Brain Imaging Does Not Help Identify Patients Who May Benefit From Endovascular Treatments for Acute Ischemic Stroke

Written by **Mary Beth Nierengarten**

Patients who undergo neuroimaging to identify a favorable penumbral pattern do not benefit from endovascular treatment any differently than people with a nonpenumbral pattern when treated within 8 hours of an acute ischemic stroke, according to Chelsea S. Kidwell, MD, Georgetown University, Washington, DC, USA, who reported results of the Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy trial [MR RESCUE; Kidwell CS et al. *N Engl J Med* 2013]. The results also showed that, regardless of penumbral pattern, clinical and imaging outcomes were no different between patients undergoing embolectomy versus those who received standard medical care for acute ischemic stroke.

MR RESCUE was a Phase 2b, multicenter, randomized, controlled trial that was undertaken to test the hypothesis that the presence of substantial penumbral tissue identifies patients most likely to respond to mechanical embolectomy for acute ischemic stroke. A secondary hypothesis tested was that embolectomy would result in improved functional outcomes compared with standard medical care.

In the study, 118 patients were randomly assigned to embolectomy (n=64) or standard care (n=54) within 8 hours of the onset of symptoms of a large-vessel, anterior-circulation ischemic stroke. All patients were aged 18 to 85 years, had a National Institute of Health Stroke Scale (NIHSS) score >6, and had a premorbid modified Rankin Scale (mRS) score of 0 to 2. Patients were excluded from the study if they were pregnant or had an NIHSS score >30, acute intracranial hemorrhage, rapidly improving symptoms, refractory iodine allergy, proximal carotid stenosis >67% or dissection, international normalized ratio >3.0 or partial thromboplastin time >3 times the normal, or renal failure.

Prior to randomization, all patients underwent pretreatment multimodal MRI or CT neuroimaging and were then stratified according to whether they had a favorable penumbral pattern (ie, substantial salvageable tissue and small infarct core) or a nonpenumbral pattern (ie, large core, or small or absent penumbra). Of the 118 patients, 58% had a favorable penumbral pattern.

In the embolectomy group, 34 had a favorable penumbral pattern and 30 had a nonpenumbral pattern. In the standard-care group, 34 patients had a favorable penumbral pattern and 29 had a nonpenumbral pattern.

The study found no difference in the benefit of endovascular therapy based on penumbral pattern, with a statistically insignificant mean difference of 0.88 between patients with a favorable penumbral pattern versus those with a nonpenumbral pattern based on a 90-day mRS score comparing embolectomy with standard care (p=0.14; Table 1).

Table 1. Primary Outcome Analyses

	E/Pen n=34	S/Pen n=34	E/Non-Pen n=30	S/Non-Pen n=20	p Value
Mean (95% CI) Day 90 mRS	3.9 (3.3–4.4)	3.4 (2.8–4.0)	4.0 (3.4–4.6)	4.4 (3.6–5.2)	0.14

E=embolectomy; Pen=favorable penumbral pattern; mRS=modified Rankin Scale; S=standard care.

There was no difference in clinical or imaging outcomes between patients treated by embolectomy versus standard care regardless of imaging pattern. Among all patients, no difference was found in the 90-day mRS score between embolectomy and standard care (3.9 vs 3.9; p=0.99), and the 90-day mortality (21%) and symptomatic intracranial hemorrhage rate (4%) did not differ between groups.

The study also found no superior benefit with embolectomy over standard care based on imaging pattern. Outcomes of embolectomy and standard care were a mean 90-day mRS score of 3.9 versus 3.4, respectively (p=0.23), for patients with a favorable penumbral pattern and a mean score of 4.0 versus 4.4, respectively (p=0.38), for patients with a nonpenumbral pattern. According to Dr. Kidwell, the study underscores the importance of confirming hypotheses in randomized, controlled trials prior to implementing treatment approaches in clinical practice.

MISTIE II Trial: 365-Day Results Demonstrate Improved Outcomes and Cost Benefit

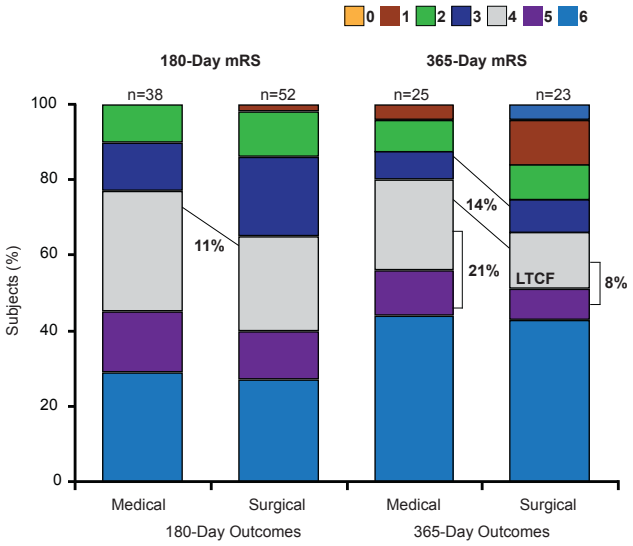
Written by **Phil Vinall**

Daniel Hanley, MD, Johns Hopkins University, Baltimore, Maryland, USA, presented results from the Minimally Invasive Surgery Plus tPA for Intracerebral Hemorrhage Evacuation trial [MISTIE; NCT00224770], which showed that catheter-based clot reduction plus tissue plasminogen activator (MIS + tPA) is safe and may reduce long-term disability after intracerebral hemorrhage.

Volume of intracerebral hemorrhage (ICH) is the strongest predictor of 30-day outcome for all locations of spontaneous ICH [Broderick JP et al. *Stroke* 1993]. MISTIE was a 2-stage multicenter, Phase 2 trial that examined outcomes and cost benefit of reducing clot size by using a catheter inserted into the largest part of the clot to apply tPA every 8 hours for 3 days. The study included patients with spontaneous supratentorial ICH ≥20 cc (stable ≥6 hours post diagnosis as shown on computed tomography) who were treated with either MIS plus tPA (n=54) or standard medical care (n=42) and followed for 180 days for stage I and 365 days for stage II. Participants were mean age 61 years (55.2% white, 65.6% men). Most were hypertensive (86.5%) and 26.5% had a diagnosis of diabetes. Prior smokers were more common in the surgical group (31.5%) versus those receiving standard medical therapy (7.1%). Of the subjects, 75% received their surgery between 12 and 38 hours post event.

At 365 days there was a 14% difference in functional performance (defined as 0 to 3 vs 4 to 6 on the modified Rankin Scale [mRS]) favoring MIS plus tPA (slightly greater than the 11% difference observed at 180 days). The improvement included a differential shift to higher independence levels at mRS 0 to 2 (Figure 1). Similar magnitudes of improvement (Figure 2) were also seen when the subjects were evaluated for improvements in mobility and activities of daily living using the Stroke Impact Scale [Duncan PW et al. *Stroke* 1999].

Figure 1. Functional Outcomes



LTCF=long-term care facility; mRS=modified Rankin Scale.

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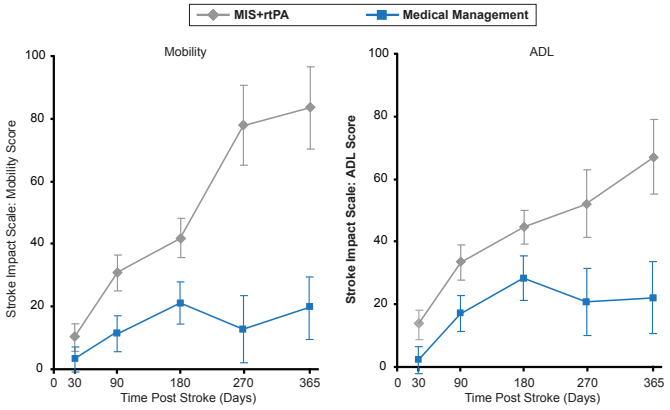
Figure 2. Functional Improvements: Stroke Impact Scale



ADL=activities of daily living; MIS=minimally invasive surgery; rtPA=recombinant tissue plasminogen activator.

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The improvements were also reflected in the cost of care. Although the median length of intensive care unit (ICU) stay was similar for both groups (9 days for patients in the surgical group vs 8 days for patients in the standard medical therapy group) the median hospital stay was 38 days shorter for the MIS plus tPA group (p=0.015). In addition, fewer surgical patients were residing in long-term care facilities both at 180 (17% vs 24%; not significant) and 365 days (8% vs 21%; not significant). After accounting for all costs (eg, ICU stay, MIS + tPA procedures), the results indicate that the experimental procedure saves an estimated $44,329 of medical care costs per patient [Hanley DF et al. ISC 2013 (abstr LB1)].