AHA/ASA Guideline

Guidelines for the Early Management of Patients with Acute Ischemic Stroke

A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

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"Size of Treatment Effect"

"Estimate of Certainty (Precision) of Treatment Effect"

	Class I *Benefit >>> Risk* **Procedure/Treatment SHOULD be performed/administered**	Class IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE to perform procedure/administer treatment**	Class IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; Additional registry data would be helpful* **Procedure/Treatment MAY BE CONSIDERED**	Class III *Risk ≥ Benefit* *No additional studies needed* **Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL**
Level A *Multiple (3-5) population risk strata evaluated** *General consistency of direction and magnitude of effect*	• Recommendation that procedure or treatment is useful/effective • Sufficient evidence from multiple randomized trials or meta-analyses	• Recommendation in favor of treatment or procedure being useful/effective • Some conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation that procedure or treatment not useful/effective and may be harmful • Sufficient evidence from multiple randomized trials or meta-analyses
Level B *Limited (2-3) population risk strata evaluated**	• Recommendation that procedure or treatment is useful/effective • Limited evidence from single randomized trial or non-randomized studies	• Recommendation in favor of treatment or procedure being useful/ effective • Some conflicting evidence from single randomized trial or non-randomized studies	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from single randomized trial or non-randomized studies	• Recommendation that procedure or treatment not useful/effective and may be harmful • Limited evidence from single randomized trial or non-randomized studies
Level C *Very limited (1-2) population risk strata evaluated**	• Recommendation that procedure or treatment is useful/effective • Only expert opinion, case studies, or standard-of-care	• Recommendation in favor of treatment or procedure being useful/ effective • Only diverging expert opinion, case studies, or standard-of-care	• Recommendation's usefulness/efficacy less well established • Only diverging expert opinion, case studies, or standard-of-care	• Recommendation that procedure or treatment not useful/effective and may be harmful • Only expert opinion, case studies, or standard-of-care
Suggested phrases for writing recommendations †	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/ beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown /unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

*Data available from clinical trials or registries about the usefulness/efficacy in different sub-populations, such as gender, age, history of diabetes, history of prior MI, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

†In 2003, the ACC/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All recommendations in this guideline have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level.

Figure. Applying classification of recommendations and level of evidence.

I. Introduction

- Despite the increase in the global burden of stroke, advances are being made
- In 2008, after years of being the third leading cause of death in the United States, stroke dropped to fourth
- This document addresses opportunities for optimal stroke care in the acute phase of the acute ischemic stroke

II. Public Stroke Education

- The chain of events favoring good functional outcome from an acute ischemic stroke begins with the recognition of stroke when it occurs
- Data show that the public's knowledge of stroke warning signs remains poor
- Many studies have demonstrated that intense and ongoing public education about the signs and symptoms of stroke improves stroke recognition

III. Prehospital Stroke Management

- The Implementation Strategies for Emergency Medical Services within Stroke Systems of Care policy statement outlines specific parameters to measure the quality if EMSS including:
  - Stroke patients are dispatched at the highest level of care available in the shortest time possible.
  - The time between the receipt of the call and the dispatch of the response team is less than 90 seconds.
  - EMSS response time is < 8 minutes (time lapsed from the time of the call by the dispatch entity to the arrival on the scene of a properly equipped ambulance and staffed ambulance)
  - Dispatch time is < 1 minute
  - Turnout time (from the call is received to the unit in route) is < 1 minute)
  - The on-scene time is < 15 minutes (barring extenuating circumstances such as extrication difficulties)
- Travel time is equivalent to trauma or myocardial infarction calls.

Class I Recommendations	Class, Level of Evidence (LOE)
To increase both the number of patients who are treated and the quality of care, educational stroke programs for physicians, hospital personnel, and EMS personnel are recommended. *(Unchanged from the previous guideline)*	Class I, LOE B
Activation of the 911 system by patients or other members of the public is strongly recommended. 9-1-1 Dispatchers should make stroke a priority dispatch, and transport times should be minimized. *(Unchanged from the previous guideline)*	Class I, LOE B
Prehospital care providers should use prehospital stroke assessment tools, such as the Los Angeles Prehospital Stroke Screen or Cincinnati Prehospital Stroke Scale. *(Unchanged from the previous guideline)*	Class I, LOE B
EMS personnel should begin the initial management of stroke in the field, as outlined in Table 4. Stroke protocol development to be used by EMS personnel is strongly encouraged. *(Unchanged from the previous guideline)*	Class I, LOE B
Patients should be transported rapidly to the closest available certified primary stroke center or comprehensive stroke center, or if no such centers exist, the most appropriate institution that provides emergency stroke care as described in the statement. In some instances, this may involve air medical transport and hospital bypass. *(Revised from the previous guideline)*	Class I, LOE A
EMS personnel should provide prehospital notification to the receiving hospital that a potential stroke patient is en route so that the appropriate hospital resources may be mobilized prior to patient arrival. *(Revised from the previous guideline)*	Class I, LOE B

IV. Designation of Stroke Centers and Stroke Care Quality Improvement Process

- The goals of creating stroke systems of care include stroke prevention, community stroke education, optimal use of EMS, effective acute and subacute stroke care, rehabilitation, and performance review of stroke care delivery
- Hospitals that have implemented organized stroke care have demonstrated sustained improvements in multiple measures of stroke care quality, including increased use of IV rtPA, increased lipid profile testing, and improved deep vein thrombosis (DVT) prophylaxis
- Neurocritical care units are essential elements of comprehensive stroke centers

IV. Designation of Stroke Centers and Stroke Care Quality Improvement Process

- Telemedicine (also called “telestroke”) may help solve the shortage of neurologists and radiologists, allowing hospitals to become acute stroke ready
- All patients with stroke and at risk for stroke benefit from the development of stroke systems of care
- States and regions should be encouraged to engage all regional stakeholders to build stroke systems

IV. Designation of Stroke Centers and Stroke Care Quality Improvement Process

Class I Recommendations	**Class, Level of Evidence (LOE)**
The creation of PSCs is recommended. The organization of such resources will depend on local resources. The stroke system design of regional ASRH and PSCs that provide emergency care and that are closely associated with a CSC, which provides more extensive care, has considerable appeal. *(Revised from the previous guideline)*	(Class I, LOE B
Certification of stroke centers by an independent external body, such as The Joint Commission or state health department, is recommended. Additional medical centers should seek such certification. *(Revised from the previous guideline)*	Class I, LOE B
Healthcare institutions should organize a multidisciplinary quality improvement committee to review and monitor stroke care quality benchmarks, indicators, evidence-based practices and outcomes. Forming a clinical process improvement team and establishing a stroke care data bank is helpful for such quality of care assurances. The data repository can be used to identify the gaps or disparities of quality stroke care. Once the gaps have been identified, specific interventions can be initiated to address these gaps or disparities. *(New recommendation)*	Class I, LOE B
For patients with suspected stroke, EMS should bypass hospitals that do not have resources to treat stroke and go to the closest facility most capable of treating acute stroke. *(Unchanged from the previous guideline)*	Class I, LOE B
For sites without in-house imaging interpretation expertise, teleradiology systems approved by the Food and Drug Administration (FDA) (or equivalent organization) are recommended for timely review of brain CT and MRI scans in patients with suspected acute stroke. *(New recommendation)*	Class I, LOE B
When implemented within a telestroke network, teleradiology systems approved by the FDA (or equivalent organization) are useful in supporting rapid imaging interpretation in time for fibrinolysis decision making. *(New recommendation)*	Class I, LOE B
The development of CSCs is recommended. *(Unchanged from the previous guideline)*	Class I, LOE C

IV. Designation of Stroke Centers and Stroke Care Quality Improvement Process

Class II Recommendations	Class, Level of Evidence (LOE)
Implementation of telestroke consultation in conjunction with stroke education and training for healthcare providers can be useful in increasing the use of IV rtPA at community hospitals without access to adequate onsite stroke expertise. *(New recommendation)*	Class IIa, LOE B
The creation of Acute Stroke Ready Hospitals (ASRHs) can be useful. Like PSC, the organization of such resources will depend on local resources. The stroke system design of regional ASRH and PSCs that provide emergency care and that are closely associated with a CSC, which provides more extensive care, has considerable appeal. *(New recommendation)*	Class IIa, LOE C

V. Emergency Evaluation and Diagnosis of Acute Ischemic Stroke

- The evaluation and initial treatment of patients with stroke should be performed expeditiously
- Because time is critical, a limited number of essential diagnostic tests are recommended
- Stroke protocols and pathways should clearly define which tests must be performed prior to acute treatment decisions and which may be performed subsequent to acute stroke therapies

V. Emergency Evaluation and Diagnosis of Acute Ischemic Stroke

Class I Recommendations	**Class, Level of Evidence (LOE)**
An organized protocol for the emergency evaluation of patients with suspected stroke is recommended. The goal is to complete an evaluation and to begin fibrinolytic treatment within 60 minutes of the patient's arrival in an ED. Designation of an acute stroke team that includes physicians, nurses, and laboratory/radiology personnel is encouraged. Patients with stroke should have a careful clinical assessment, including neurological examination. *(Unchanged from the previous guideline)*	Class I, LOE B
The use of a stroke rating scale, preferably the NIHSS, is recommended. *(Unchanged from the previous guideline)*	Class I, LOE B
A limited number of hematologic, coagulation, and biochemistry tests are recommended during the initial emergency evaluation, and only the assessment of blood glucose must precede the initiation of IV rtPA (Table 7). *(Revised from the previous guideline)*	Class I, LOE B
Baseline ECG assessment is recommended in patients presenting with acute ischemic stroke but should not delay initiation of IV rtPA. *(Revised from the previous guideline)*	Class I, LOE B
Baseline troponin assessment is recommended in patients presenting with acute ischemic stroke but should not delay initiation of IV rtPA. *(Revised from the previous guideline)*	Class I, LOE C

V. Emergency Evaluation and Diagnosis of Acute Ischemic Stroke

Class II Recommendation	**Class, Level of Evidence (LOE)**
Usefulness of chest radiographs in the hyperacute stroke setting in the absence of evidence of acute pulmonary, cardiac or pulmonary vascular disease is unclear. If obtained, they should not unnecessarily delay administration of fibrinolysis. *(Revised from the previous guideline)*	Class IIb, LOE B

VI. Early Diagnosis: Brain and Vascular Imaging

- Head CT
  - Noncontrast head CT (NECT) is excellent in discriminating the presence of an intracranial hemorrhage which will preclude patients from thrombolytics
  - Detection of early ischemic changes on NECT is variable, but structured scales such as ASPECTS may assist
  - Presence of a hyperdense MCA sign is seen in roughly 1/3 of cases but correlates to large vessel occlusion
  - Presence of extensive early ischemic changes on NECT correlates to an 8-fold risk of symptomatic hemorrhage with IV tPA

VI. Early Diagnosis: Brain and Vascular Imaging

- MRI Brain
  - Diffusion weighted imaging highly specific and sensitive in detecting ischemia
  - The GRE sequence may assist in detecting thrombus with higher sensitivity compared to NECT
  - MR is sensitive at detecting acute hemorrhage and comparable to NECT and reasonable to use for early imaging
  - Limitation of MR is patient movement, pacemakers, metal implants or claustrophobia

VI. Early Diagnosis: Brain and Vascular Imaging

- CT Angiography
  - The accuracy of CTA for evaluation of large-vessel intracranial stenoses and occlusions is very high
  - Because CTA provides a static image of vascular anatomy, it is inferior to DSA for the demonstration of flow rates and direction
  - Direct comparisons of CTA source images (CTA-SI) and MRI/DWI have demonstrated very similar sensitivity of these two techniques for detecting ischemic regions

VI. Early Diagnosis: Brain and Vascular Imaging

- MR Angiography
  - Time of flight MRA is useful in identifying acute proximal large-vessel occlusions but cannot reliably identify distal or branch occlusions
- Transcranial Doppler
  - TCD accuracy is less compared to CTA and MRA for steno-occlusive disease, with a sensitivity and specificity of TCD ranging from 55-90% and 90-95%, respectively
  - TCD usefulness is limited in patients with poor bony windows, and its overall accuracy is dependent on the experience of the technician, interpreter, and the patient's vascular anatomy

VI. Early Diagnosis: Brain and Vascular Imaging

- Conventional Angiography
  - DSA remains the ‘gold standard’ for the detection of many types of cerebrovascular lesions and diseases
  - DSA is an invasive test and can cause serious complications such as stroke and death
  - The largest series of cases to date reported a rate of stroke or death of less than 0.2%
  - A CTA or MRA may obviate the need for catheter angiography

VI. Early Diagnosis: Brain and Vascular Imaging

Class I Recommendations (For patients with acute cerebral ischemic symptoms that have not yet resolved)	**Class, Level of Evidence (LOE)**
Emergency imaging of the brain is recommended before initiating any specific therapy to treat acute ischemic stroke. In most instances, NECT will provide the necessary information to make decisions about emergency management. *(Unchanged from the previous guideline)*	Class I, LOE A
Either NECT or MRI is recommended before IV rtPA administration to exclude ICH (absolute contraindication) and to determine whether CT hypodensity or MRI hyperintensity of ischemia is present. *(Revised from the 2009 imaging scientific statement)*	Class I, LOE A
IV fibrinolytic therapy is recommended in the setting of early ischemic changes (other than frank hypodensity) on CT, regardless of their extent. *(Revised from the 2009 imaging scientific statement)*	Class I, LOE A
A non-invasive intracranial vascular study is strongly recommended during the initial imaging evaluation of the acute stroke patient if either IA fibrinolysis or mechanical thrombectomy is contemplated for management but should not delay IV rtPA if indicated. *(Revised from the 2009 imaging scientific statement)*	Class I, LOE A
In IV fibrinolysis candidates, the brain imaging study should be interpreted within 45 minutes of patient arrival in the ED by a physician with expertise in reading CT and MRI studies of the brain parenchyma. *(Revised from the previous guideline)*	Class I, LOE C

VI. Early Diagnosis: Brain and Vascular Imaging

Class II Recommendation **(For patients with acute cerebral ischemic symptoms that have not yet resolved)**	**Class,** **Level of Evidence (LOE)**
CT perfusion and MRI perfusion and diffusion imaging, including measures of infarct core and penumbra, may be considered for selecting patients for acute reperfusion therapy beyond IV fibrinolytic time windows. These techniques provide additional information that may improve diagnosis, mechanism, and severity of ischemic stroke and allow more informed clinical decision-making. *(Revised from the 2009 imaging scientific statement)*	Class IIb, LOE B

VI. Early Diagnosis: Brain and Vascular Imaging

Class III Recommendation (For patients with acute cerebral ischemic symptoms that have not yet resolved)	**Class, Level of Evidence (LOE)**
Frank hypodensity on NECT may increase the risk of hemorrhage with fibrinolysis and should be considered in treatment decisions. If frank hypodensity involves more than one third of the MCA territory, IV rtPA treatment should be withheld. *(Revised from the 2009 imaging scientific statement)*	Class III, LOE A

VI. Early Diagnosis: Brain and Vascular Imaging

Class I Recommendations (For patients with cerebral ischemic symptoms that have resolved)	**Class, Level of Evidence (LOE)**
Noninvasive imaging of the cervical vessels should be performed routinely as part of the evaluation of patients with suspected TIAs. *(Unchanged from the 2009 TIA scientific statement)*	Class I, LOE A
Noninvasive imaging by means of CTA or MRA of the intracranial vasculature is recommended to exclude the presence of proximal intracranial stenosis and/or occlusion and should be obtained when knowledge of intracranial steno-occlusive disease will alter management. Reliable diagnosis of the presence and degree of intracranial stenosis requires the performance of catheter angiography to confirm abnormalities detected with noninvasive testing. *(Revised from the 2009 TIA scientific statement)*	Class I, LOE A
Patients with transient ischemic neurologic symptoms should undergo neuroimaging evaluation within 24 hours of symptom onset or as soon as possible in patients with delayed presentations. MRI, including DWI, is the preferred brain diagnostic imaging modality. If MRI is not available, head CT should be performed. *(Unchanged from the 2009 TIA scientific statement)*	Class I, LOE B

VII. General Supportive Care and Treatment of Acute Complications

- Stroke is a primary failure of focal tissue oxygenation and energy supply
- Systemic hypoxemia and hypotension should be avoided and, if present, corrected to limit further cellular damage

VII. General Supportive Care and Treatment of Acute Complications

Class I Recommendations	Class, Level of Evidence (LOE)
Cardiac monitoring is recommended to screen for atrial fibrillation and other potentially serious cardiac arrhythmias that would necessitate emergency cardiac interventions. Cardiac monitoring should be performed for at least the first 24 hours. *(Revised from the previous guideline)*	Class I, LOE B
Patients who have elevated blood pressure and are otherwise eligible for treatment of with IV rtPA should have their blood pressure carefully lowered (Table 9) so that their systolic blood pressure is <185 mm Hg and their diastolic blood pressure is <110 mm Hg before fibrinolytic therapy is initiated. If medications are given to lower blood pressure, the clinician should be sure that the blood pressure is stabilized at the lower level before treating with IV rtPA and maintained below 180/105 mm Hg for at least the first 24 hours after IV rtPA treatment. *(Unchanged from the previous guideline)*	Class I, LOE B
Airway support and ventilatory assistance are recommended for the treatment of patients with acute stroke who have decreased consciousness or who have bulbar dysfunction causing compromise of the airway. *(Unchanged from the previous guideline)*	Class I, LOE C
Supplemental oxygen should be provided to maintain oxygen saturation > 94%. *(Revised from the previous guideline)*	Class I, LOE C
Sources of hyperthermia (temperature >38°C) should be identified and treated, and antipyretic medications should be administered to lower temperature in hyperthermic patients with stroke. *(Unchanged from the previous guideline)*	Class I, LOE C

VII. General Supportive Care and Treatment of Acute Complications

Class I Recommendations	Class, Level of Evidence (LOE)
Until other data become available, consensus exists that the previously described blood pressure recommendations should be followed in patients undergoing other acute interventions to recanalize occluded vessels, including IA fibrinolysis. (Unchanged from the previous guideline)	Class I, LOE C
In patients with markedly elevated blood pressure who do not receive fibrinolysis a reasonable goal is to lower blood pressure by 15% during the first 24 hours after onset of stroke. The level of blood pressure that would mandate such treatment is not known, but consensus exists that medications should be withheld unless the systolic blood pressure is >220 mm Hg or the diastolic blood pressure is >120 mm Hg. *(Revised from the previous guideline)*	Class I, LOE C
Hypovolemia should be corrected with IV normal saline, and cardiac arrhythmias that might be reducing cardiac output should be corrected. *(Revised from the previous guideline)*	Class I, LOE C
Hypoglycemia (blood glucose < 60 mg/dL) should be treated in patients with acute ischemic stroke. The goal is to achieve normoglycemia. *(Revised from the previous guideline)*	Class I, LOE C

VII. General Supportive Care and Treatment of Acute Complications

Class II Recommendations	Class, Level of Evidence (LOE)
Evidence from one clinical trial indicates that initiation of antihypertensive therapy within 24 hours of stroke is relatively safe. Restarting antihypertensive medications is reasonable after the first 24 hours for patients who have preexisting hypertension and are neurologically stable unless a specific contraindication to restarting treatment is known. *(Revised from the previous guideline)*	Class IIa, LOE B
No data are available to guide selection of medications for the lowering of blood pressure in the setting of acute ischemic stroke. The antihypertensive medications and doses included in Table 8 are reasonable choices based on general consensus. *(Revised from the previous guideline)*	Class IIa, LOE C
Evidence indicates that persistent in-hospital hyperglycemia during the first 24 hours after stroke is associated with worse outcomes than normoglycemia, and thus it is reasonable to treat hyperglycemia to achieve blood glucose levels in a range of 140-180 mg/dL, and to closely monitor to prevent hypoglycemia in patients with acute ischemic stroke. *(Revised from the previous guideline)*	Class IIa, LOE C
The management of arterial hypertension in patients not undergoing reperfusion strategies remains challenging. Data to guide recommendations for treatment are inconclusive or conflicting. Many patients have spontaneous declines in blood pressure during the first 24 hours after onset of stroke. Until more definitive data are available, the benefit of treating arterial hypertension in the setting of acute ischemic stroke is not well established. Patients who have malignant hypertension or other medical indications for aggressive treatment of blood pressure should be treated accordingly. *(Revised from the previous guideline)*	Class IIb, LOE C

VII. General Supportive Care and Treatment of Acute Complications

Class III Recommendation	**Class, Level of Evidence (LOE)**
Supplemental oxygen is not recommended in nonhypoxic patients with acute ischemic stroke. *(Unchanged from the previous guideline)*	Class III, LOE B

VIII. Intravenous Fibrinolysis

- In the NINDS rtPA Stroke Trial, treatment with IV rtPA was associated with an increase in the odds of a favorable outcome (OR 1.9; 95% CI 1.2-2-9); the benefit was similar 1 year after stroke.
- The earlier that treatment is initiated, the better the result.
- Early minimal neurologic symptoms or neurologic deterioration temporally associated with any intracranial hemorrhage occurred in 6.4% of patients treated with IV rtPA and 0.6% of patients given placebo; however, mortality in the 2 treatment groups was similar at 3 months (17% versus 20%)

VIII. Intravenous Fibrinolysis

Extended IV rtPA window

- ECASS III results indicated that IV rtPA can improve outcomes for, carefully selected patients treated 3 – 4.5 hours after stroke.
- A meta-analysis of 12 IV rtPA trials confirmed the benefits of IV rtPA administered within 6 hours from symptom onset (OR 1.17, 95% CI 1.06 – 1.29; *p*=0·001) and reinforced the importance of timely treatment because the benefit of IV rtPA is greatest in patients treated within 3 hrs from symptom onset.
- Health systems should set a goal of increasing their percentage of stroke patients treated within 60 minutes of presentation to hospital (door to needle time of 60 minutes) to at least 80%.

VIII. Intravenous Fibrinolysis

Minor and isolated or rapidly improving neurological signs

- the practice of withholding IV fibrinolytic therapy because of mild or rapidly improving symptoms has been questioned, justifying further study

Patients taking direct thrombin inhibitors and direct factor Xa inhibitors

- In patients known to have taken one of these agents in the past, but for whom history and/or readily available assay suggest no current substantial anticoagulant effects of the agent, cautious treatment may be pursued.

VIII. Intravenous Fibrinolysis

Class I Recommendations	Class, Level of Evidence (LOE)
IV rtPA (0.9 mg/kg, maximum dose 90 mg) is recommended for selected patients who may be treated within 3 hours of onset of ischemic stroke. *(Unchanged from the previous guideline)*.	Class I, Level of Evidence A
In patients eligible for IV rtPA, benefit of therapy is time-dependent, and treatment should be initiated as quickly as possible. The Door to Needle time (time of bolus administration) should be within 60 minutes from hospital arrival. *(New recommendation).*	Class I, Level of Evidence A
IV rtPA (0.9 mg/kg, maximum dose 90 mg) is recommended for administration to eligible patients who can be treated in the time period of 3 – 4.5 hours after stroke onset. The eligibility criteria for treatment in this time period are similar to those for persons treated at earlier time periods within 3 hours, with the following additional exclusion criteria: patients older than 80 years, those taking oral anticoagulants regardless of INR, those with a baseline NIHSS score > 25, those with imaging evidence of ischemic injury involving more than one-third of the middle cerebral artery territory, or those with both a history of stroke and diabetes. *(Revised from the 2009 IV rtPA Science Advisory)*	Class I, Level of Evidence B
IV rtPA is reasonable in patients whose blood pressure can be lowered safely (to below 185 / 110 mm Hg) with antihypertensive agents, with the physician assessing the stability of the blood pressure before starting IV rtPA. *(Unchanged from the previous guideline)*	Class I, Level of Evidence B
In patients undergoing fibrinolytic therapy, physicians should be aware of and prepared to emergently treat potential side effects including bleeding complications and angioedema that may cause partial airway obstruction. (*Revised from the previous guideline)*	Class I, Level of Evidence B

VIII. Intravenous Fibrinolysis

Class II Recommendations	**Class, Level of Evidence (LOE)**
IV rtPA is reasonable in patients with a seizure at the time of onset of stroke if evidence suggests that residual impairments are secondary to stroke and not a postictal phenomenon. *(Unchanged from the previous guideline)*	Class IIa, Level of Evidence C
The effectiveness of sonothrombolysis for treatment of patients with acute stroke is not well established. *(New recommendation)*	Class IIb, Level of Evidence B
The usefulness of IV administration of tenecteplase, reteplase, desmoteplase, urokinase, or other fibrinolytic agents, and the IV administration of ancrod or other defibrinogenating agents is not well established and should only be used in the setting of a clinical trial. *(Revised from the previous guideline)*	Class IIb, Level of Evidence B
For patients who can be treated in the time period of 3 – 4.5 hours after stroke but have one or more of the following exclusion criteria: 1) patients older than 80 years, 2) those taking oral anticoagulants, even with INR ≤ 1.7 , 3) those with a baseline NIHSS > 25, or 4) those with both a history of both stroke and diabetes, the effectiveness of IV treatment with rtPA is not well-established, and requires further study. *(Revised from the 2009 IV rtPA Science Advisory)*	Class IIb, Level of Evidence C
Use of IV fibrinolysis in patients with conditions of mild stroke deficits, rapidly improving stroke symptoms, major surgery in the preceding 3 months, and recent myocardial infarction may be considered, and potential increased risk should be weighed against the anticipated benefits. These circumstances require further study. *(New recommendation)*	Class IIb, Level of Evidence C

VIII. Intravenous Fibrinolysis

Class III Recommendations	**Class, Level of Evidence (LOE)**
The IV administration of streptokinase for treatment of stroke is not recommended. (*Revised from the previous guideline)*	Class III, Level of Evidence A
The use of IV rtPA in patients taking direct thrombin inhibitors or direct factor Xa inhibitors may be harmful and is not recommended unless sensitive laboratory tests such as aPTT, INR, platelet count, and ECT, or TT, or appropriate direct factor Xa activity assays are normal, or the patient has not received a dose of these agents for more than 2 days (assuming normal renal metabolizing function). Similar consideration should be given to patients being considered for IA rtPA. *(New recommendation)* Further study is required.	Class III, Level of Evidence C

IX. Endovascular Interventions

- Intra-Arterial (IA) Fibrinolysis
  - PROACT II study showed a 15% absolute difference in good outcome favoring IA pro-urokinase ($p<0.04$)
  - MELT terminated early but showed for mRS 0-1 better outcomes compared to control
  - Results of IA fibrinolysis are likely dependent on efficient and timely systems based approach similar to IV tPA

IX. Endovascular Interventions

- Combination Intravenous and Intra-arterial Fibrinolysis
  - A series of pilot trials have evaluated the combined IV/IA fibrinolytic approach using low-dose rtPA
  - The phase III IMS III trial, with a planned enrollment of 900 patients with NIHSS ≥10 treated within three hours of stroke symptom onset was recently stopped for reported futility; further results from the study are pending
  - As with IV fibrinolysis, reducing the time to reperfusion with endovascular therapies is likely pivotal in achieving the best clinical outcomes

IX. Endovascular Interventions

- Mechanical Clot Disruption/Extraction
  - Recanalization by mechanical thrombectomy may occur due to a combination of thrombus fragmentation, thrombus retrieval, and enhancement of fibrinolytic penetration
  - There are currently four devices cleared by the FDA for recanalization of arterial occlusion in patients with ischemic stroke (Merci, Penumbra, Solitaire, Trevo)

Endovascular Interventions

Class I Recommendations	Class, Level of Evidence (LOE)
Patients eligible for IV rtPA should receive IV rtPA even if IA treatments are being considered (Unchanged from the previous guideline)	Class I, Level of Evidence A
IA fibrinolysis is beneficial for treatment of carefully selected patients with major ischemic strokes of < 6 hours duration due to occlusions of the MCA, who are not otherwise candidates for IV rtPA. The optimal dose of IA rtPA remains is not well established and does not have FDA approval for IA use. (Revised from the previous guideline)	Class I, Level of Evidence B
As with IV fibrinolytic therapy, reduced time from symptom onset to reperfusion with intra-arterial therapies is highly correlated with better clinical outcomes, and all efforts must be undertaken to minimize delays to definitive therapy. New recommendation	Class I, Level of Evidence B
IA treatment requires the patient to be at an experienced stroke center with rapid access to cerebral angiography and qualified interventionalists. An emphasis on expeditious assessment and treatment should be made. Facilities are encouraged to define criteria to credential individuals who can perform IA revascularization procedures. Outcomes on all patients should be tracked. Revised from the previous guideline	Class I, Level of Evidence C
When mechanical thrombectomy is pursued, stent retrievers, such as Solitaire FR and Trevo, are generally preferred to coil retrievers such as Merci. The relative effectiveness of the Penumbra System vs stent retrievers is not yet characterized. (New recommendation)	Class I, Level of Evidence A

Endovascular Interventions

Class II Recommendations	Class, Level of Evidence (LOE)
The Merci, Penumbra System, Solitaire FR, and Trevo thrombectomy devices can be useful in achieving recanalization alone or in combination with pharmacological fibrinolysis in carefully selected patients. Their ability to improve patient outcomes has not yet been established. These devices should continue to be studied in randomized controlled trials to determine the efficacy of such treatments in improving patient outcomes. Revised from the previous guideline	Class IIa, Level of Evidence B
IA fibrinolysis or mechanical thrombectomy are reasonable in patients who have contraindications to the use of IV fibrinolysis. Revised from the previous guideline	Class IIa, Level of Evidence C
Rescue IA fibrinolysis or mechanical thrombectomy may be reasonable approaches to recanalization in patients with large artery occlusion who have not responded to IV fibrinolysis. Additional randomized trial data are needed. New recommendation	Class IIb, Level of Evidence B
The usefulness of mechanical thrombectomy devices other than the Merci retriever, the Penumbra System, Solitaire FR, and Trevo is not well established. These devices should be used in the setting of clinical trials. Revised from the previous guideline	Class IIb, Level of Evidence C
The usefulness of emergent intracranial angioplasty and/or stenting is not well established. These devices should be used in the setting of clinical trials. New recommendation	Class IIb, Level of Evidence C
The usefulness of emergent angioplasty and/or stenting of the extracranial carotid or vertebral arteries in unselected patients is not well established. Use of these techniques may be considered in certain circumstances, such as in the treatment of acute ischemic stroke from cervical atherosclerosis or dissection. () Additional randomized trial data are needed. (New recommendation)	Class IIb, Level of Evidence C Class IIb, Level of Evidence C

Anticoagulants

- The results of several clinical trials demonstrate an increased risk of bleeding complications with early administration of either UFH or LMWH
- Early administration of UFH or LMWH does not lower the risk of early recurrent stroke, including among persons with cardioembolic sources.
- The role of anticoagulants as an adjunct in addition to mechanical or pharmacological fibrinolysis has not been established.
- The PREVAIL study gives the strongest evidence of the superiority of LMWH in prevention of venous thromboembolism following ischemic stroke.

Anticoagulants

Class II Recommendations	**Class, Level of Evidence (LOE)**
At present, the usefulness of argatroban or other thrombin inhibitors for treatment of patients with acute ischemic stroke is not well established. These agents should be used in the setting of clinical trials. (*New recommendation*)	Class IIb, Level of Evidence B
The usefulness of urgent anticoagulation in patients with severe stenosis of an ICA ipsilateral to an ischemic stroke is not well established. (*New recommendation*)	Class IIb, Level of Evidence B

X. Anticoagulants

Class III Recommendations	**Class, Level of Evidence (LOE)**
Urgent anticoagulation, with the goal of preventing early recurrent stroke, halting neurological worsening, or improving outcomes after acute ischemic stroke, is not recommended for treatment of patients with acute ischemic stroke. (*Unchanged from previous guideline*)	Class III, Level of Evidence A
Urgent anticoagulation for the management of noncerebrovascular conditions is not recommended for patients with moderate-to-severe strokes because of an increased risk of serious intracranial hemorrhagic complications. (*Unchanged from previous guideline*)	Class III, Level of Evidence A
Initiation of anticoagulant therapy within 24 hours of treatment with IV rtPA is not recommended. (*Unchanged from previous guideline*)	Class III, Level of Evidence B

XI. Antiplatelet Agents

- Currently available data demonstrate a small but statistically significant decline in mortality and unfavorable outcomes with the administration of aspirin within 48 hours following stroke
- Data regarding the utility of other antiplatelet agents, including clopidogrel alone or in combination with aspirin, for the treatment of acute ischemic stroke are limited
- Research of intravenously administered antiplatelet agents is ongoing

Antiplatelet Agents

Class I Recommendations	Class, Level of Evidence (LOE)
Oral administration of aspirin (initial dose is 325 mg) within 24 to 48 hours after stroke onset is recommended for treatment of most patients. Unchanged from the previous guideline	Class I, Level of Evidence A

Antiplatelet Agents

Class II Recommendations	Class, Level of Evidence (LOE)
The usefulness of clopidogrel for the treatment of acute ischemic stroke is not well established. Further research testing the usefulness of the emergency administration of clopidogrel in the treatment of patients with acute stroke is required. Revised from the previous guideline	Class IIb, Level of Evidence C
The efficacy of intravenous tirofiban and eptifibatide are not well established and should be used in the setting of clinical trials. New recommendation	Class IIb, Level of Evidence C

Antiplatelet Agents

Class III Recommendations	Class, Level of Evidence (LOE)
Aspirin is not recommended as a substitute for other acute interventions for treatment of stroke, including IV rtPA. Unchanged from the previous guideline	Class III, Level of Evidence B
The administration of other IV antiplatelet agents that inhibit the glycoprotein IIb/IIIa receptor is not recommended. Further research testing the usefulness of emergency administration of these medications as a treatment option in patients with acute ischemic stroke is required. Revised from the previous guideline.	Class III, Level of Evidence B
The administration of aspirin (or other antiplatelet agents) as an adjunctive therapy within 24 hours of IV fibrinolysis is not recommended. Revised from the previous guideline	Class III, Level of Evidence C

XII. Volume Expansion, Vasodilators, and Induced Hypertension

- For over 3 decades, investigators have studied interventions aimed at increasing cerebral perfusion in acute ischemic stroke
- These approaches have targeted acute alterations of blood rheology, expansion of blood volume, and increased global or local blood pressure

Volume Expansion, Vasodilators, and Induced Hypertension

Class I Recommendations	Class, Level of Evidence (LOE)
In exceptional cases with systemic hypotension producing neurologic sequelae, a physician may prescribe vasopressors to improve cerebral blood flow. If drug-induced hypertension is used, close neurological and cardiac monitoring is recommended. Revised from the previous guideline	Class I, Level of Evidence C

Volume Expansion, Vasodilators, and Induced Hypertension

Class II Recommendations	Class, Level of Evidence (LOE)
The administration of high dose albumin is not well established as a treatment for most patients with acute ischemic stroke until further definitive evidence regarding efficacy becomes available. New recommendation	Class IIb, Level of Evidence B
At present, use of devices to augment cerebral blood flow for the treatment of patients with acute ischemic stroke is not well established. These devices should be used in the setting of clinical trials. New recommendation	Class IIb, Level of Evidence B
The usefulness of drug-induced hypertension in patients with acute ischemic stroke is not well established. Induced hypertension should be performed in the setting of clinical trials. Revised from the previous guideline	Class IIb, Level of Evidence B

Volume Expansion, Vasodilators, and Induced Hypertension

Class III Recommendations	Class, Level of Evidence (LOE)
Hemodilution by volume expansion is not recommended for treatment of patients with acute ischemic stroke. Revised from the previous guideline	Class III, Level of Evidence A
The administration of vasodilatory agents, such as pentoxifylline, is not recommended for treatment of patients with acute ischemic stroke. Unchanged from the previous guideline	Class III, Level of Evidence A

XIII. Neuroprotective Agents

- Neuroprotection refers to the concept of applying a therapy that directly affects the brain tissue to salvage or delay the infarction of the still-viable ischemic penumbra
- Newer agents and innovative clinical trial designs which adhere to the STAIR criteria are needed to demonstrate that neuroprotective strategies could be helpful in treatment of stroke

XIII. Neuroprotective Agents

Class II Recommendations	**Class, Level of Evidence (LOE)**
Among patients already taking statins at the time of onset of ischemic stroke, continuation of statin therapy during the acute period is reasonable. (*New recommendation*)	Class IIa, Level of Evidence B
The utility of induced hypothermia for the treatment of patients with ischemic stroke is not well established, and further trials are recommended. *(Revised from the previous guideline)*	Class IIb, Level of Evidence B
At present, transcranial near-infrared laser therapy is not well established for the treatment of acute ischemic stroke, and further trials are recommended. (*New recommendation*)	Class IIb, Level of Evidence B

XIII. Neuroprotective Agents

Class III Recommendations	**Class, Level of Evidence (LOE)**
At present, no other pharmacologic agents with putative neuroprotective actions have demonstrated efficacy in improving outcomes after ischemic stroke, and therefore other neuroprotective agents are not recommended. (*Revised from the previous guideline*)	Class III, Level of Evidence A
Data on the utility of hyperbaric oxygen are inconclusive, and some data imply that the intervention may be harmful. Thus, with the exception of stroke secondary to air embolization, this intervention is not recommended for treatment of patients with acute ischemic stroke. (*Unchanged from the previous guideline*)	Class III, Level of Evidence B

XIV. Surgical Interventions

- Emergent carotid endarterectomy and other operations for treatment of patients with acute ischemic stroke may have serious risks and the indications must be considered carefully for each individual patient

- Additional randomized clinical trials should be designed and undertaken to examine the safety and efficacy of CEA in various subsets of patients with acute stroke, to establish the optimal timing for revascularization, and to define its role in the emergency management of stroke

XIV. Surgical Interventions

Class II Recommendations	**Class, Level of Evidence (LOE)**
The usefulness of emergent or urgent CEA when clinical indicators or brain imaging suggest a small infarct core with large territory at risk (e.g. penumbra), compromised by inadequate flow from a critical carotid stenosis or occlusion, or in the case of acute neurologic deficit after CEA, where acute thrombosis of the surgical site is suspected, is not well established. *(New recommendation)*	Class IIb, Level of Evidence B
In patients with unstable neurologic status--either stroke-in-evolution or crescendo TIA-- the efficacy of emergent or urgent CEA is not well established. *(New recommendation)*	Class IIb, Level of Evidence B

XV. Admission to the Hospital and General Acute Treatment (After Hospitalization)

- Approximately 25% of patients may have neurological worsening during the first 24 to 48 hours after stroke and it is difficult to predict which patients will deteriorate
- The importance of dedicated stroke nursing care in the management of stroke patients cannot be overstated

XV. Admission to the Hospital and General Acute Treatment (After Hospitalization)

Class I Recommendations	**Class, Level of Evidence (LOE)**
The use of comprehensive specialized stroke care (stroke units) incorporating rehabilitation is recommended. *(Unchanged from the previous guideline)*	Class I, LOE A
Patients with suspected pneumonia or urinary tract infections should be treated with appropriate antibiotics. *(Revised from the previous guideline)*	Class I, LOE A
Subcutaneous administration of anticoagulants is recommended for treatment of immobilized patients to prevent deep vein thrombosis. *(Unchanged from the previous guideline)*	Class I, LOE A
The use of standardized stroke care order sets is recommended to improve general management. *(Unchanged from the previous guideline)*	Class I, LOE B
Assessment of swallowing before starting eating, drinking, or receiving oral medications is recommended. *(Unchanged from the previous guideline)*	Class I, LOE B

XV. Admission to the Hospital and General Acute Treatment (After Hospitalization)

Class I Recommendations	**Class, Level of Evidence (LOE)**
Patients who cannot take solid food and liquids orally should receive NG, nasoduodenal, or PEG tube feedings to maintain hydration and nutrition while undergoing efforts to restore swallowing. *(Revised from the previous guideline)*	Class I, LOE B
Early mobilization of less severely affected patients and measures to prevent subacute complications of stroke are recommended. *(Unchanged from the previous guideline)*	Class I, LOE C
Treatment of concomitant medical diseases is recommended. *(Unchanged from the previous guideline)*	Class I, LOE C
Early institution of interventions to prevent recurrent stroke is recommended. *(Unchanged from the previous guideline)*	Class I, LOE C

XV. Admission to the Hospital and General Acute Treatment (After Hospitalization)

Class II Recommendations	**Class, Level of Evidence (LOE)**
The use of aspirin is reasonable for treatment of patients who cannot receive anticoagulants for DVT prophylaxis. *(Revised from the previous guideline)*	Class IIa, LOE A
In selecting between nasogastric versus PEG tube routes of feeding in patients who cannot take solid food or liquids orally, it is reasonable to prefer nasogastric tube feeding until 2-3 weeks post stroke onset. *(Revised from the previous guideline)*	Class IIa, LOE B
The use of intermittent external compression devices is reasonable for treatment of patients who cannot receive anticoagulants. (Revised from the previous guideline.)	Class IIa, LOE B

XV. Admission to the Hospital and General Acute Treatment (After Hospitalization)

Class III Recommendations	**Class, Level of Evidence (LOE)**
Routine use of nutritional supplements has not been shown to be beneficial. *(Revised from the previous guideline)*	Class III, LOE B
Routine use of prophylactic antibiotics has not been shown to be beneficial. *(Revised from the previous guideline)*	Class III, LOE B
Routine placement of indwelling bladder catheters is not recommended because of the associated risk of catheter associated urinary tract infections. *(Unchanged from the previous guideline)*	Class III, LOE C

XVI. Treatment of Acute Neurological Complications

- Given the complexity of severe stroke and potential complications, multidisciplinary care teams comprised of neurologists, neurointensivists, and neurosurgeons, as well as dedicated stroke nursing, are required to optimally manage these complex patients.

XVI. Treatment of Acute Neurological Complications

Class I Recommendations	Class, Level of Evidence (LOE)
Patients with major infarctions are at high risk for complicating brain edema and increased intracranial pressure. Measures to lessen the risk of edema and close monitoring of the patient for signs of neurological worsening during the first days after stroke are recommended. Early transfer of patients at risk for malignant brain edema to an institution with neurosurgical expertise should be considered. *(Revised from the previous guideline)*	Class I, LOE A
Decompressive surgical evacuation of a space occupying cerebellar infarction is effective in preventing and treating herniation and brain stem compression. *(Revised from the previous guideline)*	Class I, LOE B
Decompressive surgery for malignant edema of the cerebral hemisphere is effective and potentially life-saving. Advanced patient age and patient/family valuations of achievable outcome states may affect decisions regarding surgery. *(Revised from the previous guideline)*	Class I, LOE B
Recurrent seizures after stroke should be treated in a manner similar to other acute neurological conditions and anti-epileptic agents selected by specific patient characteristics. *(Unchanged from the previous guideline)*	Class I, LOE B
Placement of a ventricular drain is useful in patients with acute hydrocephalus secondary to ischemic stroke. *(Revised from the previous guideline)*	Class I, LOE C

XVI. Treatment of Acute Neurological Complications

Class II Recommendation	**Class, Level of Evidence (LOE)**
Although aggressive medical measures have been recommended for treatment of deteriorating patients with malignant brain edema after large cerebral infarction, the usefulness of these measures is not well established. *(Revised from the previous guideline)*	Class IIb, LOE C
Class III Recommendations	**Class, Level of Evidence (LOE)**
Because of lack of evidence of efficacy and the potential to increase the risk of infectious complications, corticosteroids (in conventional or large doses) are not recommended for treatment of cerebral edema and increased intracranial pressure complicating ischemic stroke. *(Unchanged from the previous guideline)*	Class III, LOE A
Prophylactic use of anticonvulsants is not recommended. *(Unchanged from the previous guideline)*	Class III, LOE C