ISCHEMIC STROKE BEST PRACTICES: TRANSLATING RESEARCH TO THE BEDSIDE

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Learning Objectives

• The learner will be able to discuss the burden, etiology, and complications of ischemic stroke.

• The learner will understand the current evidence-based guidelines for the management of ischemic stroke.

• The learner will understand the role of stroke systems of care in managing acute and chronic stroke.
Ischemic Stroke
Stroke Burden

• **Individual**
  4\textsuperscript{rd} leading cause of death, leading cause of disability
  • ~6.8 million Americans ≥ 20 years of age have had a stroke
  • By 2030, an additional 3.4 million people aged≥ 18 years will have had a stroke, a 20.5% increase in prevalence from 2012.

• **Family/Caregiver**
  1/3 stroke will be dependent on others

• **Community**
  Majority of stroke survivors need community services

• **Nation**

<table>
<thead>
<tr>
<th>COST (billions)</th>
<th>2010</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical</td>
<td>$28.3</td>
<td>$95.6</td>
</tr>
<tr>
<td>Loss of Productivity</td>
<td>$25.6</td>
<td>$44.4</td>
</tr>
</tbody>
</table>
Stroke Etiology

Ischemic stroke ~87%

Hemorrhagic stroke ~13%

Cryptogenic

Cardiogenic embolism

Small vessel disease “lacunes”

Atherosclerotic cerebrovascular disease

SAH

ICH

Other

Albers et al. Chest 2004; 126 (3 Suppl): 438S–512S.
Ischemic vs. hemorrhagic stroke

- Danish registry of ~39,500 stroke patients
- Compared with ischemic strokes, HS was associated with an overall higher mortality risk (HR, 1.564; 95% CI, 1.441–1.696).
- The increased risk is time-dependent
  - Initially, risk is 4-fold
  - At 1 week risk was 2.5-fold
  - 3 weeks risk is 1.5-fold
  - After 3 months stroke type did not correlate to mortality
- Patients with HS had more severe strokes, more often had high alcohol intake, and more often were smokers. No difference in sex, age, and prevalence of hypertension was found between patients with IS and HS.

Transient Ischemic Attack (TIA): a tissue (not time) definition

- Same risk factors & symptoms of stroke that are transient, but in TIA, no (measureable) brain cell death occurs; diagnosis made by DW-MRI

- 1/3 of episodes characterized as TIA according to the classic definition (ie, focal neurological deficits that resolve within 24 hours) would be considered infarctions on the basis of diffusion-weighted magnetic resonance imaging findings.

- Requires immediate evaluation and treatment of risk factors to avoid a major stroke.
  - ~5% will have a major stroke in 2 days
  - ~11% will have a major stroke in 90 days

Major arteries and territories they supply

Anterior circulation

Posterior circulation

ACA

MCA superior division

MCA inferior division

MCA deep branches

PCA deep branches

Anterior choroidal artery

PCA
Anterior Circulation Strokes (~80%)

- Occlusion of carotid, middle cerebral artery, anterior cerebral arteries which, supply cortical and subcortical structures of the cerebrum

- **Typified by lateralizing signs**, eg:
  - Vision loss, complete, dimmed or foggy (ophthalmic artery)
  - Aphasia, hemianopsia (MCA)
  - Weakness, paralysis, sensory loss in contralateral face, arm, leg
    - Arm > leg (MCA)
    - Leg > arm, abulia (slow to respond) (ACA)
  - Hemineglect and impulsiveness (right MCA)
  - Gradual loss of consciousness (hemispheric MCA)

Posterior Circulation Strokes (~20%)

- Occlusion of vertebral, basilar arteries and their branches
- Typified by diffuse findings (no lateralizing signs); both ipsilateral and contralateral findings, combination brainstem and cerebellar findings, and "unusual" stroke symptoms, eg:
  - Ataxia, vertigo, ipsilateral deafness, facial paralysis and loss of sensation (AICA)
  - Ipsilateral Horner’s syndrome (ptosis, CNIII injury) with contralateral loss of pain, temperature (Wallenberg’s or lateral medullary syndrome) (PICA or VA)
  - Quadriplegia with only preserved upward gaze and consciousness (“locked in syndrome” or ventral pontine occlusion)
  - Complete sensory loss in all modalities (PCA, thalamus injury)

Recognize Symptoms FAST

One or more of these symptoms are present in 88% of all strokes and TIAs (posterior circulation strokes under-represented).

In one study, 100% of lay individuals remembered 3 months after education that facial droop and slurred speech are stroke warning signs, and 98% recalled arm weakness or numbness.

Nationwide, only ~50% of stroke patients arrive by EMS

Acute Stroke Complications

- Hyper- or hypotension (1-2 days)
- Hemorrhage (large territory infarction, post-tPA)
- Edema, increased ICP (3-5 days)
- Recurrent stroke or progression of ischemia
- Arrhythmia, myocardial infarction
- Aspiration/pneumonia (~30%)
- UTI
- Falls, neglect
- Cognitive decompensation
- Seizures (~10%)

Evidence Based Guidelines for Stroke
# Levels of Evidence

**Legend**

- **CLASS I**
  - Benefit >> Risk
  - Procedure/Treatment SHOULD be performed/administered

- **CLASS Ia**
  - Benefit >> Risk
  - Additional studies with focused objectives needed
  - IT IS REASONABLE to perform procedure/administer treatment

- **CLASS Iib**
  - Benefit ≥ Risk
  - Additional studies with broad objectives needed; additional registry data would be helpful
  - Procedure/Treatment MAY BE CONSIDERED

- **CLASS III** (No Benefit or CLASS III (Harm)
  - Procedure/Test
  - Treatment
  - Cor III: No benefit
  - Helpful
  - No Proven Benefit
  - Cor III: Harm
  - Excess Cost w/o Benefit or Harmful
  - Harmful to Patients

**LEVEL A**
- Multiple populations evaluated*
- Data derived from multiple randomized clinical trials or meta-analyses

**LEVEL B**
- Limited populations evaluated*
- Data derived from a single randomized trial or nonrandomized studies

**LEVEL C**
- Very limited populations evaluated*
- Only consensus opinion of experts, case studies, or standard of care

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Evidenced-Based Stroke Guidelines

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association


on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Peripheral Vascular Disease, and Council on Clinical Cardiology

Stroke. 2013;44:870-947; originally published online January 31, 2013;
Goals of Acute Stroke Management

- Reperfusion therapies
- Prevent complications
- Address risk factors
- Plan for recovery

*ABCD2: score that can help predict early risk of stroke in the first two days after transient ischemic attack (TIA); Johnston et al, *Lancet*, 369:283-292, 2007*
# Emergency Evaluation

<table>
<thead>
<tr>
<th>Immediate Assessment/Diagnostic Studies</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIHSS</td>
<td>Class I, Level B</td>
</tr>
<tr>
<td>Non-contrast CT or MRI</td>
<td>Class I, Level A</td>
</tr>
<tr>
<td>Blood glucose</td>
<td>Class I, Level B</td>
</tr>
<tr>
<td>ECG</td>
<td>Class I, Level B</td>
</tr>
<tr>
<td>Oxygen saturation</td>
<td>Class I, Level B</td>
</tr>
<tr>
<td>Complete blood count including platelet count*</td>
<td>Class I, Level B</td>
</tr>
<tr>
<td>Markers of cardiac ischemia*</td>
<td>Class I, Level C</td>
</tr>
<tr>
<td>Serum electrolytes and renal function tests*</td>
<td>Class I, Level B</td>
</tr>
<tr>
<td>PT, INR, aPTT*</td>
<td>Class I, Level B</td>
</tr>
</tbody>
</table>

*tPA decision should not be delayed while waiting on results unless there is clinical suspicion of bleeding abnormalities, thrombocytopenia or patient has received heparin, warfarin or other oral anticoagulants*
National Institute of Health Stroke Scale (NIHSS) (Class I, Level B)

NIHSS “the common language” for assessing stroke severity. It is a validated tool used worldwide.

An 11 item scale that measures five areas of neurologic function:
Wakefulness (1a, 1b, 1c)
Vision (3, some of 9-10)
Motor (4, 5, 6, 7, some of 2)
Sensory (8, 11)
Language and Speech (9, 10)

## NIHSS

<table>
<thead>
<tr>
<th>Score</th>
<th>Stroke Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No Stroke Symptoms</td>
</tr>
<tr>
<td>1-4</td>
<td>Minor Stroke</td>
</tr>
<tr>
<td>5-15</td>
<td>Moderate Stroke</td>
</tr>
<tr>
<td>16-20</td>
<td>Moderate to Severe Stroke</td>
</tr>
<tr>
<td>21-42</td>
<td>Severe Stroke</td>
</tr>
</tbody>
</table>

With practice, the NIHSS can be performed in 5 min.

Maximal possible score is 42, minimum is 0.

The NIHSS is used to assess stroke severity and to determine benefit/risk of delivering rtPA. Current guidelines urge against using a low NIHSS score (<5) being used as the sole reason for declaring a patient as ineligible for tPA treatment.
National Institute of Health Stroke Scale

Free NIHSS certification available from the National Stroke Association:
www.nihss-english.trainingcampus.net

A decent demonstration (*not* a certification)
http://www.youtube.com/watch?v=wzjWAJgGjTw
Reperfusion Therapies

- Timely reperfusion is the optimal therapy to reduce expansion of damage beyond the ischemic core.

- Even though neurons begin to die after ~4 minutes without blood, there will be billions of neurons in the penumbra whose blood supply may be compromised but not necrotic; survival depends on how the patient is managed.
• Early administration of tPA after ischemic stroke improves outcome at 3 months after stroke (Class I, Level A)
• Time window extended from 3 hrs to 4.5 hrs based on ECASS (European Cooperative Acute Stroke Study) III data

• Although not technically FDA approved for extended time window, recommended by AHA and ASA
rtPA for ischemic stroke (Class I, Level A)

- Nationwide estimates are that <5% of eligible patients are able to receive this treatment (double the 2005 rate)
- **Must be given within 3-4.5 hours of onset**
- Percent of patients with excellent outcomes is increased by 15% if treated within 3 hours and 7% if treated in 3-4.5 hours
- The percent of poor outcomes (Rankin 4-5) is reduced.
- Those treated within 3 hours are 30-50% more likely to have minimal or no disability at 3 mos, 16% more likely if treated 3-4.5 hours.
- **Hemorrhage rate**
  - 6.4% (1 in 16) hemorrhage rate (3 hour window)
  - 7.9% (1 in 12) hemorrhage rate (3-4.5 hour window)
  - Hemorrhage is correlated with administration and post care protocol violations

rtPA: Favorable Outcomes and Treatment Times
tPA for Ischemic Stroke: the earlier the better

- ~58,353 patients with ischemic stroke treated with tPA within 4.5 hours of symptom onset in 1,395 hospitals participating in GWTG® registry

- Every 15-minute acceleration in start of tPA after onset was associated with
  - 4% greater odds of walking independently at discharge
  - 3% greater odds of being discharged to home rather than an institution
  - 4% lower odds of death before discharge
  - 4% lower odds of experiencing symptomatic hemorrhagic transformation

Endovascular Therapy for Acute Stroke

A promising idea, but.....what evidence do we have?
RCTs of Endovascular Therapy for Acute Ischemic Stroke – Feb 7, 2013

**IMS III**
No benefit of IV-tPA + ET vs. IV tPA alone < 3 Hrs

**MR RESCUE**
No benefit of ET vs. standard care < 8 hours in pts with or without penumbra

**SYNTHESIS**
No benefit of ET < 6.0 hrs vs. IV tPA < 4.5 Hrs
Main Criticism of All 3 Trials

- Less than ideal patient selection
- Performed with 1st generation devices

Merci Retriever

New Generation Stent Retriever
So Where Does This Leave Us?

- As with intravenous fibrinolytic therapy, reduced time from symptom onset to reperfusion with intraarterial therapies is highly correlated with better clinical outcomes, and all efforts must be undertaken to minimize delays to definitive therapy (Class I, Level B).

- Ongoing randomized controlled trials are needed with new generation devices (Solitaire FR and Trevo) and better patient selection (Class I, Level A).

- Intra-arterial fibrinolysis or mechanical thrombectomy is reasonable in patients who have contraindications to the use of intravenous fibrinolysis (Class IIa, Level C).
MRI-guided patient selection: penumbra and mismatch

Mismatch = Penumbra

DWI+ = infarct

Increased TTP = at risk

No Mismatch = No Penumbra
Unlikely to Benefit
May Benefit
Blood pressure management aimed at saving the penumbra

Morphology
- Infarction
- Inflammation and apoptosis

Biochemistry
- Ionic failure
- Anoxic depolarization
- Glucose use ↓
- Glutamate release
- Glucose use ↑
- Protein synthesis ↓
- Acidosis
- Oxygen extraction ↑
- Selective gene expression

Source: trends in Neurosciences
BP: too low or too high increases mortality

![Graph showing the relationship between baseline systolic blood pressure and mortality](image)

Stroke 2002;33:1315
Physiologic Monitoring

- **Blood pressure**
  - Generally elevated/labile for first 24 hours
    - Permissive SBP up to 220 mm Hg (Class I, Level C)
    - If tPA administered, BP no higher than 185/110 mm Hg (Class I, Level B)
      - Treatment typically with Labetolol IV X 2 or Nicardipine infusion
  - Stability is important
- **Blood sugar** (Class IIa, Level C)
  - Stress response
  - Glycemic control correlates with better outcomes
- **Temperature** (Class I, Level C)
  - Metabolic demand
  - Even a slight temperature increase correlates with worse outcomes
- **Cardiac rhythm & rate** (Class I, Level B)
  - Risk of arrhythmia and MI
- **Neurologic exam (NIHSS)** (Class I, Level B)
- **Oxygenation** (Class I, Level C)
- **Normovolemic** (Class I, Level C)
Risk Factor Assessment (Class I, level B)

- Repeat CT, MRI/A/angiography
- Echocardiography: TTE / TEE
- Carotid doppler
- ECG/Telemetry

Rehabilitation Evaluation

- Physical Therapy
- Occupational Therapy
- Speech
- Swallowing
- Discharge placement
  - Home with or without therapy, acute rehabilitation, skilled nursing, hospice

Additional Labs

• CBC, BMP, PT/PTT
  • Anemia, platelets, infection, renal function, coagulopathy
• Lipids, LFTs
  • Cholesterol as vascular risk
• Cardiac markers
• Toxicology screen
• Fibrinogen, homocysteine, CRP, proinflammatory proteins
  • Activated blood promotes thrombus/embolus formation
• Fasting and random glucose, HgbA1C

Medications

- Antiplatelet drugs are safely given
  - aspirin
  - clopidogrel (Plavix)
  - ASA/dipyridamole (Aggrenox)
- All patients with a-fib must be evaluated for anticoagulation with warfarin or new anticoagulants
- Blood pressure management may be a challenge
  - ACE-Is, ARBs, Renal function
- Glycemic control adds great benefit
- Statins for LDL > 100

Goals of TIA Management

- Approximately 15% of all strokes are heralded by a TIA
- ~5% have a stroke within 2 days
- ~11% have a stroke within 90 days
- Within 1 year of TIA, ≈12% of patients will die

- **Address risk factors (identical to risk factors for stroke)**
  - Predictors of stroke after TIA included age >60 years, DM, focal symptoms of weakness or speech impairment, and TIA that lasted >10 minutes.
  - TIAs with moderate secondary stroke risk (ABCD2 ≥4) should be admitted to the hospital for risk assessment and immediate management

**ABCD2: assessing risk for early second event after TIA**

<table>
<thead>
<tr>
<th>Score</th>
<th>2 day stroke risk</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>1.0%</td>
<td>Hospital observation may be unnecessary without another new indication (e.g., atrial fibrillation)</td>
</tr>
<tr>
<td>4-5</td>
<td>4.1%</td>
<td>Hospital observation justified in most cases</td>
</tr>
<tr>
<td>6-7</td>
<td>8.1%</td>
<td>Hospital observation worthwhile</td>
</tr>
</tbody>
</table>

*ABCD2: score that can help predict early risk of stroke in the first two days after transient ischemic attack (TIA); Johnston et al, *Lancet*, 369:283-292, 2007*
Non-modifiable stroke risk factors

• **Age**
  - stroke risk doubles each 10 years after age 55

• **Gender**
  - males > females
  - Women live longer, have more atrial fibrillation and uncontrolled blood pressure

• **Family History**
  - 1 to 2 times risk

• **Ethnicity**
  - Blacks > Hispanics & Native Americans > Whites
  - Disproportionate clustering of risk factors

Modifiable stroke risk factors

- **Hypertension**
  - The prevalence among patients with a recent ischemic stroke is $\approx 70\%$

- **Diabetes**
  - DM is associated with a substantially increased risk for first ischemic stroke (RR 1.5-3.7); DM may be responsible for $>8\%$ of first ischemic strokes

- **Atrial fibrillation**
  - Leading cardiac arrhythmia in the elderly; accounts for 10-12\% of all ischemic strokes

- **Obstructive sleep apnea**
  - Sleep apnea is present in approximately half to three quarters of patients with stroke or TIA.

- **Lifestyle** (diet, exercise, smoking)

- **Previous Stroke or TIA**

Kernan W et al. *Stroke*. 2014;45:2160-2236
Stroke Systems of Care
Stroke Systems of Care

- Stroke systems of care integrate regional stroke facilities, including acute stroke-ready hospitals (ASRHs) that often have telemedicine and teleradiology capability, primary and comprehensive stroke centers, EMSS, and public and governmental agencies and resources.

- The goals of creating stroke systems of care include stroke prevention, community stroke education, optimal use of EMS, effective acute and subacute stroke care, rehabilitation, and performance review of stroke care delivery.
Stroke Systems of Care

- **Emergency Medical Systems (EMS)**
  - 9-1-1 activation and dispatch, emergency medical response, triage and stabilization in the field, and ground or air ambulance transport
  - AHA policy statement established blueprint defining critical role of EMS systems in optimizing stroke care

- **Acute Stroke Ready Hospitals (ASRH)**
  - Hospitals that have made an institutional commitment to effectively and efficiently evaluate, diagnose, and treat most ED stroke patients but that do not have fully organized inpatient stroke systems of care
  - Protocols, transfer agreements, stroke leader, emergency labs and CT, ability to administer tPA

Emergency Medical System

• Put in our stroke algorithm?
Why Primary Stroke Center Designation?

- Mortality and morbidity from stroke are significantly decreased when patients are cared for in primary stroke centers.

- Primary Stroke Center designation provides an accepted framework that ensures sustained adherence to evidence based standards of care.

Certified Primary Stroke Center Quality Measures

- tPA given when indicated
- DVT prophylaxis
- Discharge with anti-thrombotics
- Anticoagulation for a-fib/flutter
- Anti-thrombotics within 48 hours
- Statin for LDL > 100
- (Dysphagia screening)
- Individualized stroke education
- (Smoking cessation)
- Plan for rehabilitation

Joint Commission Disease Specific Certification, 2009
“Golden Hour” Benchmarks

“Brain Attack!

- Suspected stroke patient arrives at ED ≤ 10 min
  - Complete initial MD evaluation, including patient history and time last known well/symptom onset
  - Initiate labwork
  - Assess using NIHSS

- ≤ 45 min
  - Interpret CT scan and labs
  - Review patient eligibility for Activase

- ≤ 60 min
  - Give Activase bolus and initiate infusion in eligible patients

- ≤ 25 min
  - Initiate CT scan

- ≤ 15 min
  - Notify stroke team (including neurologic expertise)
Inter-professional stroke team
- Faculty Stroke Coordinator as team leader
- Designated Quality Analyst
- ED, ICU, Medical floor managers and educators; Medical Director; Pharmacy, Laboratory, Therapy, Pre-Hospital Coordinator, physicians from Neurology, Neurosurgery, Neuroradiology, ED

Program CPGs, processes, protocols, order sets, etc developed and maintained by the team

Quality improvement team
- Quality improvement (QI) processes identified
- QI action plans reviewed
- Regular reports to the organization

Use of stroke database (Get With the Guidelines-Stroke®)
Designated stroke units (ICU, Medical floor)
Transitions of Care Programs for Stroke and TIA: the next phase of improved stroke care?

• While we (locally, state, nationally) have well developed evidence-based guidelines addressing the acute phase of stroke, data (and therefore guidelines) are lacking regarding stroke care related to patients transitions to recovery.

• Elements of a Doctor of Nursing Practice-led Transitions of Care Model for Stroke and Transient Ischemic Attack:
  • Point of contact
  • Lack of urgency for follow up
  • Lack of understanding of medication changes
  • Lack of knowledge regarding diagnosis and risk factors

Acknowledgements

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.....and all those touched by stroke