AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients with Acute Ischemic Stroke

A guideline for healthcare professionals from the American Heart Association/American Stroke Association

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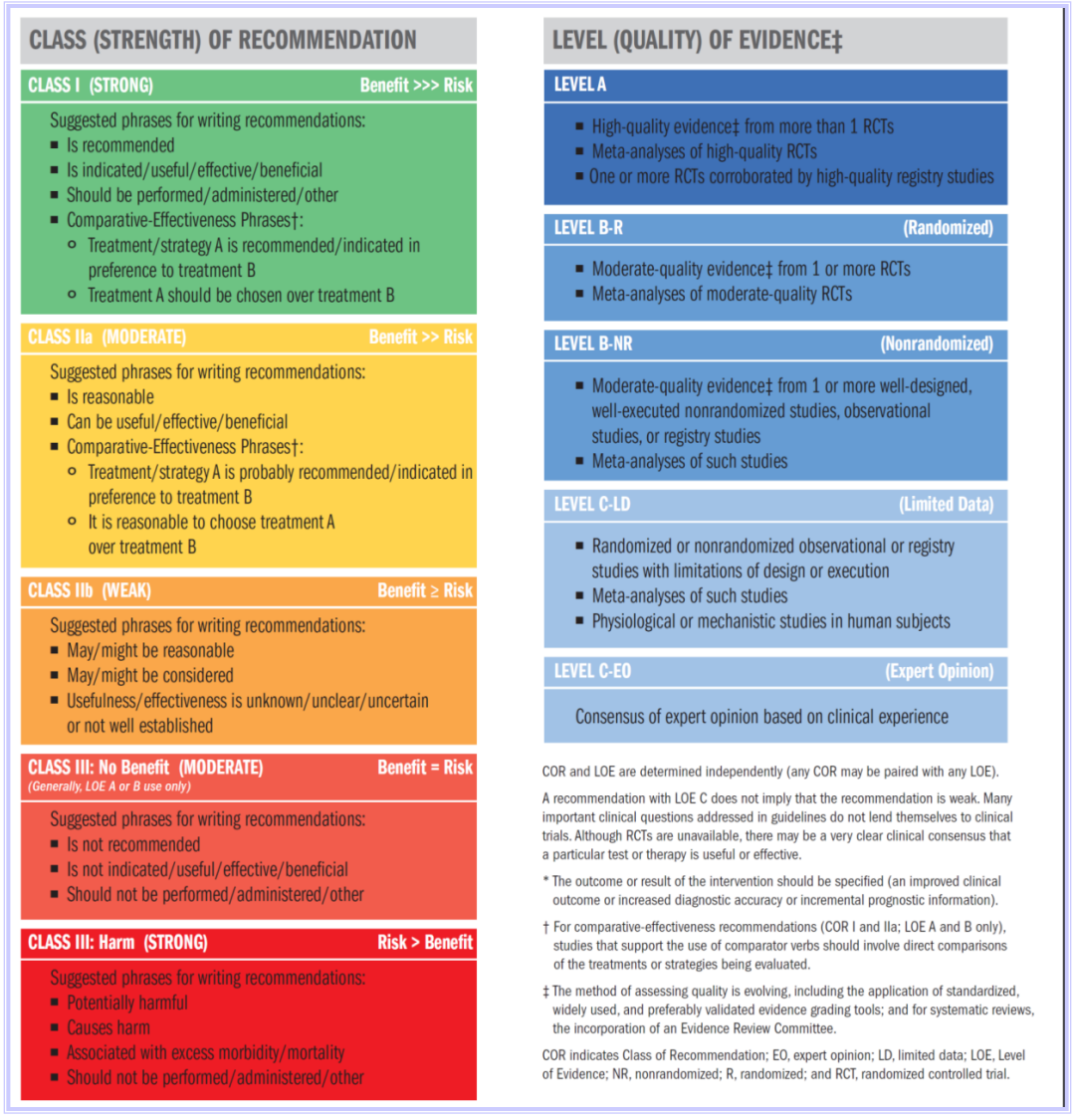
Applying classification of recommendations and level of evidence



CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — Benefit >>> Risk

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — Benefit >> Risk

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — Benefit ≥ Risk

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — Benefit = Risk
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — Risk > Benefit

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCTs
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

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Introduction

Acute Ischemic Stroke (AIS)

- Time critical, unplanned illness
- Early management is key to optimizing outcomes
- New evidence has produced major changes in treatment

This guideline is comprehensive guide to AIS management from symptom onset in the prehospital setting through 2 weeks post-stroke.

Outline

1. Prehospital Stroke Management and Systems of Care
2. Emergency Evaluation
3. Emergency Supportive Care and Treatment
4. In-hospital Supportive Care
5. Treatment of Acute Complications
6. In-hospital Evaluation and Secondary Prevention

Prehospital Stroke Management and Systems of Care

1.1 Prehospital Systems

1.2 EMS Assessment and Management

1.3 EMS Systems

1.4 Hospital Stroke Capabilities

1.5 Hospital Stroke Teams

1.6 Telemedicine

1.7 Organization and Integration of Components

1.8 Establishment of Data Repositories

1.9 Stroke Systems Care Quality Improvement Process

Prehospital Stroke Management and Systems of Care

Increase utilization of acute stroke therapies and improve outcomes via:

- Increased awareness of stroke signs and symptoms
- Maximize Utilization of EMS via 9-1-1
- Optimize prehospital management & triage
- Establish and continually improve quality of care at stroke centers
- Ensure rapid transport across hospitals when necessary

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1.1 Prehospital Systems

Recommendations	COR	LOE
Public health leaders, medical professionals, and others should design and implement public education programs focused on stroke systems and the need to seek emergency care by calling 9-1-1 rapidly. These systems should be sustained over time and reach racial/ethnically, age, and gender diverse populations.	I	B-R
Activation of 9-1-1 by patients or others is strongly recommended. 9-1-1 dispatchers should make stroke a priority dispatch; transport times should be minimized.	I	B-NR
To increase stroke treatment and quality of care, educational stroke programs for physicians, hospital personnel, and EMS are recommended.	I	B-NR

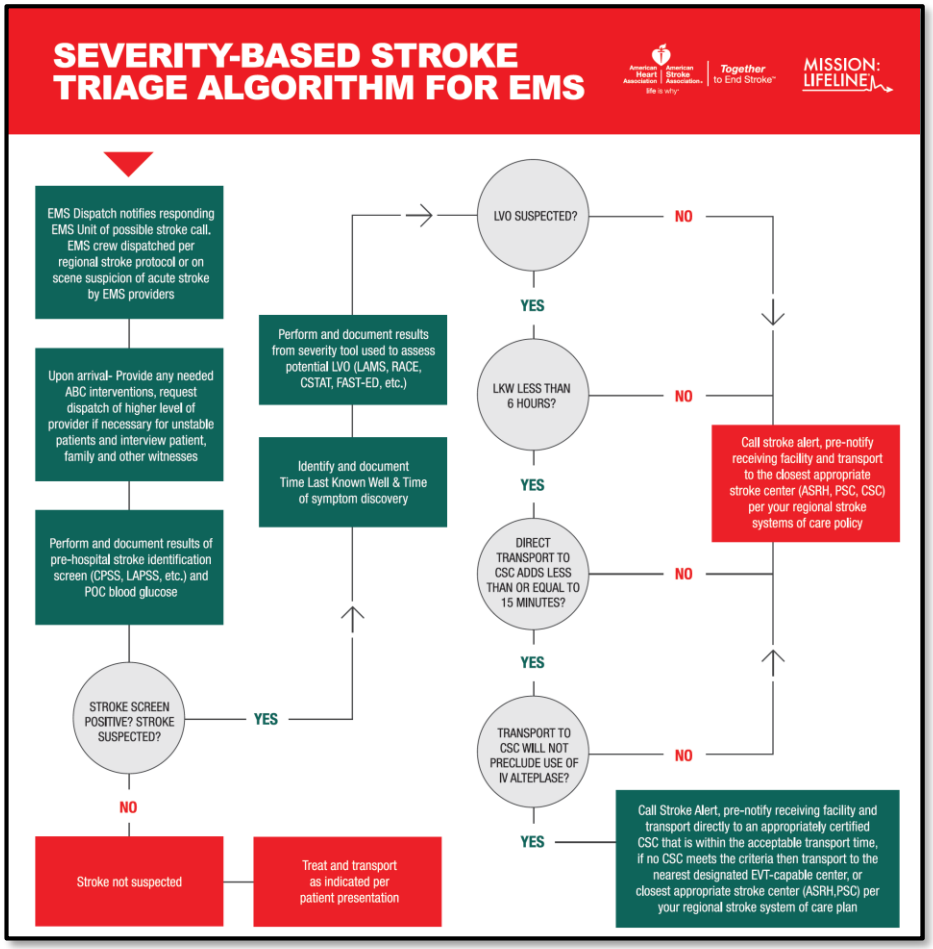
1.2 EMS Assessment and Management

Recommendations	COR	LOE
The use of stroke assessment systems by first aid providers, including EMS dispatchers, is recommended.	I	B-NR
EMS personnel should begin the initial management of stroke in the field. Implementation of a stroke protocol to be used by EMS is strongly encouraged.	I	B-NR
EMS should provide prehospital notification to the receiving hospital that a suspected stroke is en route so hospital resources may be mobilized before arrival.	I	B-NR

1.3 EMS Systems

EMS should develop triage paradigms and protocols:

- Use validated screens for stroke
- Identify regional hospitals that can give IV alteplase and those that can perform thrombectomy
- AHA Mission: Lifeline has proposed a severity based triage algorithm
  - Uncertainty exists over optimal algorithm and optimal prehospital LVO screen
  - Customization of proposed algorithm to account for local factors is needed



1.3 EMS Systems

Recommendations	COR	LOE
EMS leaders, in coordination with local, regional, and state agencies, and with medical authorities and local experts should develop triage paradigms and protocols to ensure that patients with a known or suspected stroke are rapidly identified and assessed by use of a validated and standardized instrument for stroke screening, such as the FAST scale, Los Angeles Prehospital Stroke Screen, or Cincinnati Prehospital Stroke Scale	I	B-NR
Regional systems of care should be developed, consisting of: a) Healthcare facilities that provide initial emergency care including IV alteplase. b) Centers capable of performing endovascular treatment and periprocedural care to which rapid transport can be arranged	I	A
Patients with a positive stroke screen and/or strong suspicion of stroke should be transported rapidly to the closest facility that can capably administer IV alteplase.	I	B-NR
When several IV alteplase-capable hospitals exist within a defined region, the benefit of bypassing the closest to bring the patient to one that offers a higher level of care including thrombectomy, is uncertain. Further research is needed.	IIb	B-NR

1.4 Hospital Stroke Capabilities

Certification of stroke centers by an external body is recommended

- CIHQ, DNV, HFAP, TJC, or state health department

Tiers of Stroke Hospitals have been proposed:

- Acute Stroke Ready Hospitals
- Primary Stroke Centers
- Comprehensive Stroke Centers

1.4 Hospital Stroke Capabilities

Recommendations	COR	LOE
Certification of stroke centers by an independent external body, such as Center for Improvement in Healthcare Quality, Det Norske Veritas, Healthcare Facilities Accreditation Program, and The Joint Commission (TJC),* or a state health department, is recommended. Additional medical centers should seek such certification. *AHA has a cobranded, revenue-generating stroke certification with TJC.	I	B-NR

1.5 Hospital Stroke Teams

Stroke centers should have:

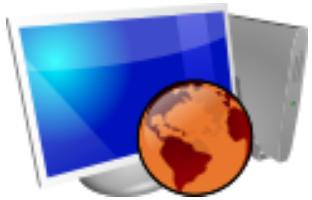
- Organized protocol for emergent evaluation of suspected stroke
- Designated acute stroke team
- Among patients receiving IV alteplase:
  - **Primary goal:** door to needle time of 60 minutes or less in ≥50% of cases
  - Secondary goal door-to-needle time of 45 minutes or less in ≥50% of cases may be reasonable

1.5 Hospital Stroke Teams

Recommendations	COR	LOE
An organized protocol for the emergency evaluation of patients with suspected stroke is recommended.	I	B-NR
It is recommended that DTN time goals be established, with a primary goal of achieving DTN times within 60 minutes in ≥ 50% of AIS patients treated with IV alteplase.	I	B-NR
It may be reasonable to establish a secondary DTN time goal within 45 minutes in ≥ 50% of AIS patients treated with IV alteplase.	IIb	C-EO
Designation of acute stroke teams that include physicians, nurses, and laboratory/radiology personnel is recommended. Patients with stroke should have a careful assessment, including neurologic examination.	I	B-NR
Multicomponent quality improvement initiatives, which include ED education and multidisciplinary teams with access to neurological expertise, are recommended to safely increase IV alteplase treatment.	I	A

1.6 Telemedicine

Telemedical solutions can help to improve care when on-site expertise is not available



- Teleradiology shown to be useful for rapid image interpretation
- Telestroke can be effective for IV alteplase decision making
  - Meta-analysis comparing telestroke to stroke centers showed no difference in mortality or functional outcomes at 3 months
- Telestroke may be reasonable for triaging patients for mechanical thrombectomy
  - A single observational study showed similar rates of reperfusion and functional outcomes between telestroke patients and those admitted directly to a tertiary care center

Prehospital Stroke Management and Systems of Care

1.6 Telemedicine

Recommendations	COR	LOE
For sites without in-house imaging interpretation expertise, FDA approved teleradiology are recommended for timely imaging review.	I	A
Within a telestroke network, FDA approved teleradiology systems are useful for rapid imaging interpretation for IV alteplase decisions.	I	A
Because of the limited distribution and availability of neurological, neurosurgical, and radiological expertise, the use of telemedicine resources and systems can be beneficial and should be supported by healthcare institutions, governments, payers, and vendors of a method to ensure adequate 24/7 coverage and care for AIS.	IIa	C-EO
Telestroke/teleradiology evaluations of AIS patients can be effective for correct IV alteplase eligibility decision making.	IIa	B-R
Administration of IV alteplase guided by telestroke consultations may be as safe and as beneficial as that of stroke centers.	IIb	B-NR
Providing alteplase decision-making support via telephone consultation to community physicians is feasible and safe and may be considered when a hospital has neither access to an in-person stroke team, nor a telestroke system.	IIb	C-LD

1.6 Telemedicine

Recommendations	COR	LOE
Telestroke networks may be reasonable for triaging patients with AIS who may be eligible for inter-facility transfer in order to be considered for mechanical thrombectomy.	IIb	B-NR

1.7 Organization and Integration of Components

Stroke systems must integrate IV alteplase capable and mechanical thrombectomy capable centers

- Thrombectomy requires patients to be at an experienced center
- Noninvasive vascular imaging can select patients for transfer to a thrombectomy capable center
  - Decisions around developing this capability require realistic expectations that account for local resource availability
- Guidelines and protocols must ensure rapid transfer 24/7

1.7 Organization and Integration of Components

Recommendations	COR	LOE
It may be useful for primary stroke centers and other healthcare facilities that provide initial emergency care, including administration of IV alteplase, to develop the capability of performing emergency noninvasive intracranial vascular imaging to most appropriately select patients for transfer for endovascular intervention and to reduce the time to EVT.	IIb	C-LD
Mechanical thrombectomy requires the patient to be at an experienced stroke center with rapid access to cerebral angiography, qualified neurointerventionalists, and comprehensive periprocedural care. Systems should emphasize expeditious assessment and treatment. Outcomes for all patients should be tracked. Facilities are encouraged to define criteria that can be used to credential individuals who can perform safe and timely intra-arterial revascularization procedures.	I	C-EO
All hospitals caring for stroke patients within a stroke system of care should develop, adopt, and adhere to care protocols that reflect current care guidelines as established by national and international professional organizations, state and federal agencies, and laws.	I	C-EO

1.7 Organization and Integration of Components

Recommendations	COR	LOE
Different services within a hospital that may be transferring patients through a continuum of care, as well as different hospitals that may be transferring patients to other facilities, should establish hand-off and transfer protocols and procedures that ensure safe and efficient patient care within and between facilities. Protocols for interhospital transfer of patients should be established and approved beforehand so that efficient patient transfers can be accomplished at all hours of the day and night.	I	C-EO
It may be beneficial for government agencies and third-party payers to develop and implement reimbursement schedules for patients with acute stroke that reflect the demanding care and expertise that such patients require to achieve an optimal outcome, regardless of whether they receive a specific medication or procedure.	IIb	C-EO

1.8-9 Data Repositories and Quality Improvement

Quality Improvement (QI) efforts improve outcomes

- QI efforts across the entire spectrum of care, from initial patient identification prehospital to post-stroke care can improve outcomes.
- Participation in GWTG-Stroke, a data repository, has been shown to improve outcomes after AIS.
- Within hospitals participating in GWTG-Stroke, a multi-disciplinary QI process has also been shown to improve outcomes.
- Stroke severity, as measured by the NIHSS, strongly influences outcomes. Outcome measures should include adjustments for baseline severity.

1.8 Establishment of Data Repositories

Recommendations	COR	LOE
Participation in a stroke data repository is recommended to promote consistent adherence to current treatment guidelines, to allow continuous quality improvement, and to improve patient outcomes.	I	B-NR

1.9 Stroke Systems Care QI Process

Recommendations	COR	LOE
Healthcare institutions should organize a multidisciplinary quality improvement committee to review and monitor stroke care quality benchmarks, indicators, evidence-based practices, and outcomes. The formation of a clinical process improvement team and the establishment of a stroke care data bank are helpful for such quality of care assurances. The data repository can be used to identify gaps/disparities in care; once identified, specific interventions can be initiated to address these gaps/disparities.	I	B-NR
Continuous quality improvement processes, implemented by each major element of a stroke system of care and the system as a whole, can be useful in improving patient care or outcome.	IIa	B-NR
Stroke outcome measures should include adjustments for baseline severity.	I	B-NR

Emergency Evaluation

2.1 Stroke Scales

2.2 Brain Imaging

2.3 Other Diagnostic Tests

2.1 Stroke Scales

Standardized severity scales quantify neurologic deficit.

- Facilitate communication
- Identify patients for acute treatments
- Monitor for improvement or worsening

National Institute of Health Stroke Scale

- Preferred severity scale
  - Rapid
  - Accurate
  - Reliable
  - Can be performed by broad spectrum of providers

2.1 Stroke Scales

NIH Stroke Scale

Item	Title	Responses and Scores
1a.	Level of consciousness	0—alert 1—drowsy 2—obtunded 3—coma/unresponsive
1b.	Orientation questions (2)	0—answers both correctly 1—answers one correctly 2—answers neither correctly
1c.	Response to commands (2)	0—performs both tasks correctly 1—performs one task correctly 2—performs neither
2.	Gaze	0—normal horizontal movements 1—partial gaze palsy 2—complete gaze palsy
3.	Visual fields	0—no visual field defect 1—partial hemianopia 2—complete hemianopia 3—bilateral hemianopia
4.	Facial movement	0—normal 1—minor facial weakness 2—partial facial weakness 3—complete unilateral palsy
5.	Motor function (arm) a. Left b. Right	0—no drift 1—drift before 10 seconds 2—falls before 10 seconds 3—no effort against gravity 4—no movement
6.	Motor function (leg) a. Left b. Right	0—no drift 1—drift before 5 seconds 2—falls before 5 seconds 3—no effort against gravity 4—no movement
7.	Limb ataxia	0—no ataxia 1—ataxia in 1 limb 2—ataxia in 2 limbs
8.	Sensory	0—no sensory loss 1—mild sensory loss 2—severe sensory loss
9.	Language	0—normal 1—mild aphasia 2—severe aphasia 3—mute or global aphasia
10.	Articulation	0—normal 1—mild dysarthria 2—severe dysarthria
11.	Extinction or inattention	0—absent 1—mild loss (1 sensory modality lost) 2—severe loss (2 modalities lost)

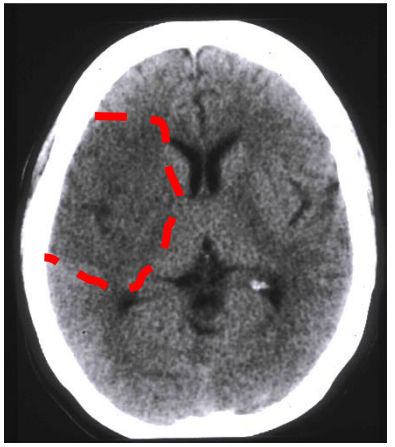
2.1 Stroke Scales

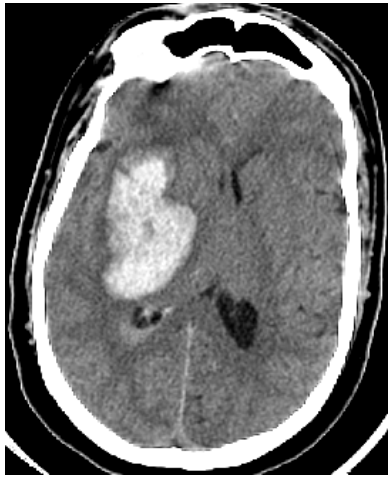
Recommendations	COR	LOE
The use of a stroke severity rating scale, preferably the NIHSS, is recommended.	I	B-NR

2.2 Brain Imaging

Urgent brain imaging is required in suspected stroke

- All should be imaged ≤ 20min of ED arrival
  - The benefit of IV alteplase and thrombectomy are time dependent
  - Reducing time from arrival to imaging can improve door to needle time
- Non-contrast CT is adequate in most cases
  - Primary goal is to exclude ICH
  - Routine MRI is not cost-effective
    - MRI will only change management in minority of cases
    - Inadequate data to establish who requires MRI

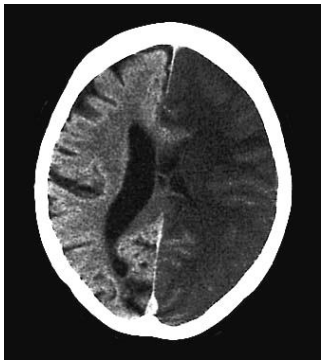


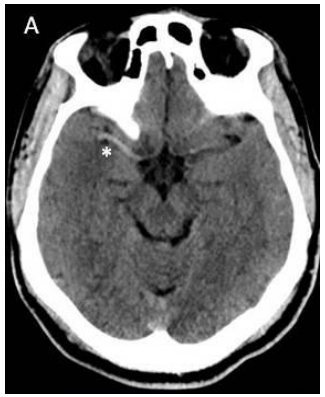


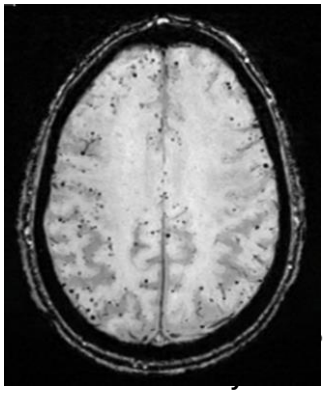
2.2 Brain Imaging

Studies show:

- Insufficient evidence to withhold treatment with alteplase based on NCCT hypodensity
  - No interaction between NCCT hypodensity (ASPECTS score) and functional outcome in RCT pooled-analysis
    - NINDS tPA trial and IST-3 did not exclude patients based on degree of CT hypoattenuation
- Should not withhold alteplase based on presence of a hyperdense MCA sign
- Routine use of MRI to exclude cerebral microbleeds (CMB) is not recommended
  - CMBs are associated with increased risk of sICH
  - BUT, rate of sICH in those with CMB is ~6%, which is similar to the risk of sICH overall in the NINDS tPA trial.



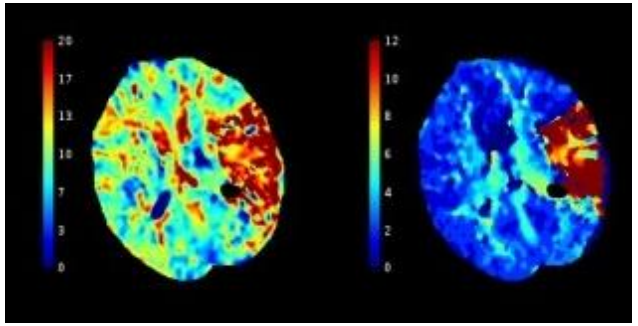


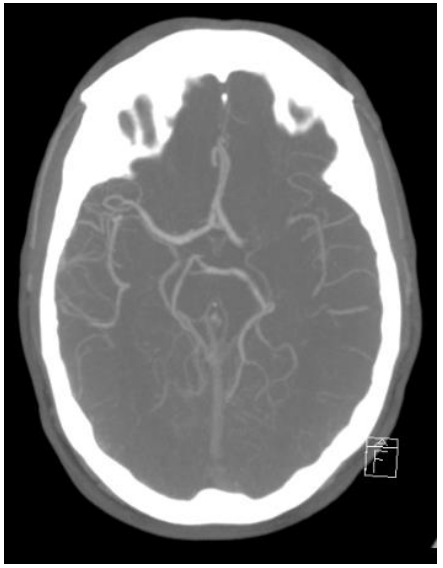


2.2 Brain Imaging

Advanced Imaging:

- Vascular and perfusion imaging should not delay alteplase treatment
- Use of imaging to select AIS cases for alteplase treatment with uncertain symptom duration is not recommended
- For patients who meet criteria for endovascular treatment, it is reasonable to proceed with CTA
  - Clinical prediction of LVO is imprecise.
  - NIHSS is best instrument, but even cut-point of ≥6 will miss cases of LVO
  - No need to wait for creatinine

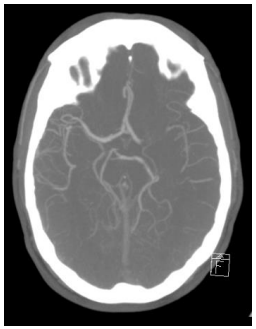


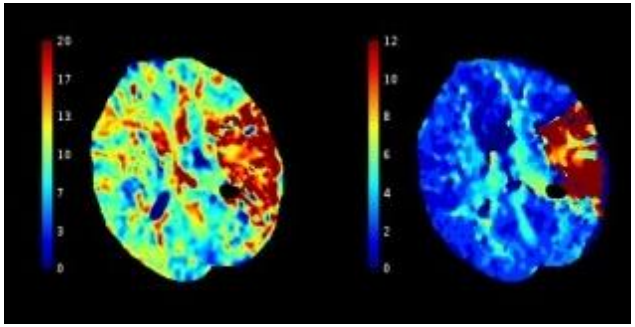


2.2 Brain Imaging

Advanced imaging can select patients for thrombectomy 6-24 hours from last normal.

- Two recent RCTs
  - CT Perfusion, or MRI/MR perfusion to select patients with salvageable brain tissue, despite prolonged time from last normal
  - Randomized to thrombectomy vs no-thrombectomy
  - Both trials showed ***large*** benefit for thrombectomy
    - DAWN Trial: Good outcome (mRS 0-2) in 49% vs. 13%
    - DEFUSE 3 Trial: Good outcome (mRS 0-2) in 45% vs. 17%





Emergency Evaluation

2.2 Brain Imaging

Recommendations	COR	LOE
All patients admitted to the hospital with suspected acute stroke should receive brain imaging evaluation on arrival. In most cases, non-contrast CT (NCCT) will provide the necessary information to make decisions about acute management.	I	B-NR
Systems should be established so that brain imaging studies can be performed within 20 minutes of arrival in the ED in at least 50% of patients who may be candidates for IV alteplase and/or mechanical thrombectomy.	I	B-NR
There remains insufficient evidence to identify a threshold of acute CT hypoattenuation severity or extent that affects treatment response to IV alteplase. The extent and severity of acute hypoattenuation or early ischemic changes should not be used as a criterion to withhold therapy for such patients who otherwise qualify.	III (NB)	B-R
The CT hyperdense MCA sign should not be used as a criterion to withhold IV alteplase from patients who otherwise qualify.	III (NB)	B-R

Emergency Evaluation

2.2 Brain Imaging

Recommendations	COR	LOE
Routine use of magnetic resonance imaging **(**MRI) to exclude cerebral microbleeds (CMBs) before administration of IV alteplase is not recommended.	III (NB)	B-NR
Use of imaging criteria to select ischemic stroke patients who awoke with stroke or have unclear time of symptom onset for treatment with IV alteplase is not recommended outside of a clinical trial.	III (NB)	B-NR
Multimodal CT and MRI, including perfusion imaging, should not delay administration of IV alteplase.	III (Harm)	B-NR
For patients who otherwise meet criteria for endovascular treatment, a noninvasive intracranial vascular study is recommended during the initial imaging evaluation of the acute stroke, but should not delay IV alteplase if indicated. For patients who qualify for IV alteplase, initiating IV alteplase before non-invasive vascular imaging is recommended for patients who have not had it as part of their initial imaging assessment. Non-invasive intracranial vascular imaging should then be obtained as quickly as possible.	I	A

Emergency Evaluation

2.2 Brain Imaging

Recommendations	COR	LOE
For patients who otherwise meet criteria for EVT, it is reasonable to proceed with CTA if indicated in patients with suspected intracranial LVO before obtaining a serum creatinine concentration in patients without a history of renal impairment.	IIa	B-NR
In patients who are potential candidate for mechanical thrombectomy, imaging of the extra-cranial carotid and vertebral arteries, in addition to the intracranial circulation, is reasonable to provide useful information regarding patient eligibility and endovascular procedural planning.	IIa	C-EO
Additional imaging beyond CT and CTA or MRI and MRA, such as perfusion studies, for selecting patients for mechanical thrombectomy <6 hours is not recommended.	III (NB)	B-R

2.2 Brain Imaging

Recommendations	COR	LOE
In selected patients with AIS within 6-24 hours of last known normal who have large vessel occlusion in the anterior circulation, obtaining CT perfusion, diffusion weighted MRI or MRI perfusion is recommended to aid in patient selection for mechanical thrombectomy, but only when imaging and other eligibility criteria from RCTs showing benefit are being strictly applied in selecting patients for mechanical thrombectomy.	I	A
It may be reasonable to incorporate collateral flow status into clinical decision making in some candidates to determine eligibility for mechanical thrombectomy.	IIb	C-LD

2.3 Other Diagnostic Tests

Other diagnostic testing should be individualized

- **Critical not to delay** initiation of IV alteplase
  - Only assessment of glucose must precede IV alteplase
  - Baseline ECG and troponins are recommended, but should not delay treatment
  - Utility of chest radiographs is uncertain.
    - Cohort study comparing AIS patients with and without CXR showed longer DTN time in those with a CXR, no difference in cardiopulmonary events

Emergency Evaluation

2.3 Other Diagnostic Tests

Recommendations	COR	LOE
Only assessments of blood glucose must precede the initiation of IV alteplase in all patients.	I	B-R
Baseline ECG assessment is recommended in patients presenting with AIS, but should not delay initiation of IV alteplase.	I	B-NR
Baseline troponin assessment is recommended in patients presenting with AIS, but should not delay initiation of IV alteplase.	I	B-NR
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 IV alteplase.	IIb	B-NR

Emergency Supportive Care and Treatment

3.1 Airway, Breathing, and Oxygenation

3.2 Blood Pressure

3.3 Temperature

3.4 Blood Glucose

3.5 Intravenous Alteplase

3.6 Other IV Thrombolytics and Sonothrombolysis

3.7 Mechanical Thrombectomy

3.8 Other Endovascular Treatments

3.9 Antiplatelet Treatment

3.10 Anticoagulants

3.11 Volume Expansion/Hemodilution, Vasodilators, Hemodynamic Augmentation

3.12 Neuroprotective Agents

3.13 Emergency Carotid Revascularization

3.14 Other

3.1 Airway, Breathing, and Oxygenation

Recommendations	COR	LOE
Airway support and ventilatory assistance are recommended for the treatment of patients with acute stroke who have decreased consciousness or who have bulbar dysfunction that causes compromise of the airway.	I	C-EO
Supplemental oxygen should be provided to maintain oxygen saturation >94%.	I	C-LD
Supplemental oxygen is not recommended in nonhypoxic patients.	III (NB)	B-R
Hyperbaric oxygen (HBO) is not recommended for patients with AIS except when caused by air embolization.	III (NB)	B-NR

3.2 Blood Pressure

- Ideal blood pressure in AIS remains unknown
  - Observational studies variable
- No clear data on fluid choice, volume, or duration
- BP with IV alteplase:
  - BP <185/110 prior to administration
  - BP <180/105 for 24 hours after administration
  - Target based on BPs in RCT of IV alteplase
    - Some data to suggest hemorrhage risk higher with higher BPs and BP variability, but exact BP that increases risk unknown
- BP with Intra-arterial Therapy
  - Optimal BP unknown
  - RCTs largely excluded BP >185/110
  - Reasonable to use <185/110 as guideline

3.2 Blood Pressure

Recommendations	COR	LOE
Hypotension and hypovolemia should be corrected to maintain systemic perfusion levels necessary to support organ function.	I	C-EO
Patients who have elevated BP and are otherwise eligible for treatment with IV alteplase should have their BP carefully lowered so that their systolic BP is <185 mm Hg and their diastolic BP is <110 mm Hg before IV fibrinolytic therapy is initiated.	I	B-NR
Until additional data become available, in patients for whom intra-arterial therapy is planned and who have not received IV thrombolytic therapy, it is reasonable to maintain BP ≤185/110 mm Hg before the procedure.	IIa	B-R
The usefulness of drug-induced hypertension in patients with AIS is not well established.	IIb	C-LD

3.2 Blood Pressure

BP treatment options in AIS patients eligible for reperfusion:

- *Labetalol:* 10-20mg IV over 1-2 min, may repeat x1
  - If continues to be elevated, 10mg IV x1 followed by infusion 2-8mg/min
- *Nicardipine:* 5mg/h IV, titrate 2.5mg/h every 5-15 min (max 15 mg/h)
- *Clevidipine:* 1-2mg/h IV, double dose every 2-5 minutes to titrate (max 21 mg/h)
- Other agents may be considered (hydralazine, enalaprilat)

Monitoring BP after reperfusion:

- Every 15 min x 2 hours
- Every 30 min x 6 hours
- Every 60 min x 16 hours

3.3 Temperature

- Peak temperature in first 24 hours <37°C and >39°C associated with increased risk of in hospital death compared to normothermia
  - Retrospective cohort study of 9366 pts w/ AIS
- Hypothermia is a promising strategy but benefit not proven and studies suggest increased risk of infection

Recommendations	COR	LOE
Sources of hyperthermia (temperature >38°C) should be identified and treated. Antipyretic medications should be administered to lower temperature in hyperthermic patients with stroke.	I	C-EO
The benefit of induced hypothermia for treating patients with ischemic stroke is not well established. Hypothermia should be offered only in the context of ongoing clinical trials.	IIb	B-R

3.4 Blood Glucose

Recommendations	COR	LOE
Evidence indicates that persistent in-hospital hyperglycemia during the first 24 hours after AIS 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 to 180 mg/dL and to closely monitor to prevent hypoglycemia in patients with AIS.	IIa	C-LD
Hypoglycemia (blood glucose <60 mg/dL) should be treated in patients with AIS.	I	C-LD

3.5 Intravenous Alteplase

- Benefit of IV alteplase well established in RCTs and confirmed by extensive experience
  - Alteplase is beneficial regardless of age and stroke severity
    - Although ECASS-III excluded age >80, patients on warfarin regardless of INR, patients with NIHSS >25, and patients with combined diabetes and prior stroke, analysis of available data indicates these exclusion criteria may not be justified in practice
- Eligibility criteria have evolved over time as usefulness and risks better established
- If patient or representative not available for consent, justifiable to proceed without consent in an otherwise eligible patient

3.5 Intravenous Alteplase

Recommendations	COR	LOE
IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is recommended for selected patients who may be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined to determine patient eligibility.	I	A
IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is also recommended for selected patients who can be treated within 3 and 4.5 hours of ischemic stroke symptom onset or patient last known well. Physicians should review the criteria outlined to determine patient eligibility.	I	B-R
IV alteplase may be reasonable for mild stroke patients in 3-4.5 hr window. Treatment risks should be weighed against possible benefits.	IIb	B-NR

Eligibility criteria reviewed on subsequent slides

3.5 Intravenous Alteplase: Cortical Microbleeds

- Clinically silent CMBs in 25% of IV alteplase patients
- No randomized trials have directly addressed tPA in those with CMBs
- Data from two meta-analyses showed sICH more common with CMBs, but not higher than NINDS tPA trial
  - Rates higher if >10 CMBs (40%), but small numbers
  - Functional outcomes worse in patients with CMBs
  - Unclear if these negative effects fully negate benefit of thrombolysis

Recommendations	COR	LOE
In otherwise eligible patients who had had a previously demonstrated small number (1-10) of cortical microbleeds on MRI, administration of IV alteplase is reasonable.	IIa	B-NR
In otherwise eligible patients who had had a previously demonstrated high burden of CMBs (>10) on MRI, treatment with IV alteplase may be associated with an increased risk of sICH and the benefits of treatment are uncertain. Treatment may be reasonable if there is potential for substantial benefit.	IIb	B-NR

3.5 Intravenous Alteplase: Sickle Cell Disease

- IV alteplase can be beneficial for patients with sickle cell disease and AIS
  - Case-control analysis of GWTG-Stroke found no significant impact on safety or outcomes in treatment with IV alteplase among 832 cases with sickle cell disease.

Recommendations	COR	LOE
IV alteplase for adults presenting with an AIS with known sickle cell disease can be beneficial.	IIa	B-NR

3.5 Intravenous Alteplase: Other Antithrombotics

Recommendations	COR	LOE
Abciximab should not be administered concurrently with IV alteplase	III (Harm)	B-R
IV alteplase should not be administered to patients who have received a treatment dose of low molecular weight heparin (LMWH) within the previous 24 hours. • *The recommendation refers to full treatment doses and not to prophylactic doses*	III (Harm)	B-NR

3.5 Intravenous Alteplase: Pre-Administration

Recommendations	COR	LOE
The potential risks should be discussed during thrombolysis eligibility deliberation and weighed against the anticipated benefits during decision making.	I	C-EO
Given the extremely low risk of unsuspected abnormal platelet counts or coagulation studies in a population, it is reasonable that urgent IV alteplase treatment not be delayed while waiting for hematologic or coagulation testing if there is no reason to suspect an abnormal test.	IIa	B-NR
Treating clinicians should be aware that hypoglycemia and hyperglycemia may mimic acute stroke presentations and determine blood glucose levels before IV alteplase initiation. IV alteplase is not indicated for nonvascular conditions.	III (NB)	B-NR
Because time from onset of symptoms to treatment has such a powerful impact on outcomes, treatment with IV alteplase should not be delayed to monitor for further improvement.	III (Harm)	C-EO
In patients eligible for IV alteplase, benefit of therapy is time dependent, and treatment should be initiated as quickly as possible.	I	A

3.5 Intravenous Alteplase: Post-Administration

Recommendations	COR	LOE
In patients undergoing fibrinolytic therapy, physicians should be prepared to treat potential emergent adverse effects, including bleeding complications and angioedema that may cause partial airway obstruction.	I	B-NR
BP should be maintained <180/105 mm Hg for at least the first 24 hours after IV alteplase treatment.	I	B-NR
The risk of antithrombotic therapy within the first 24 hours following IV alteplase (with or without EVT) is uncertain. Use might be considered in the presence of concomitant conditions for which such treatment given in the absence of IV alteplase is known to provide substantial benefit or withholding such treatment is known to cause substantial risk.	IIb	B-NR

3.5 Intravenous Alteplase: Indications

Alteplase Dosing: 0.9mg/kg, maximum 90mg, over 60 minutes with initial 10% given as a bolus over 1 minute.

Indications (Class I): Within 3 hours	
Age	≥18 years of age; equally recommended for <80 and >80 years of age under 3 hours.
Severity	Recommended for severe strokes and for mild but disabling strokes.

Indications (Class I): 3-4.5 hours	
Age, Severity and Other Considerations	<80 and without history of both diabetes and prior stroke, NIHSS <25, not on OACs, and without imaging evidence of ischemia of >1/3 of the MCA territory.

3.5 Intravenous Alteplase: Indications

Indications (Class I): Overall	
Urgency	Treatment should be initiated as quickly as possible. Time to treatment strongly associated with outcomes.
BP	Recommended in those whose BP can be safely lowered to <185/110 prior to starting IV alteplase.
Glucose	Recommended in otherwise eligible patients with glucose >50 mg/dL.
CT	Recommended in setting of mild to moderate early ischemic changes on NCCT.
Prior Antiplatelets	Recommended in those taking single antiplatelet drug; benefit outweighs possible small increased risk of sICH.
End-stage renal disease	Recommended in those with normal aPTT; those with elevated aPTT might be at higher risk of hemorrhage.

3.5 Intravenous Alteplase: Contraindications

Contraindications (Class III Overall)	
Time of onset	Not recommended if unclear time of onset or >3 or 4.5 hours Not recommended in wake-up strokes last normal >3 or 4.5 hours.
CT	Not recommended if CT shows acute intracranial hemorrhage Insufficient evidence to identify clear threshold for hypoattenuation severity or extent that affects treatment response, but treating with IV alteplase not recommended with extensive hypoattenuation.
AIS within 3 months	May be harmful in patients with AIS within 3 months Potential for increased risk of hemorrhage and associated morbidity and mortality exists but not well established.
Severe head trauma	Contraindicated within 3 months given risk of bleeding.
Intracranial/ Intraspinal surgery	Potentially harmful within 3 months of procedure.
History of Intracranial Hemorrhage	Potentially harmful in patients with a history of ICH.
Subarachnoid Hemorrhage	Contraindicated in patients presenting with signs/symptoms most consistent with SAH.
GI malignancy or GI bleed	GI malignancy or GI bleed within 21 days is high risk.
Coagulopathy	IV alteplase should not be administered if platelets <100,000/mm3, INR >1.7, aPTT >40, or PT >15 as safety and efficacy unknown.

3.5 Intravenous Alteplase: Contraindications

Contraindications (Class III): Continued	
Low-molecular-weight Heparin	Should not be administered if treatment dose LMWH given within 24 hours.
Thrombin or Xa inhibitors	Use not fully established, but may be harmful. IV alteplase should not be administered in those taking these agents unless no dose given in prior 48 hours or laboratory tests (aPTT, INR, platelets, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assays) are normal.
Glycoprotein IIb/IIIa inhibitors	Should not be administered concurrently with IV alteplase outside of clinical trials.
Infective Endocarditis	IV alteplase should not be administered due to increased risk of hemorrhage.
Aortic arch dissection	Potentially harmful and should not be administered.
Intra-axial intracranial neoplasm	IV alteplase potentially harmful.

3.5 Intravenous Alteplase: Additional Recommendations

Additional Recommendations (Class II)	
Extended 3-4.5 hour window	Safe in patients >80 and may be as effective as in younger patients Safe and may be beneficial in those taking warfarin with INR <1.7 May be as effective in those with prior stroke and diabetes and may be a reasonable option.
Severity	Treating mild, non-disabling stroke symptoms may be considered in both 0-3 and 3-4.5 hour windows weigh risks against possible benefits. Benefit of treating severe strokes (NIHSS >25) in 3-4.5 hour window uncertain.
Pre-existing disability	Does not seem to increase risk of sICH but may be associated with less improvement and higher mortality. Treatment may be reasonable
Early improvement	Treatment reasonable if patients remain moderately impaired and potentially disabled.
Seizure at onset	Reasonable if evidence suggests residual impairments secondary to stroke, not postictal phenomenon.
Blood glucose	Treatment in those initially presenting with glucose <50 or >400 that subsequently normalized and are otherwise eligible may be reasonable.
Coagulopathy	Safety and efficacy in those with bleeding diathesis or coagulopathy unknown, can consider case-by-case. Reasonable in patients on warfarin with INR ≤1.7 or PT <15 sec.

3.5 Intravenous Alteplase: Additional Recommendations

Additional Recommendations (Class II)	
Dural Puncture	May be considered, even when lumbar puncture within 7 days.
Arterial Puncture	Safety and efficacy within 7 days of puncture at noncompressible site is uncertain.
Recent major trauma	Within 14 days, not involving head, may be carefully considered.
Recent major surgery	May be carefully considered within 14 days weighing surgical-site bleeding risk against anticipated benefits.
GI/GU bleeding	Low risk in setting of past GI/GU bleeding >21 days prior.
Menstruation	Probably indicated without history of menorrhagia. If history of vaginal bleeding associated with significant anemia, gynecologist consult probably indicated.
Extracranial cervical dissections	Reasonably safe and probably recommended within 4.5 hours.
Intracranial arterial dissection	Usefulness and risk unknown, uncertain, and not well established
Unruptured intracranial aneurysms	Small or moderate-sized aneurysms (<10 mm), reasonable and probably recommended. Giant unruptured and unsecured aneurysms not well established but may be considered based on severity of stroke.
Intracranial Vascular Malformations	Usefulness and risk not well established. Because of increased risk of ICH, may be considered based on stroke severity.

3.5 Intravenous Alteplase: Additional Recommendations

Additional Recommendations (Class II): Cardiac Disease	
Cortical Microbleeds	Treatment is reasonable in otherwise eligible patients with small number (1-10) of CMBs. Treatment may be associated with increased risk of sICH in patients with high burden of CMBs (>10), may be reasonable if there is potential for substantial benefit.
Extra-axial intracranial neoplasms	Probably recommended.
Acute MI	For concurrent AIS and MI, treat at cerebral ischemia dose, then coronary angioplasty and stenting if indicated.
Recent MI (within 3 months)	Reasonable if non-STEMI. Also reasonable if STEMI involving right or inferior myocardium. May be reasonable if STEMI involving left anterior myocardium.
Other cardiac diseases	May be reasonable in acute pericarditis if major stroke. Uncertain benefit in acute pericarditis if moderate stroke. May be reasonable with LA or LV thrombus if major stroke. Uncertain benefit with LA or LV thrombus if moderate stroke. May be reasonable with cardiac myxoma and major stroke. May be reasonable with papillary fibroelastoma and major stroke

3.5 Intravenous Alteplase: Additional Recommendations

Additional Recommendations (Class II): Other Considerations	
Procedural stroke	Reasonable for stroke as a complication of cardiac or cerebral angiographic procedures.
Systemic malignancy	Not well established. May be of benefit if reasonable (>6 months) life expectancy.
Pregnancy	May be considered for moderate or severe stroke if benefits exceed risks of uterine bleeding. Safety and efficacy in early postpartum period (<14 days) not well established.
Ophthalmological conditions	Reasonable in those with history of diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmologic conditions, weigh risk of vision loss with benefit.
Sickle cell disease	Can be beneficial.
Illicit drug use	Reasonable in instances of illicit drug use without other exclusions.
Stroke mimics	Risk of hemorrhage in stroke mimics quite low, thus, reasonable to start treatment rather than delay for additional diagnostic studies.

Management of sICH after IV Alteplase

- Stop alteplase infusion
- CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match
- STAT non-enhanced head CT
- Cryoprecipitate (includes factor VIII)
  - 10 units over 10-30 minutes
  - If fibrinogen <200 mg/dL, administer additional dose
- Tranexamic acid (TXA) 1,000 mg IV infused over 10 minutes or ε-aminocaproic acid (EACA) 4-5 g over 1 hour, followed by 1 g IV until bleeding controlled
- Hematology and Neurosurgery consults
- Supportive therapy: BP management, ICP, CPP, MAP, temperature, and glucose control

Management of Angioedema after IV Alteplase

- Maintain airway
  - Intubation may not be necessary if edema limited to anterior tongue and lips
  - Edema of larynx, palate, floor of mouth, or oropharynx with rapid progression poses higher risk of requiring intubation
  - Awake, fiber optic intubation optimal
    - Nasal-tracheal intubation poses risk of epistaxis
- Discontinue IV alteplase and hold ACEIs
- Administer IV methylprednisolone 125 mg
- Administer IV diphenhydramine 50 mg
- Administer ranitidine 50 mg IV or famotidine 20 mg IV
- Epinephrine (0.1%) 0.3 ml subcutaneously or nebulizer 0.5 ml if further increase in angioedema
- Agents used in hereditary angioedema and ACE-I related angioedema
  - Incatibant, selective bradykinin B2 receptor antagonist, 3 ml (30 mg) subcutaneously in abdominal area, can be administered at intervals of 6 hours
  - Plasma-derived C1 esterase inhibitor (20 IU/kg)

3.6 Other IV Thrombolytics and Sonothrombolysis

IV Tenecteplase

- Administered as a 0.4mg/kg single IV bolus
- 3 phase II and 1 phase III trials comparing to alteplase
  - Appears to be similarly safe
  - Unclear if it is as or more effective
  - Largest trial of tenecteplase vs. alteplase:
    - 1100 subjects
    - Minor deficits, with median NIHSS 4 and no LVO
    - Failed to show superiority
    - Similar safety and efficacy between treatments

3.6 Other IV Thrombolytics and Sonothrombolysis

Recommendations	COR	LOE
The benefit of IV defibrinogenating agents and of IV fibrinolytic agents other than alteplase and tenecteplase is unproven; therefore, their administration is not recommended outside a clinical trial.	III (NB)	B-R
Tenecteplase administered as a 0.4-mg/kg single IV bolus has not been proven to be superior or noninferior to alteplase but might be considered as an alternative to alteplase in patients with minor neurological impairment and no major intracranial occlusion.	IIb	B-R
The use of sonothrombolysis as adjuvant therapy with IV thrombolysis is not recommended.	III (NB)	B-R

3.7 Mechanical Thrombectomy

Multiple randomized trials have shown thrombectomy benefit, up to 24 hours after symptom onset.

- MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, EXTEND-IA, THRACE, DAWN, DEFUSE 3 Trials
- Benefit was consistent across age groups
- Patient selection criteria varies based on time
  - 6-24 hours since last normal, advanced imaging with CT perfusion or MRI/MR Perfusion is necessary to select patients
- Reperfusion to TICI 2b/3 should be achieved as early as possible
  - Better outcomes with faster times to reperfusion
- Stent retrievers are preferred devices

3.7 Mechanical Thrombectomy: Alteplase

- **Eligible patients should receive IV alteplase even if thrombectomy is being considered.**
- **Proceed to thrombectomy immediately after alteplase**
  - **Benefits of thrombectomy are time-dependent and treatment delays may worsen outcomes**

Recommendations	COR	LOE
Patients eligible for IV alteplase should receive it even if endovascular treatments being considered	I	A
In patients under consideration for mechanical thrombectomy, observation after IV alteplase to assess for clinical response should not be performed.	III (Harm)	B-R

General Supportive Care and Emergency Treatment

3.7 Mechanical Thrombectomy: within 6 hours

Recommendations	COR	LOE
Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.	I	A
Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the MCA segment 2 (M2) or MCA segment 3 (M3) portion of the MCAs.	IIb	B-R
Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries.	IIb	C-EO
Although its benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score >1, ASPECTS <6, or NIHSS score <6, and causative occlusion of the ICA or proximal MCA (M1). Additional randomized trial data are needed.	IIb	B-R

3.7 Mechanical Thrombectomy: Over 6 hours

DAWN and DEFUSE 3 Trials

- CT Perfusion, or MRI/MR perfusion to select patients with salvageable brain tissue, despite prolonged time from last normal
- Randomized to thrombectomy vs no-thrombectomy
- Both trials showed ***large*** benefit for thrombectomy
  - DAWN Trial: Good outcome (mRS 0-2) in 49% vs. 13%
  - DEFUSE 3 Trial: Good outcome (mRS 0-2) in 45% vs. 17%

Recommendations	COR	LOE
In selected patients with AIS onset within 6-16 hours, anterior circulation large vessel occlusion, and who meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A
In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa	B-R

3.7 Mechanical Thrombectomy: Procedure Guidelines

Recommendations	COR	LOE
The technical goal of the thrombectomy procedure should be reperfusion to a modified Thrombolysis in Cerebral Infarction (mTICI) 2b/3 angiographic result to maximize the probability of a good functional clinical outcomes.	I	A
As with IV alteplase, reduced time from symptom onset to reperfusion with endovascular therapies is highly associated with better clinical outcomes. To ensure benefit, reperfusion to TICI grade 2b/3 should be achieved as early as possible within the therapeutic window.	I	B-R
Use of stent retrievers is indicated in preference to the MERCI device.	I	A
The use of mechanical thrombectomy devices other than stent retrievers as first-line devices for mechanical thrombectomy may be reasonable in some circumstances, but stent retrievers remain the first choice.	IIb	B-R
The use of a proximal balloon guide catheter or a large-bore distal-access catheter, rather than a cervical guide catheter alone, in conjunction with stent retrievers may be beneficial. Future studies should examine which systems provide the highest recanalization rates with the lowest risk for nontarget embolization.	IIa	C-LD
Use of salvage technical adjuncts including intra-arterial thrombolysis may be reasonable to achieve mTICI 2b/3 angiographic results.	IIb	C-LD
EVT of tandem occlusions (both extracranial and intracranial occlusions) at the time of thrombectomy may be reasonable.	IIb	B-R
It is reasonable to select an anesthetic technique during endovascular therapy for AIS on the basis of individualized assessment of patient risk factors, technical performance of the procedure, and other clinical characteristics. Further randomized trial data are needed.	IIa	B-R

3.7 Mechanical Thrombectomy: Blood Pressure

- Limited data, no RCTs specifically for BP in thrombectomy
- Data from existing trials:
  - Majority of trials in <6hr period enrolled patients post-tPA, thus BP ≤180/105 mm Hg for first 24 hours
    - ESCAPE protocol stated SBP ≥ 150 mm Hg probably useful in maintaining collateral flow while vessel occluded
    - DAWN protocol recommended SBP <140mm Hg for 24 hours in reperfused patients

Recommendations	COR	LOE
In patients who undergo mechanical thrombectomy, it is reasonable to maintain the BP ≤180/105 mm Hg during and for 24 hours after the procedure.	IIa	B-NR
In patients who undergo mechanical thrombectomy with successful reperfusion, it might be reasonable to maintain BP at a level <180/105 mm Hg.	IIb	B-NR

3.8 Other Endovascular Treatments

Recommendations	COR	LOE
Initial treatment with intra-arterial thrombolysis is beneficial for carefully selected patients with major ischemic strokes of <6 hours' duration caused by occlusions of the MCA.	I	B-R
Regarding the previous recommendation about intra-arterial thrombolysis, these data are derived from clinical trials that no longer reflect current practice, including the use of fibrinolytic drugs that are not available. A clinically beneficial dose of intraarterial alteplase is not established, and alteplase does not have US Food and Drug Administration approval for intra-arterial use. As a consequence, mechanical thrombectomy with stent retrievers is recommended over intra-arterial thrombolysis as first-line therapy.	I	C-EO
Intra-arterial thrombolysis initiated within 6 hours of stroke onset in carefully selected patients who have contraindications to the use of IV alteplase might be considered, but the consequences are unknown.	IIb	C-EO

3.9 Antiplatelet Treatment: Aspirin

Recommendations	COR	LOE
Administration of aspirin is recommended in patients with AIS within 24 to 48 hours after onset. For those treated with IV alteplase, aspirin administration is generally delayed until 24 hours later but might be considered in the presence of concomitant conditions for which such treatment given in the absence of IV alteplase is known to provide substantial benefit or withholding such treatment is known to cause substantial risk.	I	A
Aspirin is not recommended as a substitute for acute stroke treatment in patients who are otherwise eligible for IV alteplase or mechanical thrombectomy.	III (NB)	B-R

3.9 Antiplatelet Treatment: Other

Recommendations	COR	LOE
The efficacy of IV tirofiban and eptifibatide is not well established. Further clinical trials are needed.	IIb	B-R
The administration of other glycoprotein IIb/IIIa receptor antagonists, including abciximab, in the treatment of AIS is potentially harmful and should not be performed. Further research testing the safety and efficacy of these medications in patients with AIS is required.	III (Harm)	B-R
In patients presenting with minor stroke, treatment for 21 days with dual antiplatelet therapy (aspirin and clopidogrel) begun within 24 hours can be beneficial for early secondary stroke prevention for a period of up to 90 days from symptom onset.	IIa	B-R
Ticagrelor is not recommended (over aspirin) in the acute treatment of patients with minor stroke.	III (NB)	B-R

3.10 Anticoagulants

Recommendations	COR	LOE
Urgent anticoagulation with the goal of preventing early recurrent stroke, halting neurological worsening, or improving outcomes after AIS is not recommended for treatment of patients with AIS.	III (NB)	A
The usefulness of urgent anticoagulation in patients with severe stenosis of an internal carotid artery ipsilateral to an ischemic stroke is not well established.	IIb	B-NR
The safety and usefulness of short-term anticoagulation for nonocclusive, extracranial intraluminal thrombus in the setting of AIS are not well established.	IIb	C-LD
At present, the usefulness of argatroban, dabigatran, or other thrombin inhibitors for the treatment of patients with AIS is not well established. Further clinical trials are needed.	IIb	B-R
The safety and usefulness of factor Xa inhibitors in the treatment of AIS are not well established. Further clinical trials are needed.	IIb	C-LD

3.11 Volume Expansion/Hemodilution

Recommendations	COR	LOE
Hemodilution by volume expansion is not recommended for treatment of patients with AIS.	III (NB)	A
The administration of high-dose albumin is not recommended for the treatment of patients with AIS.	III (NB)	A
The administration of vasodilatory agents, such as pentoxifylline, is not recommended for AIS.	III (NB)	A
At present, use of devices to augment cerebral blood flow for the treatment of patients with AIS is not well established. These devices should be used only in the setting of clinical trials.	IIb	B-R

3.12 Neuroprotective Agents

Recommendations	COR	LOE
At present, no pharmacological or non-pharmacological treatments with putative neuroprotective actions have demonstrated efficacy in improving outcomes after ischemic stroke, and therefore, other neuroprotective agents are not recommended.	III (NB)	A

3.13 Emergency Carotid Intervention

Recommendations	COR	LOE
The usefulness of emergency or urgent CEA when clinical indicators or brain imaging suggests a small infarct core with large territory at risk (eg, penumbra), compromised by inadequate flow from a critical carotid stenosis or occlusion, or in the case of acute neurological deficit after CEA, in which acute thrombosis of the surgical site is suspected, is not well established.	IIb	B-NR
In patients with unstable neurological status (eg, stroke-in-evolution), the efficacy of emergency or urgent CEA is not well established.	IIb	B-NR

3.14 Other

Recommendations	COR	LOE
Transcranial near-infrared laser therapy is not recommended for the treatment of AIS • RCT terminated due to futility	III (NB)	B-R

In-hospital Supportive Care

4.1 Stroke Units

4.2 Supplemental Oxygen

4.3 Blood Pressure

4.4 Temperature

4.5 Glucose

4.6 Dysphagia Screening

4.7 Nutrition

4.8 DVT Prophylaxis

4.9 Depression Screening

4.10 Other

4.11 Rehabilitation

4.1 Stroke Units

- Stroke Units
  - Numerous studies have demonstrated that stroke units reduce morbidity and mortality after stroke
  - Standardized stroke order sets help to ensure best practices are followed
  - Multidisciplinary teams and coordinated care
  - Continuous quality improvement

In-hospital Supportive Care

4.1 Stroke Units

Recommendations	COR	LOE
The use of comprehensive specialized stroke care (stroke units) that incorporates rehabilitation is recommended.	I	A
The use of standardized stroke care order sets is recommended to improve general management.	I	B-NR

4.2 Supplemental Oxygen

- Supplemental Oxygen
  - Guidelines unchanged from 2013 recommendations
  - Maintain O_2 sats >94%; supplemental O_2 is not recommended in nonhypoxic pts
  - New RCT with 8003 pts randomized within 24 hours
    - O_2 at 2L/min (sats >93%) or 3L/min (sats ≤93%)
    - Duration: continuously for 72 hrs or nocturnally for 3 nights
    - No benefit in functional outcomes at 90 days

In-hospital Supportive Care

4.2 Supplemental Oxygen

Recommendations	COR	LOE
Airway support and ventilatory assistance are recommended for the treatment of patients with acute stroke who have decreased consciousness or who have bulbar dysfunction that causes compromise of the airway.	I	C-EO
Supplemental oxygen should be provided to maintain oxygen saturation >94%.	I	C-LD
Supplemental oxygen is not recommended in nonhypoxic patients hospitalized with AIS.	III (NB)	B

4.3 Blood Pressure

- Blood Pressure
  - Optimal BP strategy for stroke pts remains unclear and depends on the clinical situation
    - Some may have concomitant comorbidities that require acute BP lowering (aortic dissection, acute heart failure, etc)
    - Excessive BP lowering can worsen cerebral ischemia, though
    - Lowering BP acutely by 15% is probably safe
    - Initial BP <220/120: reinitiating anti-HTN is safe but is not associated with improved outcomes
    - Initial BP >220/120: possibly reasonable to lower by 15% in the first 24 hrs
    - Neurologically stable pts: probably safe to restart anti-HTN if >140/90
    - Hypotension and hypovolemia should be corrected

4.3 Blood Pressure

Recommendations	COR	LOE
In patients with AIS, early treatment of hypertension is indicated when required by co-morbid conditions (such as concomitant acute coronary event, acute heart failure, aortic dissection, post-thrombolysis sICH, or pre-eclampsia/eclampsia). Lowering BP initially by 15% is probably safe.	I	C-EO
In patients with BP below 220/120 mmHg who did not receive IV alteplase or endovascular treatment and do not have a comorbid condition requiring acute antihypertensive treatment, initiating or reinitiating treatment of hypertension within the first 48-72 hours after an AIS is not effective to prevent death or dependency.	III (NB)	A

In-hospital Supportive Care

4.3 Blood Pressure

Recommendations	COR	LOE
In patients with BP greater than or equal to 220/120 mmHg who did not receive IV alteplase or endovascular treatment and have no comorbid conditions requiring acute antihypertensive treatment, the benefit of initiating or reinitiating treatment of hypertension within the first 48-72 hours is uncertain. It might be reasonable to lower BP by 15% during the first 24 hours after onset of stroke.	IIb	C-EO
Although no solid data are available to guide selection of medications for BP lowering after an AIS, the antihypertensive medications and doses included in Table 5 are reasonable options.	IIa	C-EO

In-hospital Supportive Care

4.3 Blood Pressure

Recommendations	COR	LOE
Starting or restarting antihypertensive therapy during hospitalization in patients with BP >140/90 mmHg who are neurologically stable is safe and it is reasonable to improve long term BP control, unless contraindicated.	IIa	B-R
Hypotension and hypovolemia should be corrected to maintain systemic perfusion levels necessary to support organ function.	I	C-EO

4.4 Temperature

- Temperature
  - Identify sources of temperature >38ºC and treat
  - New data from retrospective cohort study (9366 pts)
    - Temperatures in the first 24 hrs below 37C and above 39C associated with increased in-hospital death
  - Hypothermia is promising as a neuroprotectant but benefit in AIS pts is not proven
  - Therapeutic hypothermia should only be undertaken in clinical trials

In-hospital Supportive Care

4.4 Temperature

Recommendations	COR	LOE
Sources of hyperthermia (temperature >38°C) should be identified and treated. Antipyretic medications should be administered to lower temperature in hyperthermic patients with stroke.	I	C_EO
The benefit of induced hypothermia for treating patients with ischemic stroke is not well established. Hypothermia should only be offered in the context of ongoing clinical trials.	IIb	B-R

4.5 Glucose

- Glucose
  - Recommendations unchanged from 2013 guidelines
  - Hyperglycemia
    - Common in stroke pts (elevated admission blood glucose in >40%, most frequently in diabetic pts)
    - Persistent hyperglycemia associated with worse outcomes
    - Main risk of correction: hypoglycemia
  - Hypoglycemia (<60mg/dL)
    - Symptoms: autonomic and brain dysfunction
    - Correct with IV push of dextrose

4.5 Glucose

Recommendations	COR	LOE
Evidence indicates that persistent in-hospital hyperglycemia during the first 24 hours after AIS 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 to 180 mg/dL and to closely monitor to prevent hypoglycemia.	IIa	C-LD
Hypoglycemia (blood glucose <60 mg/dL) should be treated in patients with AIS.	I	C-LD

4.6 Dysphagia Screening

- Dysphagia Screening
  - Post-stroke dysphagia
    - Very common (37-78%)
    - Risk factor for pneumonia
    - Associated with worse pt outcomes
  - Screening
    - Insufficient data whether screening protocol decreases death or dependency, but that does not mean screening is ineffective
    - Overall, early screening is reasonable
    - Those who fail screening

      -usually older

      -more comorbidities

      -coming from a facility

      -presenting with weakness and speech difficulties

      -lower level of consciousness

      -higher stroke severity

In-hospital Supportive Care

4.6 Dysphagia Screening

Recommendations	COR	LOE
Dysphagia screening before the patient begins eating, drinking, or receiving oral medications is reasonable to identify patients at increased risk for aspiration.	IIa	C-LD
It is reasonable for dysphagia screening to be performed by a speech-language pathologist or other trained healthcare provider.	IIa	C-LD
An instrumental evaluation is reasonable for those patients suspected of aspiration to verify the presence/absence of aspiration and to determine the physiological reasons for the dysphagia to guide the treatment plan.	IIa	B-NR
It is not well established which instrument to choose for evaluation of swallowing with sensory testing, but the choice may be based on instrument availability or other considerations (i.e. fiberoptic endoscopic evaluation of swallowing, videofluoroscopy, fiberoptic endoscopic evaluation).	IIb	C-LD

4.7 Nutrition

- Nutrition
  - Stroke pts should be started on a diet within 7 days
    - FOOD RCTs
      -Supplemented diet: absolute reduction in risk of death: 0.7%
    - Cochrane review (33 RCTs)
      -Available data suggest that PEG and NG are similar with regard to case-fatality, death, and dependency but PEG is associated with fewer treatment failures, less GI bleeding, and higher food delivery
  - Oral hygiene may reduce pneumonia risk
    - Standardized screening and diet along with standardized oral hygiene with antibacterial rinse with chlorhexidine may reduce pneumonia

In-hospital Supportive Care

4.7 Nutrition

Recommendations	COR	LOE
Enteral diet should be started within 7 days of admission after an acute stroke.	I	B-R
For patients with dysphagia, it is reasonable to initially use nasogastric tubes for feeding in the early phase of stroke (starting within the first 7 days) and to place percutaneous gastrostomy tubes in patients with longer anticipated persistent inability to swallow safely (>2-3 weeks).	IIa	C-EO
Nutritional supplements are reasonable to consider for patients who are malnourished or at risk of malnourishment.	IIa	B-R
Implementing oral hygiene protocols to reduce the risk of pneumonia after stroke may be reasonable.	IIb	B-NR

4.8 DVT Prophylaxis

- DVT Prophylaxis
  - Pneumatic compression is more effective than routine care
    - Primary outcome of DVT: 9.6% vs 14%
  - Benefit of prophylactic heparin (UFH or LMWH) is not well established
    - Reductions in PE and DVT but increases in ICH and extracranial bleeds
  - LMWH vs UFH
    - LMWH is once daily but is more expensive and associated with increased bleeding in elderly pts with kidney disease
  - Elastic stockings should not be used

In-hospital Supportive Care

4.8 DVT Prophylaxis

Recommendations	COR	LOE
In immobile stroke patients without contraindications, intermittent pneumatic compression in addition to routine care (aspirin and hydration) is recommended over routine care to reduce the risk of DVT.	I	B-R
The benefit of prophylactic-dose subcutaneous heparin [unfractionated heparin (UFH) or LMWH] in immobile patients with AIS is not well established.	IIb	A
When prophylactic anticoagulation is used, the benefit of prophylactic-dose LMWH over prophylactic-dose UFH is uncertain.	IIb	B-R
In ischemic stroke, elastic compression stockings should not be used.	III (Harm)	B-R

4.9 Depression Screening

- Depression Screening
  - Post-stroke depression (PSD) is common (~25-30%)
  - Structured screening is recommended
  - Optimal screen and timing remains unclear, however
  - Pts with PSD should be treated with antidepressants and the response monitored

4.9 Depression Screening

Recommendations	COR	LOE
Administration of a structured depression inventory is recommended to routinely screen for poststroke depression, but the optimal timing of screening is uncertain.	I	B-NR
Patients diagnosed with poststroke depression should be treated with antidepressants in the absence of contraindications and closely monitored to verify effectiveness.	I	B-R

4.10 Other

- Other
  - **New recommendation**: reasonable to direct appropriate patients and families to palliative care
  - Additional recommendations:
    - Avoid prophylactic antibiotics
    - Avoid routine placement of indwelling bladder catheters
    - Perform regular skin assessments
    - Perform good skin hygiene until mobility returns

4.10 Other

Recommendations	COR	LOE
Routine use of prophylactic antibiotics has not been shown to be beneficial.	III (NB)	B-R
Routine placement of indwelling bladder catheters should not be performed because of the associated risk of catheter-associated urinary tract infections.	III (Harm)	C-LD
During hospitalization and inpatient rehabilitation, regular skin assessments are recommended with objective scales of risk such as the Braden scale.	I	C-LD

In-hospital Supportive Care

4.10 Other

Recommendations	COR	LOE
It is recommended to minimize or eliminate skin friction, to minimize skin pressure, to provide appropriate support surfaces, to avoid excessive moisture, and to maintain adequate nutrition and hydration to prevent skin breakdown. Regular turning, good skin hygiene, and use of specialized mattresses, wheelchair cushions, and seating are recommended until mobility returns.	I	C-LD
It is reasonable for patients and families with stroke to be directed to palliative care resources as appropriate. Caregivers should ascertain and include patient-centered preferences in decision making, especially during prognosis formation and considering interventions or limitations in care.	IIa	C-EO

4.11 Rehabilitation

- Rehabilitation
  - Assessment
    - Pts with stroke need formal multidomain assessments before discharge
    - Pts with residual deficits should have an assessment by a clinician with expertise in rehab
  - Timing and intensity
    - High-dose and very early (within 24 hrs) should not be performed
      --AVERT trial (46% vs 50%) compared with usual care
      Reduced likelihood of favorable outcome
    - Intensity commensurate with benefit and tolerance
    - Effectiveness of fluoxetine/other SSRIs is unclear

In-hospital Supportive Care

4.11 Rehabilitation

Recommendations	COR	LOE
It is recommended that early rehabilitation for hospitalized stroke patients be provided in environments with organized, interprofessional stroke care.	I	A
It is recommended that stroke survivors receive rehabilitation at an intensity commensurate with anticipated benefit and tolerance.	I	B-NR
High-dose, very early mobilization within 24 hours of stroke onset should not be performed because it can reduce the odds of a favorable outcome at 3 months.	III (Harm)	B-R

Rehabilitation

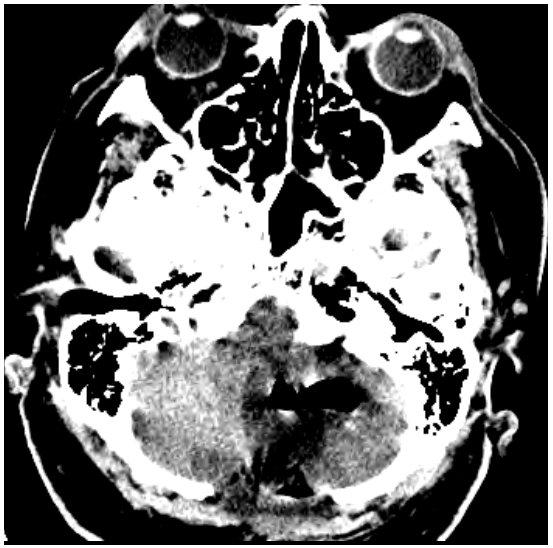
Recommendations	COR	LOE
It is recommended that all individuals with stroke be provided a formal assessment of their ADLs and IADLs, communication abilities, and functional mobility before discharge from acute care hospitalization and the findings be incorporated into the care transition and the discharge planning process.	I	B-NR
A functional assessment by a clinician with expertise in rehabilitation is recommended for patients with an acute stroke with residual functional deficits.	I	C-LD
The effectiveness of fluoxetine or other SSRIs to enhance motor recovery is not well established.	IIb	C-LD

Treatment of Acute Complications

5.1 Cerebellar and Cerebral Edema

5.2 Seizures

5.1 Cerebellar and Cerebral Edema

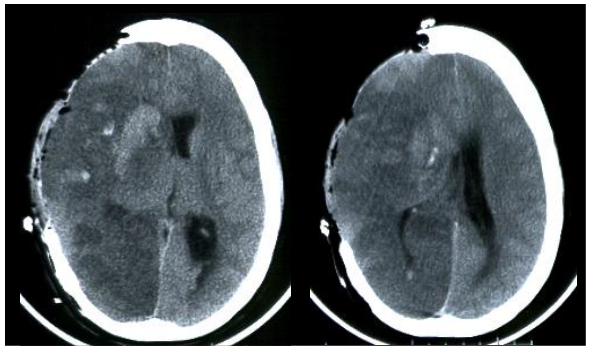


Cerebellar Edema

- Edema after large cerebellar infarction can cause neurologic deterioration via:
  - Acute obstructive hydrocephalus
  - Direct brainstem compression
- When hydrocephalus is present, emergent ventriculostomy is a reasonable first step
- When brainstem compression occurs despite medical therapy, decompressive suboccipital craniectomy should be performed
  - Outcome after suboccipital craniectomy can be good

5.1 Cerebellar and Cerebral Edema

Cerebral Edema After Large MCA Infarct



- High risk for neurologic deterioration
- Care options should be discussed early
- In those with neurologic deterioration within 48 hours, decompressive hemicraniectomy:
  - Reduces mortality and morbidity in patients ≤ 60
    - Surgical group at 12 months:
      - 14% independent (mRS=2)
      - 29% moderate disability (mRS=3)
      - 35% severely disabled (mRS=4 or 5)
      - 22% dead
  - Reduces mortality in patients >60, *but disability remains high*
    - Surgical group at 12 months:
      - 0% independent (mRS=2)
      - 6% moderate disability (mRS=3)
      - 51% severely disabled (mRS=4 or 5)
      - 43% dead

5.1 Cerebellar and Cerebral Edema

Recommendations	COR	LOE
Ventriculostomy is recommended in the treatment of obstructive hydrocephalus after a cerebellar infarct. Concomitant or subsequent decompressive craniectomy may or may not be necessary based on factors such as infarct size, neurologic condition, degree of brainstem compression, and effectiveness of medical management.	I	C-LD
Decompressive suboccipital craniectomy with dural expansion should be performed in patients with cerebellar infarction causing neurologic deterioration from brainstem compression despite maximal medical therapy. When deemed safe and indicated, obstructive hydrocephalus should be treated concurrently with ventriculostomy.	I	B-NR
When considering decompressive suboccipital craniectomy for cerebellar infarction, it may be reasonable to inform family members that the outcome after cerebellar infarct can be good after sub-occipital craniectomy.	IIb	C-LD

5.1 Cerebellar and Cerebral Edema

Recommendations	COR	LOE
Patients with large territorial infarctions are at high risk for complicating brain edema and increased intracranial pressure. Discussion of care options and possible outcomes should take place quickly with patients (if possible) and caregivers. Medical professionals and caregivers should ascertain and include patient-centered preferences in shared-decision making, especially during prognosis formation and considering interventions or limitations of care.	I	C-EO
Patients with major infarctions are at high risk for complicating brain edema. 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.	I	C-LD

5.1 Cerebellar and Cerebral Edema

Recommendations	COR	LOE
In patients ≤60 years of age with unilateral MCA infarctions who deteriorate neurologically within 48 hours despite medical therapy, decompressive craniectomy with dural expansion is reasonable because it reduced mortality by close to 50%, with 55% of the surgical survivors achieving moderate disability or better and 18% achieving independence at 12 months.	IIa	A
In patients >60 years of age with unilateral MCA infarctions who deteriorate neurologically within 48 hours despite medical therapy, decompressive craniectomy with dural expansion may be considered because it reduced mortality by close with 50%, with 11% of the surgical survivors achieving moderate disability and none achieving independence at 12 months.	IIb	B-R
Although the optimal trigger for decompressive craniectomy is unknown, it is reasonable to use a decrease in level of consciousness attributed to brain swelling as selection criteria.	IIa	A
Use of osmotic therapy for patients with clinical deterioration from cerebral swelling associated with cerebral infarction is reasonable.	IIa	C-LD

5.1 Cerebellar and Cerebral Edema

Recommendations	COR	LOE
Use of brief moderate hyperventilation (PCO2 target 30-34 mmHg) is a reasonable treatment for patients with acute severe neurological decline from brain swelling as a bridge to more definitive therapy.	IIa	C-EO
Hypothermia or barbiturates in the setting of ischemic cerebral or cerebellar swelling are not recommended.	III (NB)	B-R
Because of a lack of evidence of efficacy and the potential to increase the risk of infectious complications, corticosteroids (in conventional or large doses) should not be administered for the treatment of cerebral edema and increased intracranial pressure complicating ischemic stroke.	III (Harm)	A

5.2 Seizures

Recommendations	COR	LOE
Recurrent seizures after stroke should be treated in a manner similar to when they occur with other acute neurological conditions, and anti-seizure drugs should be selected based upon specific patient characteristics.	I	C-LD
Prophylactic use of anti-seizure drugs is not recommended.	III (NB)	B-R

In-hospital Evaluation and Secondary Prevention

6.1 Brain Imaging

6.2 Vascular Imaging

6.3 Cardiac Evaluation

6.4 Glucose

6.5 Cholesterol

6.6 Other Tests for Secondary Prevention

6.7 Antithrombotic Treatment

6.8 Statins

6.9 Carotid Revascularization

6.10 Smoking Cessation Intervention

6.11 Stroke Education

6.1 Brain Imaging

- Brain Imaging
  - Noncontrast HCT is cost-effective as it differentiates AIS from ICH
  - DW-MRI is more sensitive than HCT for AIS, but studies have not found it cost-effective
  - In some pts DW-MRI will help with the diagnosis or with stroke localization
  - Routine DW-MRI use is not recommended and more research is needed to determine criteria for its cost-effective use

6.1 Brain Imaging

Recommendations	COR	LOE
Routine use of brain MRI in all patients with AIS is not cost effective and is not recommended for initial diagnosis or to plan subsequent treatment.	III (NB)	B-NR
In some patients with AIS, the use of MRI might be considered to provide additional information for initial diagnosis or to plan subsequent treatment, although the effect on outcomes is uncertain.	IIb	C-EO

6.2 Vascular Imaging

- Vascular Imaging
  - Extracranial
    - Imaging should be performed within 24 hours of admission in pts with non-disabling AIS (mRS 0-2)
    - Revascularization via CEA or CAS feasible in a 2-7 day time window
  - Intracranial
    - Routine imaging is not recommended
      -WASID: no benefit of warfarin over ASA 325
      -SAMMPRIS: no benefit to adding stent to aggressive medical management
      -Added utility and cost-effectiveness is unproven
    - In some pts reasonable to perform intracranial imaging to help plan secondary prevention strategies

6.2 Vascular Imaging

Recommendations	COR	LOE
For patients with non-disabling (mRS 0-2) AIS in the carotid territory who are candidates for carotid endarterectomy or stenting, non-invasive imaging of the cervical vessels should be performed routinely within 24 hours of admission.	I	B-NR
In patients with AIS, routine non-invasive imaging by means of CTA or MRA of the intracranial vasculature to determine the presence of intracranial arterial stenosis and/or occlusion is not recommended to plan subsequent secondary preventative treatment.	III (NB)	A
In some patients with AIS, non-invasive imaging by means of CTA or MRA of the intracranial vasculature to provide additional information to plan subsequent secondary preventative treatment may be reasonable, although the effect on outcomes is uncertain.	IIb	C-EO

6.3 Cardiac Evaluation

- Cardiac Evaluation
  - Cardiac monitoring
    - Atrial fibrillation is a common cause of AIS and anticoagulation is associated with reduced stroke incidence compared with ASA
    - Monitoring should be performed at least 24 hrs
    - Prolonged monitoring identifies more atrial fibrillation but thus far the clinical benefit is uncertain
  - Echocardiography
    - Routine use is not recommended as evidence of cost-effectiveness is insufficient
    - In some pts ECHO data may help plan secondary preventive strategies
      -Intracardiac thrombus
      -PFO in selected pts

6.3 Cardiac Evaluation

Recommendations	COR	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.	I	B-NR
The clinical benefit of prolonged cardiac monitoring to detect atrial fibrillation after AIS is uncertain.	IIb	B-R
In some patients with AIS, prolonged cardiac monitoring to provide additional information to plan subsequent secondary preventative treatment may be reasonable, although the effect on outcomes is uncertain.	IIb	C-EO

6.3 Cardiac Evaluation

Recommendations	COR	LOE
Routine use of echocardiography in all patients with AIS to plan subsequent secondary preventative treatment is not cost effective and is not recommended.	III (NB)	B-NR
In selected patients with AIS, echocardiography to provide additional information to plan subsequent secondary preventative treatment may be reasonable.	IIb	B-R

6.4 Glucose

- Glucose
  - Screening for DM is reasonable in AIS pts
    - Fasting glucose
    - **HgbA1c (may be more accurate in the acute setting)**
    - Oral glucose tolerance test

6.4 Glucose

Recommendations	COR	LOE
After AIS, it is reasonable to screen all patients for diabetes mellitus with testing of fasting plasma glucose, HbA1c, or an oral glucose tolerance test. Choice of test and timing should be guided by clinical judgment and recognition that acute illness may temporarily perturb measures of plasma glucose. In general, HbA1c may be more accurate than other screening tests in the immediate post-event period.	IIa	C-EO

6.5 Cholesterol

- Cholesterol
  - The 2013 ACC/AHA Cholesterol Guidelines recommend statins for pts with atherosclerotic cardiovascular disease (ASCVD), including stroke of atherosclerotic origin
  - No data for treatment or titration to a specific LDL level
  - Measurement in stroke pts
    - No benefit to measuring cholesterol routinely in atherosclerotic stroke pts not already taking a high-intensity statin
    - Maybe some benefit in measuring cholesterol levels in pts already on optimized statin as they might benefit from PCSK9 inhibitor treatment
    - Maybe some benefit in measuring cholesterol levels in pts with non-atherosclerotic origin stroke as primary prevention guidelines are based on LDL-C levels

6.5 Cholesterol

Recommendations	COR	LOE
Routine measurement of blood cholesterol levels in all patients with ischemic stroke presumed to be of atherosclerotic origin who are not already taking a high-intensity statin is not recommended.	III (NB)	B-R
Measurement of blood cholesterol levels in patients with ischemic stroke presumed to be of atherosclerotic origin who are already taking an optimized regimen of statin therapy may be useful for identifying patients who would be candidates for outpatient proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor treatment to reduce the risk of subsequent cardiovascular death, MI, or stroke.	IIb	B-R

6.6 Other Tests for Secondary Prevention

- Other Tests for Secondary Prevention
  - Recommended
    - Troponin
  - Not recommended
    - Routine screening for hyperhomocysteinemia
    - Routine antiphospholipid antibody testing unless APS findings or no alternative explanation
    - Routine OSA screening
      -OSA is highly prevalent but RCTs have not found treating these pts with CPAP prevents cardiovascular events or death in pts with stroke
    - Routine thrombophilia screening

6.6 Other Tests for Secondary Prevention

Recommendations	COR	LOE
Baseline troponin assessment is recommended in patients presenting with AIS but should not delay initiation of IV alteplase or mechanical thrombectomy.	I	C-LD
Routine screening for hyperhomocysteinemia among patients with a recent ischemic stroke is not indicated.	III (NB)	C-EO
The usefulness of screening for thrombophilic states in patients with ischemic stroke is unknown.	IIb	C-LD
Anticoagulation might be considered in patients who are found to have abnormal findings on coagulation testing after an initial ischemic stroke, depending on the abnormality and the clinical circumstances.	IIb	C-LD

6.6 Other Tests for Secondary Prevention

Recommendations	COR	LOE
Routine testing for antiphospholipid antibodies is not recommended for patients with ischemic stroke who have no other manifestations of the antiphospholipid syndrome and who have an alternative explanation for their ischemic event, such as atherosclerosis, carotid stenosis, or atrial fibrillation.	III (NB)	C-LD
Routine screening of patients with recent ischemic stroke for obstructive sleep apnea (OSA) is not recommended.	III (NB)	B-R

6.7 Antithrombotic Therapy

- Antithrombotic Treatment
  - Antiplatelet therapy
    - Recommended for non-cardioembolic AIS
    - Increasing ASA or switching agents is not well established
      -SPS-3: no benefit to adding clopidogrel to ASA
      -WARSS: no difference in stroke recurrence after switching to warfarin
      -WASID: no difference after switching to warfarin
  - Anticoagulation for AIS due to atrial fibrillation
    - Reasonable to initiate 4-14 days after AIS for most pts
  - Hemorrhagic transformation: reinitiation depends on clinical scenario
  - Dissection: antiplatelet or anticoagulation is reasonable (CADISS). If recurrence, the value of stenting is not well established

6.7 Antithrombotic Therapy

Recommendations	COR	LOE
For patients with non-cardioembolic AIS, the use of antiplatelet agents rather than oral anticoagulation is recommended to reduce the risk of recurrent stroke and other cardiovascular events.	I	A
For patients who have a non-cardioembolic AIS while taking aspirin, increasing the dose of aspirin or switching to an alternative antiplatelet agent for additional benefit in secondary stroke prevention is not well established.	IIb	B-R
For patients who have a noncardioembolic AIS while taking antiplatelet therapy, switching to warfarin is not beneficial for secondary stroke prevention.	III (NB)	B-R

6.7 Antithrombotic Therapy

Recommendations	COR	LOE
For early secondary prevention in patients with noncardioembolic AIS, the selection of an antiplatelet agent should be individualized on the basis of patient risk factor profiles, cost, tolerance, relative known efficacy of the agents, and other clinical characteristics.	I	C-EO
For patients with a history of ischemic stroke, atrial fibrillation, and coronary artery disease, the usefulness of adding antiplatelet therapy to OACs is uncertain for purposes of reducing the risk of ischemic cardiovascular and cerebrovascular events. Unstable angina and coronary artery stenting represent special circumstances in which management may warrant dual antiplatelet/oral coagulation.	IIb	C-LD
For most patients with an AIS in the setting of atrial fibrillation, it is reasonable to initiate oral anticoagulation within 4-14 days after the onset of neurological symptoms.	IIa	B-NR

6.7 Antithrombotic Therapy

Recommendations	COR	LOE
For patients with AIS and hemorrhagic transformation, initiation or continuation of antiplatelet or anticoagulation therapy may be considered, depending on the specific clinical scenario and underlying indication.	IIb	B-NR
For patients with AIS and extracranial carotid or vertebral arterial dissection, treatment with either antiplatelet or anticoagulant therapy for 3 to 6 months may be reasonable.	IIb	B-R
For patients with AIS and extracranial carotid or vertebral arterial dissection who have definite recurrent cerebral ischemic events despite medical therapy, the value of EVT (stenting) is not well established.	IIb	C-LD

6.8 Statins

- Statins
  - Pts already on a statin: reasonable to continue
  - Pts ≤75yo with ASCVD: reasonable to continue or start
  - Pts ≥75yo with ASCVD: evaluate risk-reduction

  - Clinical ASCVD
    - Acute Coronary Syndrome
    - History of MI
    - Stable or unstable angina
    - Coronary or other arterial revascularization
    - Stroke/TIA
    - Peripheral artery disease

  - 'High intensity' statin: atorvastatin 80mg or rosuvastatin 20mg

6.8 Statins

Recommendations	COR	LOE
Among patients already taking statins at the time of onset of ischemic stroke, continuation of statin therapy during the acute period is reasonable.	IIa	B-R
High-intensity statin therapy should be initiated or continued as first-line therapy in women and men ≤75 years of age who have clinical ASCVD, unless contraindicated.	I	A
In individuals with clinical ASCVD in whom high-intensity statin therapy would otherwise be used, when high-intensity statin therapy is contraindicated or when characteristics predisposing to statin-associated adverse effects are present, moderate-intensity statin should be used as the second option if tolerated.	I	A

6.8 Statins

Recommendations	COR	LOE
In individuals with clinical ASCVD >75 years of age, it is reasonable to evaluate the potential for ASCVD risk-reduction benefits and for adverse effects and drug–drug interactions and to consider patient preferences when initiating a moderate- or high-intensity statin. It is reasonable to continue statin therapy in those who are tolerating it.	IIb	C-EO
Patients with ischemic stroke and other comorbid ASCVD should be otherwise managed according to the 2013 ACC/AHA cholesterol guidelines, which include lifestyle modification, dietary recommendations, and medication recommendations.	I	A
For patients with an AIS who qualify for statin treatment, in-hospital initiation of statin therapy is reasonable.	IIa	C-LD

6.9 Carotid Revascularization

- Carotid Revascularization
  - Indication
    - Minor, nondisabling stroke (mRS 0-2) in distribution of the artery
  - Timing
    - 2-7 days after index event is reasonable
      -Stroke risk is highest in the first few days after the event
      -No high quality data supporting emergent revascularization

6.9 Carotid Revascularization

Recommendations	COR	LOE
When revascularization is indicated for secondary prevention in patients with minor, nondisabling stroke, it is reasonable to perform the procedure between 48 hours and 7 days of the index event, rather than delay treatment if there are no contraindications to early revascularization.	IIa	B-NR

6.10 Smoking Cessation Intervention

Smoking Cessation Intervention

- Therapeutic options include:
  - Counseling
  - Nicotine products
  - Varenicline
- In-hospital initiation of any of the above is reasonable

6.10 Smoking Cessation Intervention

Recommendations	COR	LOE
Healthcare providers should strongly advise every patient with AIS who has smoked in the past year to quit.	I	C-EO
Counseling, nicotine products, and oral smoking cessation medications are effective in helping smokers to quit.	I	A
For smokers with an AIS, in-hospital initiation of high intensity behavioral therapies is reasonable.	IIa	B-R
For smokers with an AIS, in-hospital initiation of varenicline might be considered.	IIb	B-R
For smokers with an AIS, in-hospital initiation of interventions that incorporate both pharmacotherapy and behavioral support might be considered.	IIb	B-R
It is reasonable to advise patients after ischemic stroke to avoid second-hand (passive) tobacco smoke.	IIa	B-NR

6.11 Stroke Education

- Stroke Education
  - Unchanged from previous guideline
  - Discussion before discharge regarding:
    - What is a stroke
    - Stroke risk factors
    - Medications
    - When to call 911
    - Any other stroke-related questions

6.11 Stroke Education

Recommendations	COR	LOE
Patient education about stroke is recommended. Patients should be provided with information, advice, and the opportunity to talk about the impact of the illness on their lives.	I	C-EO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