

Reperfusion Therapy in the Acute Management of Ischemic Stroke



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KEYWORDS

- Acute ischemic stroke • Stroke system of care
- Intravenous recombinant tissue plasminogen activator (IV-tPA) • Mechanical thrombectomy
- Thrombolysis in cerebral infarction (TICI score) • American Heart Association
- American Stroke Association

KEY POINTS

- Reperfusion, or restoration of blood flow, is an effective means of reducing disability in the setting of acute stroke.
- Rapid evaluation of stroke begins with community education to recognize signs and symptoms of stroke, an organized system of care by the emergency medical services (EMS) and the emergency department (ED), timely evaluation by the stroke team, and critical care capability.
- Stroke is the fourth leading cause of death after ischemic heart disease, lung cancer, and chronic lower respiratory disease and a leading cause of disability and societal cost in the United States.

INTRODUCTION

An estimated 6.8 million Americans greater than or equal to 20 years of age have had a stroke, and there are approximately 795,000 new or recurrent cases per year with an annual direct and indirect cost of \$36.5 billion in 2010.^{1,2} Stroke is the fourth leading cause of death after ischemic heart disease, lung cancer, and chronic lower respiratory disease³ and a leading cause of disability and societal cost in the United States.³

This review provides an overview of the acute evaluation and treatment of ischemic stroke, focusing on the role of reperfusion therapy. The discussion is framed around the most recent American Heart Association/American Stroke

Association guidelines.⁴ Rapid evaluation of stroke begins with community education to recognize signs and symptoms of stroke, an organized system of care by the EMS and the ED, timely evaluation by the stroke team, and critical care capability. Intravenous (IV) thrombolysis with a recombinant tissue plasminogen activator (IV-tPA) within the first 3 hours of stroke symptom onset is the only therapy approved by the US Food and Drug Administration (FDA) for acute ischemic stroke.⁵ Recanalization rates for IV-tPA are limited, however, in large-vessel occlusions, which led to the exploration of endovascular therapy.⁶ Landmark trials in IV-tPA, endovascular perfusion therapy, and acute medical treatments, including

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blood pressure (BP) management, aspirin, statin, and anticoagulation, have shaped current understanding of acute stroke care.

EVALUATION OF ACUTE REPERFUSION THERAPY

Rapid recognition of stroke is critical for stroke outcome. The National Institutes of Neurological Disorders and Stroke (NINDS) has established target timeframes in the evaluation of stroke suspects, dubbed “stroke chain of survival” (Table 1). A fairly standardized algorithm for evaluating and treating acute ischemic stroke. The first step is to recognize traditional stroke symptoms, including acute facial paresis, arm drift, or abnormal speech, for instance. Analogous to atypical angina, many patients, in particular women, may present with nontraditional stroke symptoms, such as generalized weakness, fatigue, and cognitive changes that can make rapid diagnosis challenging.^{7,8} There are major campaigns aimed at the public to improve stroke system recognition, including the face, arm, speech, and time (FAST) educational program. Emergency dispatch operators and paramedics are also trained in stroke recognition using tools, such as the Los Angeles Prehospital Stroke Screen. Routing of patients with suspected stroke to specialized centers bypassing the nearest hospital is increasing throughout the United States.

After arrival in the ED, door-to-noncontrast CT head initiation ought to be done in less than or equal to 25 minutes, and door-to-CT head interpretation in less than or equal to 45 minutes. CT head is useful in differentiating ischemic stroke from hemorrhage stroke, because the treatment pathways of these 2 entities is different. MRI head with diffusion-weighted images is helpful in

distinguishing true stroke from stroke mimics, although a vast majority of centers in the US use CT only in the ED. Common stroke mimics include seizure, migraine, hypertensive encephalopathy, space-occupying lesions, toxic/septic/metabolic conditions, or psychogenic.⁹ Key blood work to obtain includes complete blood cell count, international normalized ratio/partial thromboplastin time, blood glucose, creatinine, toxicology screen, and troponin. Clinical assessment (history, general examination, and neurologic examination) remains the cornerstone of the evaluation. Stroke scales, such as the National Institutes of Health Stroke Scale (NIHSS), provide important information about the severity of stroke and prognostic information and influence decisions about the acute treatment.

INTRAVENOUS THROMBOLYSIS (INTRAVENOUS THROMBOLYSIS WITH A RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR)

In 1996, the FDA approved the use of IV-tPA for the treatment of acute ischemic stroke within 3 hours of symptom onset, based on the results of the NINDS tPA stroke trial.⁵ The trial showed that patients treated with tPA were 30% more likely to have minimal or no functional disability at 3 months (defined as a modified Rankin Scale score [mRS] of 0 or 1).⁴ Later, the European Cooperative Acute Stroke Study III further demonstrated global favorable outcomes when IV-tPA was administered 3 to 4.5 hours after symptom onset (52% vs 45%; OR 1.28; 95% CI, 1.0–1.6), although the effect was less pronounced than in those who received IV-tPA from 0 to 3 hours in the NINDS study (odds ratio [OR] 1.9; 95% CI, 1.2–2.9).¹⁰ Approximately 4.5 patients need to be treated within 1.5 hours, 9 from 1.5 to 3 hours, and 14.1 from 3 to 4.5 hours to have 1 additional patient with no disability at 90 days.¹¹ The primary complication of treating patients with IV-tPA for acute ischemic stroke is brain hemorrhage. In a pooled analysis, large intracranial hemorrhage (ICH) occurred in 5.2% of patients in the IV-tPA group versus 1.0% of controls (OR 5.37; 95% CI, 3.22–8.95).¹¹

Similar to recanalization of occluded coronary vessels, recanalization of intracranial vessels is clearly associated with improved clinical outcome. Zangerle and colleagues¹² reported that 58.3% of patients with recanalization had favorable 90-day mRS scores compared with 5.6% of patients without recanalization ($P < .001$). In a meta-analysis, Rha and Saver⁶ showed that recanalization significantly improved 90-day clinical

Table 1
Emergency department–based care: stroke chain of survival

Action	Time
Door-to-physician	≤10 min
Door-to-stroke team	≤15 min
Door-to-CT scan initiation	≤25 min
Door-to-CT scan interpretation	≤45 min
Door-to-drug (≥80% compliance)	≤60 min
Door-to-stroke unit admission	≤3 h

From Jauch EC, Saver JL, Adams HP, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;44:870–947; with permission.

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