Recent Endovascular Stroke Trials and Their Impact on Stroke Systems of Care

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ABSTRACT

Five recently published randomized trials of endovascular therapy versus medical management, including intravenous thrombolysis, demonstrated strong positive data in support of intra-arterial thrombectomy procedures. The American Heart Association/American Stroke Association released a focused update of the 2013 guidelines on the early management of acute ischemic strokes to specifically incorporate the findings of the 5 “positive” trials. In this review, we examine the key results of those trials and the principal changes in the updated guidelines. We discuss the ongoing and future changes in stroke systems of care, with an emphasis on the role of pre-hospital stroke triage, interhospital transfer, and the 2 main levels of stroke center certification (primary and comprehensive). (J Am Coll Cardiol 2016;67:2645-55) © 2016 by the American College of Cardiology Foundation.

Until recently, intravenous (IV) thrombolysis with recombinant tissue plasminogen activator (rtPA) was the only scientifically proven and U.S. Food and Drug Administration-approved treatment of acute ischemic stroke, on the basis of the results of the National Institute of Neurological Disorders and Stroke rtPA stroke trial (1). Acute stroke from large vessel occlusion (LVO), which
ASSOCIATION
Health Stroke Scale
NeuroInterventional Surgery
Infarction
plasminogen activator
TICI = Society of
SNIS
rtPA
PSC
NIHSS = National Institutes of
MSU
LVO = large vessel occlusion
IV = intravenous
IA = intra-arterial
IA = intra-arterial
CT = computed tomography
EMS = emergency medical service
IA = intra-arterial
IV = intravenous
LVO = large vessel occlusion
MSU = mobile stroke unit
NIHSS = National Institutes of Health Stroke Scale
PSC = primary stroke center
rtPA = recombinant tissue plasminogen activator
SNIS = Society of NeuroInterventional Surgery
TICI = Thrombolysis in Cerebral Infarction

ABBREVIATIONS AND ACRONYMS
AHA = American Heart Association
ASA = American Stroke Association
CSC = comprehensive stroke center
CT = computed tomography
EMS = emergency medical service
IA = intra-arterial
IV = intravenous
LVO = large vessel occlusion
MSU = mobile stroke unit
NIHSS = National Institutes of Health Stroke Scale
PSC = primary stroke center
rtPA = recombinant tissue plasminogen activator
SNIS = Society of NeuroInterventional Surgery
TICI = Thrombolysis in Cerebral Infarction

Typically includes the intracranial internal carotid artery, proximal middle cerebral artery, and the basilar artery, accounts for approximately 39% to 46% of all ischemic strokes and is associated with poor prognosis and neurological outcome (2-4). The most common etiology of intracranial LVO is cardioembolism, which is reported in 59% of all strokes from LVO, followed by large-artery atherosclerosis (22%) (5). However, in certain populations of patients, such as Asian subjects, large-artery atherosclerosis is more common, making it the number 1 cause of acute stroke from LVO (6). Other causes of LVO, such as a dissection and hypercoagulable and inflammatory states, are less common and tend to occur in a younger population of patients (7-9).

Parallel to the widespread use of IV rtPA, over the last 2 decades, various intra-arterial (IA) endovascular approaches were developed and tested for removal of clots from intracranial vessels. Many hospitals in the United States started to offer such therapies, but there was great variability in practice patterns, such as specific eligibility criteria when selecting patients for catheter-based interventions. Despite continuous development and the introduction of new thrombolyis and thrombectomy devices to the neurointerventional arsenal, data from randomized trials were lacking that would definitively prove that re-establishing blood flow resulted not only in angiographic success but also in clinical success.

A study by Menon et al. (10) that analyzed data from hospitals participating in Get With The Guidelines–Stroke from 2003 to 2013 serves as an excellent example of how diverse the patterns of endovascular stroke interventions were at that time. Get With The Guidelines–Stroke is a voluntary institutional program registry that tracks performance and outcomes associated with the treatment of patients who have various types of strokes. The study showed that of the 1,087 hospitals that participated in the registry, 42% provided endovascular therapy during the study period. However, only 1 out of 5 of those hospitals provided continuous endovascular coverage, and the calculated median annual number of patients receiving endovascular therapy was 6.

Five recently published randomized trials of endovascular therapy versus medical management, including IV thrombolysis with rtPA, demonstrated very strong positive data in support of IA thrombectomy procedures. These findings generated much interest and excitement in the medical community. As a result, efforts have now shifted toward the changes that existing stroke care systems need to implement, as the status of endovascular stroke therapy in certain stroke patient populations has transformed from “experimental and unproven” to “evidence-based and recommended.” These efforts are currently endorsed and supported by major medical organizations and societies, such as the American Heart Association (AHA)/American Stroke Association (ASA) and the Society of NeuroInterventional Surgery (SNIS) (11,12).

In the present review, we refer to the key results of those 5 trials, discuss the updated guidelines of endovascular stroke therapy, and focus on the current state and prospective changes in stroke care systems.

RECENT ENDOVASCULAR STROKE TRIALS AND UPDATED GUIDELINES

The 5 recent trials (MR CLEAN [Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands] [13], ESCAPE [Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times] [14], SWIFT PRIME [Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment of Acute Ischemic Stroke] [15], EXTEND-IA [Extending the Time for Thrombolysis in Emergency Neurological Deficits-Intra-arterial] [16], and REVASCAT [Randomized Trial of Revascularization with Solitaire FR Device vs Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting within Eight Hours of Symptom Onset] [17]) and, specifically, the variations in their design, screening methodologies, imaging modalities, and outcome measures, have been discussed in great detail elsewhere (we recommend referring to the special article collection in Stroke [18-21]). For the purpose of this review, we only briefly cover key findings and unique features of each trial (Table 1); our main focus is on the implications of those studies and others on stroke systems of care.

The outcomes of 2 other randomized endovascular trials (THRACE [Trial and Cost Effectiveness Evaluation of Intra-arterial Thrombectomy in Acute Ischemic Stroke], NCT01062698; and THERAPY [Assess the Penumbra System in the Treatment of Acute Stroke], NCT01429350) have not yet been finalized and published, and thus are not incorporated in this review.

In June 2015, the AHA/ASA released a focused update of the 2013 guidelines on the early management of acute ischemic stroke to specifically incorporate
TABLE 1 Recent Randomized Clinical Trials of Endovascular Stroke Therapy

| MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke) (23) | • European-based study (Netherlands), which enrolled 500 patients | • Intracerebral treatment initiated within the first 6 h (97% of which were with stent retrievers with or without preceding use of IV rtPA) was compared with standard medical therapy alone (IV rtPA in 91% of cases) |
| ESCAPE (Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times) (14) | • Mostly North America–based trial | • Compared endovascular therapy within up to 12 h (86% of cases treated with stent retrievers with or without previous administration of IV rtPA) with standard medical therapy (IV rtPA use in 79% of cases) |
| SWIFT PRIME (Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment of Acute Ischemic Stroke) (15) | • Trial predominantly conducted in North America | • Compared stent retriever thrombectomy after IV rtPA administration with IV rtPA alone (control group) |
| EXTEND IA (Extending the Time for Thrombolysis in Emergency Neurological Deficits-Intra-Arterial) (16) | • Trial based in Australia and New Zealand | • 60% in the endovascular arm and 35% in the medical treatment-only arm were functionally independent at 3 months |
| REVASCAT (Randomized Trial of Revascularization with Solitaire FR Device vs Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting within Eight Hours of Symptom Onset) (17) | • Trial conducted in Spain | • The trial mainly used perfusion-based imaging (CT or MR) for patient screening and selection |

The tremendous success of modern thrombectomy in the five recent trials was due to several key elements, which were reflected in the updated guidelines. First, all 5 trials relied primarily on the use of the most advanced thrombectomy devices, called retrievable stents or stent retrievers. The use of other types of devices was allowed in MR CLEAN and ESCAPE, but stent retrievers were used in most patients in those trials who underwent thrombectomy (97% and 86%, respectively). The AHA/ASA guidelines included a class I, Level of Evidence A recommendation in support of stent retrievers when thrombectomy is indicated. Such “mandated” use of a particular type of device for stroke interventions was criticized by some neurointerventionists as a potential barrier for further innovations. In the neuroangiography suite, recanalization is assessed by using the Thrombolysis in Cerebral Infarction (TICI) scale or the modified TICI; the 2 scales vary in what defines TICI 2b grade (28). Successful recanalization is defined as TICI 2 or modified TICI 2b/3. Rates of successful recanalization are much higher with stent retrievers than with early-generation thrombectomy devices (29,30). In the recent trials, these rates varied from 59% in MR CLEAN to 86% in SWIFT PRIME (the lowest and highest TICI 2b/3 achieved among the 5 trials, respectively). The SNIS worded their guidelines on the management of acute stroke differently, recommending “endovascular embolectomy,” rather than a specific type of a thrombectomy device (12).

The findings of the 5 recent “positive” trials (11). The guidelines committee also included the data from the preceding 3 “negative” randomized trials of endovascular therapy (IMS [Interventional Management of Stroke] III [22], SYNTHESIS Expansion [Synthesis Expansion: A Randomized Controlled Trial on Intra-Arterial Versus Intravenous Thrombolysis in Acute Ischemic Stroke] [23], and MR RESCUE [Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy] [24]), which had been published 2 years before. Much has been written about the reasons why those 3 earlier trials “failed” to show the benefit of endovascular therapy (25–27). It is important to recognize that it is the availability of both “negative” and “positive” trials that have led us to the identification of so many critical components of care for patients with acute stroke. Acute stroke care involves not only execution of a successful thrombectomy procedure leading to reperfusion of the ischemic brain but also recognition of the significance of early timing of the procedure, as well as prevention of delays and proper patient selection with various imaging modalities.
treated with endovascular therapy in the recent trials. The SWIFT PRIME and EXTEND IA trials randomized to treatment only those patients who received IV thrombolysis. The other 3 trials (MR CLEAN, ESCAPE, and REVASCAT) allowed treatment randomization of patients who were not eligible for, and thus were excluded from, receiving IV thrombolysis, but that subgroup constituted only 13%, 27%, and 22%, respectively, of all patients who underwent thrombectomy in those trials. Subgroup analyses within those 3 trials showed the clinical benefit of endovascular therapy in patients who did not receive IV rtPA, and the AHA/ASA guidelines concluded that thrombectomy is therefore “reasonable” in such patients as well.

One AHA/ASA guidelines statement that has become a subject of discussion at the scientific meetings is the effectiveness of endovascular therapy of stroke beyond the 6-h window being categorized as “uncertain” (Class IIb, Level of Evidence: C) and indicating the need for further clinical trials. In the ESCAPE trial, endovascular therapy was initiated within up to 12 h of symptom onset. However, only 49 patients were treated with endovascular therapy beyond the 6-h window. There was a trend toward favorable clinical outcomes in the interventional arm, but it did not reach statistical significance (odds ratio: 1.7; 95% confidence interval: 0.7 to 4.0).

Although results from selective retrospective studies indicate that such therapy might be safe and effective, data from randomized controlled trials are currently lacking (31–33). Ongoing randomized trials, such as DAWN (Trevo and Medical Management Versus Medical Management Alone in Wake Up and Late Presenting Strokes; NCT02142283) and POSITIVE (NCT01852201), are currently evaluating the safety and efficacy of endovascular treatment when initiated beyond the 6-h window, including in patients with wake-up strokes.

One of the main reasons why future acute stroke care systems are so complex is because despite the new evidence supporting stroke thrombectomy, endovascular therapy is not simply a replacement for IV thrombolysis. This important message was reflected in the new AHA/ASA guidelines, in which the first statement clarified that patients eligible for IV rtPA should receive IV rtPA even if endovascular therapy is being considered. At the same time, the guidelines pointed out that patients should be transported rapidly to the closest available primary stroke center (PSC) or comprehensive stroke center (CSC).

Some neurointerventionists anticipated that the AHA/ASA would define CSCs as the main targets in which all stroke patients with suspected LVO need to be immediately transported, thus bypassing those stroke centers that are not equipped with endovascular coverage; this scenario, however, was not reflected in the guidelines. Stroke systems of care vary tremendously, and not just from state to state, but even inside an individual county or a city, and real-world experience with an emphasis on clinical outcomes and cost-effectiveness analysis are needed before such a clear and strict set of rules is in place.

Examples and previous experience with triage of trauma and patients with ST-segment elevation myocardial infarction is valuable, and it is often cited as the direction of how stroke patients need to be triaged. However, we need to accept that patients with ischemic stroke are a much more diverse and complex population of patients, with various types of strokes and stroke mimics (34,35). Some patients with acute stroke are best treated with IV rtPA alone, some with a combination of IV plus IA approaches, and some are only eligible for thrombectomy alone. This mixture requires rapid and accurate identification of patients who might be potential candidates for endovascular therapy. Noninvasive imaging, such as computed tomography (CT) angiography or magnetic resonance angiography, can rapidly and accurately detect LVO; unfortunately, not all centers that serve as first-point contact with stroke patients have the infrastructure to rapidly perform and interpret such studies.

**PRE-HOSPITAL ASSESSMENT OF STROKE PATIENTS**

Several neurological tests have been developed with the goals of offering a quick “on-site” pre-hospital assessment of neurological deficits and identifying those stroke patients who are likely to harbor LVO. These tests include the Los Angeles Motor Scale (36), the Cincinnati Prehospital Stroke Severity Scale (37), and the Rapid Arterial Occlusion Evaluation (38) (Table 2) (36–42). The main advantage of such scales is their relative simplicity, allowing emergency medical personnel with different levels of training to utilize such tests as screening tools for rapid clinical assessment via the answers to 2 key questions: “Is this patient having a stroke?” and “Is the stroke likely from LVO?” Several independent studies that validated the accuracy of those 3 scales and other similar screening tests found that such pre-hospital stroke scales are (as one might expect) subject to error, with various degrees of limitations in both specificity and sensitivity, depending on the time of stroke onset and type of LVO (43–45). Still, the advantage of such simple screening tests is tremendous, as they provide immediate assessment of potential stroke patients,
When used as a predictor of LVO, for example, the National Institutes of Health Stroke Scale (NIHSS), although much more detailed in evaluating individual patients, cannot alone serve reliably as a marker of LVO but rather as screening tools to help determine the appropriate level of care (e.g., community hospital, PSC, CSC) appropriate for an individual patient. Therefore, a neurological examination, whether brief or detailed, cannot alone fail to detect LVO on angiography is one explanation as to why previous trials, such as IMS III and SYNTHESIS Expansion, found no significant benefit of endovascular therapy.

To simplify the initial on-site assessment of stroke patients, one study tested the usefulness of severe hemiparesis or hemiplegia (severe arm and leg weakness) alone as a screening tool to identify candidates for thrombectomy. Although such a basic approach might seem prone to significant error, the study found that in 3 patients who were transferred from the field to those investigators’ CSC underwent an endovascular procedure. Overall, 47% of patients included in this retrospective review received acute treatment including IV thrombolysis. With more data emerging on this subject, it is becoming clear that training of pre-hospital providers becomes essential in ensuring that potential candidates for endovascular stroke therapy are properly recognized and triaged to neuroendovascular-equipped tertiary centers.

### Current Status of Endovascular Stroke Therapy

Presently, we lack systematic data on patient access to emergent endovascular stroke therapy nationwide. Previous experience with IV thrombolysis illustrates that educating emergency medical service (EMS) dispatchers and paramedics and implementing pre-hospital acute stroke activation protocols are critically important for accurate triage of patients who are candidates for acute stroke treatment. A large body of research indicates that a simple hospital pre-notification of a potential incoming stroke patient by EMS helps greatly improve stroke treatment target times by reducing time to neurological evaluation and noninvasive CT imaging, and thus reducing “door-to-needle” time for IV thrombolysis, as well as increasing rates of rtPA administration.

In addition, active involvement by local government support increases access to stroke thrombolysis,

### Table 2: Pre-Hospital Stroke Scales to Predict LVO

<table>
<thead>
<tr>
<th>Scale Description</th>
<th>Score Range</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
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</thead>
<tbody>
<tr>
<td>Cincinnati Prehospital Stroke Severity Scale</td>
<td>0 to 4</td>
<td>83%</td>
<td>40%</td>
<td>94%</td>
</tr>
<tr>
<td>3-item stroke scale</td>
<td>0 to 6</td>
<td>86%</td>
<td>42%</td>
<td>85%</td>
</tr>
<tr>
<td>Rapid Arterial Occlusion Evaluation scale</td>
<td>0 to 9</td>
<td>68%</td>
<td>89%</td>
<td>41%</td>
</tr>
<tr>
<td>NIHSS (39-41)</td>
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<tr>
<td>A detailed scale that grades level of consciousness, speech (aphasia and dysarthria), visual field defects, gaze palsy, motor and sensory domains, presence of limb ataxia, and extinction/inattention</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Score ranges from 0 to 42</td>
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<tr>
<td>Score ≥ 8 with symptom onset within the first 3 h has predictive value of 86% for LVO</td>
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<tr>
<td>Heldner et al. (40): the best NIHSS score cutoff for LVO is 6 and has PPV 73% for anterior circulation strokes within 3 h. PPV beyond 6 h and in the posterior circulation strokes is poor</td>
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<tr>
<td>Fischer et al. (39): score ≥ 10 has PPV 97% for carotid occlusion and 96% for posterior circulation LVO</td>
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<td>Maas et al. (41): score ≥ 10 threshold has PPV 81% for LVO but only 48% sensitivity (i.e., more than one-half of all cases of LVO would be missed)</td>
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</table>

IMS = Interventional Management of Stroke; LVO = large vessel occlusion; NIHSS = National Institutes of Health Stroke Scale; PPV = positive predictive value.
as suggested by local experience in Toronto, Ontario, Canada, where a citywide pre-hospital acute stroke activation protocol was implemented as part of local government involvement in organization of local stroke care (56). The protocol was launched in 2005 and included an ambulance destination decision rule and a formal memorandum of understanding by system stakeholders. Its implementation resulted in an immediate improvement of patient access to IV thrombolysis, with an impressive 4-fold increase in patients who were treated with IV rtPA. Similar positive results of collaboration among hospitals, government agencies, and nonprofit organizations were demonstrated by the Chicago Area Stroke Taskforce initiative (49).

Multiple elements come into play when we attempt to study access to acute stroke treatment nationwide. Geographically, there is a great discrepancy in the density and availability of centers that offer IV rtPA or have neurointerventional coverage (Central Illustration). A study by Adeoye et al. (57) examined the data on ambulance response times and the use and availability of IV thrombolysis and endovascular therapy in the United States in 2011. The findings were alarming; although 81% of patients had access to hospitals that could administer IV rtPA within 60 min by ground, only approximately one-half of the hospitals (56%) had access to endovascular-capable hospitals within the first hour. With helicopter transport, endovascular centers were accessible to 85% of patients within 60 min. To allow 99% access to endovascular therapy, transport times had to be extended to 120 min.

Similar to the time-dependent effect of IV rtPA, strong proof now exists that the beneficial effect of endovascular thrombectomy is also time-dependent. By studying multiple groups of patients who underwent treatment with various endovascular approaches, such as with IA thrombolytic agents and early-generation thrombectomy devices from the IMS III data set (58), and stent retrievers in the SWIFT (Solitaire with the Intention for Thrombectomy) and STAR (Solitaire FR Thrombectomy for Acute Revascularisation) trials (59,60), there is a consistent finding of a strong association between improved clinical outcomes and shorter time to reperfusion. The pooled analysis of the SWIFT and STAR trials showed that for every 5-min delay in endovascular reperfusion, 1 of every 100 patients had a worse clinical outcome (59).

**HOSPITAL STROKE PROTOCOLS AND INTERHOSPITAL TRANSFERS**

Once the potential thrombectomy therapy candidate arrives at the treating center, any delays to establishing successful recanalization of the occluded vessel need to be prevented or minimized. A variety of imaging protocols currently exist, including the use of CT scanning, magnetic resonance imaging, and angiography, as well as advanced CT- or magnetic resonance-based perfusion imaging. Conflicting data exist on what is currently considered the “best” imaging modality to evaluate stroke patients. Some studies demonstrate benefits of advanced perfusion imaging, whereas other studies found the opposite, proving that such additional tests only create delays in the onset of intervention, without any added benefit (32,61–63). Presently, individual institutional practices range significantly in how quickly (or not) certain imaging tests can be performed and how rapidly the results of those tests can be communicated to the multidisciplinary teams that are evaluating and triaging stroke patients. Patient transport from imaging to the neurointerventional suite (known as “picture-to-puncture” time) can be greatly reduced by early mobilization of the anesthesia and neurointerventional teams in parallel, rather than after the imaging is completed and a decision is made to proceed with stroke intervention. In the study by Mehta et al. (64), a 36-min reduction in median “door-to-puncture” time was seen after the implementation of this early team arrival protocol. Clinical criteria were used to active the on-call team, and the rate of false-positive stroke intervention alerts was 23%.

Several studies have assessed factors associated with the efficacy of interhospital transfer of a potential candidate for endovascular therapy. Analysis of the IMS III trial, which tested the combined approach of IV plus IA thrombolysis versus IV thrombolysis alone, found significantly longer times from the start of IV rtPA to the start of intervention in patients who were treated in the “drip-and-ship” paradigm than in those randomized and treated at the same facility (65). Use of CT angiography and endovascular treatment at the same center was associated with shorter times to the start of intervention.

A study from a major metropolitan medical center in Chicago reported the experience with interhospital transfer delays in patients who were transferred for potential endovascular interventions (66). Data on consecutive patients transferred from 33 regional hospitals that were a part of the hub-and-spoke system of stroke transfers displayed a median transfer time of 104 min, despite relatively short distances (average, 15 miles) between the 2 facilities. The investigators concluded that after clinical exclusions, which occurred in 40% of transferred patients, transfer delay was the second most common reason...
why patients were excluded from thrombectomy (14% of all transferred patients).

Mobile stroke units (MSUs) have emerged as an elegant solution for patients who require both IV thrombolysis and endovascular therapy (Central Illustration). MSUs were first introduced in Germany, and their use led to a decrease in time to IV rtPA treatment, with no increase in adverse events (67). Such specialized ambulances are equipped with a noncontrast CT scanner and point-of-care laboratory, and they include a dedicated multidisciplinary team and telemedicine portal, allowing radiographic differentiation between ischemic stroke or intracranial hemorrhage, and pre-hospital administration of IV rtPA. Therefore, once the IV rtPA drip is initiated in the ambulance, those patients who are candidates for endovascular therapy (on the basis of pre-hospital neurological assessment scales) (Table 2) can safely bypass the nearest PCS and instead be transported directly to a hospital capable of offering endovascular therapy.

Early experience in the United States with an MSU in Houston listed funding, licensure, and establishing an effective communication system with EMS as major obstacles to this novel approach of acute stroke triage and treatment (68). The Houston group
reported treatment of approximately 2 patients with IV rtPA per week. During the first year, equipment costs were approximately $600,000 (excluding personnel costs), which, one might argue, is substantial; the cost-effectiveness of such an approach remains to be proven. The costs of an MSU may be offset by direct transport of thrombectomy-eligible patients to CSCs, thus eliminating the costs (and not just the time saved) of unnecessary patient transfer to the nearest PCS, and by a reduction in costs of long-term stroke care as a result of improved outcomes from faster rtPA administration (69). The Cleveland Clinic group also recently reported their initial MSU experience with an emphasis on patients who might be candidates for thrombectomy; they noted a substantial reduction in time to endovascular intervention after initiation of MSU- triage stroke protocols (70).

**LEVELS OF STROKE CENTER CERTIFICATION**

Presently, several pathways can be followed to determine whether a hospital meets standards for recognition as a PSC or CSC. Both the Joint Commission (in conjunction with the AHA/ASA) and Det Norske Veritas are global independent organizations that can determine whether a hospital meets the eligibility criteria. In addition, individual state health departments can also serve as stroke designation organizations. The distinction between a PSC versus a CSC is made on the basis of many factors, such as hospital size (number of beds), open neurosurgical and endovascular annual case volume, and continuous availability of stroke neurology, neurosurgery, neuroendovascular, and neurosciences intensive care unit resources (Central Illustration). Because of such heterogeneity in certification, the exact number of all combined stroke centers nationwide is difficult to track. It is estimated that with Joint Commission certification alone, >1,000 PSCs currently exist in the United States, which corresponds to 25% to 31% of all acute stroke care hospitals (71,72). The estimated number of CSCs is approximately 10 times less than the number of PCS. In addition, there are “acute stroke-ready” hospitals, which do not meet PSC qualifications but do have access, either in-person or via telemedicine, to stroke expertise and the ability to administer IV rtPA, and have transfer agreements with PSCs or CSCs.

It is unlikely that the number of CSCs will dramatically increase in the future. To provide continuous 24/7 endovascular stroke coverage, 2 to 4 neurointerventionists per 1 CSC are desirable. An estimated 1,000 neurointerventionists currently practice in the United States. Because the neurointerventional field is relatively young, and most practicing interventionists have just completed their fellowship training within the last 10 years, there will not be any shortage of operators in the next 2 decades. With decreasing reimbursement rates and lack of projected growth of other major neuroendovascular procedures (e.g., aneurysm and arteriovenous malformation embolization, carotid artery stenting), from a financial standpoint, emergent endovascular treatment of stroke alone probably will not be sufficient to support additional neurointerventionists (73,74).

Instead, focus should shift on improving communication and networking between currently existing CSCs and other health care facilities that participate in early management of acute stroke patients. In a recently launched forum by the SNIS, changes in endovascular stroke practice since the release of the results of the recent trials were discussed. The majority of neurointerventionists practicing at busy CSCs reported only a 20% to 50% increase in the number of acute stroke cases eligible for thrombectomy.

In addition to concerns for cost-effectiveness, growth in the number of CSCs, if not matched by a steady increase in the number of thrombectomy-eligible stroke patients, will lead to widespread establishment of centers that perform only few stroke interventions per year. Analysis of outcomes from catheter-based interventions performed for the treatment of acute myocardial infarction and carotid artery stenting suggest that shifting of treatment from high- to low-volume centers and performance of procedures by low-volume physicians are associated with higher complication rates and adversely affect patient outcomes (75-78). In acute stroke treatment, quicker “door-to-needle” time has been shown at high-volume centers (79). A study of 42,024 patients with acute ischemic stroke admitted to 80 hospitals in England found that patients admitted to hospitals with a treatment volume of >50 cases per year had 4.3 times greater odds (95% confidence interval: 2.21 to 8.50; p < 0.0001) of receiving IV rtPA within 60 min of arrival, which is considered the “golden” window for IV thrombolysis, with the highest chance of improving patient outcomes (80).

**PERFORMANCE STANDARDS OF ENDOVASCULAR STROKE THERAPY**

Compared with the large body of data on IV rtPA utilization collected through multiple registries, such as Get With The Guidelines-Stroke in the
United States or SITS-MOST (Safe Implementation of Thrombolysis in Stroke-Monitoring Study) in Europe, statistics on performance and outcomes of endovascular therapy are scarce. A study by Gupta et al. (81) analyzed outcomes of anterior circulation strokes treated within 8 h of symptom onset at 9 tertiary stroke centers between 2009 and 2011. High-volume centers were more likely to treat patients with endovascular therapy after administration of IV thrombolysis, and those transferred from outside hospitals and high-volume centers also demonstrated faster times to treatment, higher reperfusion rates, and higher rates of good clinical outcomes.

The most recently published 2011 AHA/ASA metrics for quality of care in CSCs collected rather limited data points on the performance of endovascular stroke interventions, such as whether thrombectomy was performed, occurrence of symptomatic intracranial hemorrhage, and 90-day functional outcomes (82). For hospitals to track a wider range of data to help improve patient outcomes through identification and correction of pre-procedural delays, additional metrics of pre-procedural delays, as well as occur in current acute ischemic stroke work-up and treatment, and outcome. Arch Neurosci 2015;2:e26670.


22. Broderick JP, Palesch YY, Demchuk AM, et al., Interventional Management of Stroke (IMS) III


77. McGrath PO, Wennis DE, Dickens JD Jr., et al. Relation between operator and hospital volume and outcomes following percutaneous coronary interventions in the era of the coronary stent. JAMA 2000;284:3139-44.


**KEY WORDS** acute ischemic stroke, endovascular therapy, randomized clinical trials, stroke centers, thrombectomy