Endovascular therapy and imaging

Is a picture worth a thousand words?

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The earliest reports of endovascular therapy for acute stroke date to the early 1980s and predate US Food and Drug Administration approval of IV tissue plasminogen activator (tPA). Initial approaches included regional infusion of urokinase in the extracranial carotid,[1–3] followed later by reports of direct infusions into intracranial arteries through a catheter embedded in a thrombus.[4] Since then, development of new devices and greater availability of interventional operators have resulted in steady growth of endovascular treatment for stroke. Despite impressive rates of recanalization, approaching 90%, good clinical outcomes occur for fewer than 50% of treated patients.[5,6]

It is likely that multiple factors contribute to the discrepancy between recanalization and good outcomes. Recanalization of the arterial occlusion does not always result in adequate restoration of perfusion to the ischemic area. Reocclusion may occur after the angiographic procedure is completed.[7] The interval from stroke onset to reestablishing adequate flow is an important variable, and evidence suggests that the more rapidly the artery is opened with endovascular therapy, the greater the probability of a good outcome.[8] This principle also holds for IV tPA, both in the time to start of infusion[9] and time to recanalization by transcranial Doppler.[10] However, some patients treated early develop infarction despite recanalization, and others at much later intervals recover considerable function. Rapid progression to irreversible infarction occurs in some cases, and others remain in a reversible state for many hours after onset of symptoms. Endovascular therapy requires considerable resources and expense, may require transfer of a patient to a tertiary care facility, and is associated with significant potential morbidity, including intracranial hemorrhage, vessel perforation, and groin hematoma. Without a randomized trial against standard treatment, either IV tPA within 4.5 hours or standard medical therapy beyond 4.5 hours, the benefit of endovascular treatment remains unproven. Even if such a trial were done and demonstrated improved outcomes in comparison with current treatments, a significant percentage of patients would not benefit from this approach. It is essential that we find ways to improve outcomes for the majority if not all acute stroke patients treated with endovascular therapy.

Perhaps better and more efficient devices will speed recanalization and help move the needle in the desired direction. However, transfer times to comprehensive stroke centers, angiographic preparation, catheter placement, and clot composition will limit the ability to minimize time to recanalization. Identification of patients with ischemic brain likely to respond to recanalization is a potentially promising approach to optimizing delivery of this expensive and resource-intensive treatment. Similarly, recognizing patients with established infarction unlikely to recover or at greater risk for complications of hemorrhage and edema would also help improve the overall yield.

One approach to improving patient selection is the use of MRI or CT imaging to measure physiologic parameters predictive of recovery or harm with recanalization. Selecting patients for IV tPA on the basis of diffusion/perfusion mismatch by MRI shows promise but has not yet demonstrated the ability to significantly increase good outcomes.[11,12] CT perfusion parameters are even less well established.[13] Perhaps the best evidence exists for MRI prediction of poor response or worsening with endovascular therapy.[14] What is needed is prospective testing of selection of acute stroke patients for endovascular treatment on the basis of MRI or CT perfusion imaging vs standard CT alone. Perfusion imaging adds another factor prolonging time to recanalization, and this disadvantage must be offset by sufficient added value to result in an overall net gain in good outcomes. The physiologic parameters measured by perfusion imaging represent only a snapshot in time in an evolving picture of ischemic changes, cellular events, and in some cases fluctuating anatomic obstruction due to occlusion/reocclusion or movement of a thrombus within the artery. The optimal thresholds of perfusion and diffusion abnormality predicting good and poor outcomes, choice of methodology, and quantitation of

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mismatch between perfusion and diffusion areas remain uncertain and require further investigation.

Selecting patients likely to benefit from endovascular therapy should not mean that those excluded are beyond help. It means that we must look for other innovative approaches for such patients, to optimize their potential for recovery. Endovascular therapy both subjects these patients to unnecessary risk and keeps us from redirecting our efforts to new and more effective treatments.

The SVIN endovascular roundtable addresses MRI and CT imaging of reversibility to select patients for endovascular therapy but also explores other concepts such as measures of collateral flow. Revascularization is a primary objective of endovascular therapy, and our current grading methods are somewhat crude and do not adequately define the spectrum of angiographic findings that might stratify outcomes. It seems logical that understanding the physiology and anatomy through imaging modalities will improve endovascular therapy and reduce morbidity. The challenge is finding the best window into this process and proving its value.

AUTHOR CONTRIBUTIONS

L.R.W. participated in drafting/revising the manuscript and in the study concept or design.

DISCLOSURE

Dr. Wechsler serves on scientific Advisory Boards for Lundbeck/DSMB, Ferrer/SAB, and Neurointerventions; served as Editor-in-Chief for *Journal of Neuroimaging*; receives research support from NIH/NINDS; and holds stock in Neurointerventions. **Go to Neurology.org for full disclosures.**

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