

An Evidence-based Update on Acute Endovascular Stroke Therapy

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Abstract

In 2015, there is now level 1 evidence from prospective randomized controlled trials proving the clinical efficacy of acute endovascular stroke therapy. Specifically, patients who would stand to benefit need to have a large vessel occlusion (LVO), need to be treated within the first 6 hours after symptom onset, and be treated by experienced neurointerventionalists who can consistently achieve high rates of Thrombolysis in Cerebral Infarction (TICI) 2b/3 recanalization.

Keywords

Acute stroke, therapy, thrombolysis, thrombectomy

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Acute endovascular stroke therapy is designed to restore perfusion for patients with large vessel occlusions (LVOs) to hopefully minimize any eventual disability. This subgroup of severely affected stroke patients comprise only a minority of the 800,000 strokes that occur annually in the US.¹ But this same group consumes a disproportionately large share of stroke care resources. Currently, the only US Food and Drug Administration (FDA)-approved treatment for acute ischemic stroke, intravenous thrombolysis, unfortunately, has been shown to have modest, if any, clinical efficacy for these severely affected patients.

Ever since 2004, when the FDA approved the first intra-arterial thrombectomy (IAT) device for clot removal in patients with acute ischemic stroke, compelling anecdotal reports and experiences have led some to consider IAT as a promising treatment option for severely affected stroke patients. But three randomized controlled trials of intra-arterial treatment, published simultaneously in *The New England Journal of Medicine* in 2013 had ambiguous results.^{2–4} In their cohort as a whole, endovascular therapy conferred no additional benefit to IAT. Additional subgroup analysis yielded noteworthy trends. Improved recanalization as measured by the Thrombolysis in Cerebral Infarction (TICI) scale yielded more favorable clinical outcomes. However, only a minority of the endovascular cohort in the Interventional Management of Stroke (IMS-III) study had a TICI 2b or 3 angiographic result, indicating clinically meaningful reperfusion. In the subset of patients with an admission National Institutes of Health Stroke Scale (NIHSS) >20, which is a surrogate marker for LVOs, there was a 7 % absolute higher rate of modified Rankin score (mRS) 0–2 among those treated with endovascular therapy.² When looking at the subset with the

largest vascular occlusions, namely carotid terminus or tandem carotid and M1 lesions, there was a 23 % absolute higher rate of mRS 0–2 in the endovascular group. As a result, it was clear that a more accurate assessment of the clinical efficacy of acute endovascular stroke therapy necessitated studying subjects with LVOs and thrombectomy devices with higher published recanalization rates.

Which brings us to the December 2014 publication in *The New England Journal of Medicine* of the Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands (MR CLEAN) study.⁵ The study aims were to see, in patients with LVO within 6 hours, if intra-arterial thrombolysis, compared with medical management, yielded improved clinical outcomes as measured by the mRS at 90 days.

A major feature in the study design was the requirement of LVO confirmation via imaging prior to enrollment. The biggest methodological difference was the decision by the Dutch government to pay for the use of thrombectomy devices only in the context of a randomized trial, thereby precluding treatment outside the trial. This policy accelerated enrollment and allowed the investigators to achieve a large sample size in a short period of time.

The results were unprecedented. Within 3 years, with about 500 subjects enrolled, 97 % had confirmation of LVO prior to enrollment. About 90 % of subjects in both groups received intravenous alteplase. In the intervention group, stent retrievers were used in 97 % of cases. Meaningful angiographic recanalization, as scored by a TICI 2b or 3 was achieved in 60 % of cases, as opposed to 41 % in the IMS-III study. In terms of the

primary outcome measure, there was an absolute increase of 13.5 % (32.6 versus 19.1 %) in the rate of functional independence at 90 days among the intervention group. Although there was a higher rate of new ischemic stroke in different vascular territory (5.6 versus 0.4 %) in the treatment group, there were no differences in mortality at 30 days (19 versus 19 %) or symptomatic intracerebral hemorrhage (ICH) (6.0 versus 5.2 %).

The data from the MR CLEAN study as well as subgroup analysis of prior studies comparing endovascular therapy to best medical management provide valuable insight into discerning any clinical benefit for intervention. A meta-analysis⁶ of the six most recent prospective randomized controlled trials comparing endovascular therapies with best medical management was published after the MR CLEAN results

were presented at the 9th World Stroke Congress (Istanbul, Turkey, 2014). They found when comparing cohorts from the six studies with LVO confirmation prior to randomization, the intervention group (n=655) had a 1.7 times greater odds of achieving mRS 0–2 at 90 days compared with best medical management (n=528). The 95 % confidence interval was between 1.29 and 2.16 with p=0.0001.

In 2015, there is now level 1 evidence from prospective randomized controlled trials proving the clinical efficacy of acute endovascular stroke therapy. Specifically, patients who would stand to benefit need to have a LVO, need to be treated within the first 6 hours after symptom onset, and be treated by experienced neurointerventionalists who can consistently achieve high rates of TIC1 2b/3 recanalization. ■

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