

## Part 9: Stroke

Stroke experts selected for the Stroke Task Force evidence evaluation process represent a variety of specialties (epidemiology, neurology, emergency medicine) and health-care settings (community hospitals and medical centers) in the United States and Canada. Conflict of interest statements completed by task force members are linked to the superscript number at the end of this sentence.<sup>W000</sup>

The 2005 Consensus Conference evaluated the evidence related to the management of acute stroke. Survival and recovery from acute ischemic stroke requires establishment of systems and programs designed to promote rapid recognition of stroke warning signs, rapid emergency medical service (EMS) transport of stroke victims with prearrival notification to the receiving hospital, and a hospital system capable of providing organized and efficient stroke care. Intravenous (IV) fibrinolytic therapy is effective for reducing morbidity from acute ischemic stroke, but evidence shows that it must be administered within a system of acute stroke care using strict protocols and quality-improvement practices. This chapter separates stroke topics into out-of-hospital management, fibrinolytic therapy, and early in-hospital management.

### Out-of-Hospital Setting

Care of the acute stroke patient ideally begins before the patient arrives at the hospital. This section considers the use of supplementary oxygen and out-of-hospital assessment and triage of patients with acute stroke. Oxygen administration is important for hypoxemic patients, but supplementary oxygen administration for all stroke victims has not yet been shown to be effective. Paramedics are able to recognize stroke with more sensitivity and specificity after receiving training in the use of specific stroke scales. Once the stroke victim is identified, transport and triage are important decisions that require the participation of hospitals and community notification. Each receiving hospital should define its capabilities for treating patients with acute stroke and should communicate this information to the EMS system and the community.

#### *Oxygen*<sup>W241</sup>

##### *Consensus on Science*

The combination of poor perfusion and hypoxemia will exacerbate and extend ischemic brain injury, and it has been associated with worse outcome from stroke.<sup>1</sup> Although one small randomized clinical trial (LOE 2)<sup>2</sup> suggested benefit of supplementary oxygen on infarct volume, a much larger trial did not show any clinical benefit (LOE 3)<sup>3</sup> from routine administration of oxygen to all patients with ischemic stroke.

In contrast, the administration of supplementary oxygen to the subset of stroke patients who are not hypoxic is indirectly supported by several studies showing improved functional outcomes and survival of stroke patients treated in dedicated stroke units in which higher rates of oxygen supplementation were used (LOE 7).<sup>1,4,5</sup>

##### *Treatment Recommendation*

Administration of supplementary oxygen to hypoxemic stroke patients by out-of-hospital and in-hospital medical personnel is recommended. Because there is conflicting evidence regarding the benefits of supplementary oxygen administration to normoxemic stroke patients, healthcare professionals may consider giving oxygen to these stroke patients on an individual basis.

#### *Out-of-Hospital Stroke Assessment Tools*<sup>W238</sup>

EMS systems must provide education and training to minimize delays in prehospital dispatch, assessment, and transport. With training in the use of relatively simple stroke assessment tools, prehospital providers can identify potential victims of stroke with high sensitivity and specificity.

##### *Consensus on Science*

When paramedics were given standard training in identification of stroke, sensitivity for identifying patients with stroke ranged from 61% to 66% (LOE 5).<sup>6–8</sup> After paramedics received training in using a stroke identification tool, sensitivity increased to 66% to 97% (LOE 3<sup>9,10</sup>; LOE 4<sup>11</sup>; LOE 5<sup>12</sup>).

##### *Treatment Recommendation*

Paramedics should be trained in the recognition of stroke with a validated, abbreviated out-of-hospital neurologic evaluation tool such as the Cincinnati Prehospital Stroke Scale or the Los Angeles Prehospital Stroke Screen.

#### *Prehospital Triage*<sup>W240A</sup>

The concept of designating stroke centers and stroke units is a source of contention within communities and among hospitals. Although many high-level studies have shown reduced length of stay and improved outcome from admission of patients to stroke units, more evidence is needed to determine criteria for the designation of stroke centers within a community and to describe time and distance limitations for transport of stroke patients to such units.

##### *Consensus on Science*

Evidence from adult case series of fair to good research design (LOE 5)<sup>13–15</sup> and additional studies of poorer quality

From the 2005 International Consensus Conference on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations, hosted by the American Heart Association in Dallas, Texas, January 23–30, 2005.

(*Circulation*. 2005;112:III-110-III-114.)

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This special supplement to *Circulation* is freely available at <http://www.circulationaha.org> DOI: 10.1161/CIRCULATIONAHA.105.166479

(LOE 7<sup>16</sup> and LOE 8<sup>17,18</sup>) suggests decreased in-hospital intervals from patient arrival to critical benchmark assessments and decreased patient mortality when triage to specific stroke hospitals for patients with potential stroke occurs in the out-of-hospital setting.

Triage of patients with potential stroke to specific stroke hospitals has not been proven to be safe, feasible, and effective. Clinical trials concerning this issue are ongoing.

#### *Treatment Recommendation*

Initial low-level evidence indicates a favorable benefit from triage of stroke patients to designated stroke centers, but this concept should be explored using more rigorous levels of evidence.

### **Fibrinolytic Therapy**

The National Institute of Neurological Disorders and Stroke (NINDS) trials published in 1995 documented improved neurologic outcome in patients with acute ischemic stroke who received tissue plasminogen activator (tPA) using strict protocols. Since that time the validity of the NINDS trials has been challenged by some who note the higher stroke severity in the placebo group and the 10-fold increase in intracranial hemorrhage (but no increase in mortality) in the tPA group. Some community hospitals and medical centers have reported a higher incidence of intracranial hemorrhage than was reported in the NINDS trials. The experts reviewed the published literature about the reported risks and benefits of tPA for acute ischemic stroke and found more large case series reporting a rate of intracranial hemorrhage equal to or lower than that reported in the NINDS trials when fibrinolytics were administered at centers with institutional commitment, strict use of protocols, and a system of continuous quality improvement.

#### *IV Fibrinolytics*<sup>W245</sup>

##### *Consensus on Science*

Level 1 studies document a higher likelihood of good to excellent functional outcome when IV tPA is given to adult patients with acute ischemic stroke <3 hours from onset of symptoms when administered by physicians in hospitals with a protocol that adheres to the eligibility criteria and therapeutic regimen of the NINDS protocol (LOE 1).<sup>19–24</sup> Evidence from level 1 studies of good to excellent quality in adults also documents greater likelihood of benefit the earlier treatment is begun (LOE 1).<sup>19,20,22,23,25</sup> Several studies report high rates of symptomatic intracerebral hemorrhage when tPA is used outside of recommended criteria (LOE 5).<sup>26,27</sup>

##### *Treatment Recommendation*

In the setting of a clearly defined protocol, a knowledgeable stroke team, and institutional commitment, IV administration of tPA to patients with acute ischemic stroke who meet the NINDS eligibility criteria is recommended. There is strong evidence to avoid all delays and treat patients as soon as possible.

Although not every hospital is capable of organizing the necessary resources to safely administer fibrinolytic therapy, every hospital with an emergency department should have a written plan describing how patients with acute stroke are to

be managed in that institution. The plan should detail the roles of healthcare professionals in the care of patients with acute stroke and define which patients will be treated with fibrinolytic therapy at that facility and when transfer to another hospital with a dedicated stroke unit is appropriate. Emergent computerized tomography (CT) or magnetic resonance imaging (MRI) scans of patients with suspected acute stroke should be reviewed quickly by a physician who is expert in the interpretation of those studies.

#### *Intra-arterial Fibrinolytics*<sup>W246</sup>

##### *Consensus on Science*

Evidence from 2 prospective randomized studies in adults (LOE 1<sup>28</sup> and LOE 2<sup>29</sup>) and additional studies including case series and meta-analysis (LOE 3<sup>30</sup> and LOE 5<sup>31–38</sup>) document improvement in the National Institutes of Health Stroke Scale scores and modified Rankin Scale score at 1 to 6 months when prourokinase, urokinase, or tPA is administered by the intra-arterial route to patients with acute ischemic stroke in the first 6 hours from onset of symptoms.

##### *Treatment Recommendation*

For patients with acute ischemic stroke who are not candidates for standard IV fibrinolysis, administration of intra-arterial fibrinolysis in centers that have the resources available may be considered within the first 6 hours after the onset of symptoms.

### **In-Patient Care**

In-patient treatment of acute stroke in dedicated units with trained personnel has proved beneficial. Hyperglycemia has been associated with poor neurologic outcome following head injury, resuscitation, and stroke. The question remains if lowering glucose will improve neurologic outcome for patients with acute stroke. Finally, therapeutic or induced hypothermia has been shown to be effective in 2 recent trials for victims of ventricular fibrillation sudden cardiac arrest who had successful return of spontaneous circulation but remained comatose. Investigators have explored the feasibility of hypothermia therapy for acute stroke.

#### *Stroke Units*<sup>W239</sup>

##### *Consensus on Science*

Evidence from multiple randomized clinical trials and meta-analyses in adults and additional studies document consistent improvement in 1-year survival rates and functional outcomes and reduced costs when care in a dedicated stroke unit is provided by dedicated stroke unit personnel to patients with acute stroke in the hospital setting (LOE 1).<sup>39–42</sup>

##### *Treatment Recommendation*

Hospitalized stroke patients experience improved outcomes when cared for by a multidisciplinary team experienced in managing stroke. Thus, when it is available, stroke patients who require hospitalization should be admitted to a stroke unit.

#### *Glucose Control*<sup>W244A</sup>

##### *Consensus on Science*

Prospective, controlled cohort studies (LOE 3)<sup>43–46</sup> and additional studies (LOE 4<sup>47–53</sup>; LOE 5<sup>54</sup>; LOE 7<sup>55</sup>) showed

worse clinical outcome in patients with hyperglycemia and acute ischemic stroke. There is no direct evidence that active control of glucose improves clinical outcome in patients with acute ischemic stroke (LOE 2).<sup>56,57</sup> There is evidence that treatment of hyperglycemia in other critically ill patients with insulin improves survival rates (LOE 7 for stroke).<sup>58</sup>

#### Treatment Recommendation

For consistency with the American Stroke Association<sup>59,60</sup> and the European Stroke Initiative Guidelines,<sup>61</sup> administration of IV or subcutaneous insulin may be considered for patients with acute ischemic stroke in the in-hospital setting to lower blood glucose when the serum glucose level is >10 mmol/L (about 200 mg/dL).

#### Therapeutic Hypothermia<sup>W243A,W243B</sup>

##### Consensus on Science

A Cochrane Database review failed to identify any evidence from prospective, randomized, controlled trials in stroke patients to support the routine use of hypothermia for patients with acute ischemic stroke (LOE 7).<sup>62</sup> Two small feasibility studies with concurrent controls (LOE 3)<sup>63,64</sup> documented the feasibility of cooling stroke patients to a body temperature of 35.5°C (95.9°F) using a cooling blanket<sup>63</sup> or a cooling helmet<sup>64</sup> with no increase in complications.

In one open study of 10 patients with a concurrent control group (LOE 3),<sup>65</sup> patients with acute ischemic stroke were cooled to 32°C to 33°C (89.6°F to 91.4°F) with minimal complications. But in 2 small case series (LOE 5),<sup>66,67</sup> including 1 using endovascular cooling (LOE 5),<sup>67</sup> a temperature reduction to ≤33°C (91.4°F) was associated with significant complications. One small case series of 25 patients with severe stroke of the middle cerebral artery and post-ischemic brain edema (LOE 5)<sup>68</sup> reported the feasibility of cooling to 33°C (91.4°F) with neutral results, but the patient outcome was poor, and in the absence of control, it is difficult to interpret complication rates. Reported complications of hypothermia in these case series include a rebound increase in intracranial pressure with rewarming, severe coagulopathy, cardiac failure and arrhythmias, pneumonia, and infection. These series were heterogeneous with respect to time between onset of stroke symptoms and cooling, method and degree of cooling, method of rewarming, and associated use of fibrinolytics.

One small series showed the feasibility of maintaining “low normothermic” temperatures (target 36°C to 37°C [96.8°F to 98.6°F]) using a cooling mattress for noncomatose, nonventilated patients with stroke (LOE 5).<sup>69</sup>

#### Treatment Recommendation

There is insufficient scientific evidence to recommend for or against the routine use of hypothermia in the treatment of acute ischemic stroke (Class Indeterminate).

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