Interventional Thrombectomy for Major Stroke —
A Step in the Right Direction
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Intravenous thrombolytic therapy is the only proven treatment for acute ischemic stroke, but its use is limited by a brief time window of up to 4.5 hours after the onset of symptoms and a recanalization rate of less than 50%. Large clots in vessels such as the distal internal carotid artery or the first segment of the middle cerebral artery respond poorly to intravenous thrombolysis. The need for a treatment for patients who do not have a good response to intravenous treatment alone remains pressing.

On the basis of compelling anecdotal experience, stroke specialists had hoped that transvascular recanalization would be an alternative to or a follow-on treatment after intravenous therapy for severe strokes with large-vessel occlusion. However, three randomized, controlled trials of intraarterial treatment, all reported in the Journal, have had negative or ambiguous results. These trials were criticized for their use of older recanalization devices, which were associated with lower recanalization rates than those found with newer devices such as retrievable stents; for the long interval between the onset of stroke and intervention; and for disappointingly low recruitment rates, which suggested that many suitable patients had been treated outside the trials. Moreover, subgroup analyses suggested that there was a benefit for patients treated in shorter time windows. Perhaps most important, two of the trials did not require evidence of an occluded vessel before randomization, thereby making intracerebral treatment futile from the start.

The lessons of these studies were that trials of intraarterial treatment should enroll patients with severe strokes, have proof of proximal vessel occlusion, initiate treatment as early as possible, and use modern thrombectomy devices. The results of the first such trial now appear in the Journal. The Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands (MR CLEAN) included patients with severe stroke and proximal-vessel occlusion. Almost 90% of the patients received intravenous thrombolysis first, and almost all the devices used were of the retrievable-stent variety, which have a track record of successful recanalization. Thrombectomy improved outcomes, with an absolute difference of 13.5 percentage points in the rate of functional independence, as assessed with the use of the modified Rankin scale. Most other prespecified clinical end points and the rate of recanalization favored transvascular treatment, although the recanalization rate with transvascular treatment was a little lower than expected. There were no significant differences in mortality or the occurrence of symptomatic intracranial hemorrhage.

Readers may wonder how the trialists from a country with only 16.8 million inhabitants succeeded in enrolling 500 patients in just over 3 years, whereas other trials from much larger regions with similarly advanced medical systems struggled with recruitment. The well-established network of investigator-initiated stroke trials in the Netherlands contributed to the success of the trial, as did the relatively short distances between the 15 intervention centers in the country. In my view, however, the most important reason for success 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 may be difficult to implement in...
other health systems, but imagine what progress the medical-device field would see if this strategy were the rule.

Finally, what does this first positive thrombectomy trial mean for interventional treatment? Is there any doubt left, or should thrombectomy now become the new standard treatment for severe stroke with proximal large-vessel occlusion up to 6 hours after stroke onset? Several similar trials are ongoing; it is premature to conclude that there is no longer equipoise regarding thrombectomy. We need and will get results from other well-designed trials, not only to confirm or refute the results of MR CLEAN but also to look at effects in subgroups (according to stroke severity, occlusion site, or time to treatment initiation), for which most single trials are underpowered. MR CLEAN is the first step in the right direction.

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