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Letter by Hill et al Regarding Article, “A Cost-Utility Analysis of Mechanical Thrombectomy as an Adjuvant to Intravenous Tissue-Type Plasminogen Activator for Acute Large-Vessel Ischemic Stroke”

To the Editor:

Therapy for acute ischemic stroke using endovascular approaches has seen widespread adoption in North America and Europe in the absence of randomized trials demonstrating better clinical outcomes. Surrogate outcomes, particularly target vessel recanalization, have been accepted by many in the neurological community and some regulatory authorities as adequate justification for clinical use. Remuneration has followed and is likely an important driver of endovascular therapy in the United States. A recent economic analysis by Kim et al serves to promote the endovascular approach by arguing the case on economic terms. However, we contest their assumptions and methodology as follows.

It is true that recanalization is a major predictor of a patient’s clinical outcome. However, other factors may show particular importance, including the time to recanalization, the susceptibility of the tissue to infarction, and the degree of established infarction already present. Thus, assuming that recanalization is the only relevant factor is an oversimplification.

Recanalization rates defined by transcranial Doppler are limited by operator dependence and a lack of clear evidence of blindness. Convincing intravenous recombinant tissue-type plasminogen activator (alteplase) recanalization rate data are lacking and may be underestimated here.

The Interventional Management of Stroke (IMS) studies have demonstrated that recanalization of the target arterial occlusion (eg, middle cerebral artery stem) does not necessarily lead to reperfusion of the distal arterial bed. As a corollary, the occurrence of distal emboli into arterial territories not initially underperfused (eg, anterior carotid artery emboli) as a consequence of the endovascular procedure can result in significant additional infarction. Thus, recanalization can be non-nutritive, but the proportion of times this occurs is poorly quantified.

Poor outcomes are not governed entirely by the symptomatic intracerebral hemorrhage rate. Symptomatic intracerebral hemorrhage is a minor overall contributor to poor outcome; the major reason for poor outcome is the severity of the initial ischemic stroke. An economic model for a condition such as stroke should use longer-term outcomes, such as 90-day outcome rates including those who did poorly because of symptomatic intracerebral hemorrhage. Further, symptomatic intracerebral hemorrhage is associated with a high 30-day mortality, which may result in endovascular therapy appearing cheaper on average.

The safety of angiography used in the model was based on a large series of patients undergoing diagnostic angiography, not intervention, for which the risk is fundamentally higher. Further, patients who undergo diagnostic cerebral angiography do not require general anesthesia, whereas general anesthesia is a frequent approach in stroke patients treated endovascularly and is a factor that has been associated with poorer outcomes.

Patients treated in the MultiMERCI study were different from those treated in CLOTBUST and in the IMS studies largely defined by time. Although a small subgroup of patients in MultiMERCI were treated with intravenous tissue-type plasminogen activator within 3 hours of stroke onset, most were treated endovascularly much later after stroke onset. Patients treated late tend to have self-selected better collateral flow, because those without good collateral flow already have had extensive infarction defined on baseline imaging, limiting their eligibility for any reperfusion strategy.

Thus, based on available data and knowledge, the conclusions reached by Kim et al are at best a promissory note to keep us hoping until there is sufficient strong evidence to change practice. It remains entirely possible that mechanical thrombectomy/thrombolysis as currently used is not cost-effective. Strong evidence for or against this practice will be forthcoming from the planned economic analysis of the IMS3 trial.

Disclosures

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