after onset, 167 of 361 (46.3%) received intravenous thrombolysis. Antiplatelet therapy was used in 67.1% of the patients in the thrombectomy group and in 77.4% of those in the control group, and anticoagulation was used in 28.6% of the patients in each group. Atrial fibrillation was present in 29.6% of the patients in the thrombectomy group and in 21.2% of those in the control group, and carotid stenosis was observed in 36.4% and 34.6%, respectively.

In the thrombectomy group, the median time from onset to arterial access was 5.3 hours. Complete reperfusion (defined as expanded Thrombolysis in Cerebral Infarction [eTICI] grade 3, on a scale from 0 [no reperfusion] to 3 [full reperfusion in the distribution of the occluded artery]) on the initial angiographic assessment was present in 16 of 277 patients (5.8%). Successful reperfusion at the end of the procedure, defined by an eTICI grade of 2b50 (reperfusion of 50 to 66% of the affected vascular territory) to 3, occurred in

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Thrombectomy Group (N=280)	Control Group (N=283)
Median age (IQR) — yr	71 (62–77)	71 (62–78)
Sex — no. (%)		
Male	164 (58.6)	158 (55.8)
Female	116 (41.4)	125 (44.2)
Modified Rankin scale score of 1 or 2 before stroke onset — no. (%)†	36 (12.9)	32 (11.3)
Median NIHSS score (IQR)‡	10 (8–16)	10 (7–15)
Cause of stroke — no. (%)§		
Large-artery atherosclerosis	134 (47.9)	160 (56.5)
Cardioembolism	111 (39.6)	110 (38.9)
Undetermined cause	33 (11.8)	13 (4.6)
Other determined cause	2 (0.7)	0
Occlusion site¶		
M2 segment	123 (43.9)	96 (33.9)
M3 segment	37 (13.2)	67 (23.7)
Anterior cerebral artery	66 (23.6)	63 (22.3)
Posterior cerebral artery	54 (19.3)	57 (20.1)
Intravenous thrombolysis — no. (%)	101 (36.1)	105 (37.1)
Antiplatelet therapy — no. (%)	188 (67.1)	219 (77.4)
Anticoagulation — no. (%)	80 (28.6)	81 (28.6)
Median duration (IQR) — hr		
From stroke onset to imaging	3.3 (1.9–6.1)	3.4 (1.6–6.4)
From stroke onset to randomization	5.0 (3.4–8.2)	5.0 (3.4–7.8)
From stroke onset to arterial access	5.3 (3.8–8.6)	NA
From stroke onset to revascularization	6.4 (5.0–9.3)	NA
From puncture to revascularization	1.0 (0.7–1.6)	NA
Final eTICI 2b50 to 3 — no./total no. (%)‖	206/277 (74.4)	NA
Variables on CT perfusion**		
Median lesion volume with cerebral blood flow <30% (IQR) — ml	8.4 (1.2–22.6)	4.2 (0–14.3)
Median lesion volume with Tmax >6 sec (IQR) — ml	53.9 (29.3–74.7)	37.1 (24.0–65.3)
Median mismatch ratio (IQR)††	4.3 (2.1–8.7)	5.0 (2.8–9.5)

* Patients were assigned to receive endovascular thrombectomy plus medical management (thrombectomy group) or medical management alone (control group). IQR denotes interquartile range, NA not applicable, and Tmax time to the maximum of the residue function.

† Scores on the modified Rankin scale of functional disability range from 0 (no disability) to 6 (death).

‡ Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating greater neurologic deficits.

§ The cause of stroke was evaluated on the basis of the medical history, clinical characteristics, and imaging results.

¶ Patients had occlusion of the medium-size segments of the middle cerebral artery (M2 or M3); segment A1, A2, or A3 of the anterior cerebral artery; or segment P1, P2, or P3 of the posterior cerebral artery.

‖ The expanded Thrombolysis in Cerebral Infarction (eTICI) scale ranges from 0 (no reperfusion) to 3 (full reperfusion in the distribution of the occluded artery). An eTICI grade of 2b50 indicates reperfusion of 50 to 66% of the affected vascular territory.

** Among 275 patients with baseline CT perfusion data, 253 (92.0%) had high-quality scans suitable for quantitative analysis.

†† The mismatch ratio is the ratio of critically hypoperfused tissue to the ischemic-core estimate.

206 of 277 patients (74.4%). The median time from onset to revascularization was 6.4 hours. General anesthesia was used in 94 of 277 patients (33.9%). The most common first-pass approach was combined stent retriever plus aspiration (in 123 of 262 patients [46.9%]), followed by aspiration alone (in 53 [20.2%]) and stent retriever alone (in 25 [9.5%]). Adjunctive techniques included intraarterial thrombolytic agents (in 53 of 262 patients [20.2%]) and balloon angioplasty (in 6 [2.3%]).

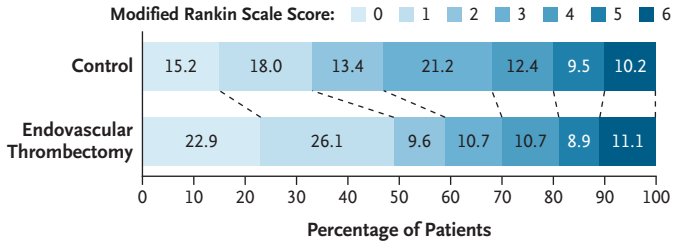

Figure 1. Distribution of Functional Outcomes at 90 Days (Intention-to-Treat Population).

Shown are scores on the modified Rankin scale for patients in the two treatment groups. Patients had been randomly assigned to receive endovascular thrombectomy plus medical management or medical management alone (control). The intention-to-treat population included all the patients who had undergone randomization, except for one patient in the thrombectomy group who withdrew shortly after randomization and was excluded. Scores on the modified Rankin scale range from 0 to 6, with 0 indicating no disability, 1 no clinically significant disability, 2 slight disability (patients are able to look after their own affairs without assistance but are unable to carry out all previous activities), 3 moderate disability (patients require some help but are able to walk unassisted), 4 moderately severe disability (patients are unable to attend to bodily needs without assistance and are unable to walk unassisted), 5 severe disability (patients require constant nursing care and attention), and 6 death. Percentages may not total 100 because of rounding.

PRIMARY AND SECONDARY OUTCOMES

The distribution of modified Rankin scale scores at 90 days in the intention-to-treat population is shown in Figure 1. The median modified Rankin scale score at 90 days was 2 (interquartile range, 1 to 4) in the thrombectomy group and 3 (interquartile range, 1 to 4) in the control group. The Brant test indicated a violation of the parallel regression assumption (P=0.02), which precluded the use of a common odds ratio. As prespecified, functional independence was therefore elevated to the primary outcome. Functional independence (modified Rankin scale score of 0, 1, or 2) was observed in 58.6% of the patients in the thrombectomy group, as compared with 46.6% of those in the control group (adjusted rate ratio, 1.24; 95% confidence interval [CI], 1.07 to 1.44; P=0.004).

An excellent outcome (modified Rankin scale score of 0 or 1) at 90 days was more common in the thrombectomy group than in the control group (in 48.9% vs. 33.2% of the patients; adjusted rate ratio, 1.47; 95% CI, 1.20 to 1.78). Other efficacy outcomes are reported in Table 2 and Table S5.

SAFETY

Mortality at 90 days was 11.1% in the thrombectomy group and 10.2% in the control group (adjusted risk ratio, 1.11; 95% CI, 0.70 to 1.76) (Table 2); overall mortality at 90 days was 10.7%. Symptomatic intracranial hemorrhage at 24 to 72 hours occurred in 4.7% of the patients in the thrombectomy group and in 2.2% of those in the control group (adjusted risk ratio, 2.21; 95% CI, 0.87 to 5.63). Any intracranial hemorrhage on imaging at 24 to 72 hours was more common in the thrombectomy group than in the control group (in 11.4% vs. 6.0% of the patients). Procedure-related adverse events occurred exclusively in the thrombectomy group and included distal embolization or occlusion (in 28 patients), embolization to a new vascular territory (in 5), arterial dissection (in 6), and vessel perforation (in 1). Other adverse events are reported in Table S6, and causes of death are listed in Table S7.

SUBGROUP ANALYSES

The prespecified subgroup analyses are shown in Figure 2. In these analyses, no clear treatment effect was observed among patients with a baseline NIHSS score of less than 8, occlusion of the M3 segment, or randomization at 8 or more hours after the time that the patient was last known to be well.

Results in the per-protocol population were similar to those in the intention-to-treat population (Tables S8 and S9 and Figs. S3 and S4). Sensitivity analyses with the use of complete cases, mixed-effects models, and 20 imputed datasets yielded results that were consistent with the primary analyses (Table S10).

Table 2. Trial Outcomes According to Assigned Treatment.*

Outcome	Thrombectomy Group (N=280)	Control Group (N=283)	Adjusted Value (95% CI)†
Primary outcome			
Median modified Rankin scale score (IQR)	2 (1 to 4)	3 (1 to 4)	—
Modified Rankin scale score of 0, 1, or 2 at 90 days — no. (%)	164 (58.6)	132 (46.6)	1.24 (1.07 to 1.44)‡
Secondary clinical outcomes§			
Modified Rankin scale score at 90 days — no. (%)			
0	64 (22.9)	43 (15.2)	1.52 (1.08 to 2.14)
0 or 1	137 (48.9)	94 (33.2)	1.47 (1.20 to 1.78)
0–3	194 (69.3)	192 (67.8)	1.01 (0.92 to 1.12)
0–4	224 (80.0)	227 (80.2)	1.00 (0.92 to 1.08)
0–5	249 (88.9)	254 (89.8)	0.99 (0.94 to 1.04)
Median NIHSS score (IQR)¶			
At 24 hr, with window of ±6 hr	9 (4 to 15)	8 (5 to 14)	0.81 (–0.27 to 1.88)
At 5–7 days or discharge	4 (1 to 10)	6 (3 to 13)	–1.27 (–2.56 to 0.03)
Barthel Index of 95 or 100 at 90 days — no. (%)‖	159 (56.8)	140 (49.5)	1.14 (0.99 to 1.31)
Median EQ-5D-5L score at 90 days (IQR)**	0.95 (0.78 to 1.00)	0.90 (0.70 to 1.00)	0.04 (–0.02 to 0.09)
Secondary imaging outcomes			
Patency at 24–72 hr on CTA or MRA — no./total no. (%)††	147/179 (82.1)	84/182 (46.2)	1.76 (1.49 to 2.09)
Intracranial hemorrhage at 24–72 hr as assessed radiologically — no. (%)	32 (11.4)	17 (6.0)	1.94 (1.12 to 3.35)
Safety outcomes			
Death — no. (%)	31 (11.1)	29 (10.2)	1.11 (0.70 to 1.76)
Symptomatic ICH at 24–72 hr — no./total no. (%)‡‡	13/275 (4.7)	6/271 (2.2)	2.21 (0.87 to 5.63)

* CTA denotes computed tomographic angiography, and MRA magnetic resonance angiography.

† Estimates were adjusted for patient age, the modified Rankin scale score before the stroke, the time from onset to randomization, stroke severity (according to the NIHSS score), and occlusion site. For NIHSS scores and EuroQoL Group 5-Dimension 5-Level (EQ-5D-5L) questionnaire scores, treatment effects are expressed as adjusted beta-coefficients with 95% confidence intervals. Effect estimates for positive binary outcomes are reported as adjusted rate ratios, and effect estimates for negative binary outcomes are reported as adjusted risk ratios.

‡ P=0.004.

§ Confidence intervals for secondary clinical outcomes were not adjusted for multiplicity and are not intended for formal hypothesis testing.

¶ Data for the NIHSS score at 24 hours were available for surviving patients. The score at 24 hours was not available for 11 patients: 2 (both in the thrombectomy group) had died before assessment, and scores were missing for 9 (1 in the thrombectomy group and 8 in the control group). The score at 5 to 7 days or discharge was not available for 26 patients: 8 (2 in the thrombectomy group and 6 in the control group) had died before assessment, and scores were missing for 18 (10 in the thrombectomy group and 8 in the control group). The worst possible score was assigned for patients who had died, in accordance with the statistical analysis plan.

‖ The Barthel Index is an ordinal scale for measuring patients' performance of self-care and activities of daily living. Scores range from 0 to 100, with 0 indicating severe disability and a score of 95 or 100 indicating no disability that interferes with daily activities. The worst possible score was assigned for patients who had died, in accordance with the statistical analysis plan.

** The EQ-5D-5L questionnaire is a standardized instrument for the measurement of health status. Scores range from –0.39 to 1.00, with higher scores indicating better quality of life. A score of 0.00 is the value of a health state equivalent to death, with negative values being worse than death and a score of 1.00 indicating full health.

†† Patency was defined as a score of 2 or 3 on the modified Arterial Occlusive Lesion scale, which ranges from 0 (complete occlusion) to 3 (complete recanalization and restoration of the target artery). Data for follow-up CTA or MRA were not available for 202 patients (101 in the thrombectomy group and 101 in the control group) because of serious illness or death.

‡‡ Symptomatic intracranial hemorrhage (ICH) was evaluated by an adverse-event committee according to the modified SITS-MOST (Safe Implementation of Thrombolysis in Stroke-Monitoring Study) criteria.[17]

DISCUSSION

In this randomized trial involving patients with acute ischemic stroke due to medium-vessel occlusion and moderate-to-severe deficits, endovascular thrombectomy plus standard medical management improved functional independence at 90 days as compared with standard care alone. The ordinal distribution was directionally concordant, with more patients having excellent outcomes in the thrombectomy group than in the control group. Mortality was similar in the two groups, although symptomatic intracranial hemorrhage was more frequent with thrombectomy than with control.

The observed treatment effect on functional independence was clinically meaningful. The absolute between-group difference of approximately 12 percentage points corresponds to a number needed to treat of 8.2 (95% CI, 3.1 to 13.3) to observe a functional-independence outcome — a magnitude similar to that reported for established

Subgroup	Endovascular Thrombectomy	Control	Adjusted Rate Ratio (95% CI)
	no. of patients with modified Rankin scale score of 0, 1, or 2 (%)		
All patients	164 (58.6)	132 (46.6)	1.24 (1.07–1.44)
Age			
<70 yr	84 (67.7)	69 (57.0)	1.13 (0.94–1.37)
≥70 yr	80 (51.3)	63 (38.9)	1.39 (1.10–1.74)
Sex			
Male	105 (64.0)	78 (49.4)	1.27 (1.06–1.52)
Female	59 (50.9)	54 (43.2)	1.30 (1.02–1.67)
NIHSS score			
<8	52 (74.3)	54 (75.0)	0.98 (0.80–1.19)
≥8	112 (53.3)	78 (37.0)	1.41 (1.15–1.74)
<10	90 (75.6)	75 (61.5)	1.22 (1.03–1.45)
≥10	74 (46.0)	57 (35.4)	1.31 (1.01–1.69)
Cause of stroke			
Large-artery atherosclerosis	73 (54.5)	75 (47.2)	1.16 (0.94–1.43)
Cardioembolism	67 (60.4)	49 (44.6)	1.31 (1.02–1.67)
Undetermined	24 (68.6)	7 (53.9)	1.26 (0.76–2.11)
Time from onset to randomization			
≤4.5 hr	69 (58.0)	57 (47.9)	1.30 (1.04–1.62)
>4.5 to <8 hr	53 (60.9)	45 (44.6)	1.38 (1.06–1.79)
≥8 hr	40 (55.6)	30 (47.6)	1.08 (0.79–1.47)
Occlusion site			
M2 segment	80 (65.0)	42 (43.8)	1.43 (1.12–1.82)
M3 segment	16 (43.2)	38 (56.7)	0.84 (0.55–1.29)
Anterior cerebral artery	37 (56.1)	29 (46.0)	1.25 (0.93–1.69)
Posterior cerebral artery	31 (57.4)	23 (40.4)	1.37 (0.95–2.00)
Intravenous thrombolysis			
No	103 (57.5)	80 (44.9)	1.26 (1.04–1.52)
Yes	61 (60.4)	52 (49.5)	1.21 (0.96–1.53)

Figure 2. Subgroup Analyses of a Modified Rankin Scale Score of 0, 1, or 2, Indicating Functional Independence, at 90 Days (Primary Outcome).

The trial was not powered and had no prespecified correction for multiple comparisons for a definitive analysis of subgroups. Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating greater neurologic deficits. Patients had occlusion of the medium-size segments of the middle cerebral artery (M2 or M3); the A1, A2, or A3 segment of the anterior cerebral artery; or the P1, P2, or P3 segment of the posterior cerebral artery. The arrow indicates that the confidence interval extends outside the graphed area.

reperfusion therapies in acute ischemic stroke and consistent with meaningful improvement in patient-centered functional outcomes.[21,22]

A potential explanation for the positive findings of the ORIENTAL-MeVO trial, in contrast to the neutral or negative results of the ESCAPE-MeVO, DISTAL, and DISCOUNT trials, could be differences in baseline stroke severity across the trial populations.[3-5] The patients in our trial presented with a higher median NIHSS score than those in the previous trials, which indicated more-severe neurologic deficits at baseline. Patients with more-severe deficits have a lower likelihood of spontaneous recovery and may derive greater benefit from reperfusion therapies. In a finding consistent with this hypothesis, no benefit was observed among patients with an NIHSS score of less than 8, a pattern that has also been suggested in previous trials.[6,23-27] The treatment effect that was observed in the ORIENTAL-MeVO trial may therefore reflect the greater responsiveness to reperfusion in patients who present with more-severe deficits.

The percentage of patients who received intravenous thrombolysis in our trial was lower than expected. Among patients who presented within 4.5 hours after onset, approximately half received thrombolysis, with the remainder excluded because of contraindications, uncertain onset time, or a decision by the patient or physician. This practice pattern probably influenced the overall percentage of patients who received thrombolysis and should be considered when interpreting the generalizability of our findings.

The high proportion of patients with large-artery atherosclerosis reflects the predominance of intracranial atherosclerotic disease in Asian populations.[28,29] This designation refers to parent-artery atherosclerosis (in the intracranial internal carotid artery, M1 segment, and vertebrobasilar arteries) leading to either artery-to-artery embolism or in situ thrombosis involving distal segments (M2 or M3, A2 or A3, or P2 or P3), as opposed to referring to primary atherosclerotic disease within the distal vessels themselves. Primary atherosclerotic disease within distal arteries rarely develops; however, these arteries are frequent targets of emboli originating from proximal intracranial atherosclerotic stenosis. This distinction is relevant when comparing our cohort with those in Western trials involving patients with medium-vessel occlusion, given that cardioembolism is more common in Western countries than in China.[6]

Other differences may also have contributed. Patients in this trial were younger and less likely to receive intravenous thrombolysis than those in previous trials. Given that thrombolysis is more effective in distal occlusions than in proximal large-vessel occlusions,[30,31] its lower use in this trial may have increased the incremental value of thrombectomy. Nonetheless, the treatment effect was similar in the two subgroups defined according to thrombolysis use, a finding that suggests that this factor only partly explains the findings. Procedural flexibility, including the use of intraarterial thrombolysis, may also have contributed.[32]

The incidence of symptomatic intracranial hemorrhage was higher with thrombectomy than with control — a finding consistent with results in previous randomized trials and registry data.[3-8] Mortality was similar in the two trial groups, and the overall 10.7% mortality in our trial is in line with previous reports.[3-8] These findings highlight the importance of careful patient selection, particularly given the smaller infarct burden that is typically associated with strokes due to medium-vessel occlusion.

This trial has limitations. First, the relatively low percentage of patients who received intravenous thrombolysis in our trial population may reflect both the longer 24-hour recruitment window and regional variations in stroke-care infrastructure and prehospital workflows, which could have influenced the observed treatment effect. Second, patients with milder deficits (NIHSS score, <6) were excluded from our trial because previous observational studies and recent randomized trials have suggested no incremental benefit of thrombectomy in patients with medium-vessel occlusion.[3,4,6,25]

Third, all the patients were enrolled in China, where the incidence of embolic stroke is lower than that in Western populations, which may limit the generalizability of the findings. A complementary randomized trial in a Western population is ongoing (DUSK; ClinicalTrials.gov number, NCT05983757). Fourth, functional independence at 90 days was ascertained primarily by means of telephone interview and relied on patient or caregiver report, which may introduce misclassification bias and influence observed treatment effects. Fifth, imaging-based

eligibility criteria excluded patients with large, established infarctions, which may limit the generalizability of the findings to patients with extensive ischemic cores.

In this trial involving patients with medium-vessel occlusion and moderate-to-severe deficits, endovascular thrombectomy plus medical management within 24 hours after symptom onset led to a significantly higher percentage of patients with functional independence than medical management alone but also led to a higher risk of symptomatic intracranial hemorrhage. These findings support the consideration of endovascular therapy in carefully selected patients with medium-vessel occlusion.

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