MRI in acute stroke

Good times are coming

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When considering IV tissue plasminogen activator (tPA) for ischemic stroke, acute imaging must ensure neurologic deficits are not due to intracerebral hemorrhage and ascertain the presence of early ischemic changes in the 3- to 4.5-hour window. The National Institute of Neurological Disorders and Stroke IV tPA study required a CT for this purpose, but the European Cooperative Acute Stroke Study (ECASS) III trial allowed both CT and MRI for screening for treatment in the 3- to 4.5-hour window.[1,2] However, of the 821 patients enrolled in ECASS III, only 50 (6%) were screened with MRI before randomization.[1] Thus, our success with IV tPA has occurred in the setting of a simple, noncontrast CT. Furthermore, the pooled IV tPA data, including more than 6,000 patients, demonstrate the convincing positive consequences of early treatment to enable a good functional outcome.[2] Every 15 minutes earlier that tPA is given provides an additional 1 month of disability-free life—indicating real-world public health implications of early treatment.[3] Therefore, using MRI as a screening tool for IV tPA decision-making, which, at present, comes at the expense of time and brain, should be approached with utmost caution.

Previous studies have shown that a multimodal MRI protocol totaling 15 to 20 minutes of scanner time and including diffusion-weighted imaging (DWI), gradient echo for hemorrhage detection, fluid-attenuated inversion recovery (FLAIR), magnetic resonance angiography, and perfusion-weighted imaging (PWI), provides far greater diagnostic accuracy and precise infarct location and size than noncontrast CT, but at the expense of excess time.[4] More recently, streamlined multimodal MRI protocols incorporate echo-planar imaging and parallel image acquisition with total scanning time less than 6 minutes.[5] Others have used DWI alone (approximately 2 minutes) for stroke screening, demonstrating accurate detection of both ischemia and hemorrhage.[6]

In this issue of *Neurology*®, Shah et al.[7] show that a multimodal MRI protocol can be expedited for tPA decision-making. The authors tracked door-to-needle (DTN) times at 2 hospitals including a large urban medical center and a nearby suburban hospital. Their stroke protocol utilizes MRI as the default screening examination rather than CT. Over the 2-year study period, they treated 157 patients with IV tPA and screened 86% with MRI. Besides the typical MRI contraindications, they used CT rather than MRI in patients arriving within 30 minutes of the 4.5-hour time window to save time. Quality improvement methods based on lean manufacturing principles (process improvement by retaining only steps that add value while eliminating those that are wasteful) to expedite IV tPA delivery identified and eliminated inherent process delays. The authors included key practical resources useful for other centers: detailed protocol flowcharts indicating how specific roles were assigned to improve flow as well as a simplified MRI screening sheet.

Process changes were implemented midway during the observational period, allowing metrics to be compared across four 6-month epochs. Impressively, DTN times decreased from 93 minutes at the beginning of 2012 to 55 minutes at the end of 2013. The proportion of patients treated in <60 minutes from hospital arrival increased from 13% to 62%. Although they did not capture symptomatic hemorrhage rates, in-hospital mortality and 90-day modified Rankin Scale scores did not differ across the epochs, allaying concerns that expediting treatment may have compromised safe tPA decision-making.

Even if acquisition times for MRI can improve to match those for CT, MRI would likely remain less used because of limited availability, greater cost, and common contraindications for MRI. Therefore, what constitutes added value of MRI over CT? First, diagnostic accuracy: the sensitivity and specificity of DWI for acute ischemic stroke exceed those for CT.[4] If performed quickly, MRI may improve clinical outcomes over CT for the subgroup of patients who have an unclear diagnosis and who have higher risk with tPA treatment. While case series have shown the safety of IV tPA even in the setting of a high stroke

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mimic rate,[8] greater diagnostic accuracy should lead to faster and safer treatment in the right direction, including patients who do not have acute stroke, but who need management for seizures, encephalitis, or other stroke mimics. The current study reports a zero stroke mimic rate, likely because all strokes were visualized on DWI. It must be noted, however, that DWI is not 100% accurate for diagnosing ischemic stroke. Approximately 5% of strokes, often those of small size and located in the posterior circulation, are "DWI negative" on initial imaging (and often below the resolution for detection on PWI), but go on to show a new stroke on follow-up FLAIR imaging.[4] In these cases, tPA should probably not be withheld when the clinical picture is consistent with stroke.

The second potential advantage of MRI includes the considerable body of data from multimodal MRI that give insight into the historical and acute state of the ischemic brain. In studies beyond the IV tPA window,[9] multimodal MRI shows promise for development of tissue-based models informing us who may benefit from tPA and in whom tPA will cause more harm than good. Predictive models will likely incorporate combined measures of irreversibly injured tissue (DWI), measures of the severity and extent of ischemia (PWI), and risk of hemorrhagic transformation (incorporating both imaging and clinical predictors).

Despite the clear need for further work, MRI for tPA decision-making may not be too far down the road. The current study reminds us of the dramatic effects on DTN times generated from focused, team-based quality improvement measures incorporating lean manufacturing principles—implementation can yield these beneficial effects within a short amount of time.[10] As technology advances, with faster parallel processing and tailoring of pulse sequences to maximize clinical yield,[5,6] scanner times continue to decrease, allowing faster and more accurate treatment. While CT remains the standard of care for acute tPA decision-making, continued work toward utilizing and interpreting MRI in a streamlined manner may eventually provide patients with the best care, balancing both time and accuracy.

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