Futile Recanalization in Mechanical Embolectomy Trials: A Call to Improve Selection of Patients for Revascularization

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It is well known that clot burden is likely a major determinant of vessel recanalization rates with the volume of thrombus to be dissolved by fibrinolytic agents much larger in the intracranial carotid artery than in the middle cerebral artery. So, the more distal the occlusion is located, the higher the likelihood of recanalization. This statement seems to be true for intravenous thrombolysis as demonstrated in several transcranial Doppler studies showing that the probability of complete recanalization at 2 hours of tissue plasminogen activator (tPA) bolus is 44%, 29%, and 10% in the distal middle cerebral artery, proximal middle cerebral artery, and terminal internal carotid artery, respectively. However, a differential treatment response according to clot size and location has not been demonstrated in patients with stroke undergoing mechanical embolectomy. Several methodological, technical, and pathophysiological differences preclude the translation of this “clot-burden effect” of intravenous tPA therapy into mechanical recanalization trials.

In this issue of Stroke, Shi et al retrospectively analyzed the pooled data of patients with middle cerebral artery strokes from the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) and Multi MERCI trials. Patients were dichotomized into 2 groups: middle cerebral artery M1 occlusions and isolated M2 occlusions. Baseline characteristics, revascularization rates, hemorrhage rates, complications, outcomes, and mortality were evaluated for both groups. The authors observed that patients with isolated M2 occlusions were revascularized at a higher rate (82.1% versus 60%), required fewer number of passes, and were associated with a trend of a shorter median procedure time than patients with M1 occlusions. However, no statistically significant differences were found between the M2 and M1 groups for favorable 90-day outcome (modified Rankin Scale score 0 to 2; 40.7% versus 33.3%) or 90-day mortality (25.9% versus 32.9%).

Although clot burden may represent a major determinant of recanalization success, other factors different than a smaller clot size may influence the higher recanalization rates seen in M2 compared with M1 occlusions. In the study by Shi et al, the mean onset-to-groin puncture time was 4.5 hours. So, the angiographic identification of a M2 clot may represent an advanced ongoing stage of M1 recanalization, particularly in those patients pretreated with intravenous tPA. In fact, Shi et al observed that recanalization rates at the end of the procedure were higher in patients who were pretreated with tPA. This finding raises the hypothesis that pretreatment with tPA may soften the clot favoring catheter penetration and retrieval. Moreover, M2 clots may have a better collateral blood supply and larger areas of clot—in 2 fronts of recanalization—exposed to circulating tPA. On the other hand, most patients with M2 occlusion were included in the Multi MERCI trial, so the higher recanalization rates in the M2 occlusion group may result from an incorporation of knowledge gained from the practitioner’s increasing experiences and the newer generation of Merci Retriever devices available in Multi MERCI.

Angiographic studies have elucidated the relationship between the location of arterial occlusion and outcome after intravenous thrombolysis. Furthermore, transcranial Doppler studies have shown that M2 recanalization increases 2-fold the likelihood of a good outcome compared with M1 recanalization. In contrast, the pooled analysis of Merci in Multi MERCI shows that despite the higher recanalization rates in M2 occlusions, short- and long-term outcomes were comparable to M1 occlusions. Although the lack of differences in clinical outcome may be due to a statistical Type II error because the sample size of patients with M2 occlusion enrolled into these 2 trials was smaller than that of the patients with M1 occlusion, a proportion of patients with M2 occlusion may have experienced nonnutritional or futile recanalization.

Futile recanalization occurs when successful recanalization fails to improve the functional outcome. In the Interventionsal Management of Stroke II trial, 45% of subjects who achieve partial or complete reperfusion (Thrombolysis In Myocardial Ischemia Grade 2 and 3) had a poor 3-month outcome (modified Rankin Scale score ≥3). In the Pro-Urokinase for Acute Cerebral Thromboembolism II trial, the mismatch between recanalization and favorable outcome was 26%. Similarly, in the Combined Lysis of Thrombus in Brain Ischemia by Using Transcranial Sonography and Systemic tPA trial, the rate of futile recanalization was 31% (82% recanalization, 51% favorable outcome), the MERCI trial 34%, and the Multi MERCI trial 36% (68% recanalization rate, 32% favorable outcome). In a recent multicenter study, Hussein et al observed futile recanalization in 49% of patients who received endovascular treatment for acute ischemic stroke. In this study, age >70 years (OR, 4.4; 95% CI, 1.9 to 10.5) and initial National Institutes of Health Stroke...
Scale score 10 to 19 (OR, 3.8; 95% CI, 1.7 to 8.4; P<0.001) emerged as independent predictors of futile recanalization.

Several factors, including stroke severity, older age, systolic hypertension, extent of hypodensity or brain swelling on pretreatment CT, and admission hyperglycemia, have been shown to be predictors of poor outcome in stroke thrombolysis. The beneficial effect of early restoration of cerebral blood flow on stroke outcome may be hampered in part by such factors as extent of irreversible brain injury before recanalization, excessive glucose burden at the time of reperfusion, and blood pressure changes during procedure. These factors are particularly crucial in the extended time window when the likelihood of success decreases over time.

MOST (a Multimodal Outcome Scale for Stroke Thrombolysis) is a 5-item score that has been shown to improve the predictive accuracy of recanalization on stroke outcome. Items of this logistic regression derived scale, based on independent predictors of poor outcome after thrombolysis, include stroke severity (National Institutes of Health Stroke Scale score >14), proximal middle cerebral artery occlusion, Alberta Stroke Programme Early CT Score (ASPECTS) <7, recanalization >5 hours, and baseline systolic blood pressure of >150 mm Hg. Interestingly, in the Shi et al study, baseline stroke severity was comparable in both M1 and M2 groups, suggesting selection bias because only M2 occlusions with severe neurological deficit were included, maybe including patients with large ischemic lesions at baseline or patients with initial M1 or even T occlusions who experience tPA- or spontaneous-induced recanalization with futile reperfusion. This may explain the comparable clinical outcome at 3 months rather than simply the imbalance in the side of stroke among groups. Because a global ASPECTS value on baseline CT of <7 points has been demonstrated to independently predict poor outcome after thrombolysis, preprocedural imaging (CT perfusion or diffusion-weighted MR imaging) may depict those patients with large already infarcted tissue and improve the selection of patients for delayed revascularization.

In the Shi et al study, admission systolic blood pressure was higher in patients with M2 occlusion compared with those with M1 occlusion. Increased blood pressure during the first few hours of acute ischemic stroke has been suggested to be reactive and indicative of a large infarction. This may suggest a large infarcted area despite M2 occlusion or high uncontrolled blood pressure among patients with M2 occlusion, both factors associated with poor long-term outcome. On the other hand, clinical trials of revascularization have been designed to achieve technical success and focused on recanalization as a primary efficacy end point. In the Shi et al study, like in other revascularization trials in acute stroke, information regarding prestroke disability is lacking. Pre-stroke disability (modified Rankin Scale score >1) may hamper the effect of treatment on stroke outcome independent of the occurrence of futile recanalization.

Given the time and resources consumed by and the logistics required for endovascular treatment in acute stroke, more careful patient selection to avoid futile recanalization is needed. Factors such as age, extent of irreversible ischemia, occlusion location, stroke severity, blood pressure, pattern of collateral flow, and pretreatment with tPA become critical in the late time window (>4.5 hours) and may play a central role in translating angiographic recanalization into a favorable clinical outcome. The development of multimodal outcome scores including these factors may help to improve the selection of patient for mechanical revascularization.

Disclosures

None.

References


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