ORIGINAL ARTICLE

Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion

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ABSTRACT

BACKGROUND

The effects and risks of endovascular thrombectomy 6 to 24 hours after stroke onset due to basilar-artery occlusion have not been extensively studied.

METHODS

In a trial conducted over a 5-year period in China, we randomly assigned, in a 1:1 ratio, patients with basilar-artery stroke who presented between 6 to 24 hours after symptom onset to receive either medical therapy plus thrombectomy or medical therapy only (control). The original primary outcome, a score of 0 to 4 on the modified Rankin scale (range, 0 to 6, with a score of 0 indicating no disability, 4 moderately severe disability, and 6 death) at 90 days, was changed to a good functional status (a modified Rankin scale score of 0 to 3, with a score of 3 indicating moderate disability). Primary safety outcomes were symptomatic intracranial hemorrhage at 24 hours and 90-day mortality.

RESULTS

A total of 217 patients (110 in the thrombectomy group and 107 in the control group) were included in the analysis; randomization occurred at a median of 663 minutes after symptom onset. Enrollment was halted at a prespecified interim analysis because of the superiority of thrombectomy. Thrombolysis was used in 14% of the patients in the thrombectomy group and in 21% of those in the control group. A modified Rankin scale score of 0 to 3 (primary outcome) occurred in 51 patients (46%) in the thrombectomy group and in 26 (24%) in the control group (adjusted rate ratio, 1.81; 95% confidence interval [CI], 1.26 to 2.60; P<0.001). The results for the original primary outcome of a modified Rankin scale score of 0 to 4 were 55% and 43%, respectively (adjusted rate ratio, 1.21; 95% CI, 0.95 to 1.54). Symptomatic intracranial hemorrhage occurred in 6 of 102 patients (6%) in the thrombectomy group and in 1 of 88 (1%) in the control group (risk ratio, 5.18; 95% CI, 0.64 to 42.18). Mortality at 90 days was 31% in the thrombectomy group and 42% in the control group (adjusted risk ratio, 0.75; 95% CI, 0.54 to 1.04). Procedural complications occurred in 11% of the patients who underwent thrombectomy.

CONCLUSIONS

Among patients with stroke due to basilar-artery occlusion who presented 6 to 24 hours after symptom onset, thrombectomy led to a higher percentage with good functional status at 90 days than medical therapy but was associated with procedural complications and more cerebral hemorrhages. (Funded by the Chinese National Ministry of Science and Technology; BAOCHE ClinicalTrials.gov number, NCT02737189.)

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Randomized trials involving patients with acute stroke due to large-artery occlusion in the anterior circulation have shown a benefit of endovascular thrombectomy.[1,2] These trials excluded patients with basilar-artery occlusion, a stroke type associated with poor prognosis. The Endovascular Treatment versus Standard Medical Treatment for Vertebrobasilar Artery Occlusion (BEST) trial[3] and the Basilar Artery International Cooperation Study (BASICS)[4] did not show a clear benefit of thrombectomy over medical care in patients with basilar-artery occlusion, but both trials had methodologic limitations.[5] It has been postulated that anatomical and pathophysiological characteristics of the brain stem and cerebellum, which are supplied by branches of the basilar artery, make them more resistant to ischemia than structures supplied by the anterior cerebral circulation. These characteristics may allow reperfusion in patients with basilar-artery stroke to have an effect over a longer time window after stroke onset than is seen in patients with anterior circulation strokes.[6] We conducted the Basilar Artery Occlusion Chinese Endovascular (BAOCHE) trial to assess the effect and safety of endovascular thrombectomy in conjunction with medical therapy, as compared with medical therapy alone, in patients with acute ischemic stroke due to basilar-artery occlusion and an absence of a large baseline infarct on neuroimaging who underwent randomization 6 to 24 hours after symptom onset.

Methods

Trial Oversight

We conducted an investigator-initiated, multicenter, open-label, randomized, controlled trial with blinded outcome evaluation. The trial protocol, available with the full text of this article at NEJM.org, was approved by the institutional review boards at all participating sites. Enrolled patients or their surrogates provided written informed consent for participation in the trial. The trial was designed and conducted by a steering committee composed of independent academic investigators, and the trial was monitored by an independent data and safety monitoring board. An independent clinical-events committee adjudicated safety outcomes, procedure-related complications, and serious adverse events. A core laboratory assessed all neuroimaging studies in a blinded manner.

The trial was funded by an unrestricted grant from the Chinese National Ministry of Science and Technology, which was not involved in the design or conduct of the trial. There was no industry involvement in the trial. The first and last authors wrote the first and subsequent drafts of the manuscript with input from all the authors. The authors vouch for the completeness and accuracy of the reported data and the fidelity of the trial to the protocol. Decisions related to the discontinuation of enrollment were made at the recommendation of an independent data and safety monitoring board.

Trial sites were certified stroke centers in China, at which more than 500 patients with acute stroke had been treated, more than 30 stroke thrombectomy procedures had been performed annually, and neurointerventionalists on the staff had performed at least 10 thrombectomies with the Solitaire (Medtronic) device (see the Supplementary Appendix, available at NEJM.org). The trial was performed in accordance with the principles of the Declaration of Helsinki.[7]

Patient Population

Patients were eligible for inclusion in the trial if they were 18 to 80 years of age; had an occlusion of the basilar artery or intracranial segments of both vertebral arteries that could be treated within 6 to 24 hours after symptom onset, which was defined as the time at which the patient was last known to be free from acute stroke symptoms except for isolated vertigo; had a pre-stroke score of 0 or 1 on the modified Rankin scale (range, 0 [no symptoms] to 6 [death]); and had a score of 10 or higher on the National Institutes of Health Stroke Scale (NIHSS; range, 0 to 42, with higher values indicating more severe deficit) at presentation. Because of slow recruitment, after the enrollment of 61 patients, the inclusion criteria were expanded to allow for the enrollment of patients with an NIHSS score of 6 or higher.

The main exclusion criteria with regard to imaging were evidence of recent intracranial hemorrhage; the presence of a large infarct in the posterior circulation, defined as a posterior

circulation Acute Stroke Prognosis Early CT Score (PC-ASPECTS) of less than 6 (range, 0 to 10, with higher values indicating less infarct burden) on computed tomography (CT), CT angiographic (CTA) source images, or diffusion-weighted magnetic resonance imaging (MRI)[8]; and the presence on CT, CTA source images, or MRI of a large infarct in the brain stem, defined as a Pons-Midbrain Index of more than 2 points (range, 0 to 8, with higher values indicating more infarct burden; 1 point is attributed to infarction of <50% and 2 points to infarction of ≥50% on one side of the pons or midbrain).[9] Details of the inclusion and exclusion criteria are provided in Table S1 in the Supplementary Appendix, and detailed information on these criteria and the trial interventions and assessments has been published previously.[10]

Patients were randomly assigned in a 1:1 ratio to undergo thrombectomy plus receive standard medical care (thrombectomy group) or to receive standard medical care alone (control group). Patients could receive intravenous thrombolysis at the referring hospital or at the endovascular center to which they were transferred if they arrived within the accepted window for thrombolytic treatment of 4.5 hours and met guidelines for safe treatment. Patients had to pay for their thrombolytic drug and were eligible for reimbursement by their insurance entity. Randomization was performed by means of a central, Web-based procedure, with the use of a minimization process to balance the two treatment groups and with stratification according to age (≤70 years or >70 years), the time from symptom onset to randomization (6 to 12 hours or >12 to 24 hours), and baseline NIHSS score (6 to 20 or >20).

All the patients were admitted to acute stroke units or neurologic intensive care units and treated according to current Chinese guidelines for acute ischemic stroke management (see the Supplementary Appendix). Thrombectomy was performed with the Solitaire device, a retrievable and detachable self-expanding stent that is used to remove occlusive thrombi and restore blood flow. Rescue reperfusion therapy with other devices or pharmacologic agents was not permitted except for balloon angioplasty or stenting of the vertebral artery or basilar artery (see the Supplementary Appendix).

Outcomes

The primary outcome was good functional status, defined as a score of 0 to 3 on the modified Rankin scale (range, 0 [no symptoms] to 6 [death]), at 90 days. Outcomes were obtained by means of a structured interview[11] conducted by local assessors (in person or by telephone) who were unaware of the treatment assignments and by central assessors (by means of video or audio recordings) who were certified to assess the modified Rankin scale scores and were unaware of the treatment assignments. All the patients who were available for evaluation at 90 days had outcome data obtained by local evaluators who were unaware of the treatment assignments. In patients who declined to have audio and video recordings, central evaluations were missing. The primary analysis used central evaluations as the default and local evaluations when central evaluations were missing (see the Supplementary Appendix). Subgroup analyses were prespecified for the primary outcome according to age (≤70 or >70 years), dichotomous baseline NIHSS score (6 to 20 or >20), baseline NIHSS score (6 to 9, 10 to 20, or >20), randomization window (6 to 12 hours or >12 to 24 hours), baseline PC-ASPECTS (9 to 10 or <9), and location of basilar-artery occlusion (proximal, middle, or distal basilar artery).

On February 23, 2021, after the enrollment of 215 patients, 211 of whom had completed 90 days of follow-up, and before the unblinding of data to the investigators or trial committees, in consensus with the trial data and safety monitoring board, the steering committee of the trial decided to implement a change in the primary outcome, from a modified Rankin scale score of 0 to 4 at 90 days to a score of 0 to 3 at 90 days. The original primary outcome was changed to a secondary outcome. This decision was made because previously unavailable data from two randomized trials[3,4] showed that the cutoff on the modified Rankin scale that was most informative of treatment benefit in patients with basilar stroke was at a score grouping of 0 to 3 as compared with 4 to 6, a transition that was relevant to patients on the basis of previous work in patient-centered outcomes.[12] In addition, the change in the primary outcome allowed for alignment with the results of contemporaneous randomized trials of endovascular treatment of basilar-artery stroke.

Secondary outcomes besides the original primary outcome included functional independence (modified Rankin scale score, ≤2); the ordinal (shift) analysis of modified Rankin scale scores between the two groups at 90 days; vessel revascularization as assessed on CTA or magnetic resonance angiography (MRA) at 24 hours; the Barthel Index (range, 0 to 100, with higher scores indicating less disability); dramatic neurologic improvement, which was defined as reduction of at least 8 points on the NIHSS or a score of 0 to 2 at 24 hours; the NIHSS score at 90 days; and health status as measured on the EuroQoL Group 5-Dimension 3-Level (EQ-5D-3L) patient-reported questionnaire (range, −0.149 to 1.00, with higher scores indicating better quality of life) at 90 days, 6 months, and 12 months. In the thrombectomy group, the core laboratory used postprocedural conventional angiography to adjudicate successful vessel revascularization, which was defined as grade 2b or 3 (indicating reperfusion of >50% of the affected territory) on the modified Thrombolysis in Cerebral Infarction (TICI) scale (range, 0 to 3, with higher grades indicating increased reperfusion).[13]

The primary safety outcomes were 90-day mortality and symptomatic intracranial hemorrhage at 24 hours, which was assessed primarily according to the definition used in the Safe Implementation of Thrombolysis in Stroke–Monitoring Study (SITS-MOST),[14] which was parenchymal hemorrhage type 2[15] on follow-up imaging and a neurologic deterioration of at least 4 points on the NIHSS. As a secondary safety outcome, we used the definition of symptomatic intracranial hemorrhage according to the second European Cooperative Acute Stroke Study (ECASS II)[16] — namely, any type of intracranial hemorrhage on post-treatment imaging with an increase of at least 4 points on the NIHSS that was judged to be the predominant cause of neurologic deterioration. Other secondary safety outcomes included procedural complications and other serious adverse events.

STATISTICAL ANALYSIS

Under the original design incorporating an effect size (difference) of 20 percentage points in the primary outcome, one interim analysis after 212 patients had completed 90 days follow-up, and a stopping rule for efficacy defined with the use of O'Brien–Fleming boundaries, we calculated a sample size of 318. On the basis of publication of two trials and a Chinese registry of stroke due to basilar-artery occlusion,[3,4,17] we concluded that the postulated treatment effect size of an absolute difference of 20 percentage points was more likely to be accurate for the revised primary outcome than for the original primary outcome (Table S2).

All the analyses were based primarily on the intention-to-treat principle and included all the patients who had undergone randomization. Analyses were also performed in the per-protocol population (which included patients without major protocol deviations) and the as-treated population (which included patients according to the treatment they received). Statistical comparisons of efficacy outcomes according to treatment group were adjusted for age, baseline NIHSS score, and the time from stroke onset and are presented as adjusted rate ratios with 95% confidence intervals. Because there was no plan for the adjustment of the widths of confidence intervals of secondary outcomes for multiple comparisons, no conclusions can be drawn from these results. In the adjusted ordinal analysis, which was carried out with the modified Rankin scale scores 5 and 6 collapsed into one category, we used the common odds ratio after confirming that the proportional-odds assumption model is preferred over a multinomial alternative according to the Akaike information criterion. If the 90-day modified Rankin scale scores were missing but the patient was known to have survived at 90 days, the last known value was imputed. A modified Rankin scale score of 6 was assigned to missing patients with unknown survival status. There was no plan for imputation of other missing data, as outlined in the statistical analysis plan, which is available with the protocol.

The planned interim analysis occurred on April 18, 2022, and included the first 212 enrolled patients who had completed 90 days of follow-up. A P value of less than 0.001 was observed for the between-group difference in the primary outcome at 90 days (modified Rankin scale score of 0 to 3), which indicated that the prespecified stopping boundary for trial termination (P<0.012) had been crossed. Therefore, the steering committee accepted the recommendation of the data and safety monitoring board to stop enrollment.

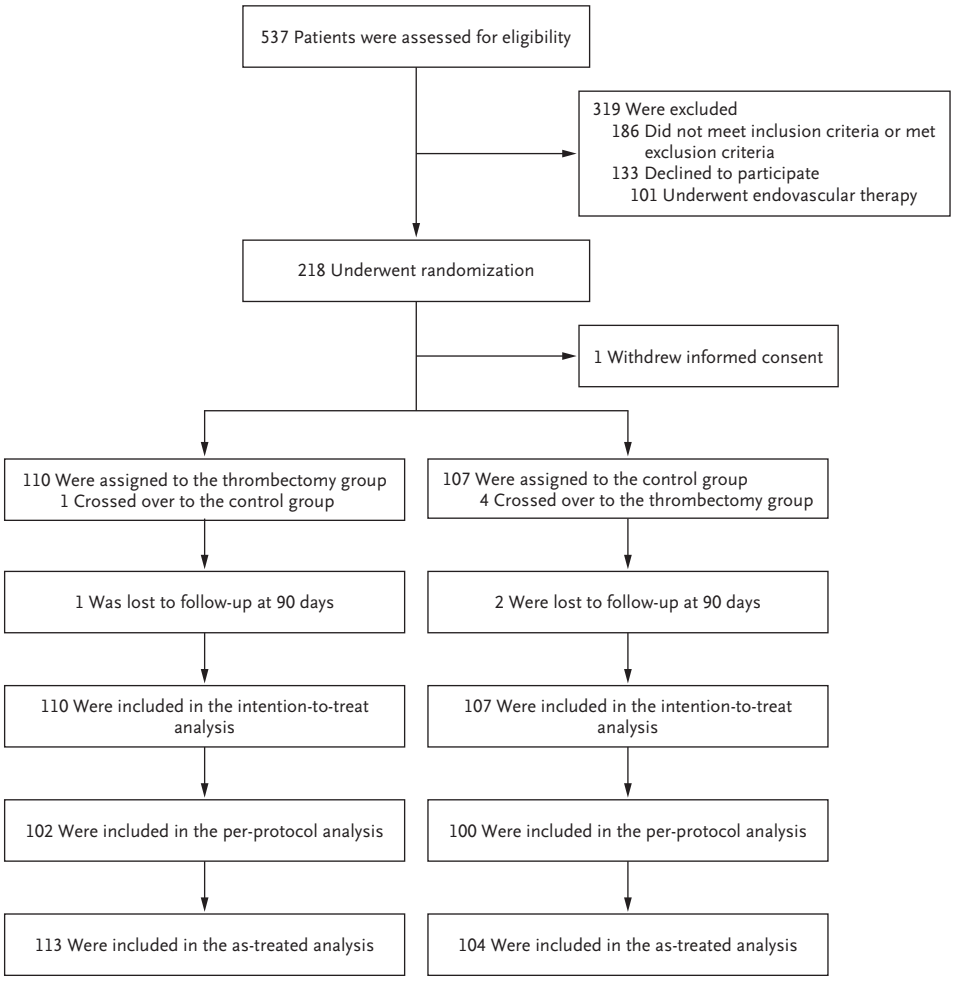

Figure 1. Screening, Randomization, and Follow-up of the Patients.

The per-protocol population included patients without major protocol deviations. The as-treated population included patients according to the treatment they received.

RESULTS

CHARACTERISTICS OF THE PATIENTS

From August 2016 through June 2021, a total of 218 patients underwent randomization (110 to the thrombectomy group and 108 to the control group) and had reached 90 days of follow-up at the time that the trial was stopped. Four patients in the control group crossed over to receive endovascular treatment, and 1 in the thrombectomy group crossed over to receive medical care only. One patient in the control group withdrew consent and was excluded from the analysis (Fig. 1). Missing primary-outcome data were imputed for 3 patients. The primary analysis used central evaluations (31 video and 59 audio) when available and local evaluations in the remaining 47 cases.

The characteristics of the patients at baseline were similar in the two trial groups (Table 1 and Table S3). The median age of the patients was 65 years, and 27% of the patients were women. Randomization occurred at a median of 663 minutes after symptom onset. The median NIHSS score was 20, and the median PC-ASPECTS was 8. Intravenous alteplase was administered to 18% of the patients overall (to 15 patients [14%] in the thrombectomy group and to 23 [21%] in the control group). In 32% of the patients, the imaging method used for selection was MRI

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Thrombectomy (N=110)	Control (N=107)
Age — yr	64.2±9.6	63.7±9.8
Male sex — no. (%)	80 (73)	79 (74)
Medical history		
Atrial fibrillation — no. (%)	14 (13)	13 (12)
Diabetes mellitus — no. (%)	30 (27)	29 (27)
Hypertension — no./total no. (%)	90/110 (82)	79/106 (75)
Modified Rankin scale score of 0 before stroke — no. (%)	85 (77)	89 (83)
NIHSS score†		
Median (IQR)	20 (15–29)	19 (12–30)
Distribution — no. (%)		
6–20	66 (60)	61 (57)
>20	44 (40)	46 (43)
Median systolic blood pressure at hospital arrival (IQR) — mm Hg‡	157 (138–175)	152 (138–166)
Median glucose level at hospital arrival (IQR) — mmol/liter§	8.0 (6.4–9.9)	7.6 (6.0–10.2)
Intravenous thrombolysis — no. (%)	15 (14)	23 (21)
Imaging characteristics		
Median PC-ASPECTS (IQR)¶	8 (7–10)	8 (7–10)
Median Pons-Midbrain Index (IQR)‖	1 (0–2)	1 (0–2)
Basilar-artery occlusion site — no./total no. (%)**		
Proximal basilar artery	53/107 (50)	45/105 (43)
Middle basilar artery	40/107 (37)	37/105 (35)
Distal basilar artery	13/107 (12)	23/105 (22)
Workflow times		
Distribution — no. (%)		
6–12 hr	64 (58)	71 (66)
>12 hr	46 (42)	36 (34)
Median duration (IQR) — min		
From stroke onset to randomization	664 (512–861)	662 (492–838)
From stroke onset to revascularization††	790 (626–1000)	NA
From hospital admission to groin puncture‡‡	153 (99–235)	NA
From groin puncture to revascularization§§	85 (59–129)	NA

* Plus–minus values are means ±SD. IQR denotes interquartile range, and NA not applicable.
† Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating more severe neurologic deficits.
‡ Data were missing for one patient in the thrombectomy group.
§ Data were missing for 11 patients in the thrombectomy group and for 13 in the control group. To convert the values for glucose to milligrams per deciliter, divide by 0.05551.
¶ The posterior circulation Acute Stroke Prognosis Early CT Score (PC-ASPECTS) is a measure of the extent of posterior circulation early cerebral ischemia. Scores ranges from 0 to 10, with higher scores indicating fewer early ischemic changes. Shown are values as assessed by the core laboratory. Scores were not available for four patients in the thrombectomy group.
‖ The Pons-Midbrain Index, a measure of the extent of early cerebral ischemia in the pons and midbrain, ranges from 0 (absence of early cerebral ischemia in the midbrain and pons) to 8 (>50% early cerebral ischemia on both sides in these brain-stem territories); 1 point is attributed to infarction of less than 50%, and 2 points to infarction of 50% or more on one side of the pons or midbrain. Scores were not available for four patients in the thrombectomy group.

Table 1. (Continued.)

** The location of the basilar-artery occlusion was adjudicated by a core laboratory. Images were lost for 3 patients in the thrombectomy group and for 2 in the control group. On the basis of assessment by the core laboratory, 1 patient in the thrombectomy group did not have basilar-artery occlusion and had a high-grade basilar-artery stenosis. There were 20 patients with occluded intracranial segments of both vertebral arteries, which were included in the proximal category.

†† Revascularization was defined as the first visualization of successful reperfusion, as indicated by a modified Thrombolysis in Cerebral Infarction (TICI) grade of 2b or 3 (on a scale from 0 [no reperfusion] to 3 [complete reperfusion]). For patients who underwent angiography only or had unsuccessful revascularization, the time of administration of the last bolus of contrast material was considered to be the time to revascularization. Data on the time from stroke onset to revascularization were missing for seven patients in the thrombectomy group.

‡‡ Data on the time from hospital admission to groin puncture were missing for five patients in the thrombectomy group.

§§ Data on the time from groin puncture to revascularization were missing for seven patients in the thrombectomy group.

(Table S4). A total of 22 patients arrived at the thrombectomy center within 4.5 hours after stroke onset, 12 (55%) of whom received intravenous thrombolysis, and 39 patients arrived at the referring hospital in less than 4.5 hours from the time of stroke onset, of whom 26 (67%) received intravenous thrombolysis.

Thrombectomy was performed in 106 of the 110 patients who had been assigned to the thrombectomy group, and core laboratory–adjudicated reperfusion occurred in 88% of the patients. General anesthesia was used in 72 patients (65%) who had been assigned to the thrombectomy group. Intracranial angioplasty or stenting after failed thrombectomy was performed in 60 patients (55%) (Table S5).

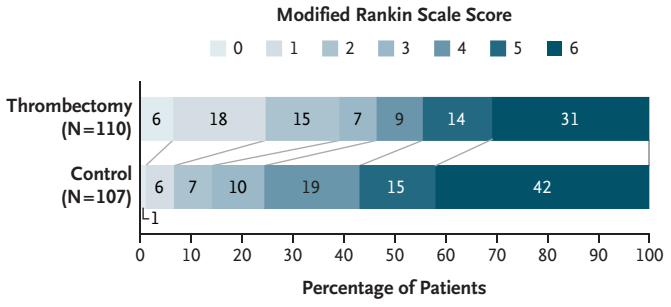

Figure 2. Distribution of Functional Scores at 90 Days (Intention-to-Treat Population).

Scores on the modified Rankin scale range from 0 to 6, with a score of 0 indicating no symptoms, 1 no clinically significant disability, 2 slight disability (able to handle own affairs without assistance but unable to carry out all previous activities), 3 moderate disability necessitating some help but ability to walk unassisted, 4 moderately severe disability (unable to attend to bodily needs and unable to walk), 5 severe disability (receiving constant nursing care and attention), and 6 death. The adjusted common odds ratio for the modified Rankin scale score toward a better outcome with endovascular thrombectomy at 90 days was 2.64 (95% CI, 1.54 to 4.50).

EFFICACY OUTCOMES

Good functional status (score of 0 to 3 on the modified Rankin scale) at 90 days was observed in 46% of the patients in the thrombectomy group and in 24% of those in the control group (adjusted rate ratio, 1.81; 95% confidence interval [CI], 1.26 to 2.60, P<0.001) (Fig. 2 and Table 2). The original primary outcome, a modified Rankin scale score of 0 to 4 at 90 days, was observed in 61 of 110 patients (55%) in the thrombectomy group and in 46 of 107 (43%) in the control group (adjusted rate ratio, 1.21; 95% CI, 0.95 to 1.54) (Table 2). For the secondary outcome of a modified Rankin scale score of 0 to 2, the percentages were 39% in the thrombectomy group and 14% in the control group (adjusted rate ratio, 2.75; 95% CI, 1.65 to 4.56). The ordinal modified Rankin scale had an adjusted common odds ratio of 2.64 (95% CI, 1.54 to 4.50) in a direction that favored thrombectomy (Fig. 2), but the width of the confidence interval for this outcome was not adjusted for multiplicity.

The median EQ-5D-3L score was higher in the thrombectomy group than in the control group (0.78 vs. 0.46 points; mean difference, 0.24 points; 95% CI, 0.10 to 0.39). Successful reperfusion in the thrombectomy group, defined as modified TICI category of 2b or 3 (signifying flow restoration in >50% of the originally affected territory)[13] was observed in 88% of the patients. Basilar-artery patency at 24 hours as assessed on CTA or MRA was observed in 92% of the patients in the thrombectomy group and in 19% of those in the control group. Results of secondary outcomes are shown in Table 2, and results of the per-protocol analyses are shown in Table S6 and Figure S1. Prespecified subgroup analyses are shown in Figure 3, Figures S2 through S8, and Table S7.

Table 2. Trial Outcomes.*

Outcome	Thrombectomy (N=110)	Control (N=107)	Measure of Effect	Adjusted Value (95% CI)†
Primary outcome				
Modified Rankin scale score of 0–3 at 90 days — no. (%)	51 (46)	26 (24)	Rate ratio	1.81 (1.26 to 2.60)‡
Secondary outcomes				
Modified Rankin scale score at 90 days§	NA	NA	Common odds ratio	2.64 (1.54 to 4.50)
Modified Rankin scale score of 0 to 2 at 90 days — no. (%)	43 (39)	15 (14)	Rate ratio	2.75 (1.65 to 4.56)
Modified Rankin scale score of 0 to 4 at 90 days — no. (%)¶	61 (55)	46 (43)	Rate ratio	1.21 (0.95 to 1.54)
Dramatic neurologic improvement at 24 hr — no./total no. (%)‖	25/101 (25)	9/94 (10)	Rate ratio	2.50 (1.23 to 5.07)
Barthel Index score of 95 to 100 at 90 days — no./total no. (%)**	26/73 (36)	10/56 (18)	Rate ratio	2.20 (1.16 to 4.17)
Basilar-artery patency at 24 hr — no./total no. (%)††	76/83 (92)	15/77 (19)	Rate ratio	4.53 (2.81 to 7.30)
Median EQ-5D-3L score at 90 days (IQR)‡‡	0.78 (0.36–1.00)	0.46 (0.11–0.73)	Mean difference	0.24 (0.10 to 0.39)
Reperfusion on digital subtraction angiography — no./total no. (%)§§	89/101 (88)	NA		
Safety outcomes				
Death within 90 days	34 (31)	45 (42)	Risk ratio	0.75 (0.54 to 1.04)
Symptomatic intracranial hemorrhage¶¶				
According to SITS-MOST criteria	6/102 (6)	1/88 (1)	Risk ratio	5.18 (0.64 to 42.18)
According to ECASS II criteria	9/102 (9)	2/88 (2)	Risk ratio	3.88 (0.86 to 17.49)
Asymptomatic intracranial hemorrhage	8/102 (8)	3/88 (3)	Risk ratio	2.30 (0.63 to 8.41)
Procedure-related complication	12 (11)	NA		—
Vessel dissection	4 (4)	NA		—
Vessel perforation	3 (3)	NA		—
Distal embolization	5 (5)	NA		—
Other serious adverse events				
Pneumonia	51 (46)	50 (47)		—
Malignant brain edema	14 (13)	11 (10)		—
Gastrointestinal hemorrhage	15 (14)	10 (9)		—
Acute renal insufficiency	3 (3)	5 (5)		—
Cardiac ischemia	0	4 (4)		—
Acute heart failure	16 (15)	22 (21)		—
Acute respiratory failure	21 (19)	26 (24)		—

* The widths of confidence intervals for secondary outcomes have not been adjusted for multiple comparisons, and no conclusions can be drawn from these results.

† The value was adjusted for the minimization factors of age (≤70 years or >70 years), baseline NIHSS (6 to 20 or >20), and therapeutic window (6 to 12 hours or >12 hours), except for the values representing the risk ratios for symptomatic intracranial hemorrhage and asymptomatic intracranial hemorrhage, which are presented as unadjusted values.

‡ P<0.001.

§ The two worst categories on the modified Rankin scale (5 and 6) were considered to be equivalent and were collapsed into one single category for the analysis of the common odds ratio.

¶ A modified Rankin scale score of 0 to 4 at 90 days was the original primary outcome.

‖ Dramatic neurologic improvement was defined as a reduction of at least 8 points on the NIHSS or a score of 0 to 2 at 24 hours. Eleven patients who died before 24 hours were classified as having no dramatic neurologic improvement. In addition to the 11 patients who had died, NIHSS scores at 24 hours were not available for 9 patients in the thrombectomy group and for 13 in the control group.

Table 2. (Continued.)

** Scores on the Barthel Index range from 0 to 100, with higher values indicating good performance of daily living activities. A score between 95 and 100 indicates no disability that interferes with daily activities. Included in this analysis were patients who were alive at 90 days.

†† Patency was defined as a score of 2 or 3 on the Arterial Occlusive Lesion scale, which ranges from 0 (complete occlusion) to 3 (complete recanalization and restoration of the target artery). Data for follow-up angiography were not available for 57 patients because of clinical instability or death.

‡‡ The EuroQoL Group 5-Dimension 3-Level (EQ-5D-3L) patient-reported questionnaire is a standardized instrument for the measurement of health status. Scores range from –0.149 to 1.00, with higher scores indicating better quality of life. Data were available for 68 patients in the thrombectomy group and for 52 in the control group.

§§ Reperfusion on digital subtraction angiography was defined as a modified TICI grade of 2b or 3. A modified TICI reperfusion grade of 2b or higher indicates antegrade reperfusion of more than half the ischemic territory of the previously occluded target artery.[13] Nine angiographic images were missing or could not be assessed for modified TICI because of poor image quality.

¶¶ Symptomatic intracranial hemorrhage was defined as parenchymal hemorrhage type 2 on follow-up imaging and neurologic worsening of at least 4 points on the NIHSS, according to the Safe Implementation of Thrombolysis in Stroke–Monitoring Study (SITS-MOST) criteria, or any symptomatic intracranial hemorrhage and neurologic worsening of at least 4 points on the NIHSS, according to the second European–Australasian Acute Stroke Study (ECASS II) criteria. Follow-up scans were unavailable because of clinical instability or death in 8 patients in the thrombectomy group and in 19 in the control group. The risk ratios are presented as unadjusted values because of nonconvergence in the adjusted analysis.

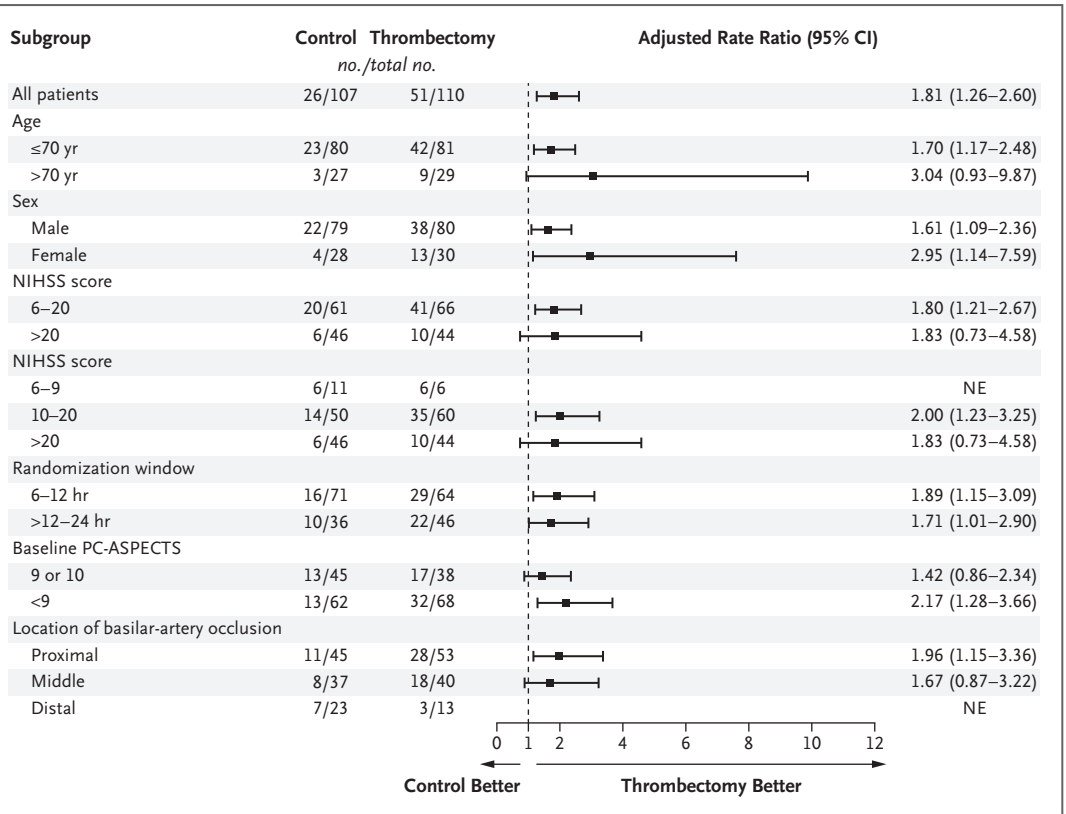

Figure 3. Subgroup Analyses of a Modified Rankin Scale Score of 0 to 3 at 90 Days (Primary Outcome).

Scores on National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating greater neurologic deficits. The posterior circulation Acute Stroke Prognosis Early CT Score (PC-ASPECTS) is a 10-point grading system that measures the extent of posterior circulation early cerebral ischemia; scores ranges from 0 to 10, with higher scores indicating fewer early ischemic changes. The adjusted rate ratio in subgroups of patients with a baseline NIHSS score of 6 to 9 and with distal basilar-artery occlusion could not be estimated (NE) because of limited sample sizes. The trial was not powered for and had no prespecified correction for multiple comparisons for a definitive analysis of subgroups.

SAFETY OUTCOMES

The incidence of symptomatic intracranial hemorrhage at 24 hours based on the primary definition (according to the SITS-MOST criteria) was higher in the thrombectomy group than in the control group (6% vs. 1%; unadjusted risk ratio, 5.18; 95% CI, 0.64 to 42.18); the incidence based on the secondary definition (according to the ECASS II criteria) was 9% in the thrombectomy group and 2% in the control group (unadjusted risk ratio, 3.88; 95% CI, 0.86 to 17.49). Mortality at 90 days was 31% in the thrombectomy group and 42% in the control group (adjusted risk ratio, 0.75; 95% CI, 0.54 to 1.04) (Fig. S9). In the thrombectomy group, procedure-related complications, including dissection, perforation, and distal embolization, occurred in 12 of 110 patients (11%). The incidence of medical complications was similar in the two groups (Table 2 and Tables S8 and S9).

DISCUSSION

Our trial showed that among eligible patients with stroke due to basilar-artery occlusion and symptom onset 6 to 24 hours earlier, the incidence of a good functional status, defined as a modified Rankin scale score of 0 to 3, was higher with thrombectomy plus standard medical care than with standard medical care alone. The 95% confidence interval for the between-group difference in the analysis of the original primary outcome of a modified Rankin scale score of 0 to 4 included zero, a finding that suggests null results. Thrombectomy was associated with procedural complications and cerebral hemorrhages that may have been the result of reperfusion, including a higher incidence of symptomatic intracerebral hemorrhage than was observed in the control group. However, mortality at 90 days was similar in the two groups.

These results differ from those of some other trials of endovascular treatment of basilar-artery stroke (BASICS and BEST) and are similar to those of the Endovascular Treatment for Acute Basilar-Artery Occlusion (ATTENTION) trial, the results of which are reported in this issue of the *Journal*.[18] BASICS restricted enrollment to patients who presented within 6 hours after estimated stroke onset, and the trial included a large proportion of patients who had received treatment with intravenous alteplase, an effective treatment for stroke due to basilar-artery occlusion.[19,20] The overall results of BASICS did not rule out a beneficial effect of thrombectomy, and there was a suggestion of benefit in favor of thrombectomy in patients with a baseline NIHSS score of at least 10. Despite the inclusion of patients who presented with an NIHSS score of at least 6 in our trial, most of our patients had a baseline NIHSS score of at least 10. Therefore, uncertainty still exists regarding the benefit of thrombectomy as compared with medical care in patients who present with an NIHSS score of less than 10.

On the basis of previous reports indicating that the extent of infarction in the posterior circulation, and particularly in the brain stem, is a predictor of outcome after thrombectomy for basilar-artery occlusion,[8,21] we restricted enrollment to patients who did not have large baseline infarcts in these anatomical regions, which may limit the generalizability of the results of our trial. Future studies may address questions regarding the use of imaging for the selection of patients with stroke due to basilar-artery occlusion to undergo thrombectomy.

Our trial has limitations. First, protocol changes were made during the trial, most notably to the primary outcome, on the basis of data from other trials that were unavailable at the time of the protocol design. The revised outcome, a modified Rankin scale score of 0 to 3 as representing good functional status, has been considered to be meaningful to patients[12] and has been used as the primary outcome in other randomized trials involving patients with basilar-artery stroke. This change was implemented by the steering committee while its members were unaware of the trial results. Second, since the population that was enrolled is representative of the Han Chinese population, the generalizability of our trial results to other populations is limited. In addition, patients underwent thrombectomy outside the trial, and consecutive enrollment did not occur. Furthermore, the cause of the underlying occlusion in our patients was predominantly atherothrombotic, and the ability to determine a benefit of thrombectomy in patients with embolic stroke, a stroke type that may be more prevalent in White populations than in the Han Chinese population, is limited.[22,23] Owing to discrepant proportions of enrolled men as compared with women in our trial, the benefit of thrombectomy for the treatment of basilar-

artery occlusion in women is less certain. Finally, a limited proportion of patients received intravenous thrombolysis, and less than two thirds of the patients who arrived at the referring hospital or endovascular center within 4.5 hours after onset received intravenous thrombolysis. The low proportion of patients with thrombolytic use may have been related to the requirement that patients had to initially pay for the thrombolytic drug.

In a trial in China that was stopped early for efficacy, we found that patients with stroke due to basilar-artery occlusion who presented 6 to 24 hours after symptom onset had a higher incidence of good functional status at 90 days with thrombectomy plus medical care than with medical care alone. Thrombectomy was associated with procedural complications and with a higher incidence of cerebral hemorrhage.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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APPENDIX

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