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AHA/ASA Updated Guidelines for the Early Management of Acute Ischemic Stroke -

"It's like déjà vu all over again."

Virginia Stroke Systems Task Force
January 24, 2020

DISCLOSURES

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RESEARCH SUPPORT

- NIH, NSF
- Coulter Translational Research Fund
- American Heart Association/American Stroke Association
- Diffusion Pharmaceuticals, Inc.

OTHER

- U.S. Patent application no. 14/910,890 (iTREAT)
- U.S. Provisional patent application no. 62/620,096 (BANDIT)
- Legal expert review (vascular neurology)

American Heart Association | American Stroke Association®

January 24, 2018

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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

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine and Neurocritical Care Society

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

William J. Powers, MD, FAHA, Chair; Alejandro A. Rabinstein, MD, FAHA, Vice Chair; Teri Ackerson, BSN, RN; Opeolu M. Adeoye, MD, MS, FAHA; Nicholas C. Bambakidis, MD, FAHA; Kyra Becker, MD, FAHA; José Biller, MD, FAHA; Michael Brown, MD, MSc; Bart M. Demaerschalk, MD, MSc, FAHA; Brian Hoh, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Chelsea S. Kidwell, MD, FAHA; Thabele M. Leslie-Mazwi, MD; Bruce Ovbiagele, MD, MSc, MAS, MBA, FAHA; Phillip A. Scott, MD, MBA, FAHA; Kevin N. Sheth, MD, FAHA; Andrew M. Southerland, MD, MSc; Deborah V. Summers, MSN, RN, FAHA; David L. Tirschwell, MD, MSc, FAHA; on behalf of the American Heart Association Stroke Council

2018 GUIDELINE OVERVIEW

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- Update from 2013 guideline (Jauch Stroke 2013)
- 19 writing group members including **neurology, neurosurgery, radiology, emergency medicine, and nursing**
- Members not allowed to discuss/vote on areas if perceived RWI
- Areas addressed:
  - Prehospital care, emergency management, acute treatment (IV tpa, EVT), in-hospital management (*including secondary prevention measures begun during initial hospitalization, **within first 2 weeks***)
- Independent evidence review committee commissioned to systematically review limited number of clinical questions
  - LVO prediction instruments, dysphagia screening
- Modified ACC/AHA class of recommendation, level of evidence
- New streamlined format with knowledge bytes, evidence tables
- 87 pgs (2013) vs. 48 pgs (2018)

2015 ACC/AHA COR/LOE FORMAT

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 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

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.

Example Rec 2013

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1. **Intravenous rtPA (0.9 mg/kg, maximum dose 90 mg) is recommended for selected patients who may be treated within 3 hours of onset of ischemic stroke *(Class I; Level of Evidence A)*. Physicians should review the criteria outlined in Tables 10 and11 (which are modeled on those used in the NINDS Trial) to determine the eligibility of the patient. A recommended regimen for observation and treatment of patients who receive intravenous rtPA is described in** Table 12. (Unchanged from the previous guideline[13])

Example Rec 2018

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STRENGTH OF RECOMMENDATION

LEVEL OF EVIDENCE

3.5. IV Alteplase	COR	LOE	New, Revised, or Unchanged
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	Recommendation reworded for clarity from 2013 AIS Guidelines. Class and LOE unchanged. See Table LXXXIII in online Data Supplement 1 for original wording.
The safety and efficacy of this treatment when administered within the first 3 hours after stroke onset are solidly supported by combined data from multiple RCTs[90,139,140] and confirmed by extensive community experience in many countries.[141] The eligibility criteria for IV alteplase have evolved over time as its usefulness and true risks have become clearer. A recent AHA statement provides a detailed discussion of this topic.[15] Eligibility recommendations for IV alteplase in patients with AIS are summarized in Table 6. The benefit of IV alteplase is well established for adult patients with disabling stroke symptoms regardless of age and stroke severity.[73,142] Because of this proven benefit and the need to expedite treatment, when a patient cannot provide consent (eg, aphasia, confusion) and a legally authorized representative is not immediately available to provide proxy consent, it is justified to proceed with IV thrombolysis in an otherwise eligible adult patient with a disabling AIS. In a recent trial, a lower dose of IV alteplase (0.6 mg/kg) was not shown to be equivalent to standard-dose IV alteplase for the reduction of death and disability at 90 days.[143] Main elements of postthrombolysis care are listed in Table 7.			See Table XXXIV in online Data Supplement 1.

KNOWLEDGE BYTE

LVO Screening

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"No scale predicted LVO with both high sensitivity and high specificity…more prospective studies are needed to assess the accuracy of LVO prediction instruments in the prehospital setting…"

AHA/ASA Systematic Review

Accuracy of Prediction Instruments for Diagnosing Large Vessel Occlusion in Individuals With Suspected Stroke

A Systematic Review for the 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine and Neurocritical Care Society

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Smith EE et al. Stroke 2018

Dysphagia Screening

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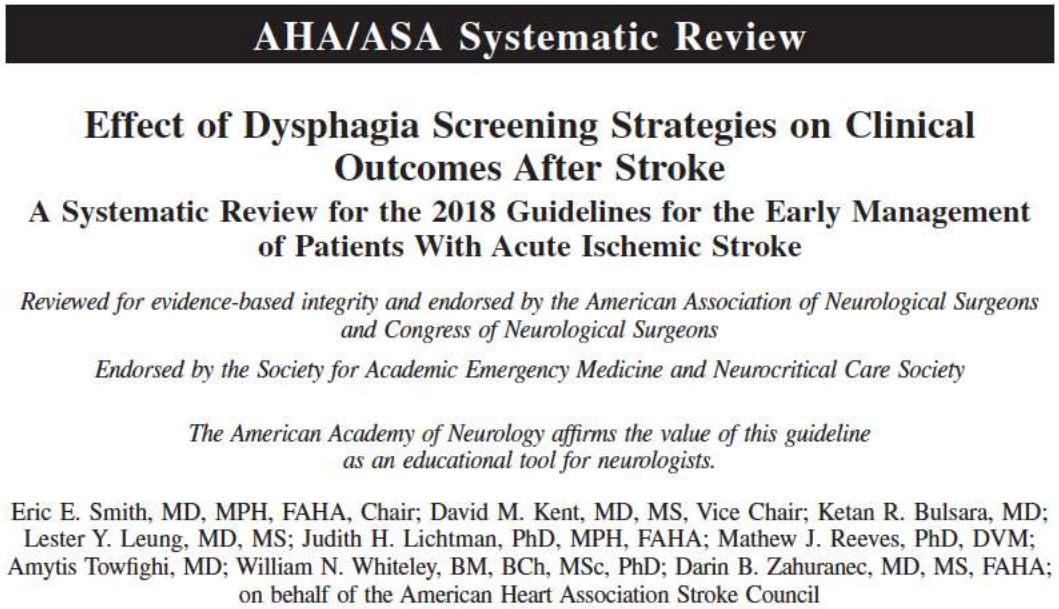
"This systematic review found insufficient RCT data to show whether implementation of a specific dysphagia screening protocol reduces the risk of death or dependency after stroke."



AHA/ASA Systematic Review

Effect of Dysphagia Screening Strategies on Clinical Outcomes After Stroke

A Systematic Review for the 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

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2018 GUIDELINE

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GOOD

- Extended Window Thrombectomy (I, A)
- Telestroke (IIa, B-R)
- TNK (IIb, B-R)
- Minor stroke/TIA (IIa, B-R)

BAD

- Dysphagia screening (IIa, C-LD)
- DVT prophylaxis (IIb, A)
- MRIs, Echo, Lipid panels (III, B-NR)

UGLY...

April 18, 2018

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CORRECTION

Correction to: 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

www.medscape.com

AHA Rescinds Large Sections of New Stroke Guidelines

Sue Hughes

April 27, 2018

2018;49:e46–e110. DOI: 10.1161/STR.0000000000000158), the American Heart Association/American Stroke Association has reviewed the guideline and is preparing clarifications, modifications, and/or updates to several sections in it. Currently, those sections, listed here, have been deleted from the guideline while this clarifying work is in process:

Section 1.3 EMS Systems Recommendation 4
Section 1.4 Hospital Stroke Capabilities Recommendation 1
Section 1.6 Telemedicine Recommendation 3
Section 2.2 Brain Imaging Recommendation 11
Section 3.2 Blood Pressure Recommendation 3
Section 4.3 Blood Pressure Recommendation 2
Section 4.6 Dysphagia Recommendation 1
Section 6.0 All subsections (11)


SOUT
51

REVISED 2019 GUIDELINE

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- Sent back to the writing group for review and revising
- 14 new peer reviewers (compared to just 4 with initial guideline)
- Addition of new RCTs published since release of 2018 guideline
- Removed recommendations reviewed/revised/edited and placed back into the guidelines
    - Attempted to change wording in several recommendations from ***negative*** statements to ***positive*** statements
- Writing group *consensus (*i.e. NOT *unanimity)*
- Final approval by AHA Stroke Council and Scientific Review Committee
- Final endorsement by peer societies

October 30, 2019

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AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

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

Endorsed by the Society for Academic Emergency Medicine and The Neurocritical Care Society

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons.

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Hospital Bypass?

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2018 & 2019

4. When several IV alteplase–capable hospital options exist within a defined geographic region, the benefit of bypassing the closest to bring the patient to one that offers a higher level of stroke care, including mechanical thrombectomy, is uncertain. Further research is needed.	IIb	B-NR

2019

5. Effective prehospital procedures to identify patients who are ineligible for IV thrombolysis and have a strong probability of large vessel occlusion (LVO) stroke should be developed to facilitate rapid transport of patients potentially eligible for thrombectomy to the closest healthcare facilities that are able to perform mechanical thrombectomy.	IIb	C-EO

Dysphagia Screening

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2013

5. Assessment of swallowing before the patient begins eating, drinking, or receiving oral medications is recommended *(Class I; Level of Evidence B)*. (Unchanged from the previous guideline[13])

2018

1. 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

2019

4.7. Dysphagia	COR	LOE
1. Dysphagia screening before the patient begins eating, drinking, or receiving oral medications is effective to identify patients at increased risk for aspiration.	I	C-LD

MRI

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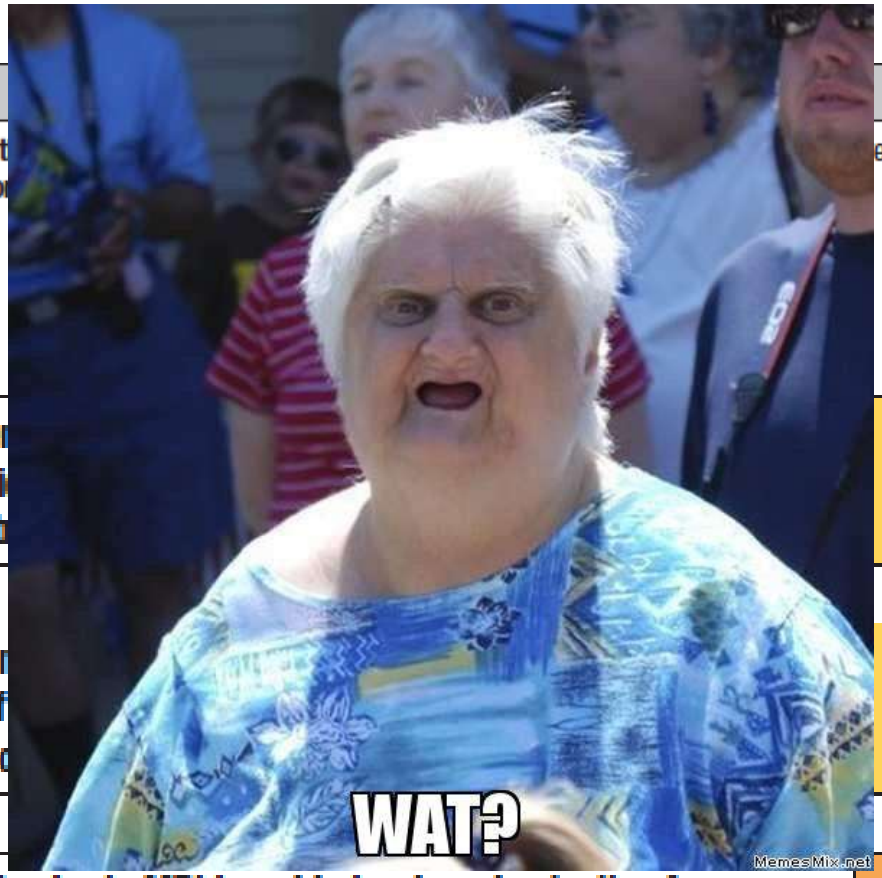
2018

6.1. Brain Imaging	New, Revised, or Unchanged
1. Routine use of brain MRI in all patients wit is not recommended for initial diagnosis o	ecommendation.

2019

1. For prevention of recurre patients with AIS to provi appropriate secondary st	IIa	C-EO
2. Brain MRI is reasonable i evaluation to determine if investigated mechanical c	IIa	B-R
3. The effectiveness of routine brain MRI to guide treatment selection for prevention of recurrent stroke is uncertain. (See knowledge byte following 6.1, recommendation 1.)	IIb	B-NR



NEW DATA!

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WAKE-UP

3. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) administered within 4.5 hours of stroke symptom recognition can be beneficial in patients with AIS who awake with stroke symptoms or have unclear time of onset >4.5 hours from last known well or at baseline state and who have a DW-MRI lesion smaller than one-third of the MCA territory and no visible signal change on FLAIR.	IIa	B-R

Mild Stroke

3. For otherwise eligible patients with mild nondisabling stroke symptoms (NIHSS score 0–5), IV alteplase is not recommended for patients who could be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state.	III: No Benefit	B-R

TNK

1. It may be reasonable to choose tenecteplase (single IV bolus of 0.25-mg/kg, maximum 25 mg) over IV alteplase in patients without contraindications for IV fibrinolysis who are also eligible to undergo mechanical thrombectomy.	IIb	B-R
2. 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

TAKE HOME

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- New AIS guidelines officially usher in the endovascular era
- Streamlined approach to guideline formation and layout
- COR/LOE more rigorous than before
- Philosophical questions
    - Evidence vs. Expert
    - Scientific vs. Practical
    - Change vs. Status quo
- Future considerations
    - Peer review
    - Additional voices
    - Transparency
- What's next?

"When any real progress is made, we unlearn and learn anew what we thought we knew before."

-Thoreau

QUESTIONS?

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American Heart Association | American Stroke Association

EXTRA SLIDES

We continue to support this corrected version of the guideline and its support for clinical decision-making. After review, a revised guideline, with consideration given to the clarifications, modifications, and/or updates of the sections noted above, will be posted over the coming weeks.

Ensuring our scientific guidelines reflect the best, most comprehensive scientific analysis has always been, and remains, the Association's top priority. We appreciate the continuing commitment and dedication of our volunteer writing group, peer reviewers, and the scientific community at large, who share our devotion to the integrity and quality of guideline development.