Commentary: Intraarterial Stroke Revascularization Training Guidelines

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Abbreviations: IA = intraarterial, IV = intravenous, NIHSS = National Institute of Health Stroke Scale, TPA = tissue plasminogen activator

STROKE is a devastating disease for patients, their families, the health care system, and society. In the United States alone there are 795,000 strokes per year, with a yearly medical cost of nearly $69 billion (1). Approximately 87% of these strokes are ischemic, and approximately 20% of these are considered "major" strokes as defined by a National Institute of Health Stroke Scale (NIHSS) score of at least 10 (2). For those patients who have experienced a major stroke, with loss of speech, difficulty swallowing, and loss of independence, life as they had known it is over. It is no surprise that the vast majority of stroke victims would prefer to risk dying rather than remain severely disabled (3).

Formerly, treatment for acute ischemic stroke was solely damage control. Swallowing is assessed to prevent aspiration pneumonia. Prophylactic anticoagulant agents are given to prevent phlebitis or recurrent stroke from atrial fibrillation. Physical and occupational therapy are consulted to maximize function in the face of persistent neurologic deficit. For a small minority of patients, acute stroke care can now reverse the deficit.

With the advent of fibrinolytic therapy—first with the use of intravenous (IV) tissue plasminogen activator (TPA) and later followed by proof of effectiveness of intraarterial (IA) prourokinase—the world of stroke therapy has vastly changed. IV TPA has been approved for treatment of acute ischemic stroke within 3 hours of onset and has demonstrated a modest improvement in neurologic deficit by 90 days, particularly in those patients with strokes of lesser severity (4). Based on the recent European Cooperative Acute Stroke Study III (5), the treatment window for IV TPA may be extended to 4.5 hours, although the average NIHSS score in the study was only 10, very severe strokes were excluded, and earlier studies have demonstrated patient harm from IV TPA treatment after 3 hours (6). Strokes that result from large vessel occlusions (i.e., internal carotid or middle cerebral arteries) usually are more severe (i.e., NIHSS >10) and respond poorly to IV TPA (7–12). For such patients, and for patients who present after 3 hours, IA thrombolysis has demonstrated better outcomes than IV TPA (13,14).

The evidence in support of IA lysis is as strong as that for IV lysis. Prolyse in Acute Cerebral Thromboembolism II (15) was a randomized placebo-controlled phase III trial that demonstrated statistically positive clinical benefit for treatment of a well defined group of patients: those with a middle cerebral artery occlusion (level 2 evidence). There is only one positive trial for treatment of acute stroke within 3 hours with the use of IV TPA (NINDS part 2) (4) and one for IV TPA in the 3–4.5-hour window (ECASS III); both provided level 2 evidence. The Prolyse in Acute Cerebral Thromboembolism II trial (15) found that IA prourokinase administered into a middle cerebral artery clot led to independent function approximately 60% more frequently, on average, than placebo (40% vs 25%). Patients with severe stroke treated with IA lysis had nearly double the rate of independent outcome (45% vs 24% for NIHSS 11–20, 13% vs 7% for NIHSS 21–30) (15). The clinical cost of treatment was a higher rate of symptomatic intracranial hemorrhage (10% vs 2%), although with no worsening of 90-day mortality rate (25% vs 27%) (15). The Food and Drug Administration did not grant prourokinase a new drug approval because, as a new drug, two positive trials were necessary and a second trial was never performed. However, similar outcomes were found with urokinase in a comparison study of IV and IA lysis (13), as well as in the randomized trial of Ogawa et al (16). This trial (16) was prematurely halted as a result of the approval of IV TPA in Japan for acute stroke, and thus the trial did not accrue enough patients to achieve statistical power for its primary endpoint (modified Rankin scale score of 0–2 at 90 d). Despite the early termination, excellent outcomes (modified Rankin scale score of 0–1 at 90 d) were nearly twice as likely in the IA lysis arm (42% vs 23%; $P = .045$). Near-complete resolution of neurologic deficit (i.e., NIHSS 0–1) was more than twice as likely in the lysis arm (35% vs 14 %; $P = .017$). At present, the large majority of neurointerventionists believe that IA lysis is clinically beneficial, but it is un-

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likely that another randomized trial of IA lysis versus placebo would be funded or even ethically viable in the United States (17). Trials to refine the role of various endovascular treatments are ongoing. Interventional Management of Stroke trial III is studying patients with stroke severity of NIHSS greater than 10 who might benefit from endovascular therapy in addition to IV TPA treatment (started within 3 h of stroke onset). A randomized trial of IA versus IV TPA is being conducted in Europe (18), but results are not available and recruitment has been hampered by controversial assumptions that (i) IA is superior to IV thrombolysis, (ii) IA should only be used as a "rescue" for IV thrombolysis, and (iii) the efficacy of IA lysis may be dependent on a particular drug (19).

Despite the general, but not uniform, acceptance that IA thrombolysis leads to improved stroke outcomes for large vessel occlusions, IA treatment is not widely available (20,21) for multiple reasons. Some major institutions in the United States still consider this therapy experimental. Physician compensation is very low relative to the long hours of work and emotional stress involved. Poor outcomes are not infrequent as a result of the severity of the emergency condition, and physicians fear being sued for a poor (but possibly unavoidable) outcome. Cases are emergent and random, disrupt the interventional room schedule during the day, and need to be performed immediately at any hour of the day or night. There is a shortage and a maldistribution of physicians trained to treat acute ischemic stroke with interventional techniques (2,22). Estimates of manpower based on the number of fellowship-trained neurointerventionists and their practice location have lead to a conclusion that 99% of the total United States population has access to IA stroke treatment within 6 hours of symptom onset and 82% has access within 3 hours (22). However, these estimates have not led to increased numbers of patients being treated with IA therapy, and perhaps as few as 10% of appropriate patients are currently receiving IA therapy (20). Many neurointerventionists, for the above reasons, choose not to treat acute ischemic stroke patients, and no single neurointerventionist can be available 24 hours a day, 7 days a week, 365 days a year. Transport frequently takes longer than expected, and the goal is not to transport patients to undergo treatment at the very end of a borderline therapeutic time window, but rather to treat patients as soon as possible. The goal is to reverse ischemia as rapidly as possible; every minute counts. In the ideal world, stroke treatment would be handled similar to treatment in trauma centers, with government regulation of facility infrastructure, personnel, expertise, transport, and reimbursement for the expenses associated with these resources. But even if stroke centers were comparable to trauma centers, a time to treatment of 6 hours, or even 3 hours, would be unacceptable if adequate care could be provided faster.

The reality is that interventional stroke therapy is underserved (19), which has led to interest by physicians from diverse specialties to provide this care (23). The Society of Interventional Radiology (SIR) has run interventional stroke training courses for nearly a decade, with an earlier survey reporting that one third of SIR members are in practices that offer IA stroke thrombolysis (24). Diagnostic neuroradiologists with interventional stroke treatment experience provide stroke care. The field of interventional cardiology is also making an effort to train interventional cardiologists in acute stroke reperfusion (25,26).

Given the previously described disincentives to provide interventional stroke care, we believe the commitment of various national societies and individual physicians to offer cerebral revascularization needs to be supported with a framework for the training that is necessary to perform cerebral revascularization with adequate competence. For this reason SIR has written physician training and competency guidelines for stroke revascularization therapy (27).

Stroke revascularization is not simply a technical procedure in which clinical success is determined by the ability to thread a catheter into the occluded cerebral artery and restore flow. Revascularization is necessary but not sufficient to produce positive clinical outcomes (28). Clinical success depends on patient selection based on multiple variables, including stroke severity, time of onset, age, blood glucose, blood pressure, volume and location of infarcted tissue, volume of ischemic penumbra, clot volume and location, and collateral perfusion. Clinical success also depends on having the hospital infrastructure and processes of care to allow rapid triage of patients from paramedics to the emergency room and then to imaging, intervention, appropriate neurointensive care, and subsequent rehabilitation. Primary and comprehensive stroke center accreditation is a way of assuring that these facility resources are available. Physician training is a way of assuring that the physician performing the procedure has the expertise to correctly select and skillfully treat patients who have experienced a stroke.

Physician training is both cognitive and technical. The physician must be able to perform a stroke specific neurologic examination and interpret complex neuroimaging, and then correlate these areas of information into a cohesive understanding of the issues related to the particular patient in question. Neurologic expertise includes recognition and specific diagnosis of stroke (including the elimination of stroke mimics), accurate evaluation of stroke severity, correlation of neurologic deficits with appropriate neuroanatomy and neurovasculature, and understanding of the clinical risk factors for revascularization outcomes. Imaging expertise is absolutely vital and includes the ability to evaluate stroke-specific imaging of brain computed tomography (CT), CT angiography and CT perfusion, multimodal magnetic resonance (MR) imaging and MR angiography, perfusion and diffusion studies, and catheter cerebral arteriography. Clinical expertise includes intra- and periprocedural clinical and pharmacological patient management. Technical expertise includes rapid and safe placement of an intracranial catheter and application of revascularization techniques.

We do not believe that technical expertise alone, with reliance on other members of a stroke team to provide the cognitive and imaging assessment, is acceptable. Nor do we believe that intracerebral microcatheter experience alone and unrelated to emergency stroke care constitutes adequate training. Our proposed training is not intended to train the interventionist to be a neurologist, a neuroradiologist, or a full-spectrum neurointerventionist. The intent of this training is to produce an excellent stroke interventionist who will know how to select correctly and then treat patients who have experienced a stroke with ap-

propriate cognitive and technical skills to produce documented excellent clinical outcomes.

These guidelines for training for interventional/endovascular stroke therapy are different from the guidelines SIR has published for other procedures. Previous guidelines have been based on time spent training and volumes of cases performed with a requirement that training outcomes meet national outcome benchmarks. For stroke revascularization, there are no national benchmarks for outcomes, and therefore confirmation of expertise is necessary beyond just time and case volume. However, some documentation of time and case volume is used in these stroke training guidelines, such as 6 months of neuroscience education (that is met in a diagnostic radiology residency program that includes verified expertise in interpretation of neurologic CT, MR, ultrasound, nuclear medicine single photon emission CT, and positron emission tomography scans, neuropathology, and angiography). Specified numbers of catheter cerebral arteriograms, superselective microcatheter placements, and neuroimaging interpretation are required in these standards. What is unique in these guidelines is a requirement to confirm mastery of this subject-specific material by examination and a requirement to track outcomes through a national registry (www.strokeregistry.org). Time and case volume requirements are a substitute for assessing true expertise. Expertise is typically confirmed by board examination. But endovascular stroke interventions are not part of the board examinations required for diagnostic radiology, interventional radiology, interventional cardiology, neurology, interventional neurology, or, for that matter, endovascular surgical neuroradiology (for which there is no board examination). SIR has no authority to require an examination to confirm competency to treat stroke, but we believe that passing a rigorous examination will affirm competency and will lead to better patient care and outcomes and will be desired by hospitals that seek to identify those who have the knowledge and skills for this care. Evidence of proficiency is the basis of hospital credentialing.

The SIR Stroke Intervention Training Guideline has not been endorsed by societies whose members have trained in neurointerventional fellowships, and these societies have written their own training guidelines (29). In our discussions with the Society of NeuroInterventional Surgery (previously the American Society of Interventional and Therapeutic Neuroradiology), the Society of Vascular and Interventional Neurology, and the American Association of Neurological Surgeons' Congress of Neurological Surgeons Cerebrovascular Section, it was their feeling that the field of stroke interventions has matured to the point at which a neurointerventional fellowship should be required, and any training other than a neurointerventional fellowship was an inappropriate shortcut likely to lead to poor outcomes. SIR has the highest respect for our neurointerventional colleagues and their expertise, but we disagree on this issue. Many neurointerventional fellowships do not provide acute ischemic stroke-specific education. Peripheral interventionists currently provide a significant amount of stroke interventions in this country successfully and have demonstrated excellent outcomes that rival those of the Prolyse in Acute Cerebral Thromboembolism II trial (30). The SIR and Society of NeuroInterventional Surgery, in association with the American Society of Neuroradiology, have previously published a statement that formally endorses peripheral interventionists providing emergency stroke revascularization therapy with appropriate training (31). This SIR guideline document conforms with that multisociety policy statement. In addition, the manpower analysis by Suzuki et al (22), cowritten by a former president of the Society of NeuroInterventional Surgery, refers to a large group of general interventional radiologists who may be available to provide acute stroke care. As a field matures, successful procedures migrate out of the specialty of origin. In addition to interventional radiologists, peripheral endovascular interventions are performed by cardiologists and vascular surgeons; spinal augmentation is performed by neurointerventionists, orthopedic surgeons and neurosurgeons, and anesthesiologists; thermal tumor ablations are performed by urologists and surgical oncologists. Such migration of procedures is a sign of the value of the technique.

What is needed now is a training pathway for physicians to acquire the expertise to deliver critically important emergency therapy on a widespread basis. Because of this important public health need, guidelines that are inclusive of all specialists with adequate training and experience are needed. Confirmation of this expertise is by examination and then by assessment of clinical outcomes through the use of a national registry. These are all components of the SIR stroke intervention training guidelines and are consistent with the Accreditation Council for Graduate Medical Education requirements that competency be confirmed with external measures of training performance and ongoing comparison with outcomes (32,33). We do not agree that poor outcomes will result from use of our training guidelines. Given the good outcomes that have been achieved so far by peripheral interventionists (30), and the rigorousness of these training guidelines, we believe that outcomes and access to care will only improve further as a result of these guidelines. With more than one societal training guideline for stroke interventions (with cardiology expected to publish yet a third such guideline), hospitals will face the same dilemma regarding credentialing for stroke interventions as they faced for carotid stent placement, for which there is more than one training guideline. Hospitals will likely require physicians to meet the requirements from one of the guidelines, perhaps the one written by the society representing the specialty of the individual physician.

The truth is that most training guidelines are not based on definitive evidence. Guidelines typically represent the consensus of a group of experts from a particular professional society as to what training will likely produce good results. Patient outcomes are the true gold standard for training and patient care. Reporting of patient outcomes is mandated in the SIR standards, and will likely also be mandated by the American Stroke Association and the Joint Commission to obtain accreditation as a comprehensive stroke center. For carotid stent placement, facility accreditation and reimbursement may soon depend on outcomes meeting national benchmarks. It is possible that accreditation and reimbursement for stroke interventions may follow the same path; SIR intends to lead the way.

SIR is creating a stroke interventions training course to allow physicians to meet the requirements of our guidelines. Some of the content will be avail-

able as online educational modules and some will be provided in a typical meeting environment, faculty will be drawn from multiple specialties, and an examination to confirm expertise will be offered. Physicians from any specialty will be welcome to attend and learn. The mission of SIR is to provide excellence in patient care. Our goal with these training guidelines and our course is to provide the means to achieve that excellence for patients needing treatment for severe acute ischemic stroke amenable to endovascular therapy.

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