When Is Stroke Thrombectomy Futile or to Be Avoided?

A discussion of the importance of patient selection, noninvasive imaging considerations, and procedural factors that contribute to futile endovascular therapy.

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Endovascular therapy (EVT) for emergent large vessel occlusion (ELVO) stroke is one of the most effective treatments in medicine, but due to the potential for harm and heavy resource requirement, proper patient selection remains important. In addition to potentially increasing costs without improving outcomes, a large number of procedures can strain the teams providing this care. Avoiding futile treatment is therefore important to the long-term sustainability of EVT.

A MAJOR ADVANCE IN STROKE CARE

EVT for ELVO strokes has undergone a monumental paradigm shift in the past 5 years. In 2015, after a series of negative trials raised questions about the application of this therapy, five major clinical trials established EVT as the standard of care for ELVO stroke patients.[1] Further clinical trials have expanded the time window for application of this therapy, and enthusiasm for this treatment has never been higher.[2,3] The most recent American Stroke Association guidelines have given a level 1 recommendation for EVT in patients with acute ischemic stroke caused by ELVO who meet the following criteria:[4]

- Age ≥ 18 years
- Occlusion located in the internal carotid artery (ICA) or M1 segment of the middle cerebral artery (MCA)
- Within 0 to 16 hours of symptom onset (level 1A) or 6 to 24 hours (level 1B)
- National Institutes of Health Stroke Scale (NIHSS) score ≥ 6
- Baseline modified Rankin Scale (mRS) score ≤ 1
- Alberta Stroke Program Early CT Score (ASPECTS) ≥ 6

Improved device technology, protocols driving efficiency, decreased time to treatment, and proper patient selection have all been identified as key reasons for the positive results seen in these trials.

After these successful clinical trials, the discussion turned to how to expand the therapy to benefit the maximum number of patients. Clinical trials aim to ensure safety and limit the study population to avoid large variability and confounders. Applying these strict criteria in clinical practice would be too restrictive, and other patients who may benefit would be denied therapy. However, applying these paradigms to all stroke patients would also be counterproductive, exposing patients who do not have ELVO or those who cannot derive benefit from the therapy to potential risks and harm.

PATIENT SELECTION

Although EVT has been successful in patients presenting with LVOs, it also has limitations. The procedure is safer and more efficient with an increasing variety of innovative tools, but it is also resource-intensive and not intended for every patient. Despite quick and effective recanalization, treatment can be futile (defined as mRS ≥ 3 or not returning to baseline mRS). In the major trials, futile treatments were seen in 20% of cases.[1] Futile therapy in endovascular intervention can be identified on initial patient selection as well as factors during the procedure. Postprocedural care and comorbidities can also significantly affect outcomes.

UNDERSTANDING IMAGING

The success of the positive endovascular trials was dependent on the selection of patients with confirmed LVOs. As such, it is critical to perform noninvasive vessel imaging (eg, CTA) to confirm that an ELVO is present. In addition to confirming the presence of occlusion, it also provides the interventional team with information about the patient's specific vascular anatomy, which can aid and improve the speed of the approach and treatment of the occlusion.

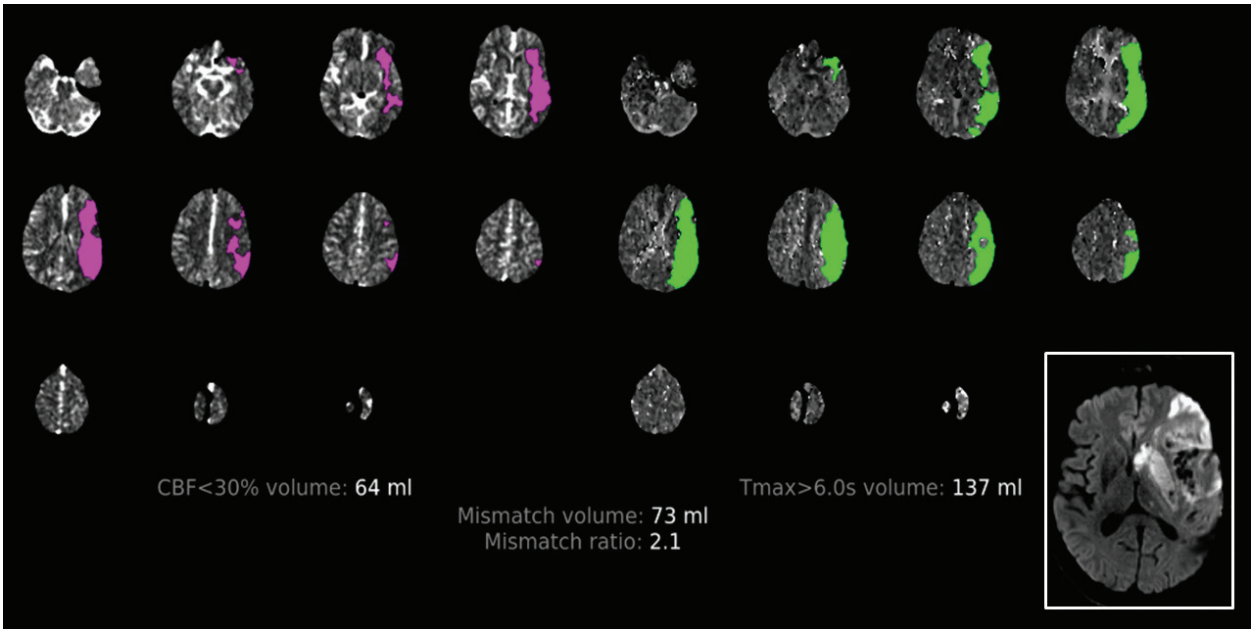

Figure 1. A 70-year-old woman presented with wake-up stroke and tandem ICA-M1 MCA occlusion. Her baseline NIHSS score was 19. Preprocedural imaging showed a moderate core infarction but a larger area of hypoperfusion, which suggested salvageable tissue. Intervention was performed with thrombolysis in cerebral infarction (TICI) 2b flow. Postprocedure MRI showed a moderate infarct with hemorrhagic conversion. The patient's 90-day mRS was 3. CBF, cerebral blood flow.

The goal of EVT is to salvage as much penumbra (tissue with reduced blood flow at risk to undergo permanent infarction) as possible. Various clinical and imaging paradigms can be used to estimate the difference between the amount of brain tissue lacking blood flow or perfusion versus the amount of brain tissue that is already infarcted (known as the core infarct). Areas lacking perfusion can be estimated via CT perfusion and magnetic resonance perfusion, which produce maps based on perfusion parameters but can be variable in their estimation of true penumbral tissue. Overall, it appears Tmax maps are the most helpful; tissue with Tmax > 6 seconds more than normal are at risk to become infarcted. Most simplistically, we can look at clinical examination findings. With the understanding that hypoperfused tissue at risk for infarction by definition is structurally intact but electrically silent (and thus produces symptoms), we can correlate findings on the clinical examination back to the brain regions responsible for those symptoms and map out the area at risk.

Core infarction can also be estimated by various imaging modalities. From noncontrast CT, a score using ASPECTS is helpful. Ten regions in the MCA territory are assessed, with a point taken away if the region loses its gray-white differentiation or has sulcal effacement. ASPECTS correlates well with core infarction on diffusion-weighted imaging (DWI), although it should be noted that CT is specific but not sensitive to ischemic changes. DWI is both sensitive and specific for acute infarction, but the phenomenon of DWI reversal can occur, which is typically seen in patients treated early after stroke onset at the periphery of the lesion and where the apparent diffusion coefficient has dropped < 20%. Perfusion imaging can also estimate the core using cerebral blood volume or cerebral blood flow < 30% maps. Using a perfusion protocol yields a higher proportion of patients with favorable outcomes compared with those without perfusion imaging.[5] Perfusion maps can be more prone to acquisition errors and other artifacts, so care must be taken in their interpretation.

For each patient, this assessment should occur rapidly, as delays in starting and obtaining reperfusion can be detrimental to patient outcomes. The assessment can be individualized, particularly depending on the time window. Those who present early after onset (< 6 hours) are very likely to have the largest proportion of penumbra, especially if they have poor collaterals, and may be very time-dependent. In this population, minimizing imaging and quickly getting to the angiography suite are critical. Among patients in the later time window (≥ 6 hours), those who have salvageable tissue will have good collaterals, and time, although important, may not be the most critical factor. Imaging can be obtained efficiently and help select patients who truly have a chance at benefiting from EVT. Postprocessing software such as Rapid (iSchemaView, Inc.) and Viz.ai (Viz.ai, Inc.) has made processing and communication of these results efficient, aiding in quick interpretation.

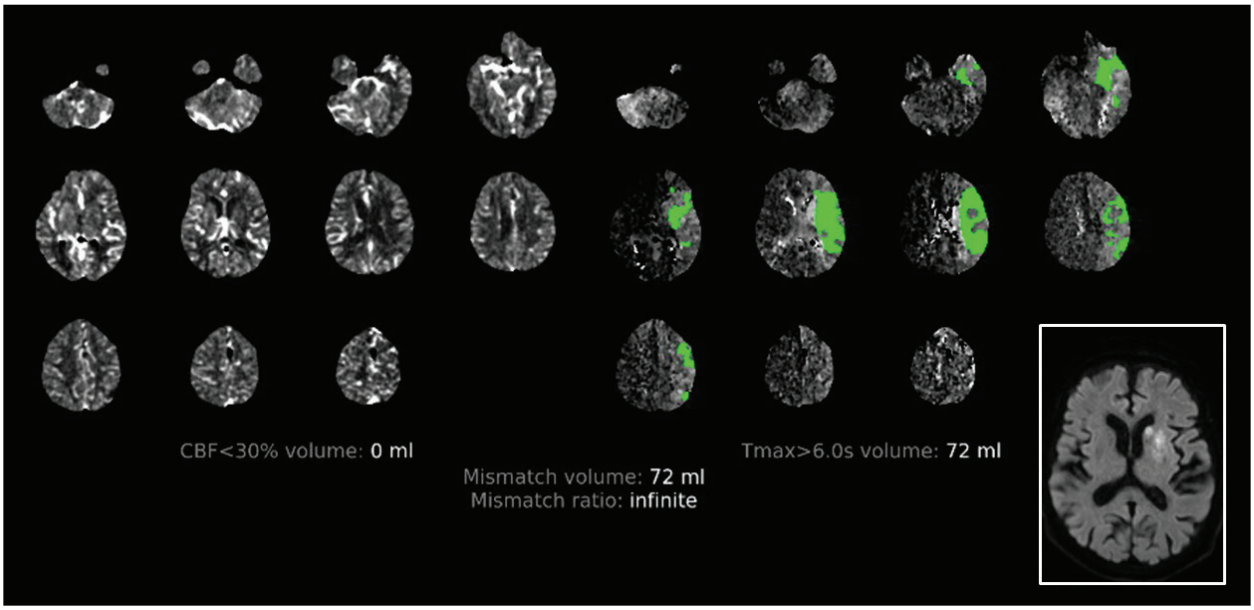

Figure 2. A 95-year-old woman presented with a wake-up stroke and was found to have a tandem left ICA–MCA occlusion. Initial NIHSS score was 24. Preprocedural imaging demonstrated no significant ischemic core and a large mismatch volume that suggested a penumbra with salvageable tissue. EVT resulted in TICI 2b flow. Inset shows small final infarct. Unfortunately, due to advanced age and comorbidities, the patient deteriorated medically and passed away in the hospital. CBF, cerebral blood flow.

PREDICTORS OF FUTILE THERAPY

Preprocedural Factors

Patient selection based on core volume may help define candidacy for EVT. Those with large core infarction are a particular population of interest when discussing futile therapy. Generally, it is believed that patients who have a large core infarct on presentation are unlikely to benefit and may also be at increased risk of harm, particularly from hemorrhagic conversion (Figure 1). Although there were variable approaches on the type of perfusion imaging and its use in the clinical trials, most trials excluded patients with large baseline ischemic core (ASPECTS 0–4).[6,7] In the SELECT trial, those with a large core ≥ 100 mL on CT perfusion or ASPECTS 0 to 2 did not have favorable outcomes and may have a higher risk of hemorrhagic conversion.[8] Up to 30% of patients presenting with a core > 70 mL will have a fatal outcome, and with every 10-mL increase in volume, the possibility of an mRS < 2 is reduced by 20% to 30%.[9] In the discussion of treating patients with large cores, the general consensus is that cores > 100 mL are unlikely to benefit from EVT. Thus, a possible opportunity arises for patients with moderate core volumes (50–100 mL). The role of EVT in patients with moderate to large core is being studied in the ongoing SELECT 2, TESLA, and TENSION trials.

There are no current age cutoffs for EVT. Certainly, some patients benefit at older ages, but there is an understanding of cumulative factors contributing to futile treatments. In the meta-analysis performed by HERMES collaborators pooling the major endovascular trials, older age combined with higher baseline NIHSS score led to poorer outcomes.[1] The effect of core size on the outcome is more pronounced in elderly populations as well, with those with larger core sizes only benefiting in very early time windows. Despite the elevated cost of EVT at first, there are encouraging cost analyses demonstrating that the lifetime direct and indirect costs are mitigated in patients ≤ 79 years. From ages 80 to 100 years, there are moderate increases in lifetime costs but added quality-adjusted life-years.[9]

Patients with a poor baseline (mRS > 2) can also be a difficult population for EVT selection. Although some patients can be returned to their previous baseline status, the addition of even moderate core infarct can often have a great effect on their final functional status. Careful and realistic discussions with patients and their family about the goals of care are important to ensure their wishes are respected, which is often challenging in these emergent situations.

Another challenging situation for selection involves patients who present with ELVO but a low NIHSS score. Data have suggested that approximately 20% to 25% will deteriorate and that intervention after deterioration generally has a poor outcome.[10] Collateral failure likely occurs in this subset, leading to the rapid progression of infarction. However, complications and other hemodynamic issues can occur intraprocedurally and potentially worsen outcomes. It is truly a situation with equipoise. Unfortunately, no reliable clinical or imaging factors have yet been found to predict deterioration, although

work is ongoing. Early intervention before deterioration will be studied in upcoming clinical trials, including the ENDOLOW study.

Intraprocedural Factors

Several intraprocedural factors can influence outcomes and lead to futile therapy. Patient anatomy, including steep arch configurations, arch and aortic comorbidities, and significant vessel tortuosity, can present a challenge for timely vascular access to the occlusion site. New device technologies, such as better guide catheters and access catheters, have helped to overcome some of these challenges. In addition, studying the CTA before the procedure can aid the interventionalist in device selection. Choosing radial access over femoral in certain situations, such as type III and bovine arches, can also help avoid frustration and increased procedure time.

Tandem ICA occlusions are a particularly challenging situation. Tandem occlusion can affect the time to recanalization and has resulted in a broad range of treatment effects in various trials.[7,11,12] The baseline ischemic core is a crucial adjunctive piece in defining the threshold of potential futile therapy. Intervention was noted as unfavorable in patients presenting ≥ 5 hours from symptom onset.[1] Also, in the THRACE trial, not a single patient with large ischemic core (> 70 mL) and a tandem ICA occlusion experienced a favorable outcome.[7]

Procedure duration has also been shown to significantly affect outcomes. Because an infarction is ongoing, the longer the procedure time, the more infarction develops and leads to poorer outcomes. Data suggest that outcomes substantially drop when groin-to-recanalization time exceeds 60 minutes.[13] Similarly, a higher number of stent retriever passes is associated with declining recanalization rates, with the odds of a successful treatment diminishing to < 10% after four stent retriever attempts.[14] As the number of passes increases, the risk of intracranial hemorrhage also rises, particularly after three passes.[15]

Postprocedural Factors

Not all patients who undergo rapid recanalization will have a good functional outcome. Aside from poor baseline status, comorbidities are often present in stroke patients and, in the setting of a critical illness, may become active or uncontrolled, leading to detrimental in-hospital complications (Figure 2). In addition, reperfusion injury—particularly hemorrhagic conversion—can occur and may be influenced by postprocedural care, especially blood pressure control. Although this should not necessarily influence patient selection, it does speak to the need for excellent postprocedural care. These patients should be treated in centers that not only have neurointerventional capabilities but also strong and experienced neurocritical care and stroke care teams.

CONCLUSION

Cumulative factors involving patient selection and procedural issues ultimately contribute to futile EVT. As the field continues to forge forward with exciting initiatives, understanding these thresholds is an opportunity for ongoing efforts to improve stroke intervention outcomes. Ongoing clinical trials for large core patients (SELECT 2, TENSION, TESLA) and mild stroke patients with ELVO (ENDOLOW) should help us gain evidence to further refine our selection paradigms. ■

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