

VIEWPOINT

The Acute Stroke Care Revolution

Enhancing Access to Therapeutic Advances

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Stroke is an important public health issue, affecting 800 000 individuals in the United States yearly and leading to 140 000 deaths.¹ The morbidity of stroke is substantial and contributes to serious neurologic disability and reduced quality of life in the majority of those affected.¹

Patients with **acute ischemic stroke**, which accounts for approximately **85%** of individuals with stroke in the United States, present to emergency departments hoping for interventions that will quickly reverse neurologic deficits and restore function. It is clear that speed matters ("**time is brain**") because **every additional minute of ischemia is estimated to lead to the death of perhaps 2 million neurons**.² Prior to 2015, acute treatment options with a good evidence base were limited to intravenous tissue plasminogen activator (**IV t-PA, alteplase**), which generally can be given within, at most, **4.5 hours** from the last time the patient was seen well without signs and symptoms of stroke. This narrow time window precluded many patients from receiving any acute therapy for stroke because they were deemed not eligible for tissue plasminogen activator treatment, often related to delayed presentations outside of this time window.³

Starting in late 2014, a series of randomized trials demonstrated the efficacy of **clot extraction (thrombectomy)** for the approximately **one-third** of patients with

from the last time they were seen well,⁶ and the DEFUSE-3 trial enrolled 182 patients up to a **16-hour limit** from the time last seen well.⁷ In both trials, patients were **selected based on perfusion imaging**, typically with computed tomography; if they demonstrated a relatively small burden of infarction but a large area of tissue at risk, they were randomly assigned to thrombectomy or medical management alone. In both trials, patients assigned to thrombectomy had significantly better functional outcomes. In the **DAWN trial**, outcomes at **90 days** were better with thrombectomy plus standard care than with standard care alone, with rates of **functional independence** at 90 days of **49% vs 13%**, respectively.⁶ In the **DEFUSE-3 trial**, endovascular therapy plus medical therapy, compared with medical therapy alone, also was associated with a higher percentage of patients who were functionally independent at **90 days (45% vs 17%, respectively)**.⁷

These findings suggest that many more eligible patients with acute ischemic stroke can receive therapy regardless of where they present in the United States, because centers that can provide these procedures can typically be reached within a few hours via flight or ground transport. Of the estimated 650 000 patients who experience ischemic stroke each year in the United States, at least 20 000 may have LVO that can now be newly eligible for thrombectomy in these extended time windows.⁸

However, the systems of care needed to provide such treatment still lag behind this new evidence. Just because patients with stroke should be able to arrive at a center with the ability to perform thrombectomy does not mean that these patients currently can. A well-developed hub-and-spoke system (ie, with the hub being a stroke center that can provide thrombectomy, and the spokes as outlying or neighboring hospitals that cannot provide this procedure, but refer patients to the thrombectomy center) analogous with a system providing care for patients with myocardial infarction does not widely exist for stroke. Although the challenges of establishing such a model quickly remain substantial, anything less than a system in which all eligible patients with stroke can receive this care should not be considered acceptable. Reducing morbidity from stroke should be a major priority for every health care system.

Selection of patients with acute stroke for these interventional procedures is a major hurdle. Even though many hospitals can perform computed tomographic angiography to identify LVOs, there is **less-widespread availability of the perfusion imaging expertise needed to**

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ischemic stroke with large-vessel occlusions (LVOs) in the anterior circulation. These trials included patients who presented early enough that they could receive thrombectomy within 6 hours of the last time they were seen well.^{4,5} While encouraging, this extended time window still excluded many patients with acute stroke, either because they presented too late for treatment or they presented to a center without neurointerventional expertise.

This landscape changed considerably in 2018 with the publication of 2 important trials that evaluated an extended time window for thrombectomy in selected patients with LVO.^{6,7} Both trials involved treatment outside of the established 6-hour window for clot extraction. The DAWN trial enrolled 206 patients up to 24 hours

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determine whether a patient might benefit from thrombectomy outside of the 6-hour treatment window. The interpretation of perfusion images remains difficult without appropriate levels of training, and although automated software is available, it requires substantial investment for an individual hospital. As hospitals work to establish regional models, an important question will be whether to invest in perfusion software and training at all outlying spoke hospitals or transfer all potentially eligible patients to receive perfusion imaging at the hub. The burden of unnecessary transfers of patients who turn out to be ineligible for treatment based on perfusion imaging at the hub hospital needs to be weighed against the cost of investing in software and training for perfusion imaging and mandating its interpretation at every referring hospital.

Access to expertise in decision making also limits the availability of thrombectomy. Many hospitals lack around-the-clock access to specialists with specific training in the care of patients with stroke. Increasingly, telemedicine is being used to fill this expertise gap. Historically, access to telestroke services has been made difficult by unreimbursed costs, but the recently passed Furthering Access to Stroke Telemedicine Act could potentially ease this challenge. It is essential to foster these types of remote arrangements as well as partnerships with and training of emergency medicine, internal medicine, and family practice physicians, who often provide care for patients with acute stroke.

Another substantial barrier to the implementation of a national system for stroke thrombectomy is the availability of proceduralists who can effectively perform clot extractions. It is unlikely that smaller hospitals will ever have the volume of patients to support a dedicated neurointerventionalist. If not, possible solutions are to set up and hone an efficient interhospital transfer protocol with a larger receiving hospital where patients could receive thrombectomy or to make arrangements for neurointerventionalists to be on call and travel to the referring hospitals as needed. At this time, almost all stroke thrombectomies are performed by radiologists, neu-

rologists, and neurosurgeons, but it is an open question whether increasing needs in stroke intervention will lead to other practitioners who are more numerous, such as interventional cardiologists, learning to deliver such care.

Regional emergency medical systems are also grappling with the best way to transport patients with acute stroke. Should these patients be taken to the nearest primary stroke center for evaluation and potential treatment with intravenous thrombolytics and then transferred if needed to a hub hospital for thrombectomy? Or should patients with a likely LVO be transported past a nearby stroke center to a more distant thrombectomy-capable center? In a country as large and heterogeneous as the United States, there will not be a uniform right answer and regional systems will need to be tailored to accommodate local factors. If stroke centers are to be bypassed, reliable out-of-hospital tools will be needed to accurately identify patients with a likely LVO. While there are currently numerous proposed scales (such as the Cincinnati Prehospital Stroke Severity Scale and the stroke vision, aphasia, neglect assessment), robust data are lacking about which is most effective.

Although acute stroke care has experienced an experimental revolution in the past several years, the United States and most other countries need a system of care to deliver these advances to all eligible patients in an efficient, effective, and coordinated fashion. Every hospital that provides emergency care should consider options for the acute treatment of patients who present with acute stroke and a possible LVO. Leaders of emergency medical services should require transparent data on procedural volume, stroke expertise, and outcomes from their partner hospitals when developing and refining out-of-hospital triage procedures. Local protocols, transfer plans, and partnerships with hub hospitals must be developed so that the quality of care for acute stroke does not depend on whether a patient is fortunate enough to present to a hospital with what is currently relatively rare expertise. These coordinated efforts are necessary for patients to fully realize the benefits of recent important advances in acute stroke care.

ARTICLE INFORMATION

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REFERENCES

- Benjamin EJ, Blaha MJ, Chiuve SE, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2017 update: a report from the American Heart Association. *Circulation*. 2017; 135(10):e146-e603. doi:10.1161/CIR.0000000000000485
- Saver JL. Time is brain—quantified. *Stroke*. 2006; 37(1):263-266. doi:10.1161/01.STR.0000196957.55928.ab
- Emberson J, Lees KR, Lyden P, et al; Stroke Thrombolysis Trialists' Collaborative Group. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. *Lancet*. 2014;384(9958):1929-1935. doi:10.1016/S0140-6736(14)60584-5
- Goyal M, Menon BK, van Zwam WH, et al; HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387(10029):1723-1731. doi:10.1016/S0140-6736(16)00163-X
- Saver JL, Goyal M, van der Lugt A, et al; HERMES Collaborators. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316(12):1279-1288. doi:10.1001/jama.2016.13647
- Nogueira RG, Jadhav AP, Haussen DC, et al; DAWN Trial Investigators. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2018;378(1):11-21. doi:10.1056/NEJMoa1706442
- Albers GW, Marks MP, Kemp S, et al; DEFUSE 3 Investigators. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378(8):708-718. doi:10.1056/NEJMoa1713973
- Jadhav AP, Desai SM, Kenmuir CL, et al. Eligibility for endovascular trial enrollment in the 6- to 24-hour time window: analysis of a single comprehensive stroke center. *Stroke*. 2018;49(4):1015-1017.