Stroke

CLINICAL TRIALS

Endovascular Therapy Versus Medical Management for Large Ischemic Infarct: 1-Year Outcomes of the ANGEL-ASPECT Trial

Xiaochuan Huo, MD, PhD*; Dapeng Sun, MD, PhD*; Thanh N. Nguyen, MD*; Gaoting Ma, MD, PhD; Yuesong Pan, PhD; Xin Tong, MD; Guangxiong Yuan, MD; Hongxing Han, PhD; Wenhuo Chen, PhD; Ming Wei, MD; Jiangang Zhang, MD; Zhiming Zhou, MD; Xiaoxi Yao, BS; Weigen Song, BS; Xueli Cai, MD; Guangxian Nan, MD; Di Li, MD; Alvin Yi-Chou Wang, MD; Wentong Ling, BS; Chuwei Cai, MD; Changming Wen, MD; En Wang, MD; Liyong Zhang, MD; Changchun Jiang, MD; Geng Liao, MD; Xiaohui Chen, MD; Tianxiao Li, MD; Shudong Liu, MD; Jinglun Li, MD; Yaxuan Sun, MD; Na Xu, MD; Zong'en Gao, MD; Dongsheng Ju, MD; Cunfeng Song, MD; Feng Zhou, MD; Qing Shi, MD; Jun Luo, MD; Yan Liu, MD; Zaiyu Guo, MD; Hongbo Zheng, MD; Linzhi Dai, MD; Junfeng Zhao, MD; Xiaokun Geng, MD; Yufeng Tang, MD; Congguo Yin, MD; Hua Yang, MD; Xuelei Zhang, MD; Shuo Li, MD; Mohamad Abdalkader, MD; Feng Gao, MD, PhD; Ning Ma, MD, PhD; Dapeng Mo, MD, PhD; Zeguang Ren, MD; Liping Liu, MD, PhD; Yongjun Wang, MD, PhD; Zhongrong Miao, MD, PhD; on behalf of the ANGEL-ASPECT Investigators†

BACKGROUND: Several trials have shown the benefit and safety of endovascular therapy (EVT) compared with medical management (MM) of patients with a large ischemic core in the 90-day follow-up. However, the 1-year outcome comparison between EVT and MM in Asian patients with a large ischemic core has not been investigated. Our aim was to evaluate the 1-year outcomes of patients in the ANGEL-ASPECT trial (Endovascular Therapy in Acute Anterior Circulation Large Vessel Occlusive Patients with a Large Infarct Core).

METHODS: In this phase 3, randomized, open-label, blinded end point assessment trial, patients with anterior circulation large vessel occlusion and an Alberta Stroke Program Early CT Score of 3 to 5 or an infarct core volume of 70 to 100 mL were enrolled across 46 hospitals in China. Patients were randomly assigned 1:1 to EVT or MM. The 90-day outcomes were previously reported. We report a prespecified analysis of the ANGEL-ASPECT trial, with 1-year functional outcome as the primary outcome in this study. The primary outcome was the shift of the modified Rankin Scale (mRS) score (range, 0–6, with a higher score reflecting greater disability) to better outcomes at 1-year. The secondary outcomes included functional independence (mRS score, 0–2), independent ambulation (mRS score, 0–3), and mortality. This trial is registered with https://www.clinicaltrials.gov (Unique identifier: NCT04551664).

RESULTS: One-year data were available for 425 of 455 (93%) patients for the primary outcome, with 214 patients in the EVT group and 211 in the MM group in the complete case analysis. The mean age was 66 years, and 38.1% were female. There was a greater likelihood of shift toward improved 1-year mRS distribution in the EVT compared with the MM group (generalized odds ratio, 1.25 [95% CI, 1.01–1.56]; P=0.04). Functional independence and independent ambulation were higher in the EVT compared with MM groups (mRS score, 0–2: 30.4% [65/214] versus 17.1% [36/211]; relative risk, 1.87 [95% CI, 1.27–2.75]; mRS score, 0–3: 50.0% [107/214] versus 35.6% [75/211]; relative risk, 1.46 [95% CI, 1.15–1.85], respectively). The 1-year mortality rate was 31.3% (67/214) in the EVT group and 26.5% (56/211) in the MM group (relative risk, 1.12 [95% CI, 0.82–1.53]). In addition, no change was found in the rate of functional independence between

Continuing medical education (CME) credit is available for this article. Go to https://cme.ahajournals.org to take the quiz.

Correspondence to: Liping Liu, MD, PhD, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, No. 119, S 4th Ring W Rd, Fengtai District, Beijing 100070, China, Email lipingsister@gmail.com; Yongjun Wang, MD, PhD, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, No. 119, S 4th Ring W Rd, Fengtai District, Beijing 100070, China, Email yongjunwang@ncrcnd.org.cn; or Zhongrong Miao, MD, PhD, Department of Neurology, Interventional Neuroradiology, Beijing Tiantan Hospital, Capital Medical University, No. 119, S 4th Ring W Rd, Fengtai District, Beijing 100070, China, Email zhongrongm@163.com

This manuscript was sent to Ajay K. Wakhloo, Guest Editor, for review by expert referees, editorial decision, and final disposition.

*X. Huo, D. Sun, and T.N. Nguyen contributed equally.

†A list of all ANGEL-ASPECT Investigators is given in the Supplemental Material.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.124.050086.

For Sources of Funding and Disclosures, see page 2406.

Stroke is available at www.ahajournals.org/journal/str

90 days and 1 year in the EVT group (29.4% [69/214] versus 30.4% [65/214], respectively); however, a gain in functional independence was observed in the MM group from 90 days to 1 year (10.9% [26/211] versus 17.1% [36/211]), narrowing the magnitude of EVT treatment effect from 18.5% at 90 days to 13.3% at 1 year.

CONCLUSIONS: In patients with large ischemic stroke from a proximal arterial occlusion presenting within 24 hours of onset, EVT reduced disability with durable 1-year benefit compared with MM.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT04551664.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: caregivers ■ infarction ■ ischemic stroke ■ prognosis ■ thrombectomy

Nonstandard Abbreviations and Acronyms

ANGEL-ACT	Endovascular Treatment Key Technique and Emergency Workflow Improvement of Acute Ischemic Stroke
ANGEL-ASPECT	Endovascular Therapy in Acute Anterior Circulation Large Vessel Occlusive Patients With a Large Infarct Core
ASPECTS	Alberta Stroke Program Early CT Score
EVT	endovascular therapy
IQR	interquartile range
MM	medical management
mRS	modified Rankin Scale
RR	relative risk
SELECT	Optimizing Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke
SELECT2	Randomized Controlled Trial to Optimize Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke
TENSION	Efficacy and Safety of Thrombectomy in Stroke With Extended Lesion and Extended Time Window
TESLA	Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke

Several clinical trials have demonstrated the benefit of endovascular therapy (EVT) compared with medical management (MM) in reducing disability for patients with large ischemic core and anterior circulation large vessel occlusion at 3 months.[1–5] These findings were reaffirmed by study-level meta-analyses and cost-effective analysis studies showing the benefit of EVT in patients with large ischemic cores.[6–8]

See related article, p 2408

The long-term outcomes of patients with large ischemic stroke have not been fully characterized. As more patients with large ischemic core and large vessel occlusion are likely to be treated with EVT,[9,10] understanding the degree of disability or death that a patient sustains beyond the 3-month time point can inform patients and caregivers on the patient's prognosis and later reintegration into the community.[11] At 1 year, the SELECT2 (Randomized Controlled Trial to Optimize Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke), the TENSION trial (Efficacy and Safety of Thrombectomy in Stroke With Extended Lesion and Extended Time Window), and preliminary data from the TESLA trial (Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke) showed that the benefit of EVT with regards to functional outcomes compared with MM was extended.[12,13]

The long-term outcomes of patients with large ischemic core treated with EVT compared with MM have not been characterized in an Asian population. In this prespecified analysis of the ANGEL-ASPECT randomized trial (Endovascular Therapy in Acute Anterior Circulation Large Vessel Occlusive Patients with a Large Infarct Core), we aimed to evaluate whether the benefit of EVT compared with MM would persist at the 1-year mark. Our hypothesis was that in light of the benefit in lower disability observed with EVT compared with MM at 3 months,[3,14] better clinical outcomes would likely be extended to 1 year.

METHODS

Data Availability

The data that support the findings of this study are available from the corresponding authors.

Ethics Approval

The ANGEL-ASPECT trial was approved by the ethics committee at Beijing Tiantan Hospital (institutional review board approval number: KY2020-072-02) and all participating centers.

Trial Design and Participants

The ANGEL-ASPECT investigator-initiated trial was approved by the institutional review board at Beijing Tiantan Hospital and at each trial site. The trial was conducted across 46 hospitals in China.[15] Written informed consent was obtained from each patient or their representative before enrollment in the trial. The study was conducted in accordance with the principles of the Declaration of Helsinki. This article is prepared following the Consolidated Standards of Reporting Trials guideline.[16] The funders of the study had no role in study design, data collection, statistical analyses, or writing of the article. The trial is registered on https://www.clinicaltrials.gov (NCT04551664), and the 1-year follow-up plan was recorded on https://www.clinicaltrials.gov.

Inclusion criteria were patients who were aged 18 to 80 years with ischemic stroke within 24 hours of symptom onset, with a National Institutes of Health Stroke Scale score of 6 to 30, with acute ischemic stroke due to occlusion of the intracranial internal carotid artery or initial segment of the middle cerebral artery (M1) or both. All patients received noncontrast computed tomography and computed tomography perfusion. The imaging inclusion criteria were either (1) an Alberta Stroke Program Early CT Score (ASPECTS) of 3 to 5 based on noncontrast computed tomography, regardless of infarct core volume; (2) ASPECTS of 0 to 2 and infarct core 70 to 100 mL; and (3) in patients presenting 6 to 24 hours of onset, ASPECTS >5 on noncontrast computed tomography, and infarct core of 70 to 100 mL. The infarct core volume was evaluated with the use of the automated RAPID system (version 5.0.4; iSchemaView), and the infarct core was defined as an area with a relative cerebral blood flow of <30% on computed tomography perfusion imaging or an apparent diffusion coefficient value of $<620\times10^{-6}$ mm^2/s on magnetic resonance imaging. In addition, patients had prestroke modified Rankin Scale (mRS) score of 0 or 1 indicating no disability. Only patients with available 1-year outcome data were included in the complete case analysis. Key exclusion criteria were the presence of midline shift, clinical signs of herniation, mass effect, bilateral stroke, and multiple intracranial occlusions. The complete inclusion and exclusion criteria are described in the Supplemental Material (Table S1). The ethics committees of each participating center approved this study. Informed consent was obtained from all patients or their legally authorized representatives before enrollment. We followed the Consolidated Standards of Reporting Trials reporting guidelines.

Randomization and Masking

ANGEL-ASPECT was a multicenter, randomized, open-label clinical trial with blinded end point assessment. Eligible patients were randomly assigned 1:1 to either EVT plus MM or MM alone (Figure S1).[3] A randomization code from a Web-based central randomization system was generated and provided to the investigator at each trial site. Randomization was generated by a 24-hour, real-time central network and based on the simple randomization method with no stratification.

Interventions

Thrombectomy with a stent retriever, contact aspiration, or its combination were utilized as first-line techniques. Balloon angioplasty, stent-deployment, or intra-arterial thrombolysis were permitted as other techniques. MM in both treatment groups was conducted according to the Chinese Stroke Association Guidelines.[17] Eligible patients received intravenous thrombolysis with alteplase at 0.9 mg/kg or urokinase at 1.0 to 1.5 million IU.

Outcomes

We report a prespecified analysis of the ANGEL-ASPECT trial, with 1-year functional outcome as the primary outcome in this study. The primary outcome was the mRS score at 1 year according to the mRS shift. The mRS scores of 5 and 6 were merged for the analysis to avoid the shift of 6 to 5 considered as an improvement in functional status. The 1-year secondary outcomes included functional independence (mRS score, 0–2), independent ambulation (mRS score, 0–3), poor outcome (mRS score, 5–6), and mortality.

The 90-day and 1-year outcomes were assessed through telephone interviews with recording at their respective time points and centralized follow-up by trained staff who were unaware of the assigned patient groups. Adverse events were adjudicated by an independent clinical event committee unaware of the trial-group assignments. All imaging data were adjudicated by an independent imaging core laboratory that assessed baseline ASPECTS, site of arterial occlusion, reperfusion, and intracranial hemorrhage.

Sample Size

The sample size of the trial was drawn from the SELECT trial (Optimizing Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke) and ANGEL-ACT trial (Endovascular Treatment Key Technique and Emergency Workflow Improvement of Acute Ischemic Stroke) and was previously described in detail.[3] Brief, EVT was estimated to improve the 90-day outcomes with a common odds ratio of 1.73 for a 1-point improvement in the mRS. Accounting for 10% attrition, we estimated a 90% power to detect mRS shift between the trial groups, assuming that EVT would improve the mRS.

There were 2 interim analyses planned (when one-third and two-thirds of enrolled patients would complete 3-month follow-up). The trial would be stopped early either for efficacy if a prespecified threshold (P<0.0123) was met for EVT benefit on the basis of mRS shift or for futility if a conclusion about treatment effect could not be drawn from the sample size.

Statistical Analysis

The primary and secondary analyses of the 1-year cohort were conducted in the intention-to-treat population. In the primary efficacy analysis, the proportional odds assumption for the ordinal logistic regression was not satisfied, and therefore, the Wilcoxon-Mann-Whitney U test generalized odds ratio and 95% CI were calculated in an assumption-free ordinal analysis to detect a shift in the distribution of scores on the mRS. There were no missing data in the primary outcome analysis. The primary outcome in prespecified subgroups was analyzed.

Sensitivity analyses were conducted in the per-protocol population, which consisted of patients who received the assigned treatment without clinically significant protocol deviation. The as-treated analyses included patients who received the EVT or MM assignment.

 Stroke. 2025;56:2398–2407. DOI: 10.1161/STROKEAHA.124.050086

For the secondary outcomes analyses, differences between groups were assessed with the Cochran-Mantel-Haenszel method with an adjustment for the side effects. The relative risks (RRs) with 95% CIs are reported. $P<0.05$ (2-tailed) was considered statistically significant. All statistical analyses were performed by using SAS (version 9.4, SAS Institute, Inc, Cary, NC).

Early Study Termination

The ANGEL-ASPECT trial was stopped early because of the efficacy of EVT after the second interim analysis on May 17, 2022. Outcome data at 90 days were available for 336 patients. An additional 120 patients had undergone randomization by

Table 1. Baseline Clinical Characteristics of Patients Treated With Endovascular Therapy Versus Medical Management in the Complete Case Analysis

	Endovascular therapy group (N=214)	Medical management group (N=211)	*P* value
Median age, y (IQR)	68 (61–73)	67 (59–73)	0.370
Male sex, n (%)	126 (58.9)	137 (65.0)	0.199
Hypertension	127 (59.4)	130 (61.6)	0.633
Atrial fibrillation	51 (23.8)	44 (20.9)	0.461
Diabetes	41 (19.2)	37 (17.5)	0.666
Affected hemisphere			0.653
Right	113 (52.8)	116 (55.0)	
Left	101 (47.2)	95 (45.0)	
Wake-up stroke, n (%)	64 (30.0)	74 (35.0)	0.256
Transfer patient	119 (52.4)	108 (51.2)	0.361
Median NIHSS score at admission (IQR)*	16 (13–20)	15 (12–19)	0.129
Occlusion site, n (%)			0.845
Internal carotid artery	79 (36.9)	77 (36.5)	
M1 middle cerebral artery segment	133 (62.2)	133 (63.0)	
M2 middle cerebral artery segment	2 (0.9)	1 (0.5)	
Ipsilateral extracranial ICA occlusion	39 (18.2)	32 (15.2)	0.398
ASPECTS value based on CT†			
Median value (IQR)	3 (3–4)	3 (3–4)	0.972
0, n (%)	5 (2.3)	2 (1.0)	0.230
1, n (%)	12 (5.6)	19 (9.0)	
2, n (%)	12 (5.6)	8 (3.8)	
3, n (%)	91 (42.5)	94 (44.6)	
4, n (%)	61 (28.5)	46 (21.8)	
5, n (%)	33 (15.4)	42 (19.9)	
Median infarction volume,mL (IQR)‡	60 (28–86)	64 (34–88)	0.463
Intravenous thrombolysis, n (%)	51 (23.8)	52 (24.6)	0.845
Alteplase	48 (22.4)	51 (24.2)	
Tenecteplase	3 (1.4)	1 (0.5)	
Median interval between time of stroke onset and hospital arrival, min (IQR)	348 (197–632)	341 (180–652)	0.971
Median interval between time of stroke onset and time of imaging, min (IQR)	399 (241–697)	412 (236–738)	0.782
Interval between the time of stroke onset and time of randomization			
Median (IQR), min	459 (299–713)	456 (305–781)	0.804
<4.5 h, n (%)	45 (21.0)	48 (22.8)	0.724
4.5–<6.0 h, n (%)	32 (15.0)	32 (15.2)	
6.0–<12.0 h, n (%)	84 (39.3)	72 (34.1)	
12.0–24.0 h, n (%)	53 (24.8)	59 (28.0)	

ASPECTS indicates Alberta Stroke Program Early CT Score; CT, computed tomography; ICA, internal carotid artery; IQR, interquartile range; M1, main trunk of the middle cerebral artery; M2, first-order branch of the main trunk; and NIHSS, National Institutes of Health Stroke Scale.

*The NIHSS score is an ordinal scale to evaluate the severity of stroke ranging from 0 to 42, with higher scores indicating a more severe deficit.

†ASPECTS values range from 0 to 10, with lower scores indicating larger infarction.

‡Infarction volume was assessed by apparent diffusion coefficient $<620\times10^{-6}$ mm^2/s based on magnetic resonance imaging in 38 patients, whereas others were assessed by relative cerebral blood flow <30% based on computed tomography perfusion.

the time of the second interim analysis, and 455 completed 90-day follow-up by August 13, 2022.

RESULTS

Participants

From October 2, 2020, to May 18, 2022, 1504 patients were screened for eligibility, of whom 456 were enrolled with 231 patients in the EVT group and 225 in the MM group. One patient in the EVT group withdrew consent, leaving 455 patients in the randomized population. Of the 455 patients, 30 patients were without 1-year follow-up. Overall, 425 patients were in the present analysis. The median age was 68 years (interquartile range [IQR], 60–73), and 38.1% were female. Vascular risk factors including hypertension, atrial fibrillation, and diabetes were similar between groups. The median (IQR) baseline National Institutes of Stroke Scale score (16 [13–20] versus 15 [12–19]; *P*=0.129), median (IQR) ASPECTS (3 [3–4] versus 3 [3–4]; *P*=0.972), median (IQR) baseline core infarct volume (60 [28–86] versus 64 [34–88] mL; *P*=0.463), and the time from onset to randomization (459 [299–713] versus 456 [305-781] minutes; *P*=0.804) were similar between the EVT and MM groups. Intravenous thrombolysis, mostly alteplase, was administered in 24% of both groups. The site of occlusion was the internal carotid artery in 36.7% of patients and the M1 middle cerebral artery segment in 62.5% of patients (Table 1). The baseline characteristics of patients with (n=425) and without 1-year follow-up (n=30) are presented in Table S2. A comparison of key characteristics between patients demonstrating various transitions between 90-day and 1-year follow-up is presented in Table S3.

Primary Outcome

At 1-year follow-up, completed in May 2023, data were available for 425 of 455 (93%) patients for the primary outcome compared with 455 (100%) patients at 90 days (Figure 1). In the complete case analysis, there were 214 patients in the EVT group and 211 in the MM group. At 1 year, the median (IQR) mRS was 3 (2–6) in the EVT group and 4 (3–6) in the MM group. For the primary outcome of the distribution of the 1-year mRS, there was a greater likelihood of shift toward better outcomes in the EVT compared with the MM group (generalized odds ratio, 1.25 [95% CI, 1.01–1.56]; *P*=0.04; Figure 2; Table 2).

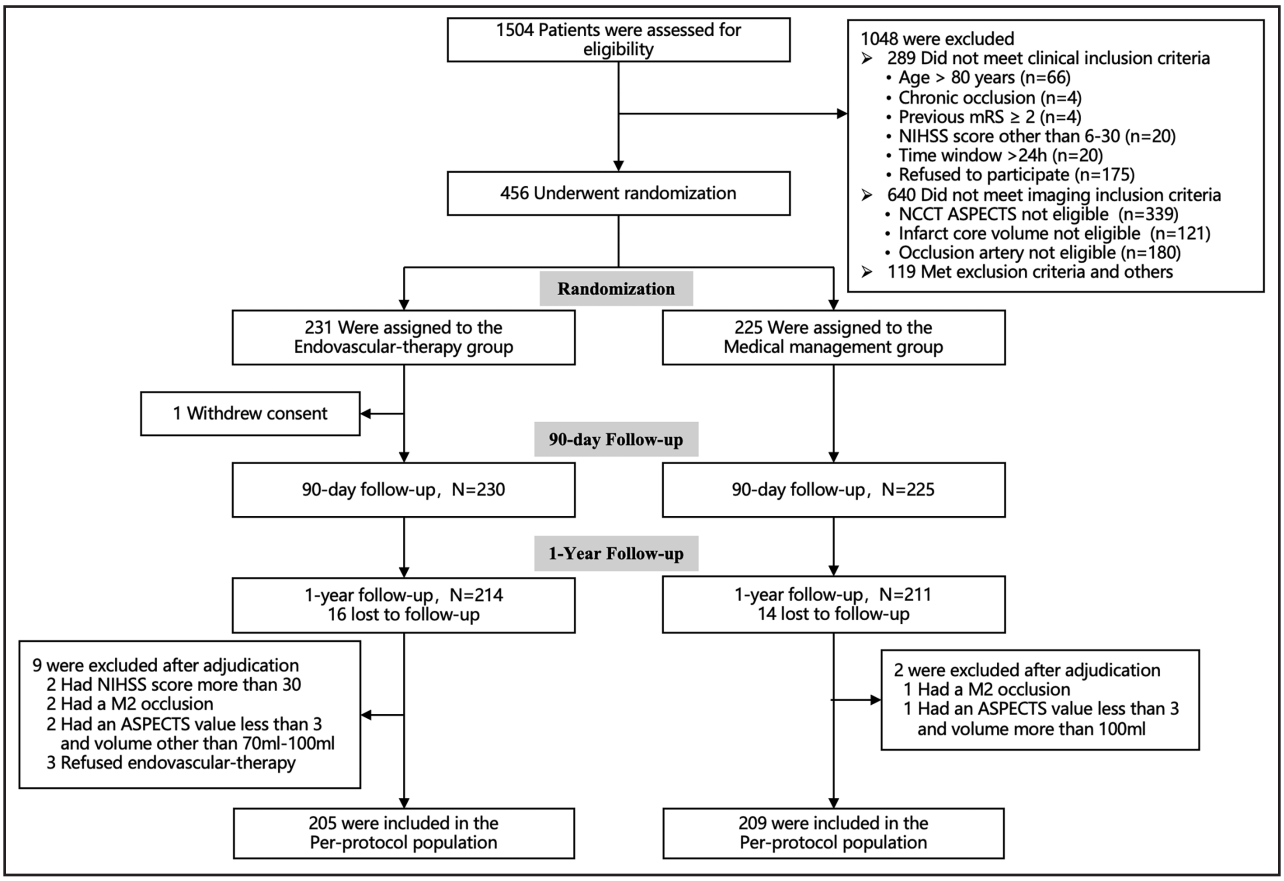
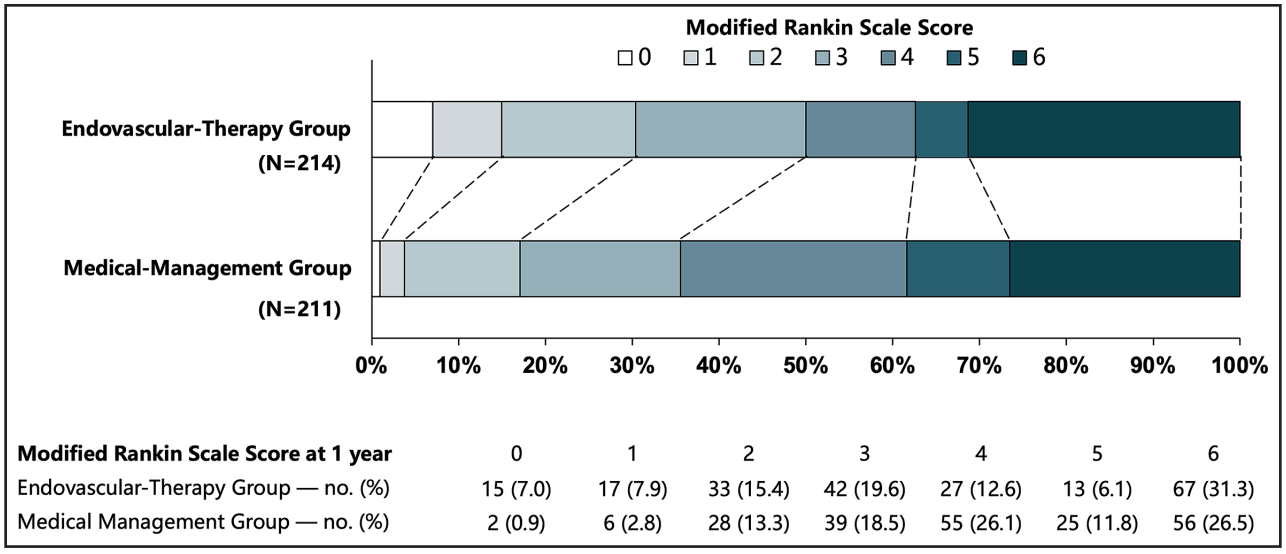


Figure 1. Participant flow diagram and 1-year loss to follow-up.
ASPECTS indicates Alberta Stroke Program Early CT Score; mRS, modified Rankin Scale; NCCT, noncontrast computed tomography; and NIHSS, National Institutes of Health Stroke Scale.



Modified Rankin Scale Score at 1 year	0	1	2	3	4	5	6
Endovascular-Therapy Group — no. (%)	15 (7.0)	17 (7.9)	33 (15.4)	42 (19.6)	27 (12.6)	13 (6.1)	67 (31.3)
Medical Management Group — no. (%)	2 (0.9)	6 (2.8)	28 (13.3)	39 (18.5)	55 (26.1)	25 (11.8)	56 (26.5)

Figure 2. Distribution of scores on the modified Rankin Scale at 1-year follow-up, stratified on the basis of treatment assignment in the intention-to-treat population.

Secondary Outcomes

In the 1-year secondary outcomes, functional independence and independent ambulation were higher in the EVT compared with MM groups (mRS score, 0–2: 30.4% versus 17.1%; RR, 1.87 [95% CI, 1.27–2.75]; mRS score, 0–3: 50.0% versus 35.6%; RR, 1.46 [95% CI, 1.15–1.85], respectively). Poor outcomes were similar in both groups (mRS score, 5–6: 37.4% versus 38.4%; RR, 0.94 [95% CI, 0.73–1.20]). The 1-year mortality rate was 31.3% in the EVT group and 26.5% in the MM group (RR, 1.12 [95% CI, 0.82–1.53]).

In the per-protocol population, there were 11 patients who were removed because of a National Institutes of Stroke Scale score >30, M2 occlusion, an ASPECTS <3, and volume other than 70 to 100 mL, and refusing EVT, leaving 205 patients in the EVT group and 209 patients in the MM group. The as-treated population consisted of 211 patients in the EVT group and 214 patients in the MM group. The 1-year treatment effects for the aforementioned primary and secondary outcomes were similar for the per-protocol (Table S4; Figure S2) and as-treated (Table S5; Figure S3) populations as that for the complete case analysis.

Subgroup Analyses

Analyses of the primary outcome showed that the treatment effect of EVT was consistent across subgroups including age, stroke onset to randomization time, presenting National Institutes of Stroke Scale, use of intravenous thrombolysis, occlusion site, ASPECTS, infarct core volume, and stroke cause (Figure 3). However, the trial was not powered to detect differences by subgroups.

One-Year Versus 90-Day Outcomes

Event rates at 1 year were compared with 90 days (Table 3). There was no change in the rate of functional

Table 2. Efficacy and Safety Outcomes at 1 Year, the Complete Case Analysis

Outcome	Endovascular therapy group (N=214)	Medical management group (N=211)	Treatment effect (95% CI)*	*P* value
Primary outcome				
mRS score at 1 y, median (IQR)	3 (2–6)	4 (3–6)	1.25 (1.01–1.56)	0.04
Secondary outcome, n (%)				
mRS score of 0–2 at 1 y	65 (30.4)	36 (17.1)	1.87 (1.27–2.75)	0.001
mRS score of 0–3 at 1 y	107 (50.0)	75 (35.6)	1.46 (1.15–1.85)	0.001
mRS score of 5–6 at 1 y	80 (37.4)	81 (38.4)	0.94 (0.73–1.20)	0.60
Mortality at 1 y	67 (31.3)	56 (26.5)	1.12 (0.82–1.53)	0.48

IQR indicates interquartile range; and mRS, modified Rankin Scale.

*The treatment effect is reported for the primary outcome as a generalized odds ratio with the 95% CI for the ordinal shift in the distribution of scores on the mRS toward a better outcome; the treatment effect is reported for the secondary outcome as the relative risks with 95% CIs by adjustment for the side effect with the Cochran-Mantel-Haenszel method. The widths of the CIs for the secondary outcomes were not adjusted for multiple comparisons and may not be used for hypothesis testing.

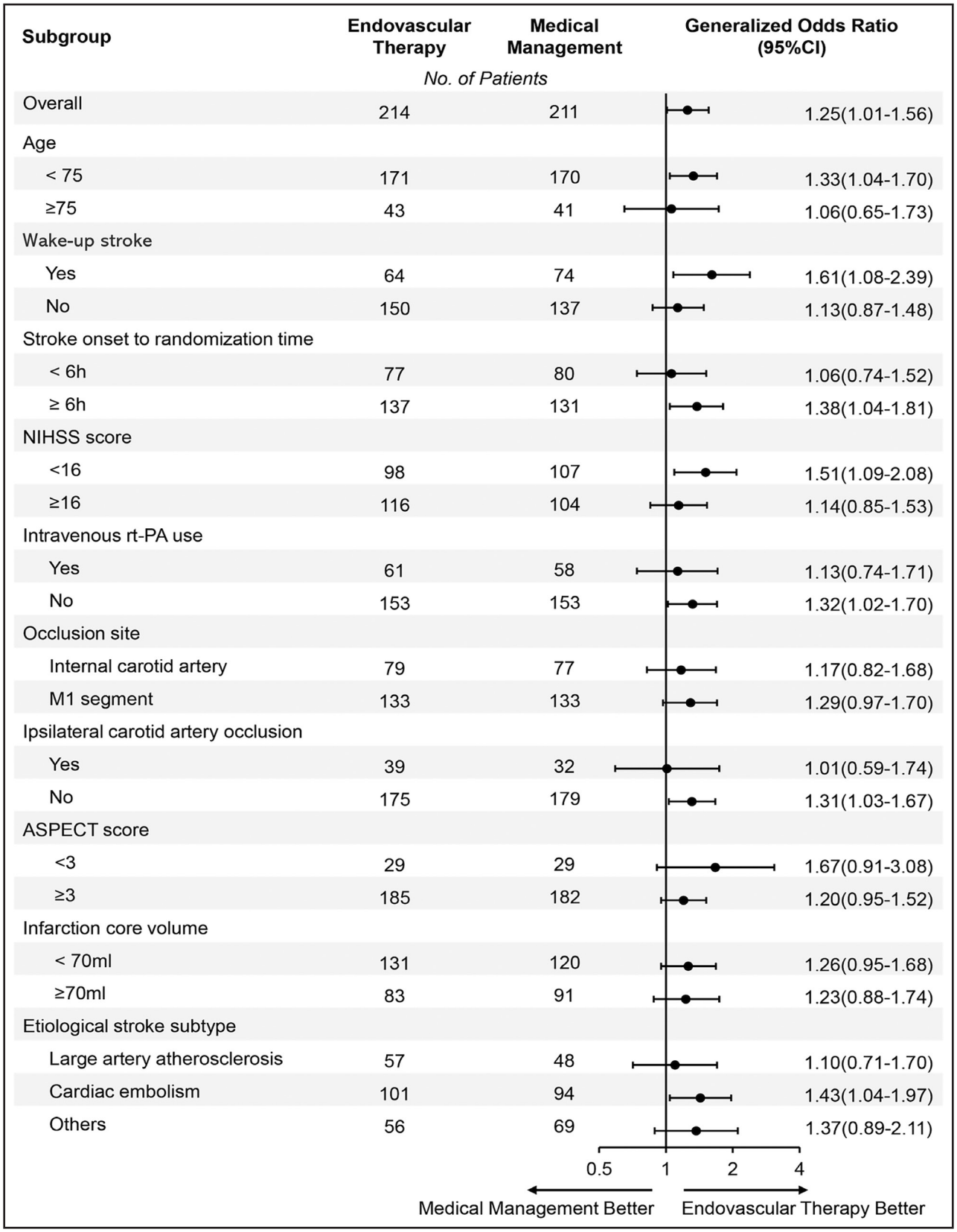


Figure 3. Subgroup analyses on modified Rankin Scale at 1-year follow-up.
The subgroup analysis of the modified Rankin Scale indicating the odds that the trial patients would have better functional recovery at 1-year follow-up. The trial was not powered to allow definite conclusions based on the results of the subgroup analyses. The M1 segment is the main trunk of the middle cerebral artery. ASPECTS indicates Alberta Stroke Program Early CT Score; NIHSS, National Institutes of Health Stroke Scale; and rt-PA, recombinant tissue-type plasminogen activator.

 Stroke. 2025;56:2398–2407. DOI: 10.1161/STROKEAHA.124.050086

Table 3. Comparison of 90-Day and 1-Year Outcomes, the Complete Case Analysis

Outcome	Treatment (90 d/1 y)	Outcome rates (%)		Absolute difference (%)	
		90 d (N=425)	1 y (N=425)	90 d (N=425)	1 y (N=425)
mRS score, 0–2	Thrombectomy (n=214/n=214)	63 (29.4)	65 (30.4)	18.5	13.3
	Medical management (n=211/n=211)	23 (10.9)	36 (17.1)		
mRS score, 0–3	Thrombectomy (n=214/n=214)	97 (45.3)	107 (50.0)	13.1	14.4
	Medical management (n=211/n=211)	68 (32.2)	75 (35.6)		
Mortality	Thrombectomy (n=214/n=214)	50 (23.4)	67 (31.3)	2.1	4.8
	Medical management (n=211/n=211)	45 (21.3)	56 (26.5)		

mRS indicates modified Rankin Scale.

independence (mRS score, 0–2) between 90 days and 1 year in the EVT group (29.4% versus 30.4%, respectively). However, a gain in functional independence was observed in the MM group from 90 days to 1 year (10.9% versus 17.1%), narrowing the magnitude of the EVT treatment effect from 18.5% at 90 days to 13.3% at 1 year. With regards to independent ambulation (mRS score, 0–3), event rates were similar between 90 days and 1 year across the EVT (45.3% versus 50.0%) and MM (32.2% versus 35.6%) groups, respectively. Mortality rates were higher from 90 days to 1 year in both the EVT (23.4% versus 21.3%) and MM (31.3% versus 26.5%) groups.

DISCUSSION

In a randomized trial of patients in China with large ischemic stroke and anterior circulation large vessel occlusion, at the 1-year time point, patients who received EVT achieved lower disability, higher rates of functional independence, and independent ambulation than those who received MM. There was no significant difference in poor outcomes or mortality between groups. The treatment effect was present across subgroups according to age, time of presentation, site of arterial occlusion, and the extent of baseline infarct core. To our knowledge, it is the first trial to show the benefit of EVT in patients with a large infarct core extended to the 1-year time point in an Asian population.

As the degree of baseline infarction at presentation is an important prognostic factor for patient outcome,[14,18,19] patients with large infarct cores were excluded from most of the initial thrombectomy trials.[20,21] As the results of multiple large ischemic core randomized trials comparing EVT versus MM have now been reported, the presence of a large infarct core remains a poor prognostic factor but not a modifier of the treatment effect of EVT.[1–5,22] As such, an understanding of the long-term patient outcomes is important to provide estimates as to the durability of the benefit of thrombectomy to counsel patients and their families. Moreover, the 1-year results of our analyses, of the Chinese population, may further inform the cost-effectiveness of our intervention, which may have ramifications in the allocation of health care resources in the second most populous nation in the world.[6,8,23]

The results of our trial are in line with other EVT trials of patients with smaller infarct cores, such as the REVASCAT (Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy in the Treatment of Acute Stroke due to Anterior Circulation Large Vessel Occlusion Presenting Within Eight Hours of Symptom Onset) and MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) trials, which showed that the treatment effect of EVT does not change over the extended follow-up to 1 and 2 years.[24,25] Our findings are concordant with that of the SELECT2, TENSION, and preliminary results of the TESLA randomized trials of patients with large estimated infarct core, which showed better functional outcomes at 1 year among those treated with EVT compared with MM.[12,13]

With regards to safety outcomes, mortality both at 90 days and 1 year was lower in the ANGEL-ASPECT trial (mortality, overall 28.9% at 1 year) compared with the SELECT2 trial (mortality, overall 45% at 1 year). This may be reflective of the fact that the baseline median infarct core volume in ANGEL-ASPECT was smaller than that of the SELECT 2 trial (62 versus 80 mL),[2,3] possibly indicative of a lower baseline severity of disease presentation in the ANGEL-ASPECT trial. Another possibility is cultural differences in patient, and family perspectives on continuing rehabilitation versus withdrawal of care may affect the continuation or discontinuation of life-sustaining treatments between non-Asian and Asian populations.

We acknowledge the limitations of our trial. Missing data for the primary outcome were present in 6.6% of participants but are comparable with that of the SELECT2 trial at 1 year (7%).[13] Nonetheless, the benefit of EVT in reducing disability compared with MM was observed in sensitivity analyses of the per-protocol and as-treated populations. We did not record quality of life metrics including cognitive or social score, which was found to be better in patients receiving EVT in the SELECT2 trial.[12] Data on the cause of mortality were not recorded. As the

results of our trial align with those from the SELECT2, TENSION, and TESLA trials, its generalizability may be broadened to other nations.

CONCLUSIONS

In patients with large ischemic stroke from a proximal arterial occlusion within 24 hours of onset, a reduction in disability with EVT compared with MM was maintained at 1 year. There was no difference between groups in mRS 5-6 or mortality at 1 year.

ARTICLE INFORMATION

Received November 15, 2024; final revision received April 27, 2025; accepted May 27, 2025.

The podcast and transcript are available at https://www.ahajournals.org/str/podcast.

Affiliations

Cerebrovascular Disease Department, Neurological Disease Center, Beijing Anzhen Hospital (X.H., X.T., X.Z., S. Li), Department of Neurology, Beijing Xuanwu Hospital (G.M.), and Department of Neurology, Beijing Luhe Hospital (X.G.), Capital Medical University, China. Department of Neurology, Interventional Neuroradiology (D.S., Y.P., F.G., N.M., D.M., Z.M.) and Department of Neurology (L.L., Y.W.), Beijing Tiantan Hospital, Capital Medical University, China. China National Clinical Research Center for Neurological Diseases, Beijing (D.S., Y.P., F.G., N.M., D.M., L.L., Y.W., Z.M.). Department of Neurology, Radiology, Boston Medical Center, MA (T.N.N., M.A.). Department of Emergency, Xiangtan Central Hospital, Hunan, China (G.Y.). Department of Neurology, Linyi People's Hospital, Shandong, China (H.H.). Department of Neurology, Fujian Medical University Union Hospital, Fuzhou, China (W.C.). Department of Neurosurgery, Tianjin Huanhu Hospital, China (M.W.). Department of Neurology, Anyang People's Hospital, Henan, China (J. Zhang). Department of Neurology, Yijishan Hospital of Wannan Medical College, Anhui, China (Z.Z.). Department of Neurology, The First People's Hospital of Chenzhou, Hunan, China (X.Y.). Department of Neurology, Yancheng Third People's Hospital, Jiangsu, China (W.S.). Department of Neurology, Lishui Municipal Central Hospital, Zhejiang, China (X. Cai). Department of Neurology, China-Japan Union Hospital of Jilin University, Jilin (G.N.). Department of Neurointervention, Dalian Municipal Central Hospital of Dalian University of Technology, Liaoning, China (D.L.). Department of Neurosurgery, The First Hospital of Hebei Medical University, China (A.Y.-C.W.). Department of Neurology, Zhongshan City People's Hospital, Guangdong, China (W.L.). Department of Neurology, Shantou Central Hospital, Guangdong, China (C.C.). Department of Neurology, Nanyang Central Hospital, Henan, China (C.W.). Department of Neurology, Taizhou Hospital of Zhejiang Province, Zhejiang, China (E.W.). Department of Neurosurgery, Liaocheng People's Hospital, Shandong, China (L.Z.). Department of Neurology, Baotou Central Hospital, Inner Mongolia, China (C.J.). Department of Neurology, Maoming People's Hospital, Guangdong, China (G.L.). Department of Neurology, The Second Affiliated Hospital of Guangzhou Medical University, Guangdong, China (X. Chen). Department of Cerebrovascular Disease, Henan Provincial People's Hospital Zhengzhou University, China (T.L.). Department of Neurology, Yongchuan Hospital of Chongqing Medical University, China (S. Liu). Department of Neurology, The Affiliated Hospital of South West Medical University, Sichuan, China (J. Li). Department of Neurology, Shanxi Provincial People's Hospital, China (Y.S.). Department of Neurology, The Second Affiliated Hospital to Xiamen Medical College, Fujian, China (N.X.). Department of Neurology, Shengli Oilfield Central Hospital, Shandong, China (Z. Gao). Department of Neurology, Songyuan Jilin Oil Field Hospital, China (D.J.). Department of Interventional Neuroradiology, Liaocheng the Third People's Hospital, Shandong, China (C.S.). Department of Neurology, Taiyuan Central Hospital, China (F.Z.). Department of Neurology, Affiliated Jiangmen Traditional Chinese Medicine Hospital of Ji'nan University, Guangdong, China (Q.S.). Department of Neurology, Sichuan Mianyang 404 Hospital, China (J.L.). Department of Neurology, Jingjiang People's Hospital, The Seventh Affiliated Hospital of Yangzhou University, Jiangsu, China (Y.L.). Department of Neurosurgery, Tianjin TEDA Hospital, China (Z.G.). Department of Neurology, West China Hospital, Sichuan University, (H. Zheng.). Department of Neurosurgery, First Affiliated Hospital School of Medicine Shihezi University, Xinjiang, China (L.D.). Department of Neurology, Siping Central People's Hospital, Jilin, China (J. Zhang). Department of Neurology, Mianyang Central Hospital, Guangzhou, China (Y.T.). Department of Neurology, Hangzhou First People's Hospital, Zhejiang, China (C.Y.). Department of Neurosurgery, The Affiliated Hospital of Guizhou Medical University, China (H.Y.).

Acknowledgments

Drs D. Sun, Huo, and Miao contributed to the conception and design of the study. Drs Wei and Pan contributed to the acquisition and analysis of data. Drs D. Sun and Nguyen contributed to drafting the text and preparing the figures. Dr Nguyen critically reviewed and edited the article. All authors reviewed and approved the final article.

Sources of Funding

The study is supported by the Noncommunicable Chronic Diseases-National Science and Technology Major Project (grant 2023ZD0505400).

Disclosures

Dr Nguyen is an associate editor of *Stroke*; is a speaker for Genentech and Kaneka; is on the advisory board for Brainomix and Aruna Bio; and is consulting for Medtronic. The other authors report no conflicts.

Supplemental Material

Tables S1–S5
Figures S1–S3
CONSORT Checklist

REFERENCES

1. Costalat V, Jovin TG, Albucher JF, Cognard C, Henon H, Nouri N, Gory B, Richard S, Marnat G, Sibon I, et al; LASTE Trial Investigators. Trial of thrombectomy for stroke with a large infarct of unrestricted size. *N Engl J Med*. 2024;390:1677–1689. doi: 10.1056/NEJMoa2314063
2. Sarraj A, Hassan AE, Abraham MG, Ortega-Gutierrez S, Kasner SE, Hussain MS, Chen M, Blackburn S, Sitton CW, Churilov L, et al; SELECT2 Investigators. Trial of endovascular thrombectomy for large ischemic strokes. *N Engl J Med*. 2023;388:1259–1271. doi: 10.1056/NEJMoa2214403
3. Huo X, Ma G, Tong X, Zhang X, Pan Y, Nguyen TN, Yuan G, Han H, Chen W, Wei M, et al; ANGEL-ASPECT Investigators. Trial of endovascular therapy for acute ischemic stroke with large infarct. *N Engl J Med*. 2023;388:1272–1283. doi: 10.1056/NEJMoa2213379
4. Bendszus M, Fiehler J, Subtil F, Bonekamp S, Aamodt AH, Fuentes B, Gizewski ER, Hill MD, Krajina A, Pierot L, et al; TENSION Investigators. Endovascular thrombectomy for acute ischaemic stroke with established large infarct: multicentre, open-label, randomised trial. *Lancet*. 2023;402:1753–1763. doi: 10.1016/S0140-6736(23)02032-9
5. Yoshimura S, Sakai N, Yamagami H, Uchida K, Beppu M, Toyoda K, Matsumaru Y, Matsumoto Y, Kimura K, Takeuchi M, et al. Endovascular therapy for acute stroke with a large ischemic region. *N Engl J Med*. 2022;386:1303–1313. doi: 10.1056/NEJMoa2118191
6. Gao L, Churilov L, Johns H, Pujara D, Hassan AE, Abraham M, Ortega-Gutierrez S, Hussain MS, Chen M, Blackburn S, et al; For SELECT2 investigators. Cost-effectiveness of endovascular thrombectomy in patients with large ischemic stroke. *Ann Neurol*. 2025;97:222–231. doi: 10.1002/ana.27119
7. Li Q, Abdalkader M, Siegler JE, Yaghi S, Sarraj A, Campbell BCV, Yoo AJ, Zaidat OO, Kaesmacher J, Pujara D, et al. Mechanical thrombectomy for large ischemic stroke: a systematic review and meta-analysis. *Neurology*. 2023;101:e922–e932. doi: 10.1212/wnl.0000000000207536
8. Pan Y, Huo X, Jin A, Nguyen TN, Ma G, Tong X, Zhang X, Gao F, Ma N, Mo D, et al. Cost-effectiveness of endovascular therapy for acute ischemic stroke with large infarct in China. *J Neurointerv Surg*. 2023;16:453–458. doi: 10.1136/jnis-2023-020466
9. Starikova N, Räty S, Strbian D, Kaiser DPO, Gerber JC, Huo X, Qiu Z, Chen HS, Kaesmacher J, Pallesen LP, et al. Endovascular thrombectomy for anterior circulation large vessel occlusion stroke: an evolution of trials. *Semin Neurol*. 2023;43:397–407. doi: 10.1055/s-0043-1771454
10. Sahoo A, Abdalkader M, Yamagami H, Huo X, Sun D, Jia B, Weyland CS, Diana F, Kaliaev A, Klein P, et al. Endovascular therapy for acute stroke: new evidence and indications. *J Neuroendovasc Ther*. 2023;17:232–242. doi: 10.5797/jnet.ra.2023-0047
11. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, Deruyter F, Eng JJ, Fisher B, Harvey RL, et al; American Heart Association Stroke Council, Council on Cardiovascular and Stroke

Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2016;47:e98–e169. doi: 10.1161/STR.0000000000000098
12. Thomalla G, Fiehler J, Subtil F, Bonekamp S, Aamodt AH, Fuentes B, Gizewski ER, Hill MD, Krajina A, Pierot L, et al; TENSION Investigators. Endovascular thrombectomy for acute ischaemic stroke with established large infarct (TENSION): 12-month outcomes of a multicentre, open-label, randomised trial. *Lancet Neurol*. 2024;23:883–892. doi: 10.1016/S1474-4422(24)00278-3
13. Sarraj A, Abraham MG, Hassan AE, Blackburn S, Kasner SE, Ortega-Gutierrez S, Hussain MS, Chen M, Johns H, Churilov L, et al; SELECT2 Investigators. Endovascular thrombectomy plus medical care versus medical care alone for large ischaemic stroke: 1-year outcomes of the SELECT2 trial. *Lancet*. 2024;403:731–740. doi: 10.1016/S0140-6736(24)00050-3
14. Sun D, Guo X, Nguyen TN, Pan Y, Ma G, Tong X, Raynald, Wang M, Ma N, Gao F, Mo D, Huo X, Miao Z; ANGEL-ASPECT Study Group. Alberta stroke program early computed tomography score, infarct core volume, and endovascular therapy outcomes in patients with large infarct: a secondary analysis of the ANGEL-ASPECT trial. *JAMA Neurol*. 2024;81:30–38. doi: 10.1001/jamaneurol.2023.4430
15. Huo X, Ma G, Zhang X, Pan Y, Tong X, Sun D, Liu L, Wang Y, Liebeskind DS, Wang Y, et al. Endovascular therapy in acute anterior circulation large vessel occlusive patients with a large infarct core (ANGEL-ASPECT): protocol of a multicentre randomised trial. *Stroke Vasc Neurol*. 2023;8:169–174. doi: 10.1136/svn-2022-001865
16. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *Trials*. 2010;11:32. doi: 10.1186/1745-6215-11-32
17. Liu L, Chen W, Zhou H, Duan W, Li S, Huo X, Xu W, Huang L, Zheng H, Liu J, et al. Chinese Stroke Association guidelines for clinical management of cerebrovascular disorders: executive summary and 2019 update of clinical management of ischaemic cerebrovascular diseases. *Stroke Vasc Neurol*. 2020;5:159–176. doi: 10.1136/svn-2020-000378
18. Sun D, Nguyen TN, Pan Y, Wang M, Abdalkader M, Masoud HE, Ma A, Tong X, Ma G, Sun X, et al. Unsuccessful recanalization versus medical management of patients with large ischemic core: analysis of the ANGEL-ASPECT randomized trial. *Clin Neuroradiol*. 2024;34:441–450. doi: 10.1007/s00062-024-01384-5
19. Sarraj A, Hassan AE, Abraham MG, Ortega-Gutierrez S, Kasner SE, Hussain MS, Chen M, Churilov L, Johns H, Sitton CW, et al; SELECT2 Investigators. Endovascular thrombectomy for large ischemic stroke across ischemic injury and penumbra profiles. *JAMA*. 2024;331:750–763. doi: 10.1001/jama.2024.0572
20. Nguyen TN, Raymond J, Nogueira RG, Fischer U, Siegler JE. The problem of restrictive thrombectomy trial eligibility criteria. *Stroke*. 2022;53:2988–2990. doi: 10.1161/STROKEAHA.122.040006
21. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CB, van der Lugt A, de Miquel MA, et al; HERMES Collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731. doi: 10.1016/S0140-6736(16)00163-X
22. Zheng L, Nie X, Wang M, Liu X, Duan W, Zhang Z, Liu J, Wei Y, Wen M, Yang Z, et al; ANGEL-ASPECT Investigators. Endovascular therapy in acute ischaemic stroke with large infarction with matched or mismatched clinical-radiological severities: a post-hoc analysis of the ANGEL-ASPECT trial. *EClinicalMedicine*. 2024;72:102595. doi: 10.1016/j.eclinm.2024.102595
23. Moreu M, Scarica R, Pérez-García C, Rosati S, López-Frías A, Egido JA, Gómez-Escalonilla C, Simal P, Arrazola J, Bocquet AL, et al. Mechanical thrombectomy is cost-effective versus medical management alone around Europe in patients with low ASPECTS. *J Neurointerv Surg*. 2023;15:629–633. doi: 10.1136/jnis-2022-019849
24. Dávalos A, Cobo E, Molina CA, Chamorro A, de Miquel MA, Román LS, Serena J, López-Cancio E, Ribó M, Millán M, et al; REVASCAT Trial Investigators. Safety and efficacy of thrombectomy in acute ischaemic stroke (REVASCAT): 1-year follow-up of a randomised open-label trial. *Lancet Neurol*. 2017;16:369–376. doi: 10.1016/S1474-4422(17)30047-9
25. van den Berg LA, Dijkgraaf MG, Berkhemer OA, Fransen PS, Beumer D, Lingsma HF, Majoie CB, Dippel DW, van der Lugt A, van Oostenbrugge RJ, et al; MR CLEAN Investigators. Two-year outcome after endovascular treatment for acute ischemic stroke. *N Engl J Med*. 2017;376:1341–1349. doi: 10.1056/NEJMoa1612136