Editorial

Distal Vessel Occlusions

When to Consider Endovascular Thrombectomy

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In recent years, endovascular thrombectomy (EVT) has revolutionized care for stroke patients with occlusions of the internal carotid or M1 segment middle cerebral artery.[1] In the patient population with distal occlusions, for example, M2 segment, we face increasing heterogeneity with regards to clinical presentation (nondisabling versus disabling symptoms, high versus low eloquence), anatomic variability (number, location, and diameter of different M2 segments) and to our perception of imaging (relative amount of ischemic changes in the segment artery's territory). Yet, there is growing evidence on safety and efficacy of EVT over standard care practice for M2 segment occlusions.[2–4]

Distally located clots have not been a primary focus of EVT trials thus far. In this issue, Grossberg et al[5] report their experience on EVT for distal vessel occlusions beyond the M2 segment and in any anterior or posterior cerebral artery segment. The most frequent occlusions that were treated were in the M3 segment. From a strict procedural point of view, this report demonstrates the technical feasibility of reopening distal vessel occlusions in 83%. The chosen treatments were stent-retriever technology in 38% of cases, intraarterial thrombolysis in 37% of cases, and aspiration in 31% of cases. Notably, the reperfusion rates were highest when stent-retrievers could be deployed (92%).

The report by Grossberg et al[5] provides us with insight on the safety profile of EVT in distal occlusions. The rate of parenchymal hematoma in the territory of the distal occlusion was 4%. No vessel perforations were observed, and no secondary proximal occlusions occurred during procedures. A large multicenter retrospective cohort of EVT versus medical management of M2 occlusions demonstrated overall improved functional outcomes with EVT, yet reported symptomatic intracranial hemorrhage rates of 5.6% for EVT versus 2.1% for medical management (P=0.10).[2] Compared with M1 occlusions, a meta-analysis of 12 studies on 1080 patients with M2 occlusions identified an increased risk of symptomatic intracranial hemorrhage (odds ratio=3.39).[4]

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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Context Is Key

An important distinction must be made within Grossberg et al[5] report between primary distal occlusions that caused the presenting neurological symptoms versus secondary occlusions that resulted during EVT procedures for more proximal vessel occlusions or under bridging intravenous thrombolysis (IVT) treatment. This reshapes our approach to decision-making and how we extrapolate the evidence we have from randomized trials.

Primary Distal Vessel Occlusions in IVT-Eligible Patients

If patients present with vessel occlusions distal to the M2 segments, the current guidelines recommend treatment with IVT.[6] In this population, IVT provides larger benefit when compared with IVT-treated stroke patients without evidence of any occlusion on imaging.[7,8] In select cases, a careful risk-benefit assessment of EVT may be justified. This reflection in clinical decision-making is evident in Grossberg et al[5] report, which was biased toward patients with severe symptoms as indicated by the high National Institutes of Health Stroke Scale scores. It comes down to a judgment call of whether EVT opens vessels faster and better than IVT, and if that would lead to a clinically meaningful improvement?

Primary Distal Vessel Occlusions in IVT-Ineligible Patients

Two-thirds of the patients with distal occlusions reported by Grossberg et al[5] were treated primarily with EVT. Notably, the rate of IVT administration in this retrospective cohort was relatively low, indicating selection bias. If we suppose a scenario in which a patient presents with disabling symptoms yet is IVT-ineligible, we may extrapolate our knowledge from large to distal vessel occlusions. We do know that rapid reperfusion saves brain tissue and that EVT has a good safety profile. However, we need to adjust our perceived threshold of unfavorable imaging with respect to the territory at risk in the individual patient: is there an area of eloquence that can possibly be saved?

In addition, the identification of distal vessel occlusions may represent a challenge in noninvasive imaging. Conventional single-phase computed tomography angiography has limitations in distal occlusions, caused by scan timing and vessel-to-background contrast. Techniques like multiphase computed tomography angiography or computed tomography perfusion reconstructions may be useful to improve sensitivity and specificity for distal occlusion detection.[8,9] In particular for nonexpert readers, the additional imaging information of contrast hold-up on later phases of multiphase computed tomography angiography or the presence of a perfusion deficit will trigger a closer look and increase the chance to detect a possibly decision-relevant vessel occlusion.

Considering the natural history of untreated distal occlusion stroke, we know that patients with M2 occlusions have a better prognosis than patients with more proximal occlusions, yet still around half of these patients may suffer poor outcomes.[10] Overall, we face a paucity of data on the natural history of untreated M2 and more distally located occlusions. Knowing more about the natural history would allow us to extrapolate our understanding into the context of IVT-ineligible patients with distal occlusions. In most reports that investigate EVT in distal occlusions, significant proportions of patients were also eligible for IVT.[2,11]

Secondary Distal Vessel Occlusions During Thrombectomy Procedures

EVT procedures for large vessel occlusions carry a risk of thrombus fragmentation[12] and for secondary infarcts in new vascular territories.[13] These secondary vessel occlusions may limit the treatment effect of EVT as there is emerging evidence on the benefit of modified Thrombolysis In Cerebral Infarction (mTICI) 2c/3 reperfusion over mTICI 2b reperfusion.[14,15] Improving mTICI 2b to 2c/3 reperfusion has been demonstrated feasible in a proportion of patients in retrospective studies, including this report by Grossberg et al.[5,16] Procedural strategies to achieve complete reperfusion should be further assessed for safety and feasibility, even when initial reperfusion seems to be adequate. Technical and procedural innovations like the CAPTIVE technique (continuous aspiration before intracranial vascular embolectomy) should be further investigated and improved to decrease the likelihood of distal emboli and achieve better first pass TICI 2c/3.[17]

How Do We Move Forward?

The question that precedes any design of a randomized controlled trial is do we have equipoise on the interventional versus medical management of distal vessel occlusions?[18] In patients with disabling symptoms and proximal M2 occlusions, we suspect there is consensus on the benefit of EVT. This fact may hinder randomization. Another issue is a likely smaller effect size in distal occlusions than in recent EVT trials, which in turn considerably increases the needed sample sizes.[19] From a practical perspective, we would be confronted with markedly slower enrolment and with cherry-picking. All the permutations that arise in clinical presentation, anatomic variability and imaging make it also tough to control for in a randomized trial. Therefore, other options include matched comparisons of multiple large registry data. Finally, we will have to use our best clinical judgment with extrapolation of everything we learned on EVT and on IVT and be humble in recognizing the limitations of current technology and individual procedural skills.

Disclosures

None.

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