

TOPIC COLLECTION: ENDOVASCULAR THROMBECTOMY FOR ACUTE ISCHEMIC STROKE

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Letter from the Editor

Endovascular thrombectomy (EVT) has become an important treatment for patients with acute ischemic stroke who can be treated within 6 hours of stroke onset, and was one focus of a recent guideline update from the American Heart Association/American Stroke Association. Select patients who meet certain imaging criteria can be treated up to 24 hours after stroke onset. Clinical trials have established the value of EVT in “high-resource” locations such as western Europe, North America, and Australia. The RESILIENT trial evaluated whether EVT can be of benefit in a lower-resource setting.

In 12 hospitals in the public health system of Brazil, 35% of the patients who received thrombectomy achieved functional independence, compared to 20% of those who did not receive thrombectomy. The rate of symptomatic intracranial hemorrhage was 4.5% in both groups, and there was no significant difference in mortality. The RESILIENT trial demonstrates the feasibility of implementing EVT in a limited-resource health system, and the findings should encourage clinicians in other settings to implement a pathway for EVT.

Other articles in this collection examine different aspects of the current practice of EVT for acute ischemic stroke. The DIRECT-MT study from China evaluated whether alteplase can be withheld prior to thrombectomy. Although the overall trial results did not show a difference in outcomes in the EVT-alone group vs. the EVT + alteplase group, the vast majority of patients were treated at the initial hospital. Many patients in the U.S. are treated with thrombolysis at a primary stroke center and then transferred to a comprehensive stroke center; it's likely that thrombolysis is useful for these patients. Therefore, confirmatory studies in different countries are needed.

The study on outcomes of EVT in elderly patients showed worse overall results in patients older than 80. Only 1 in 5 patients achieved functional independence, and 90-day mortality was 51%. Therefore, careful patient selection among elderly patients is paramount.

In the study on EVT for patients with mild deficits at presentation, there appeared to be a potential role for thrombectomy in patients with proximal middle cerebral artery occlusion presenting with mild deficits, but this requires confirmation in randomized trials.

Finally, a multicenter study reviewed outcomes in patients with different imaging strategies and found that CT or CT angiography alone and CT with perfusion imaging were both acceptable approaches. Each hospital should examine its radiology metrics and decide which imaging strategy is most practical and leads to best patient outcomes.

Seemant Chaturvedi, MD

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Thrombectomy for Stroke in the Public Health Care System of Brazil

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ABSTRACT

BACKGROUND

Randomized trials involving patients with stroke have established that outcomes are improved with the use of thrombectomy for large-vessel occlusion. These trials were performed in high-resource countries and have had limited effects on medical practice in low- and middle-income countries.

METHODS

We studied the safety and efficacy of thrombectomy in the public health system of Brazil. In 12 public hospitals, patients with a proximal intracranial occlusion in the anterior circulation that could be treated within 8 hours after the onset of stroke symptoms were randomly assigned in a 1:1 ratio to receive standard care plus mechanical thrombectomy (thrombectomy group) or standard care alone (control group). The primary outcome was the score on the modified Rankin scale (range, 0 [no symptoms] to 6 [death]) at 90 days.

RESULTS

A total of 300 patients were enrolled, including 79 who had undergone thrombectomy during an open-label roll-in period. Approximately 70% in the two groups received intravenous alteplase. The trial was stopped early because of efficacy when 221 of a planned 690 patients had undergone randomization (111 to the thrombectomy group and 110 to the control group). The common odds ratio for a better distribution of scores on the modified Rankin scale at 90 days was 2.28 (95% confidence interval [CI], 1.41 to 3.69; $P=0.001$), favoring thrombectomy. The percentage of patients with a score on the modified Rankin scale of 0 to 2, signifying an absence of or minor neurologic deficit, was 35.1% in the thrombectomy group and 20.0% in the control group (difference, 15.1 percentage points; 95% CI, 2.6 to 27.6). Asymptomatic intracranial hemorrhage occurred in 51.4% of the patients in the thrombectomy group and 24.5% of those in the control group; symptomatic intracranial hemorrhage occurred in 4.5% of the patients in each group.

CONCLUSIONS

In this randomized trial conducted in the public health care system of Brazil, endovascular treatment within 8 hours after the onset of stroke symptoms in conjunction with standard care resulted in better functional outcomes at 90 days than standard care alone. (Funded by the Brazilian Ministry of Health; RESILIENT ClinicalTrials.gov number, NCT02216643.)

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*A complete list of sites and investigators in RESILIENT is provided in the Supplementary Appendix, available at NEJM.org.

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Thrombectomy for Acute Stroke in Brazil

Endovascular treatment within 8 hours of stroke onset improved functional outcomes at 90 days for patients in the public healthcare system of Brazil.

Endovascular thrombectomy (EVT) has become an important treatment for patients with acute ischemic stroke who can be treated within 6 hours of stroke onset and for select patients up to 24 hours of onset. Trials supporting the use of EVT in this setting were conducted in Europe, North America, and Australia. Whether EVT can be adopted and whether it will be efficacious in a lower-resource setting are unknown.

Now, investigators have conducted a multicenter, randomized trial (RESILIENT) involving 221 patients with acute stroke (mean age, 66 years) in the public healthcare system of Brazil. Patients were eligible if they could be treated within 8 hours of stroke onset and had occlusion in the internal carotid artery or middle cerebral artery. Median NIH Stroke Scale score at entry was 18, and 70% received alteplase.

Patients were assigned to mechanical thrombectomy plus standard care or standard care alone; the median time from stroke onset to randomization was approximately 4 hours. The primary study endpoint was functional outcome on the modified Rankin scale at 90 days, with a score of 0–2 indicating functional independence. A key safety endpoint was intracranial hemorrhage.

More patients who received thrombectomy versus standard care alone achieved functional independence (35% vs. 20%). The rate of symptomatic intracranial hemorrhage was similar with thrombectomy or standard care alone (4.5%), as was mortality (24% and 30%, respectively).

COMMENT

This study demonstrates that the benefits of EVT for acute ischemic stroke can be realized in a variety of healthcare settings. Even with the constrained resources of the Brazilian public health system, the steps needed for appropriate patient evaluation and treatment with thrombectomy were achievable, and results were comparable to other EVT trials. These results should encourage clinicians in resource-constrained systems to implement an EVT pathway for appropriate patients with acute stroke. — **Seemant Chaturvedi, MD**

Martins SO et al. Thrombectomy for stroke in the public health care system of Brazil. N Engl J Med 2020 Jun 11; 382:2316. (https://doi.org/10.1056/NEJMoa2000120)

Risks and Benefits of Endovascular Thrombectomy in Older Adults

A comparison of outcomes in patients 80 years and older with outcomes in younger patients

Endovascular thrombectomy (EVT) is an established treatment for patients with acute ischemic stroke and large vessel occlusion (LVO), but clinical trials of EVT have included relatively few elderly patients (≥80 years). High rates of comorbidities in older adults have raised concerns about EVT utility in the elderly.

Using data from a national EVT registry in the Netherlands from 2014 to 2016, the authors included 1526 patients (25% elderly) with an anterior circulation LVO who were treated at an approved study center. The primary outcome was a favorable shift on the modified Rankin Scale (mRS), and achieving functional independence (mRS score, 0–2) was the secondary endpoint; follow-up was 90 days. At baseline, the elderly patients were more often women and had higher median NIH Stroke Scale scores and higher rates of prestroke disability. Atrial fibrillation was more common in the elderly, as was prior use of anticoagulants, and elderly patients had longer onset-to-groin-puncture times.

Regarding outcomes, elderly patients had a lower likelihood of favorable shift on the mRS. Functional independence was also lower in the elderly (20% vs. 46%), and 90-day mortality was higher (51% vs. 22%). However, if there was successful reperfusion, then elderly patients had a slightly higher benefit compared with younger patients. No difference was seen in symptomatic intracranial hemorrhage.

COMMENT

This study demonstrates that elderly patients have relatively high mortality and lower chance of a good outcome following EVT for acute stroke. However, about one in five achieve functional independence. Use of advanced imaging to identify patients with salvageable brain tissue will likely help clinicians target EVT to elderly patients with the best chance for a favorable outcome.

— **Seemant Chaturvedi, MD**

Groot AE et al. Endovascular treatment in older adults with acute ischemic stroke in the MR CLEAN Registry. Neurology 2020 Jun 11; 10.1212/WNL.0000000000009764; [e-pub]. (https://doi.org/10.1212/WNL.0000000000009764)

Is There a Role for Endovascular Thrombectomy in Stroke with Mild Deficits?

Perhaps only in patients with M1 occlusion

Current guidelines recommend consideration of endovascular thrombectomy (EVT) for acute ischemic stroke only when the clinical deficit measured by the NIH stroke scale is >5. The role of EVT is unclear in patients with milder clinical deficits, especially in the presence of a large vessel occlusion, such as in the distal internal carotid or middle cerebral artery.

In a multicenter retrospective study, researchers compared outcomes in patients with minor stroke (NIH stroke scale ≤5) and presence of a large vessel occlusion who received intended therapy with intravenous thrombolysis (IVT; alteplase) alone or with adjunctive EVT. Propensity-score weighting was used to account for baseline differences. A modified Rankin Scale score of 0 to 1 at 3 months was the primary outcome, considered excellent functional outcome.

Among 598 patients, 384 received IVT alone and 214 patients received IVT + EVT. One third of IVT-alone recipients had a first-segment middle cerebral artery (M1) occlusion, compared with 59% of the IVT + EVT group. Conversely, the IVT-alone group had a higher rate of second-segment middle cerebral artery (M2) occlusion.

Overall, adjunctive treatment with EVT was not associated with higher odds of excellent outcome, but this varied by site of occlusion. In patients with M1 occlusion, odds of excellent outcome were significantly higher with IVT + EVT treatment (odds ratios, 3.3 for proximal and 1.7 for distal), whereas in those with M2 occlusions, odds of excellent outcome were significantly lower with IVT + EVT (OR, 0.5). The IVT + EVT group had higher odds of symptomatic intracranial hemorrhage for M2 but not M1 occlusions. An analysis based on actual treatments received (vs. those intended) showed similar results.

COMMENT

These findings suggest that clinicians should employ IVT alone for minor stroke with M2 occlusions. For minor stroke with M1 occlusion, there is a potential role for EVT, but larger, prospective trials are needed to establish whether there is a true clinical benefit.

— *Seemant Chaturvedi, MD*

Seners P et al. Bridging therapy or IV thrombolysis in minor stroke with large vessel occlusion. Ann Neurol 2020 Apr 29; [e-pub]. (https://doi.org/10.1002/ana.25756)

Can Thrombolysis Be Avoided Prior to Thrombectomy for Acute Ischemic Stroke?

A randomized trial found thrombectomy alone to be noninferior to thrombectomy plus thrombolysis.

In studies establishing the utility of endovascular thrombectomy (EVT) for patients with acute ischemic stroke, patients also received treatment with a thrombolytic agent such as alteplase if they could be treated within a 4.5-hour time window, but there have been concerns that thrombolysis could increase the risk for brain hemorrhage and lead to delays in initiation of EVT. Now, researchers have conducted a randomized trial comparing EVT alone to EVT plus alteplase in 656 patients (median age, 69) at 41 healthcare centers in China. Median NIH stroke scale score was 17; median duration from randomization to groin puncture was 31 minutes in the EVT-alone group and 36 minutes in the combination-treatment group. The primary endpoint was the score on the modified Rankin scale (mRS), with lower scores indicating better neurologic recovery.

At 90 days, there was no difference in the proportion of the two groups with a mRS score of 0 to 2 (37% of the combination-treatment group vs. 36% of the EVT-alone group). The combination-treatment group had higher rates of recanalization before EVT (7.0% vs. 2.4%) and successful angiographic recanalization was also higher in the combination group (85% vs. 79%). There was no difference between groups in mortality or symptomatic intracranial hemorrhage.

COMMENT

The authors concluded that EVT alone was noninferior to combination treatment with regard to functional outcome. However, most of these patients in Chinese centers received both treatments at the same hospital. In the U.S. and other countries, it is common for patients to receive thrombolysis at one hospital and then be transferred for EVT (“drip and ship” model). Further studies are needed to see

if these results can be confirmed in other healthcare systems and among “drip and ship” patients. — *Seemant Chaturvedi, MD*

Yang P et al. Endovascular thrombectomy with or without intravenous alteplase in acute stroke. N Engl J Med 2020 May 21; 382:1981. (https://doi.org/10.1056/NEJMoa2001123)

Imaging Selection and Outcomes of Thrombectomy for Acute Stroke

CT and CTP fared similarly in identifying good thrombectomy candidates; unfavorable CTP findings might indicate increased risk for adverse events.

Endovascular thrombectomy (EVT) improves stroke outcomes for select patients when performed within 24 hours after ischemic stroke onset. Imaging practices to determine EVT eligibility vary among hospitals: Some use brain CT and the Alberta Stroke Program Early CT Score (ASPECTS) to judge extent of infarction. Others use CT perfusion (CTP) to identify a “favorable profile” of small infarct core and medium/large hypoperfused area. To expand on the limited data on outcomes when these imaging methods are discordant versus concordant, researchers conducted a multicenter, observational trial to assess EVT outcomes in patients with acute stroke. A core imaging lab reviewed acute radiology results to determine if the CT was favorable (ASPECTS score ≥ 6) or if the CTP pattern was favorable (infarct core < 70 cc, mismatch ratio ≥ 1.2 , mismatch volume ≥ 10 cc). Functional status was considered a good outcome if the modified Rankin scale (mRS) score was 0 to 2.

Of 361 enrolled patients, 285 were treated with EVT and the rest with medical management. Most patients (78%) were treated within 6 hours after stroke onset, and most (231) had favorable imaging on both CT and CTP; 58% of these concordant-imaging patients had a good outcome from EVT. The rates of good outcome from EVT were 24% of 17 patients with favorable CT but unfavorable CTP, 46% of 28 patients with unfavorable CT but favorable CTP, and 0 of 9 patients with both unfavorable CT and unfavorable CTP findings. Among patients with a favorable CT/unfavorable CTP, 24% had symptomatic intracranial hemorrhage and 53% died. The rate of good outcome was similar in patients with a favorable CT pattern (56%) and favorable CTP appearance (57%).

COMMENT

This study illustrates that either a CT-only imaging approach or a CTP approach is acceptable in determining good candidates for EVT. Current guidelines recommend a CTP approach for patients beyond 6 hours after stroke onset. The finding that patients with a favorable CT/unfavorable CTP have a high hemorrhage and mortality rate deserves confirmation in larger studies.

— *Seemant Chaturvedi, MD*

At the time we reviewed this paper, its publisher noted that it was not in final form and that subsequent changes might be made.

Sarraj A et al. Optimizing patient selection for endovascular treatment in acute ischemic stroke (SELECT): A prospective, multicenter cohort study of imaging selection. Ann Neurol 2020 Jan 9; [e-pub]. (https://doi.org/10.1002/ana.25669)