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2018 AHA/ASA Acute Ischemic Ischemic Stroke Guidelines: The *Good*, the *Bad*, and the *Ugly*

NECC Summit Newport, RI October 25, 2018

Disclosures



- Research Support
 - HRSA GO1RH27869-01-00
 - Coulter Translational Research Fund
 - Virginia Alliance of Emergency Medicine Research
 - American Heart Association/American Stroke Association
 - American Academy of Neurology (AAN), American Board of Psychiatry and Neurology (ABPN)

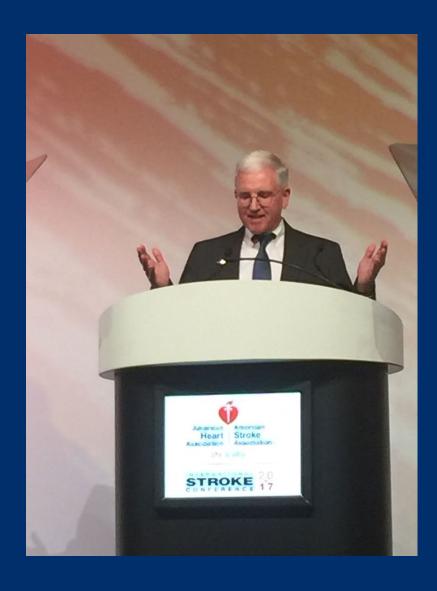




- U.S. Patent Application No. 14/910,890 (iTREAT)
- U.S. Provisional Patent Application No. 62/620,096 (BANDIT)



EC Haley, Jr. - UVA Neurology 1984 - 2017







Learning Objectives



- 1) The Good: New recommendations and areas of emphasis in the 2018 Update
- 2) The Bad: Recommendations in need of further research and clarity
- 3) The Ugly: Corrections and controversy, what's next?
- 4) Discussion/Q&A



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.

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Guideline Overview



- 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), Inhospital management (*Including secondary prevention measures begun during initial hospitalization, within first 2 weeks*)
- Independent <u>evidence review committee</u> commissioned to systematically review of a 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)

Renefit >> Rist

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 III (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 Dat

- 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

EVEL 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 Ila; 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.

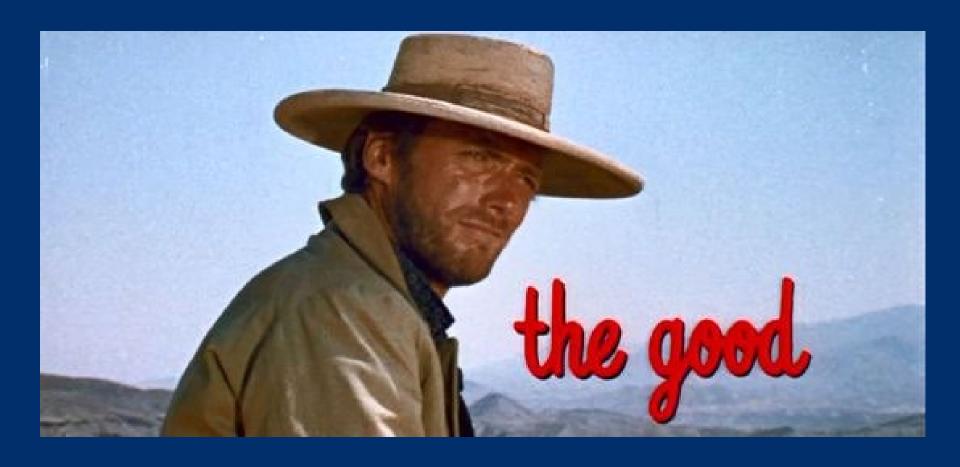
COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Example Rec 2013

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 and 11 (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

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.	ı	Α	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 supported by combined data from multiple RCTs ^{90,139,140} and confirmed by in many countries. ¹⁴¹ The eligibility criteria for IV alteplase have evolved or risks have become clearer. A recent AHA statement provides a detailed disrecommendations for IV alteplase in patients with AIS are summarized in Tawell established for adult patients with disabling stroke symptoms regardles Because of this proven benefit and the need to expedite treatment, when a paphasia, confusion) and a legally authorized representative is not immediately it is justified to proceed with IV thrombolysis in an otherwise eligible adult patiental, a lower dose of IV alteplase (0.6 mg/kg) was not shown to be equivalent reduction of death and disability at 90 days. ¹⁴³ Main elements of postthrombol	extensive community or time as its use scussion of this to ble 6. The benefit as of age and strok patient cannot proving available to proving to standard-dose ly	nity experience ofulness and true pic. 15 Eligibility of IV alteplase is the severity. 73,142 wide consent (eg, ide proxy consent, g AIS. In a recent V alteplase for the	See Table XXXIV in online Data Supplement 1.

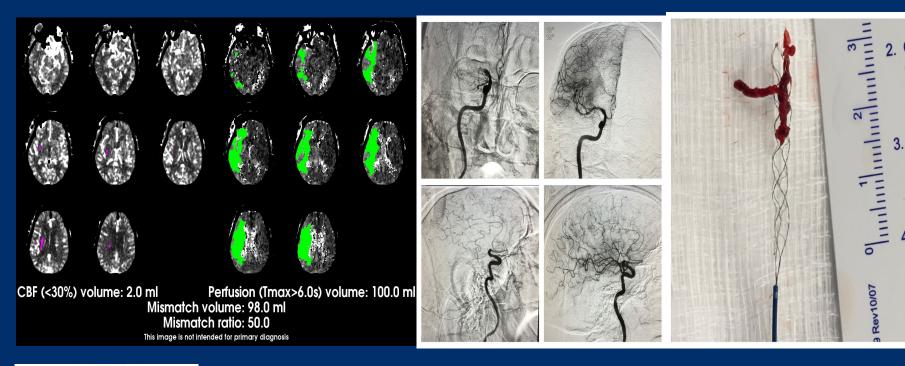




A New DAWN...



Presented at ESOC in Prague – April 2017 73% relative risk reduction of dependency in ADL's NNT for any lower disability = 2







DAWN, DEFUSE-3



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuva,

D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.J. B.P. Mehta, B.W. Baxter, M.G. Abraham, P. F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lope V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. F. J.-M. Olivot, W.G. Tekle, R. Shields, T. Gra D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

G.W. Albers, M.P. Marks, S. Kemp, S. Christensen, J.P. Tsai, S. Ortega-Gutierrez, R.A. McTaggart, M.T. Torbey, M. Kim-Tenser, T. Leslie-Mazwi, A. Sarraj, S.E. Kasner, S.A. Ansari, S.D. Yeatts, S. Hamilton, M. Mlynash, J.J. Heit, G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators*



Thrombectomy Recs

Thrombectomy 0-6 hrs (revised from 2015 Statement)

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. Recommendation revised from 2015 Endovascular.

Extended Window Thrombectomy 6-24 hrs (DAWN and DEFUSE 3)

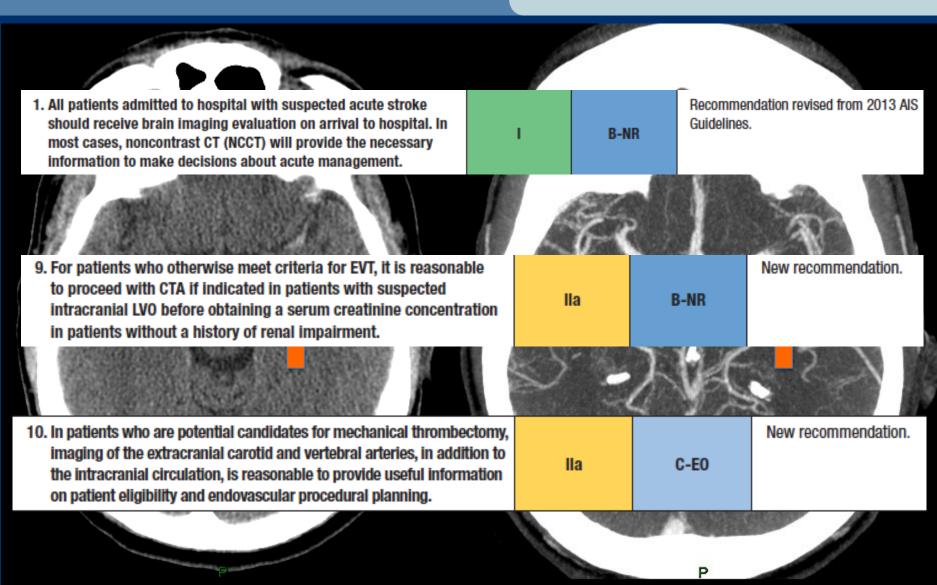
7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.

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.

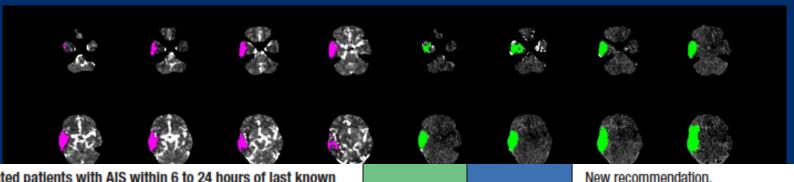
New recommendation.

New recommendation.

Acute Neuroimaging



Perfusion Imaging



Total Mismatch difference: 115 ml Total Mismatch ratio: 4.4

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.

iSchemaView!

CBF<30% volume: 7 ml

Imaging mbectomy.

Tmax>6.0s volume: 105 ml

Mismatch volume: 98 ml

Total CBF<30% volume: 34 ml

Total Tmax>6.0s volume: 149 ml



Acute Thrombolysis

tPA + EVT

3.7. Mechanical Thrombectomy	COR	LOE	New, Revised, or Unchanged
Patients eligible for IV alteplase should receive IV alteplase even if EVTs are being considered.	ı	Α	Recommendation reworded for clarity from 2015 Endovascular. See Table LXXXIII in online Data Supplement 1 for original wording.
In patients under consideration for mechanical thrombectomy, observation after IV alteplase to assess for clinical response should not be performed.	III: Harm	B-R	Recommendation revised from 2015 Endovascular.

Tenecteplase (TNK)

 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. 	llb	B-R	New recommendation.
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EMS Systems



1.3. EMS Systems	COR	LOE	New, Revised, or Unchanged
1. EMS leaders, in coordination with local, regional, and state agencies and in consultation 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 (face, arm, speech test) scale, Los Angeles Prehospital Stroke Screen, or Cincinnati Prehospital Stroke Scale.	_	B-NR	Recommendation reworded for clarity from 2013 Stroke Systems of Care. Class and LOE added to conform with ACC/AHA 2015 Recommendation Classification System. See Table LXXXIII in online Data Supplement 1 for original wording.
	See Table IV in online Data Supplement 1.		
2. Regional systems of stroke care should be developed. These should consist of the following: (a) Healthcare facilities that provide initial emergency care, including administration of IV alteplase, and, (b) Centers capable of performing endovascular stroke treatment with comprehensive periprocedural care to which rapid transport can be arranged when appropriate.	ı	Α	Recommendation reworded for clarity from 2015 Endovascular. Class and LOE unchanged. See Table LXXXIII in online Data Supplement 1 for original wording.
Patients with a positive stroke screen and/or a strong suspicion of stroke should be transported rapidly to the closest healthcare facilities that can capably administer IV alteplase.	I	B-NR	Recommendation reworded for clarity from 2013 AIS Guidelines. See Table LXXXIII in online Data Supplement 1 for original wording.

sudden signs of a stroke and what you need to do when it happens. When you spot the signs, call 9-1-1 right away.

gets to the hospital, the sooner they can begin treatment. And that can make a remarkable difference in recovery.



LVO Screening

"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

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Telestroke



	4. Telestroke/teleradiology evaluations of AIS patients can be effective for correct IV alteplase eligibility decision making.	lla	B-R	New recommendation.
Jo	The STRokEDOC (Stroke Team Remote Evaluation Using a Digital Observation the hypothesis that telemedicine consultations, which included teleradiology, resulted in statistically significantly more accurate IV alteplase eligibility decis symptoms and signs of an acute stroke syndrome in EDs. ⁴⁶	See Table XI in online Da		
	 Administration of IV alteplase guided by telestroke consultation for patients with AIS may be as safe and as beneficial as that of stroke centers. 	New recommendation.		
	A systematic review and meta-analysis was performed to evaluate the safety delivered through telestroke networks in patients with AIS. Symptomatic intra were similar between patients subjected to telemedicine-guided IV alteplase at stroke centers. There was no difference in mortality or in functional indepetelestroke-guided and stroke center-managed patients. The findings indicate telestroke networks is safe and effective in the 3-hour time window. ⁴⁷	See Table XII in online Da		
	6. Providing alteplase decision-making support via telephone consultation to community physicians is feasible and safe and may be considered when a hospital has access to neither an in-person stroke team nor a telestroke system.	New recommendation.		
	The advantages of telephone consultations for patients with acute stroke synuse, simplicity, availability, portability, short consultation time, and facile imp	See Table XIII in online D		
	7. Telestroke networks may be reasonable for triaging patients with AIS who may be eligible for interfacility transfer in order to be considered for acute mechanical thrombectomy.	llb	B-NR	New recommendation.

Antiplatelet Therapy

CHANCE Trial

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.

New recommendation.

B-R

POINT Trial...to be continued



Hospital Bypass?

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.

llb

B-NR

Hospital Certification



1.4. Hospital Stroke Capabilities	COR	LOE	New, Revised, or Unchanged
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.	-	B-NR	Recommendation reworded for clarity from 2013 AlS Guidelines. Class unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System. See Table LXXXIII in online Data Supplement 1 for original wording.

Perfusion Imaging <6 hrs



11. Additional imaging beyond CT and CTA or MRI and magnetic resonance angiography (MRA) such as perfusion studies for selecting patients for mechanical thrombectomy in <6 hours is not recommended.

III: No Benefit

B-R

New recommendation.



Dysphagia Screening



"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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Dysphagia Screening



2013

 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 guideline¹³)

2018

 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



DVT Prophylaxis



The benefit of prophylactic-dose subcutaneous heparin (unfractionated heparin [UFH] or LMWH) in immobile patients with AIS is not well established.

IIb

A

New recommendation.

Diagnostic Testing

MRI

6.1. Brain Imaging	COR	LOE	New, Revised, or Unchanged
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: No Benefit	B-NR	New recommendation.

Intracranial Imaging

2. In patients with AIS, routine noninvasive imaging by means of CTA
or MRA of the intracranial vasculature to determine the presence
of intracranial arterial stenosis or occlusion is not recommended to
plan subsequent secondary preventive treatment.

		New recommendation.
III: No Benefit	Α	

Echo

4. Routine use of echocardiography in all patients with AIS to plan			New recommendation.
subsequent secondary preventive treatment is not cost-effective	III: No Benefit	B-NR	
and is not recommended.			

Cholesterol

1. Routine measurement of blood cholesterol levels in all patients with			New recommendation.
ischemic stroke presumed to be of atherosclerotic origin who are	III: No Benefit	B-R	
not already taking a high-intensity statin is not recommended.			



April 18, 2018



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

Based on recent feedback received from the clinical stroke community related to the article by Powers et al, "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," which published ahead of print January 24, 2018, and appeared in the March 2018 issue of the journal (*Stroke*. 2018;49:e46–e110. DOI: 10.1161/STR.00000000000000158), 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)

AHA Rescinds Large Sections of New Stroke Guidelines

Sue Hughes

April 27, 2018

The AHA sent the following statement to Medscape Medical News:

"A new guideline often generates healthy discussion and debate. Following questions from our volunteers and others in the stroke community regarding some of the recommendations in this guideline, there were several issues of clarity in wording that emerged after publication that we felt needed to be addressed.

"We believe that much of this occurred because we continually refine our system of categorizing evidence and the system used for the AIS guideline was the first time this Writing Group had used it," the statement notes.

"We have reconvened the writing group to consider whether clarifications, modifications or updates would address the concerns about clarity. Their work to review and clarify select sections of the guideline is currently underway. We anticipate the updated guideline will be ready for publication this summer."



Take Home



- 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
 - Transparency
- Next steps
 - Revised guideline coming soon…so stay tuned!

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

Thoreau

Questions?



Contact:
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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.