

2018 AHA/ASA Ischemic Stroke Guidelines

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Just another night in
Montana...



Disclosures

- Nothing to disclose

Objectives

- Review the 2018 AHA/ASA Stroke Guidelines
 - Internal Medicine Focused
- Highlight indications for dual antiplatelet therapy (DAPT) after stroke
- Discuss indications for PFO closure
- Identify future research avenues

2018 Updates

- Represents first large update since 2013 guidelines
- Based on “**2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke**”
- Notably – shortly after release large sections recalled
 - This review based on post recall guidelines
 - Will focus on what’s applicable to IM
 - Rapid fire tPA review

Class 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 of Evidence

LEVEL A

- High-quality evidence‡ from more than 1 RCT
- 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

Stroke Teams and Telemedicine

4. Designation of an acute stroke team that includes physicians, nurses, and laboratory/radiology personnel is recommended. Patients with stroke should have a careful clinical assessment, including neurological examination.	I	B-NR
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Unchanged from 2013 guidelines

4. Telestroke/teleradiology evaluations of AIS patients can be effective for correct IV alteplase eligibility decision making.	IIa	B-R
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New in 2018 guidelines

5. Administration of IV alteplase guided by telestroke consultation for patients with AIS may be as safe and as beneficial as that of stroke centers.	IIb	B-NR
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New in 2018 guidelines

Case Presentation

- A 71 yo F presents to the emergency department for left arm and leg weakness.
 - Woke up normal
 - Symptoms started during breakfast
 - Presented to ED 2 hours after last known well
- Medications include metformin, sitagliptin, lisinopril, HCTZ, amlodipine and albuterol. She uses Tylenol and ibuprofen as needed for her pain



Case Presentation

- Physical Exam

- Vitals – HR 72, RR 16, BP 165/82, T 98.6, 93% on RA
- Gen – well appearing elderly female in NAD
- Heart – regular and nontachycardic
- Neuro – LUE and LLE weak compared to RUE and RLE with L sided facial droop. Sensory deficits to gross touch over LUE and LLE.
- NIH Stroke Scale (NIHSS) - 9



Case Question #1

Which of the following need to be checked prior to consideration for tPA? (Select all correct answers)

- a) Fingertstick glucose
- b) CT head
- c) MRI brain (to exclude cerebral microbleeds)
- d) CBC (specifically platelets)
- e) INR
- f) ECG
- g) Troponin



Initial Imaging

2.2. Brain Imaging	COR	LOE
1. All patients admitted to hospital with suspected acute stroke should receive brain imaging evaluation on arrival to hospital. In most cases, noncontrast CT (NCCT) will provide the necessary information to make decisions about acute management.	I	B-NR

Revised from 2013 guidelines

5. Routine use of magnetic resonance imaging (MRI) to exclude cerebral microbleeds (CMBs) before administration of IV alteplase is not recommended.	III: No Benefit	B-NR
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New in 2018 guidelines

Initial Labs and Tests

2.3. Other Diagnostic Tests	COR	LOE
1. Only the assessment of blood glucose must precede the initiation of IV alteplase in all patients.	I	B-R
2. Baseline ECG assessment is recommended in patients presenting with AIS, but should not delay initiation of IV alteplase.	I	B-NR
3. Baseline troponin assessment is recommended in patients presenting with AIS, but should not delay initiation of IV alteplase.	I	B-NR

Unchanged from 2013 guidelines

Unchanged from 2013 guidelines

Unchanged from 2013 guidelines

Oxygenation

3.1. Airway, Breathing, and Oxygenation (Continued)	COR	LOE
2. Supplemental oxygen should be provided to maintain oxygen saturation >94%.	I	C-LD
3. Supplemental oxygen is not recommended in nonhypoxic patients with AIS.	III: No Benefit	B-R

Unchanged from 2013 guidelines

Unchanged from 2013 guidelines

Case Question #2

A head CT shows no evidence of hemorrhage and fingerstick blood glucose is 156. A decision is made to administer tPA. Which of the following is the blood pressure goal in this patient?

- a) <220/120 mmHg
- b) <200/115 mmHg
- c) <185/110 mmHg
- d) <160/100 mmHg



Blood Pressure Management

4.3. Blood Pressure	COR	LOE
1. In patients with AIS, early treatment of hypertension is indicated when required by comorbid conditions (eg, concomitant acute coronary event, acute heart failure, aortic dissection, postthrombolysis sICH, or preeclampsia/eclampsia). Lowering BP initially by 15% is probably safe.	I	C-EO
3. In patients with BP \geq 220/120 mm Hg who did not receive IV alteplase or EVT and have no comorbid conditions requiring acute antihypertensive treatment, the benefit of initiating or reinitiating treatment of hypertension within the first 48 to 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
5. Starting or restarting antihypertensive therapy during hospitalization in patients with BP >140/90 mm Hg who are neurologically stable is safe and is reasonable to improve long-term BP control unless contraindicated.	IIa	B-R

New in the 2018 guidelines

New in the 2018 guideline – 2013 said “...not to lower blood pressure unless >220/110...”.
Canadian guideline – start treatment at 72h

New in 2018 guideline. Caveat – expert opinion in large vessel intracranial stenosis

Blood Pressure Management

2. 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
1. Hypotension and hypovolemia should be corrected to maintain systemic perfusion levels necessary to support organ function.	I	C-E0

Unchanged in 2018 guideline

New in 2018 guideline. Based on observational studies, benefit intermittent. No guidance on how to resuscitate

A Brief Word on tPA

1. 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 in Table 6 to determine patient eligibility.	I	A
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Reworded from 2013 guidelines. Need to address exclusion criteria carefully

2. 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 in Table 6 determine patient eligibility.	I	B-R
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Reworded from 2013 guidelines

3. For otherwise eligible patients with mild stroke presenting in the 3- to 4.5-hour window, treatment with IV alteplase may be reasonable. Treatment risks should be weighed against possible benefits.	IIb	B-NR
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New in 2018 guideline

A Brief Word on tPA

<p>4. In otherwise eligible patients who have had a previously demonstrated small number (1–10) of CMBs on MRI, administration of IV alteplase is reasonable.</p>	<p>IIa</p>	<p>B-NR</p>
<p>8. 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.</p>	<p>III: Harm</p>	<p>B-NR</p>
<p>15. The risk of antithrombotic therapy within the first 24 hours after treatment with 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.</p>	<p>IIb</p>	<p>B-NR</p>

New in 2018 guideline. Can also consider if >10 CMB

Clarified from 2015 tPA guidelines to reflect only for therapeutic doses

New in 2018 guideline. Based on a single study from South Korea with admitted selection bias

The Future of tPA?

- Recent systematic review and meta-analysis of 3 trials
 - EXTEND, ECASS4-EXTEND, EPITHET
- 414 patients, 213 received alteplase, 201 received placebo
 - Patients were within 4.5-9 hours of last known well, or with a “wake up stroke”
 - All had evidence of salvageable brain tissue on diffusion-perfusion MRI
- Conclusion - benefits of alteplase outweighed risk of hemorrhage

Case Presentation

- Immediately after receiving tPA your patient is taken for a CT angiogram of their neck/head.
 - CT angiogram of the head/neck shows evidence of a thrombus in the middle cerebral artery with some associated hypoattenuation in the left parietal lobe. ASPECT score is 8
 - You consider need for endovascular thrombectomy, but it is currently 3.5 hours since last known well and it will be 3-4 hours before the patient would arrive at an EVT center.



Case Question

Should this patient be transferred for endovascular therapy?

- a) Yes
- b) No



Endovascular Therapy

8. For patients who otherwise meet criteria for EVT, a noninvasive intracranial vascular study is recommended during the initial imaging evaluation of the acute stroke patient, but should not delay IV alteplase if indicated. For patients who qualify for IV alteplase according to guidelines from professional medical societies, initiating IV alteplase before noninvasive vascular imaging is recommended for patients who have not had noninvasive vascular imaging as part of their initial imaging assessment for stroke. Noninvasive intracranial vascular imaging should then be obtained as quickly as possible.

I

A

New in the 2018 guideline

12. In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation, obtaining CTP, DW-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

New in the 2018 guidelines

Endovascular Therapy

1. Patients eligible for IV alteplase should receive IV alteplase even if EVTs are being considered.	I	A
2. In patients under consideration for mechanical thrombectomy, observation after IV alteplase to assess for clinical response should not be performed.	III: Harm	B-R
3. 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
7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A
8. 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

Revised from 2015 Endovascular guidelines

Revised from 2015 Endovascular guidelines

New in the 2018 guidelines

From DAWN/DEFUSE 3 – biggest thing is NIHSS was >9

Alberta Stroke Program Early CT Score (ASPECTS) ☆

Determines MCA stroke severity using available CT data.

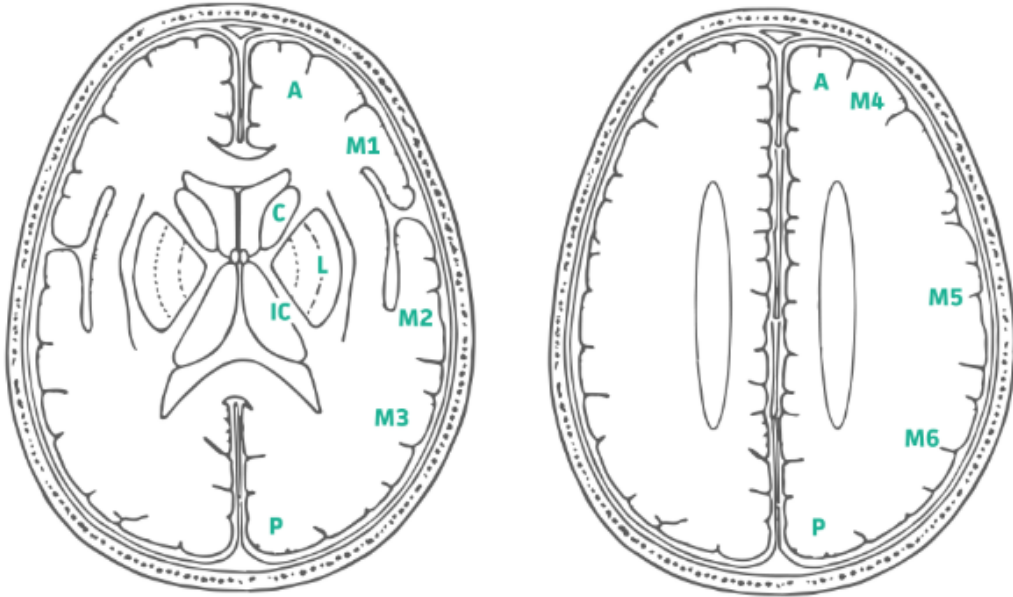
INSTRUCTIONS

To compute the ASPECTS, 1 point is subtracted from 10 for any evidence of early ischemic change for each of the defined regions.

When to Use ▾

Pearls/Pitfalls ▾

Why Use ▾



ASPECT Score

10 points

Normal CT Scan

Copy Results 📄

Next Steps >>>

(Not a case) Question

How long should dual antiplatelet therapy (DAPT) be continued in a patient for whom it is indicated?

- a) 14 days
- b) 21 days
- c) 45 days
- d) 90 days



Antiplatelets and DAPT

3.9. Antiplatelet Treatment	COR	LOE
1. 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
6. Ticagrelor is not recommended (over aspirin) in the acute treatment of patients with minor stroke.	III: No Benefit	B-R
5. 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

Change from 2013 guideline – removed specific dosing of 325mg as new trials have shown benefit of 160mg-300mg

New in the 2018 guidelines

New in the 2018 guidelines

A little more on DAPT

- CHANCE Trial – 2013 – 5170 patients at 114 Chinese centers
 - Included minor ischemic stroke or high risk TIA
 - Clopidogrel 300mg on day 1 followed by 75mg daily with aspirin 75mg-300mg on day 1 followed by 75mg daily. DAPT continued for 21 days
 - DAPT reduced risk of recurrent stroke without increased risk of major bleeding

A little more on DAPT

- POINT trial – 2018 –4881 patients at 269 international clinical sites (including North America)
 - Included minor ischemic stroke or high risk TIA
 - Clopidogrel 600mg on day 1 followed by 75mg daily with aspirin 150mg-200mg x 5 days followed by 75mg-100mg daily. DAPT continued for 90 days
 - DAPT reduced recurrent ischemia, but increased risk of major bleed

A little more on DAPT

- SPS3 trial – 2012 – Clopidogrel + ASA 325mg in 3020 patients
 - Looked at lacunar strokes, therapy had no set end point
 - DAPT increased mortality and bleeds, no effect on recurrent ischemia
- SAMMPRIS trial – 2011 – Clopidogrel + ASA 325mg in 451 patients
 - DAPT was superior to invasive intervention in symptomatic intracranial large vessel stenosis

What is a “minor” stroke?

- High risk TIA – ABCD2 score >3
- Minor Stroke – NIHSS <4
- DAPT contraindicated in major stroke due to increased risk of hemorrhagic conversion

What are “we” doing?

- Based primarily on CHANCE trial (and subgroup of POINT) as well as recent meta-analysis by Hao et al.
 - Clopidogrel 300mg on day 1 with aspirin 325mg on day 1 followed by clopidogrel 75mg daily with aspirin 81mg daily for 21 days, at which point clopidogrel is discontinued
 - Start within 24 hours of symptom onset

Anticoagulation

3.10. Anticoagulants	COR	LOE
1. 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: No Benefit	A
4. 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
5. 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

Unchanged from 2013 guidelines

Revised from 2013 guidelines. Studies ongoing

New in the 2018 guidelines

Case Presentation

- Your patient received tPA and overall did very well. On day 2 of her admission her muscle strength was markedly improved in her LLE and LUE, now scoring 4/5 in both. She continued with L facial droop although she was able to eat without food spillage. NIHSS is now 2.
- On day 2, she had an echocardiogram bubble study performed per protocol. This showed evidence of a PFO as indicated by injection of agitated saline moving into the L atrium.



Case Question

When is closure of a PFO potentially indicated?

- a) In patients <60 yo after their first cryptogenic stroke
- b) In patients <90 yo after their first cryptogenic stroke
- c) In patients <60 yo after their second cryptogenic stroke
- d) In patients <90 yo after their second cryptogenic stroke
- e) It has never been shown to have a statistically significant benefit



PFO's

- PFO's – should we close them in cryptogenic strokes?
 - Cryptogenic strokes – stroke not due to large vessel atherosclerosis, small artery disease or embolism despite extensive work up
- Until 2017 – No
 - Closure I (2012) and PC (2013) looked at closure of PFO vs medical therapy
 - Closing PFO reduced recurrence of ischemic stroke, but not significantly

PFO's

- 2017 came and went – 3 new trials published
 - RESPECT, Gore REDUCE and CLOSE
 - Enrolled patients with cryptogenic ischemic stroke
 - Patients were <60 years old in all 3 trials
 - Endpoint included recurrent clinical ischemic stroke
 - REDUCE also looked at “silent ischemia”
 - Gore REDUCE and CLOSE saw increased risk of atrial fibrillation/flutter
 - Gore REDUCE and CLOSE used aspirin + clopidogrel (DAPT) in closure group

PFO's

- RESPECT (long term follow up – initially published in 2013)
 - 980 patients, 499 with PFO closure (**+DAPT 1 months**), 481 with medical therapy (antiplatelet or warfarin alone)
 - 2013 – no stat. sig benefit with intention to treat analysis (ITT)
 - 2017 – ITT analysis shows stat sig reduction in closure group (HR 0.55)

PFO's

- Gore REDUCE

- 664 patients, 441 with PFO closure (+antiplatelet), 223 with antiplatelet therapy
- Study showed a significant reduction in closure group (HR 0.23)

- CLOSE

- 663 patients, 238 with PFO closure (**+DAPT 3 months**), 235 with single antiplatelet, 187 in anticoagulant group (warfarin or NOAC)
- Study showed a significant reduction in closure group (HR 0.03) versus antiplatelet
- Study showed a non-significant reduction in anticoagulant group (HR 0.43, $p=0.17$) versus antiplatelet

PFO's

- So should we close PFO's?
 - Nothing in the new guidelines
 - Variable as to whether insurance covers
 - Notably 2 studies gave DAPT to closure arm, but comparison arms received traditional single antiplatelet
 - Would this change results if comparing closure to DAPT?
 - MKSAP and certification exams are saying it should be considered, but not recommending one or the other

Nutritional Support

2. It is reasonable for dysphagia screening to be performed by a speech-language pathologist or other trained healthcare provider.	IIa	C-LD
1. Enteral diet should be started within 7 days of admission after an acute stroke.	I	B-R
2. 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-E0

Reworded from 2016 Rehab guidelines

New in the 2018 guidelines

New in the 2018 guidelines

DVT Prophylaxis

1. In immobile stroke patients without contraindications, intermittent pneumatic compression (IPC) in addition to routine care (aspirin and hydration) is recommended over routine care to reduce the risk of deep vein thrombosis (DVT).	I	B-R
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Revised from 2016 Rehab guidelines

2. The benefit of prophylactic-dose subcutaneous heparin (unfractionated heparin [UFH] or LMWH) in immobile patients with AIS is not well established.	IIb	A
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New in the 2018 guideline – did not affect morbidity/mortality but decreased PE/DVT

4. In ischemic stroke, elastic compression stockings should not be used.	III: Harm	B-R
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New in the 2018 guidelines

Depression Management

1. 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
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New in the 2018 guideline

2. Patients diagnosed with poststroke depression should be treated with antidepressants in the absence of contraindications and closely monitored to verify effectiveness.	I	B-R
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New in the 2018 guideline

5. 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
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New in the 2018 guidelines

Research Avenues

- Depression inventory interventions



Questions?
