Current Guidelines for Acute Ischemic Stroke Management

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Canon Stroke and Vascular Research Center
Jacobs Institute, Gates Vascular Institute, and Kaleida Health
Disclosures

• Research and consultant support: Canon, Stryker, Penumbra, Medtronic, Jacobs Institute
• Founding member: Neurovascular Diagnostics
• Stockholder: Blockade Medical
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

Stroke. 2018;49:e46–e99
Live Case Presentations

• Congress of Neurologic Surgeons (3k physicians)
• TCT - Transcatheter Cardiovascular Therapeutics (5k physicians, 10k attendees)
• World Live Neurovascular Conference (1k physicians)
• LINC – Leipzig Interventional Course (5k, global)
Trials - AIS

• **Tiger**- Treatment with Intent to Generate Endovascular Reperfusion
• **Vigor**- VIGOR: Volumetric Impedance to Guide Stroke Response
• **Confidence**- Carotid Stent Trial to Evaluate the Safety and Efficacy of the Roadsaver Stent Used in Conjunction with the Nanoparasol® Embolic Protection System for Patients at Increased Risk for Adverse Events from Carotid Endarterectomy
• **CREST2**- CAROTID REVASCULARIZATION AND MEDICAL MANAGEMENT FOR ASYMPTOMATIC CAROTID STENOSIS TRIAL
• **CREST H**- Carotid Revascularization and Medical Management for Asymptomatic Carotid stenosis – Hemodynamics
• **CREST Registry**- The Need for CREST-2 Registry (C2R) While the CMS coverage decision in 2005 made CAS available to a subset of high-risk patients with carotid artery stenosis, the vast majority of carotid occlusive disease exists in an asymptomatic standard surgical risk patient population.
• **Stance**- Statin Neuroprotection and Carotid Endarterectomy: Safety, Feasibility and Outcomes
<table>
<thead>
<tr>
<th>Institution</th>
<th>Location</th>
<th>CAST/Accreditation</th>
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Academic impact and rankings of neuroendovascular fellowship programs across the United States

Ashish Sonig, MD, MS, MCh, Hussain Shalwani, MD, Bennett R. Levy, Hakeem J. Shakir, MD, and Adnan H. Siddiqui, MD, PhD
Public Health Impact of Stroke

- 4th leading cause of death in US (Expected to be 5-6), #2 worldwide
  - Relative Rate of Stroke Deaths has declined by 40% in US since 2000
- #1 cause of Disability! Most prevalent neurologic condition, most comment discharge diagnosis to nursing homes and rehab
  - > 2/3 of survivors need rehabilitation after hospitalization
  - Large scale rigorous clinical trials on stroke rehab have been few (VR and AR opportunities)
- WNY is 25% higher than national stroke rate with one regional zip code at 200%
Need Improvements in Assessment Guidelines

• NIHSS:
  • good prognostics of mortality and some level of morbility
  • poor for predicting in level of impairment and deficits such as depression, hand-motor deficits, swallowing, or cognitive dysfunction

• 3 major dimensions to Complete Assessment:
  • body structures/body functions (impairments), activities (activity limitations), and participation (participation restrictions)

• Barthel Index, Functional Independence Measure (FIM), mRS
• MMSE
• Computer based Assessments
Unmet needs of Current Assessments

• Apathy in >50% of survivors
• Fatigue is often a common and debilitating symptom
• Daily physical activity in community living stroke survivors are low
• Depressive symptoms are high
• >30 % of stroke survivors report difficulty with autonomy, engagement, or fulfilling societal roles (meaningful)
Clinical Evaluation

• NIHSS

• AHA certification
  • [www.americanheart.org](http://www.americanheart.org)
    • Go to “For Healthcare Professionals/stroke resources”
<table>
<thead>
<tr>
<th>Instructions</th>
<th>Scale Definition</th>
<th>Score</th>
</tr>
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</table>
| **1a. Level of Consciousness:** The investigator must choose a response if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/condition. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation. | 0 = Alert; keenly responsive.  
1 = Not alert; but arousable by minor stimulation to obey, answer, or respond.  
2 = Not alert; requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped).  
3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and arreflexic. | ____ |
| **1b. LOC Questions:** The patient is asked the month and his/her age. The answer must be correct. There is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysphasia from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not “help” the patient with verbal or non-verbal cues. | 0 = Answers both questions correctly.  
1 = Answers one question correctly.  
2 = Answers neither question correctly. | ____ |
| **1c. LOC Commands:** The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him or her (pantomime), and the result scored (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored. | 0 = Performs both tasks correctly.  
1 = Performs one task correctly.  
2 = Performs neither task correctly. | ____ |
| **2. Best Gaze:** Only horizontal eye movements will be tested. Voluntary or reflexive (oculoccephalic) eye movements will be scored, but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI), score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements, and a choice made by the investigator. Establishing eye contact and then moving the patient from side to side will occasionally clarify the presence of a partial gaze palsy. | 0 = Normal.  
1 = Partial gaze palsy; gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present.  
2 = Forced deviation, or total gaze paresis not overcome by the oculoccephalic maneuver. | ____ |
<table>
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<tr>
<th>Test Category</th>
<th>Scores</th>
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| Visuals: | 0 = No visual loss.  
1 = Partial hemianopia.  
2 = Complete hemianopia.  
3 = Bilateral hemianopia (blind including cortical blindness). |
| Facial Palsy: | 0 = Normal symmetrical movements.  
1 = Minor paralysis (flattened nasolabial fold, asymmetry on grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient).  
2 = Partial paralysis (total or near-total paralysis of lower face).  
3 = Complete paralysis of one or both sides (absence of facial movement in the upper and lower face). |
| Motor Arms: | 0 = No drift; limb holds 0 or 45 degrees for 10 seconds.  
1 = Drift; limb holds 0 or 45 degrees, but drifts down before full 10 seconds; does not hit bed or other support.  
2 = Some effort against gravity; limb cannot get to or maintain (if used) 0 or 45 degrees, drifts down to bed, but has some effort against gravity.  
3 = No effort against gravity; limb falls.  
4 = No movement.  
UN = Amputation or joint fusion, explain: |  
5a. Left Arm  
5b. Right Arm |
| Motor Legs: | 0 = No drift; leg holds 30-degree position for full 5 seconds.  
1 = Drift; leg falls by the end of the 5-second period but does not hit bed.  
2 = Some effort against gravity; leg fails to bed by 5 seconds, but has some effort against gravity.  
3 = No effort against gravity; leg fails to bed immediately.  
4 = No movement.  
UN = Amputation or joint fusion, explain: |  
6a. Left Leg  
6b. Right Leg |
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<th>Section</th>
<th>Description</th>
<th>Scores</th>
<th>Notes</th>
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<td>7.</td>
<td>Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-to-nose and heel-to-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot answer or is paralyzed. Only in the case of amputation or joint fusion, the examiner should record the score as unstable (UN), and clearly write the explanation for this choice. In case of blindness, test by having the patient touch nose from extended arm position.</td>
<td>0 = Absent. 1 = Present in one limb. 2 = Present in two limbs. UN = Amputation or joint fusion, explain:</td>
<td></td>
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<td>8.</td>
<td>Sensory: Sensation or grimace to pinprick when tested, or withdrawal from noxious stimuli in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for homonymous loss. A score of 2, &quot;severe or total sensory loss,&quot; should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will, therefore, probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (item 16-19) are automatically given a 2 on this item.</td>
<td>0 = Normal; no sensory loss. 1 = Mild to moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side, or there is a loss of superficial pain with pinprick, but patient is aware of being touched. 2 = Severe to total sensory loss; patient is not aware of being touched in the face, arm, and leg.</td>
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<td>9.</td>
<td>Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For this scale item, the patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet and to read from the attached list of sentences. Comprehension is judged from responses here, as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in a coma (item 16-19) will automatically score 3 on this item. The examiner must choose a score for the patient with slurred or limited cooperation, but a score of 3 should be used only if the patient is mute and following no one-step commands.</td>
<td>0 = No aphasia; normal. 1 = Mild to moderate aphasia; some obvious loss of fluency or facility of comprehension; without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in a conversation about provided materials, examiner can identify picture or naming content from patient's response. 2 = Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = mute, global aphasia; no usable speech or auditory comprehension.</td>
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<td>10.</td>
<td>Dysarthria: If patient is thought to be normal, an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barriers to producing speech, the examiner should record the score as unstable (UN), and clearly write the explanation for this choice. Do not tell the patient why he or she is being tested.</td>
<td>0 = Normal. 1 = Mild to moderate dysarthria; patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = Severe dysarthria; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/aphasic. UN = Intubated or other physical barrier, explain:</td>
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<td>11. Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.</td>
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<td>0 = No abnormality.</td>
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<td>1 = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities.</td>
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<td>2 = Profound hemi-inattention or extinction to more than one modality; does not recognize own hand or orients to only one side of space.</td>
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## mRS

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<td>1</td>
<td>No significant disability despite symptoms; able to carry out all usual duties and activities</td>
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<tr>
<td>2</td>
<td>Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability; requiring some help, but able to walk without assistance</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance</td>
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<td>5</td>
<td>Severe disability; bedridden, incontinent and requiring constant nursing care and attention</td>
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<td>6</td>
<td>Dead</td>
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Data derived from Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. N Engl J Med. 2018
Classification of Stroke

• Ischemic (80%)
  • ICAD
  • Lacunar
  • Carotid Occlusive disease (25%)

• Hemorrhagic (20%)
  • Intracerebral hemorrhage
  • Subarachnoid hemorrhage
Thrombus lodges in the cerebral artery causing a stroke.

Thrombus in the carotid artery breaks off and travels to the cerebral artery in the brain.

Diseased carotid artery.

Normal carotid artery.
Stroke Treatment Options in 2013

• ASA within 24-48 hrs is recommended
• IV rtPA in appropriate patients (<3-4.5 hours)
• IA thrombolysis an option in major MCA stroke patients <6 hours if not IV rtPA candidates (dose not determined and NOT FDA approved)
• Mechanical thrombectomy devices can be offered in carefully selected patients and should continue to be studied in randomized trials

AHA/ASA Stroke Guidelines Stroke 2013
TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE rt-PA STROKE STUDY GROUP*

Abstract Background  Thrombolytic therapy for acute ischemic stroke has been approached cautiously because there were high rates of intracerebral hemorrhage in early clinical trials. We performed a randomized, double-blind trial of intravenous recombinant tissue plasminogen activator (t-PA) for ischemic stroke after recent pilot studies suggested that t-PA was beneficial when treatment was begun within three hours of the onset of stroke.

Methods. The trial had two parts. Part 1 (in which 291 patients were enrolled) tested whether t-PA had clinical activity, as indicated by an improvement of 4 points over baseline values in the score of the National Institutes of Health stroke scale (NIHSS) or the resolution of the neurologic deficit within 24 hours of the onset of stroke. Part 2 (in which 333 patients were enrolled) used a global test statistic to assess clinical outcome at three months, according to scores on the Barthel index, modified Rankin scale, Glasgow outcome scale, and NIHSS.

Results. In part 1, there was no significant difference between the group given t-PA and that given placebo in the percentages of patients with neurologic improvement at 24 hours, although a benefit was observed for the t-PA group at three months for all four outcome measures. In part 2, the long-term clinical benefit of t-PA predicted by the results of part 1 was confirmed (global odds ratio for a favorable outcome, 1.7; 95 percent confidence interval, 1.2 to 2.6). As compared with patients given placebo, patients treated with t-PA were at least 30 percent more likely to have minimal or no disability at three months on the assessment scales. Symptomatic intracerebral hemorrhage within 36 hours after the onset of stroke occurred in 6.4 percent of patients given t-PA but only 0.6 percent of patients given placebo (P<0.001). Mortality at three months was 17 percent in the t-PA group and 21 percent in the placebo group (P = 0.30).

Conclusions. Despite an increased incidence of symptomatic intracerebral hemorrhage, treatment with intravenous t-PA within three hours of the onset of ischemic stroke improved clinical outcome at three months. (N Engl J Med 1995;333:1581-7.)
• Any NIHSS > 0 included

• Part 1: (~300 pts) NIHSS improvement of 4 point by 24 hours
  • No difference

• Part 2: (~300 pts) 3 month mRS
  • 30 percent more mRS 0-1

  ![Modified Rankin Scale Diagram]

  • 6% vs 0.6% s ICH

  • Asx rate of 12%! 
IV-tPA Contraindications

- TBI or stroke within 3 mo
- SAH
- Previous ICH
- Recent surgery or arterial puncture
- Elevated BP (> 185)
- Active bleeding
- Hypoglycemia (< 50)
- Platelet < 100,000

- Heparin received within 48 hrs
- Anticoagulation
- Large infarction
- Minor stroke or rapidly improving symptoms
There remains insufficient evidence to identify a threshold of hypoattenuation severity or extent that affects treatment response to alteplase. However, administering IV alteplase to patients whose CT brain imaging exhibits extensive regions of clear hypoattenuation is not recommended. These patients have a poor prognosis despite IV alteplase, and severe hypoattenuation defined as obvious hypodensity represents irreversible injury.† (Class III: No Benefit; LOE A)§
3.5. IV Alteplase

<table>
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<th>3.5. IV Alteplase</th>
<th>COR</th>
<th>LOE</th>
<th>New, Revised, or Unchanged</th>
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<tbody>
<tr>
<td>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.</td>
<td>I</td>
<td>A</td>
<td>Recommendation reworded for clarity from 2013 AIS Guidelines. Class and LOE unchanged. See Table LXXXIII in online Data Supplement 1 for original wording.</td>
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</tbody>
</table>

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 and confirmed by extensive community experience in many countries. 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. 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. 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. Main elements of postthrombolysis care are listed in Table 7.

| 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 to determine patient eligibility. | I   | B-R  | Recommendation reworded for clarity from 2013 AIS 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. |

One trial (ECASS-III) specifically evaluating the efficacy of IV alteplase within 3 and 4.5 hours after symptom onset and pooled analysis of multiple trials testing IV alteplase within various time windows support the value of IV thrombolysis up to 4.5 hours after symptom onset. ECASS-III excluded octogenarians, patients taking warfarin regardless of international normalized ratio, patients with combined history of diabetes mellitus and previous ischemic stroke, and patients with very severe strokes (NIHSS score >25) because of a perceived excessive risk of intracranial hemorrhage in those cases. However, careful analysis of available published data summarized in an AHA/American Stroke Association scientific statement indicates that these exclusion criteria from the trial may not be justified in practice (Table 6).
Additional exclusion criteria Between 3 and 4.5 hours:
- Age >80 years
- Severe stroke (NIHSS > 25)
- History of diabetes and prior stroke
- Taking an oral anticoagulant regardless of INR
Intravenous Thrombolysis

- IV thrombolysis received approval by the FDA for treatment of acute ischemic stroke within 0-3 hours
- Approval granted based on 1995 NINDS rtPA stroke trial
- IV thrombolysis within 3-4.5 hours (for selected group of patients, Class I; Level of Evidence B) is recommended by AHA/ASA but not FDA-approved
IV tPA and Large-Vessel Occlusion (35-40% of Ischemic Stroke)

• Clinical response to thrombolysis is influenced by the site of occlusion

• Rate of recovery from IV tPA by occlusion
  • 33% for distal MCA occlusion
  • 15% for proximal MCA occlusion
  • 0% with ICA-T occlusions

• Mortality of LVO

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>53%</td>
</tr>
<tr>
<td>MCA</td>
<td>27%</td>
</tr>
<tr>
<td>Basilar Artery</td>
<td>89-90%</td>
</tr>
</tbody>
</table>

2. Furlan A et al. PROACT II Trial

Stroke. 2007;38:948-954
Volume of Patients within Presenting NIHSS Category

Research/Technology to increase presentations of High NIHSS
Stroke Treatment Options in 2013

- **ASA** within 24-48 hrs is recommended
- **IV rtPA** in appropriate patients (<3-4.5 hours)
- **IA thrombolysis** an option in major MCA stroke patients <6 hours if not IV rtPA candidates (dose not determined and NOT FDA approved)
- Mechanical thrombectomy devices can be offered in carefully selected patients and should continue to be studied in randomized trials

_AHA/ASA Stroke Guidelines Stroke 2013_
Prospective Acute Ischemic Stroke Outcomes After Endovascular Therapy: A Real-World Experience

Sabareesh K. Natarajan¹,³, Yuval Karmon¹,³, Kenneth V. Snyder¹,³, Hajime Ohta¹,³, Erik F. Hauck¹,³, L. Nelson Hopkins¹,²,³, Adnan H. Siddiqui¹,²,³, Elad I. Levy¹,²,³

OBJECTIVE: To report results of endovascular therapy for acute ischemic stroke (AIS) in patients who were not candidates for intravenous thrombolysis (IVT) or in whom IVT failed.

METHODS: Prospectively collected data for patients treated between January 2006 and June 2009 were analyzed retrospectively. After careful patient and therapy selection, 213 AIS patients with a mean NIHSS score of 14.2 at presentation underwent intervention. End points analyzed were Thrombolysis in Myocardial Infarction (TIMI) 2/3 reperfusion, symptomatic intracranial hemorrhage (SICH) rates, and 90-day outcomes (modified Rankin Scale [mRS] and mortality). Multivariate binary logistic regression analysis was used to assess independent predictors of end points.

RESULTS: Of 189 patients with anterior circulation occlusions, 135 were treated within 0–8 hours, 33 were treated after 8 or more hours, and 21 were treated after wake-up stroke (WUS). Among 24 patients treated with posterior circulation occlusions, 4 had WUS. After treatment, 72.3% patients had TIMI 2/3 reperfusion; SICH rate was 8.7%; at 90 days, 36.6% recovered to mRS 2 or less. SICH rate was higher in patients with anterior circulation strokes who received treatment 8 or more hours after symptom onset (odds ratio [OR] = 3.8) and patients with WUS (OR = 4.9). In patients treated within 8 hours of onset of symptoms of anterior circulation stroke, SICH rate was only 6.7%. There was no difference in outcomes in patients with WUS compared with patients treated less than 8 hours after stroke onset.

CONCLUSIONS: This is the first and largest prospective study to the authors’ knowledge that shows endovascular therapy for AIS patients in a real-world setting. High recanalization rates with low SICH rates were achieved using careful patient and therapy selection.
Clinical History

34 yo F s/p fall from a high ropes course while harnessed approximately 30 feet off the ground (‘Trust training’)

Patient c/o of neck pain, then left-sided weakness, slurred speech, left-sided facial droop -> progressive quadraparesis, required intubation/ventilation

NIHSS = 18

A CT of the head and revealed no hemorrhage and the patient was out of the window for medical stroke treatment
MRI brain POD
#2
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
5. 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.

6. 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 internal carotid artery (ICA) or proximal MCA (M1). Additional randomized trial data are needed.

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 6 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.

9. 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 outcome.
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.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 StrokeCapabilities 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)

(Stroke. 2018;49:e233–e234. DOI: 10.1161/STR.0000000000000172.)
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Stroke is available at http://stroke.ahajournals.org
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.

New recommendation.

<table>
<thead>
<tr>
<th>III: No Benefit</th>
<th>B-R</th>
</tr>
</thead>
</table>

Of the 6 RCTs that independently demonstrated clinical benefit of mechanical thrombectomy with stent retrievers when performed <6 hours from stroke onset, 4 trials (REVASCAT [Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting Within Eight Hours of Symptom Onset], SWIFT PRIME [Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment], EXTEND-IA [Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial], and ESCAPE [Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times])\textsuperscript{102–105} used some form of advanced imaging to determine eligibility, whereas 2 (THRACE [Trial and Cost Effectiveness Evaluation of Intra-Arterial Thrombectomy in Acute Ischemic Stroke] and MR CLEAN [Multicenter Randomized Clinical Trial of Endovascular Treatment for AIS in the Netherlands])\textsuperscript{106,107} required only NCCT and demonstration of LVO. Because the last 2 studies independently demonstrated benefit in the treated group, additional imaging-based eligibility criteria could lead to the exclusion of patients who would benefit from treatment and are therefore not indicated at this time. Further RCTs may be helpful to determine whether advanced imaging paradigms using CTP, CTA, and MRI perfusion and diffusion imaging, including measures of infarct core, collateral flow status, and penumbra, are beneficial for selecting patients for acute reperfusion therapy who are within 6 hours of symptom onset and have an ASPECTS score <6.

See Table XXIII in online Data Supplement 1.
What’s A Retrievable Stent?
2015: Endovascular vs Best Medical Therapy

- 5 major studies evaluating the role of endovascular therapy in stroke treatment
  - MR CLEAN
  - EXTEND-IA
  - ESCAPE
  - SWIFT PRIME
  - REVASCAT
- Endovascular Therapy within 6 hours, NIHSS >7
- ALL 5 trials stopped because of significant benefit in the Endovascular arms
Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke

SWIFT PRIME
Medtronic- US

• Proximal anterior circulation occlusion
• Randomized patients who received IV-tPA to undergo endovascular therapy with Solitaire or continue receiving IV-tPA alone

• RESULTS:
• Endovascular showed improvement in mRS at 90 days
  • 60.2% vs 35.5% , P<0.001
• No significant differences in mortality or the occurrence of symptomatic ICH
• NNT = 4
Imaging Exclusion Criteria*

1. Computed tomography (CT) or Magnetic Resonance Imaging (MRI) evidence of hemorrhage on presentation.
2. CT or MRI evidence of mass effect or intra-cranial tumor (except small meningioma).
3. CT or MRI evidence of cerebral vasculitis.
4. CT showing hypodensity or MRI showing hyperintensity involving greater than 1/3 of the middle cerebral artery (MCA) territory (or in other territories, >100 cc of tissue) on presentation.
5. **Baseline non-contrast CT or DWI MRI evidence of a moderate/large core defined as extensive early ischemic changes of Alberta Stroke Program Early CT score (ASPECTS) < 6.†
6. CT or MRI evidence of a basilar artery (BA) occlusion or posterior cerebral artery (PCA) occlusion.
7. CTA or MRA evidence of carotid dissection or complete cervical carotid occlusion requiring stenting at the time of the index procedure (i.e., mechanical thrombectomy).
8. Imaging evidence that suggests, in the opinion of the investigator, the subject is not appropriate for mechanical thrombectomy intervention (e.g., inability to navigate to target lesion, moderate/large infarct with poor collateral circulation, etc.).

*Qualifying imaging had to be obtained at the study hospital. Patients with initial imaging at an outside hospital had to undergo additional qualifying CT or MR imaging at the study hospital.

**Before imaging entry criteria revision, this criterion stated: “Core Infarct and hypoperfusion: a) MRI- or CT-assessed core infarct lesion greater than 50 cc; b) Severe hypoperfusion lesion (10 sec or more Tmax lesion larger than 100 cc); c) Ischemic penumbra < 15 cc and mismatch ratio ≤ 1.8.” After imaging entry criteria revision, sites could enroll based on ASPECTS findings only, but were still encouraged to obtain perfusion imaging and use this information if available. A total of 71 patients were enrolled under the initial imaging entry criteria and 125 patients under the revised imaging entry criteria.

†ASPECTS, range 0 to 10, with higher scores indicating smaller infarct core
ischemic penumbra

core ischemic zone
<table>
<thead>
<tr>
<th>Imaging Selection Criteria</th>
<th>NIHSS&gt;=2 &lt;6 hr MR CLEAN</th>
<th>NIHSS (tPA) &lt;6 hr, dual EXTEND-IA</th>
<th>NIHSS&gt;=6 &lt;12 hr, consecutive ESCAPE</th>
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</thead>
<tbody>
<tr>
<td>Small core</td>
<td>Not required</td>
<td>RAPID perfusion infarct &lt;70 mL (relCBF&lt;30% threshold)</td>
<td>ASPECTS score 6–10</td>
<td>ASPECTS score 6–10 on NCCT or DWI, RAPID perfusion infarct &lt;50 mL (relCBF&lt;30% threshold)</td>
<td>ASPECTS score &gt;6 on NCCT, ASPECTS score &gt;5 on DWI (NCCT ASPECTS &gt;8 for age 80–85)</td>
</tr>
<tr>
<td>Penumbra</td>
<td>Not required</td>
<td>Target mismatch: RAPID perfusion ischemic core mismatch ratio &gt;1.2, absolute mismatch &gt;10 mL ($T_{max}&gt;6$ s threshold)</td>
<td>Not required</td>
<td>Target mismatch: RAPID perfusion penumbra/ infarct ratio &gt;1.8, penumbra absolute volume &gt;15 mL ($T_{max}&gt;6$ s threshold) - $T_{max}&gt;10$ s, Lesion ≤100 mL</td>
<td>Not required (clinical/core mismatch [NIHSS&gt;5])</td>
</tr>
<tr>
<td>Collaterals</td>
<td>Not required</td>
<td>Not required</td>
<td>Adequate collateral circulation defined as some filling of 50% or greater of the ischemic territory pial circulation beyond occlusion on CT angiography (preferably multiphase CTA)</td>
<td>Not required</td>
<td>Not required</td>
</tr>
</tbody>
</table>

**mRS <=2**

| 32.6% vs 19.1% | 71% vs 40% | 53% vs 29.3% | 60.2% vs 35.5% | 43.7% vs 28.2% |
Treatment Strategies

• Conscious Sedation vs General
• Balloon Guide
• J microwire
• Always image distally
• Stent Triever for fastest recan and immediate temporary bypass
• Time before attempt to pull?
• Suction aspiration if very good collateral imaging
• Balloon only for clot retrieval
International Stroke Conference
Los Angeles, CA
January 25, 2018

Principal Investigator & Study Management
Aquilla Turk, DO
Medical University of South Carolina

Principal Investigator & Data Management
J Mocco, MD
Mount Sinai Hospital

Principal Investigator & Core Lab
Adnan Siddiqui, MD, PhD
University at Buffalo Neurosurgery
Outcomes
Secondary Efficacy Endpoints:

90d mRS Shift OR (95% CI) = 0.98 (0.64, 1.51)

<table>
<thead>
<tr>
<th></th>
<th>ADAPT</th>
<th>SRFL</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TICI 2c or greater within 45 minutes</td>
<td>50%</td>
<td>44%</td>
<td>0.2998</td>
</tr>
<tr>
<td>TICI 3 or greater within 45 minutes</td>
<td>34%</td>
<td>23%</td>
<td>0.0486</td>
</tr>
<tr>
<td>Time to TICI 2b or greater</td>
<td>22 min</td>
<td>33 min</td>
<td>0.0194</td>
</tr>
</tbody>
</table>
There is now Level I evidence that Stent Retrievers and primary Aspiration have non-inferior clinical outcomes in the treatment of ELVO.
Volume of Patients within Presenting NIHSS Category

Research/Technology to increase presentations of High NIHSS
### Natural History

<table>
<thead>
<tr>
<th>OUTCOMES</th>
<th>NIHSS=16-20</th>
</tr>
</thead>
<tbody>
<tr>
<td>D/C to home, n (%)</td>
<td>6 (3.3 %)</td>
</tr>
<tr>
<td>D/C to rehabilitation unit</td>
<td>60 (33.0 %)</td>
</tr>
<tr>
<td>D/C to nursing facility</td>
<td>41 (22.5 %)</td>
</tr>
<tr>
<td>Hospice, n (%)</td>
<td>27 (14.8 %)</td>
</tr>
<tr>
<td>Expired, n (%)</td>
<td>44 (24.2 %)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (2.2 %)</td>
</tr>
</tbody>
</table>

90 day mortality > 80%, with 10% severely disabled
Stroke Imaging Strategies
NCCT

- NCCT remains sufficient at identifying contraindications to fibrinolysis
  - Widespread, fast, low cost
  - Door to CT should be < 25 min
- Rule out Hemorrhagic Stroke
- 3-6 hrs after infarct for hypodensities to be obvious.
  - Complicated by edema
- > 1/3 MCA EIC on NCCT predicts poor functional outcome and risk of ICH
  - Sensitivity 65%, Specificity 65%
Early Ischemic Change (EIC)

http://www.aspectsinstroke.com
Alberta Stroke Program Early CT Score (ASPECTS)

- Standardize the detection and reporting of the extent of EIC on NCCT
- Scoring system of 1 or 0 for 10 predefined locations
- C- Caudate, I- Insular ribbon, IC- Internal Capsule, L- Lentiform nucleus, and M1 to M6 MCA territories
- < 8 is correlated with both poor functional outcome and sICH

http://www.aspectsinstroke.com
MRI

• DWI – Diffusion Weighted Imaging
  • Sensitivity 90%, Specificity 95%
  • Within min of onset of sx
  • Small lesions
  • NOT all completed stroke (includes irreversible and reversible regions—especially < 24 hrs)

• GRE
  • Rule out ICH

• FLAIR
  • Importance to calculate Final Infarct Volume at 3-5 days

Schellinger, 2010, Neurology; Fiebach et al., 2002, Stroke
Diffusion Lesion Reversal After Thrombolysis
A MR Correlate of Early Neurological Improvement

Marc-Antoine Labeyrie, MD; Guillaume Turc, MD; Agathe Hess, MD; Patrice Hervò;
Jean-Louis Mas, MD; Jean-François Meder, PhD; Jean-Claude Baron, ScD;
Emmanuel Touzé, PhD; Catherine Oppenheim, PhD

Background and Purpose—In acute stroke, diffusion-weighted imaging (DWI) lesions are commonly considered markers of irreversible ischemia yet can occasionally reverse. However, the extent and clinical correlates of DWI reversal in thrombolysed patients remain unclear. We assessed the extent of reversible acute DWI lesions (RADs) and their relationships with clinical outcome in patients thrombolysed ≤4.5 hours from onset.

Methods—Data were retrospectively analyzed. RAD was defined as an acute DWI lesion not part of a 24-hour DWI lesion as determined voxelwise. Associations with an early neurological improvement (early neurological improvement=ΔNational Institutes of Health Stroke Scale ≥8 or National Institutes of Health Stroke Scale ≤2 at 24 hours) or an excellent outcome (modified Rankin Scale ≤1) were assessed in multivariate analyses.

Results—One hundred seventy-six patients were included. The median (interquartile range) time to treatment from onset was 150 minutes (120–194). Eighty-nine patients (50%) exhibited visually-detectable RAD irrespective of its extent. Over the whole population, the median percentage and volume of RAD were 11% (4–36) and 2.4 mL (0.5–8). Subtracting RAD from initial DWI altered perfusion-weighted imaging–DWI classification in 5 of 100 patients (shift from “no mismatch” to “mismatch” profile in all). Percent RAD was significantly greater in patients treated ≤3 hours (P=0.049), without proximal occlusion (P=0.003), and in 24-hour recanalizers (P<0.001). Early neurological improvement was independently associated with percent RAD. This association increased with percent RAD split in quartiles in a “dose-dependent” manner (P for trend=0.01). Excellent outcome was independently associated with percent RAD (P for trend <0.001).

Conclusion—DWI reversal was often sizeable in patients treated ≤4.5 hours. It was strongly associated with, albeit not necessarily causal for, early neurological improvement. (Stroke. 2012;43:2986-2991.)
CTA Collaterals

http://www.aspectsinstroke.com
Future of Stroke Imaging

The greatest challenge is to show that advanced neuroimaging, used as a biomarker to select patients for reperfusion therapy (in an extended time window), improves patient outcomes
Advanced Imaging

• Dynamic Studies capturing one cycle of the full transit of a contrast bolus though the tissue

• Physiologic Imaging: Transit Time, Blood Flow, Blood Volume
  • Parenchyma (Capillary phase NOT large vessels)
  • Intravascular surrogate for Intracellular process (not biological, Xenon)

• Ability to distinguish core (infarcted tissue) from penumbra (salvageable tissue)

• Individualize stroke treatment
Buffalo Protocol

• NIHSS and CTSS (CTA head and neck and CTP)
  • Intervention based on perfusion parameters, clinical exam, and Time of Onset
  • MRI if no obvious deficit on CTP
• Post intervention CT/ LCI /MRI GRE
• CTP POD #1, NIHSS at 24hrs
• MRI at 3-5 days
• Discharge disposition, NIHSS and mRS
• CT or MRI at 1-3 months, mRS and NIHSS
• All patients collected in prospective registry

• Raw DICOM imaging saved for over 3000 cases
Millard Fillmore Gates Circle Hospital in Buffalo, N.Y., has installed a Toshiba America Medical Systems’ Aquilion One dynamic volume CT system at its Kaleida Health Stroke Center.

The Aquilion One can image the entire brain and show real-time brain function in less time than traditional multi-detector CT systems, according to Toshiba.

The 189-bed acute care medical center is home to a multi-disciplinary team trained in stroke care that comprises the hospital’s Kaleida Health Stroke Center. It is the first stroke center in the United States to offer dynamic volume CT, the Tustin, Calif.-based Toshiba said.
Neuro One Protocol

• Perfusion
  • 50 cc at 5cc/s 19 volumes
• Equivalent to 1.5 NCCT Rad Dose
Time/Tissue Attenuation Curve
CT Perfusion Models (4 min processing time)

• Maximum Slope

• Deconvolution
  • Parametric $R(t)$ has specific distribution
  • Non-parametric – $R(t)$ is an unknown
    • Transform – Fourier
    • SVD
    • Delay Insensitive Deconvolution (SVD+)

• Bayesian
CT Perfusion Parameters

- CBF mL blood/100g brain tissue/min
- CBV mL blood/100g brain tissue
- Mean transit time (MTT)
- Time to peak (TTP)
- Delay Map
<table>
<thead>
<tr>
<th>Condition</th>
<th>rTTP</th>
<th>rCBF</th>
<th>rCBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Art stenosis/occl with comp</td>
<td>Prolonged</td>
<td>Normal</td>
<td>Normal or Hyper</td>
</tr>
<tr>
<td>Oligemic</td>
<td>Prolonged</td>
<td>&gt; 60%</td>
<td>&gt; 80%</td>
</tr>
<tr>
<td>Tissue at risk</td>
<td>Prolonged</td>
<td>&gt; 30%</td>
<td>&gt; 60%</td>
</tr>
<tr>
<td>Dead tissue</td>
<td>Strong prolonged</td>
<td>&lt; 30%</td>
<td>&lt; 30-40%</td>
</tr>
</tbody>
</table>

Tomandl, 2003; Mayer 2000; Koenig 2001
Cerebral Perfusion

- CBF = 50-60 mL/100 g/min, normal
- CBF = 35: protein synthesis ceases, oligemic stage, tissue can survive.
- CBF = 20: disturbance of synaptic transmission, loss of function (still viable)
- CBF = 10: irreversible cell death
Heiss and Rosner (1983)
Differences in CT Perfusion Maps Generated by Different Commercial Software: Quantitative Analysis by Using Identical Source Data of Acute Stroke Patients

Kohsuke Kudo, MD, PhD
Makoto Sasaki, MD, PhD
Kei Yamada, MD, PhD
Suketaka Momoshima, MD, PhD
Hidetsuna Utsunomiya, MD, PhD
Hiroki Shirato, MD, PhD
Kuniaki Ogasawara, MD, PhD

Purpose:
To examine the variability in the qualitative and quantitative results of computed tomographic (CT) perfusion imaging generated from identical source data of stroke patients by using commercially available software programs provided by various CT manufacturers.

Materials and Methods:
Institutional review board approval and informed consent

• Up to 30% variability of variables between vendors
• rCBV the most reliable
<table>
<thead>
<tr>
<th>Imaging Selection Criteria</th>
<th>NIHSS&gt;=2 &lt;6 hr MR CLEAN</th>
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<th>NIHSS&gt;=6 &lt;12 hr, consecutive ESCAPE</th>
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<td>Target mismatch: RAPID perfusion penumbra/infarct ratio&gt;1.8, penumbra absolute volume &gt;15 mL ($T_{max}$&gt;6 s threshold) - $T_{max}$&gt;10 s Lesion ≤100 mL</td>
<td>Not required (clinical/core mismatch [NIHSS&gt;5])</td>
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<td>Collaterals</td>
<td>Not required</td>
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<td>Adequate collateral circulation defined as some filling of 50% or greater of the ischemic territory pial circulation beyond occlusion on CT angiography (preferably multiphase CTA)</td>
<td>Not required</td>
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<td>mRS &lt;=2</td>
<td>32.6% vs 19.1%</td>
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<td>60.2% vs 35.5%</td>
<td>43.7% vs 28.2%</td>
</tr>
</tbody>
</table>
RAPID (iSchemaView) Dr. G Albers

• At Risk (Penumbra)
  • Tmax > 6s

• Core
  • CBF < 30% (70 % reduction) or Tmax >10 s

• Multiple different thresholds used:
  • < 70 cc and Mismatch >1.2 (Extend IA)
  • < 50 cc and Mismatch >1.8 (Swift prime)
  • < 20 cc, < 30 cc, < 50 cc (Dawn – depending on age and presenting NIHSS)
  • < 70 cc and Mismatch >1.8 (Diffuse 3)
MISMATCH

Mismatch Volume: 51 ml
Mismatch Ratio: 7.6
Baseline scans were compared to 27 hr CT or MRI FLAIR for measure FIV
Thresholds were adjusted to find best fit
rCBF of 0.3-0.34 and rCBV of 0.32-0.34 best matched FIV
Acute Stroke Imaging Research Roadmap III

• Exclude Large Core (>70 ml),
• Define other futile perfusion parameters (age, time of onset, presenting NIHSS)
• Improve correlation of FIV and CS
• Validation of core thresholds with ultrafast reperfusion data
• Anatomic location of ischemic core

• FIV:
  • < 24 hrs DWI reversible
  • 24-48 hrs: lesion volume and signal intensity may be changing, complicated by edema, parenchymal ICH, contrast staining
  • 30-90 d: mortalities complicate and bias data
    • Tissue atrophy, underestimates
    • Index infarct from chronic difficult
• FLAIR 3-5 d
  • Reduces risk of late infarct growth
  • Edema prominent
  • Distinguish acute from chronic challenging
• Penumbra/Core – volume mismatch

• Clinical Exam/Core – appropriate for patient selection
**Study Methods: Workflow**

**NCCT/DWI:**
- <1/3 MCA Territory

**CTA/MRA:**
- ICA-T and/or MCA-M1 (Tandem Occlusions Allowed)

**RAPID CTP/DWI CIM:**
A. ≥80 y/o:
   1. NIHSS ≥10 + core <21cc
B. <80 y/o:
   2. NIHSS ≥10 + core <31cc
   3. NIHSS ≥20 + core <51cc
Primary endpoint

Nogueira R.G. et. al., NEJM 2017
### Co-primary endpoints

<table>
<thead>
<tr>
<th></th>
<th>Trevo</th>
<th>MM</th>
<th>Treatment benefit (95% CI)</th>
<th>Bayesian probability of superiority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 90 weighted mRS</td>
<td>5.5 ± 3.8</td>
<td>3.4 ± 3.1</td>
<td>2.1 (1.20, 3.12)</td>
<td>&gt;0.9999*</td>
</tr>
<tr>
<td>Day 90 mRS (0-2)</td>
<td>48.6%</td>
<td>13.1%</td>
<td>35.5% (23.9%, 47.0%)</td>
<td>&gt;0.9999*</td>
</tr>
</tbody>
</table>

**NNT for 90-day functional independence = 2.8**

*Similar to p<0.0001*
Secondary effectiveness endpoints

**Pre and 24 hour median core size**

- **Trevo**
  - Pre: 9
  - 24 Hours: 8

- **MM**
  - Pre: 11
  - 24 Hours: 22

\[ P = 0.02 \]

**NIHSS early responders**

- **Trevo**
  - 47.7%

- **MM**
  - 19.2%

\[ P < 0.001 \]

140% Improvement
Defuse 3- Thrombectomy for Stroke at 6-16 hours with selection by Perfusion Imaging

- NEJM 2018: 378:708-18
- Multicenter, randomized, MCA or ICA, Primary outcome mRS at 90 days
- Less than 70 cc core, and Ratio of >1.8

- RESULTS:
  - Terminated Early for efficacy (92 endo and 90 BMT)
  - mRS 0-2 (45% vs 17%)
  - 90 day mortality (14% vs 26%)
  - No sign difference in sICH (7% vs 4%)
DAWN

• Age: > 18
• NIHSS: >= 10
• Vessel: ICA/M1
• LSN: 6-24
• CTP Core: <20, <30, <50
• CTP Ratio: none

DEFUSE 3

• 18-90
• >= 6
• ICA/M1
• 6-16
• < 70
• >1.8
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
5. 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.

<table>
<thead>
<tr>
<th>Recommendation</th>
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<tbody>
<tr>
<td>IIb</td>
<td>C-EO</td>
</tr>
</tbody>
</table>

Recommendation reworded for clarity from 2015 Endovascular. Class unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System. See Table LXXXIII in [online Data Supplement 1](#) for original wording.

6. 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 internal carotid artery (ICA) or proximal MCA (M1). Additional randomized trial data are needed.

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<tr>
<td>IIb</td>
<td>B-R</td>
</tr>
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</table>

Recommendation unchanged from 2015 Endovascular.

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.

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<td>A</td>
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New recommendation.

8. In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.

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<tbody>
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<td>B-R</td>
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</table>

New recommendation.

9. 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 outcome.

<table>
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Recommendation reworded for clarity from 2015 Endovascular. See Table LXXXIII in [online Data Supplement 1](#) for original wording.
Clinical History

- 50 yo who woke up with left hemiplegia, dysarthria, and facial droop.
- NIHSS = 16.
- PMH - Anxiety disorder, tobacco dependence, alcohol dependence
Deployment of TREVO retrieval device
1st pull of the microcatheter with the retrieval device

Total intervention time ~20 min
Complete recanalization
TIMI-3 after 1 pull
• In the angio suite – the patient could lift his Rt arm antigravity, improved gaze, NIHSS 16 to 5 immediately

• POD#1 NIH -3

• POD#2– NIH -0
Clinical History

• 75 yo WM last seen normal at 10 pm, ? Issues at 2 am, awoke thrashing at 4 am with Right gaze preference and left HP

• NIHSS 18
Workflow and Time on Treatment Outcomes

Figure 3

(a) % Functional independence at 90 days vs. Time from onset to reperfusion (min) for Solitaire reperfused (n=70).

(b) % Functional independence at 90 days vs. Time from qualifying imaging to reperfusion (min) for Solitaire reperfused (n=43).
Speed to Reperfusion is Critical

• Even though physiologic imaging allows more people to be offered treatment at later time points, realize...

• IT IS STILL A RACE

• Streamlining Stroke triage from ambulance to CTP has helped tremendously
Volumetric Impedance Phase Shift Spectroscopy (various bandwidth radiowaves)
The VIPS device was able to differentiate severe stroke from minor strokes with a sensitivity of 93% (95% CI 83 to 98), specificity of 92% (95% CI 75 to 99)
See. Diagnose. Treat.
Future Advanced Imaging Considerations

• Improvements in validation studies and/or deterministic models (Xenon?)
  • Especially for Physiology Imaging near time of onset

• Define Futility Thresholds for grey and white matter

• Validation of Semi automated methods across vendor platforms and modalities

• Applications to other organ systems

• Generation of Physiologic Maps from Angiography
Time Density Curves

![Diagram of time density curves with annotations for peak, 0.5 peak, 0.1 peak, BAT, A, TTP, MIT, and contrast density over time.]
Time Density Curves
On table Physiology Surrogate

TIMI/TICI Scoring
Thank you!