Stroke Update 2015

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PeaceHealth
Objectives

1. Review successes in systems of care approach to acute ischemic stroke
2. Evaluate the results of recent landmark acute stroke endovascular trials
3. Renew enthusiasm for population based primary prevention

Disclosures: None
Epidemiology

- Annually, 15 million people worldwide suffer a stroke

- One-third of these individuals die and another one-third are left permanently disabled

- The World Health Organization (WHO) estimates that a stroke occurs every 5 seconds
Epidemiology

• In the United States, approximately 795,000 people have a new or recurrent stroke each year.

• About 600,000 are new strokes and 195,000 are recurrent strokes.

• A stroke occurs approximately every 40 seconds, which is 2160 strokes per day.
Epidemiology

• In the U.S., stroke is the primary cause of long term disability with an estimated 6.5 million survivors among adults age 20 and older (2.6 million males and 3.9 million females)

• The estimated 2015 direct and indirect cost of stroke is $95 billion
Proportion of patients dead 1 year after first stroke.

<table>
<thead>
<tr>
<th>Group</th>
<th>45-64 years of age</th>
<th>≥65 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Men</td>
<td>14</td>
<td>25</td>
</tr>
<tr>
<td>White Women</td>
<td>18</td>
<td>28</td>
</tr>
<tr>
<td>Black Men</td>
<td>18</td>
<td>24</td>
</tr>
<tr>
<td>Black Women</td>
<td>19</td>
<td>23</td>
</tr>
</tbody>
</table>

Legend:
- Blue: 45-64 years of age
- Red: ≥65 years of age
### Table. Trends in Age-Standardized Death Rates

<table>
<thead>
<tr>
<th>Death Rate†</th>
<th>1970</th>
<th>2002</th>
<th>% Change‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td>1242.2</td>
<td>844.6</td>
<td>-32.0</td>
</tr>
<tr>
<td>Heart disease</td>
<td>502.6</td>
<td>240.5</td>
<td>-52.1</td>
</tr>
<tr>
<td>Cancer</td>
<td>198.8</td>
<td>193.5</td>
<td>-2.7</td>
</tr>
<tr>
<td>Stroke</td>
<td>151.9</td>
<td>56.1</td>
<td>-63.1</td>
</tr>
<tr>
<td>COPD</td>
<td>21.4</td>
<td>43.4</td>
<td>102.8</td>
</tr>
<tr>
<td>Accidents</td>
<td>62.5</td>
<td>36.9</td>
<td>-41.0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>24.6</td>
<td>25.4</td>
<td>3.2</td>
</tr>
</tbody>
</table>
Stroke is now the fifth leading cause of death in the U.S.
Major Shifts in Population Risks and Expanded Treatment, U.S.

- **Risk Factors worse**: +17%
  - Obesity (increase) +7%
  - Diabetes (increase) +10%

- **Risk Factors better**: -65%
  - Population BP fall -20%
  - Smoking -12%
  - Cholesterol (diet) -24%
  - Physical activity -5%

- **Treatments**: -47%
  - AMI treatments -10%
  - Secondary prevention -11%
  - Heart failure -9%
  - Angina: CABG & PTCA -5%
  - Hypertension therapies -7%
  - Statins (primary prevention) -5%

341,745 fewer deaths in 2000
Infarct core and The Ischemic Penumbra
During a stroke 32,000 neurons die per second...
Emergent Stroke Care and the Chain of Survival
Acute management: thrombolysis
Modified Rankin Scale (mRS)

The scale runs from 0-6, running from perfect health without symptoms to death.

- 0 - No symptoms.
- 1 - No significant disability. Able to carry out all usual activities, despite some symptoms.
- 2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
- 3 - Moderate disability. Requires some help, but able to walk unassisted.
- 4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
- 5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
- 6 - Dead.
Acute management: thrombolysis

• Only a select group of patients are eligible to receive rt-PA

• The major adverse affect of rt-PA is hemorrhage

• The symptomatic intracranial hemorrhage rate in the NINDS trial was 6.4%

• Symptomatic ICH was seen primarily from hemorrhagic transformation of the ischemic infarct
NIH TPA ACUTE STROKE STUDY
THREE MONTH OUTCOME

Modified Rankin Scale
Percentage of Patients

Placebo
- No Significant Disability: 26%
- Slight-Moderate Disability: 25%
- Moderately Severe-Severe Disability: 27%
- Death: 21%

t-PA
- No Significant Disability: 39%
- Slight-Moderate Disability: 21%
- Moderately Severe-Severe Disability: 23%
- Death: 17%
CATH LAB
Intra-arterial Thrombolysis
Acute management: endovascular thrombolysis

• 4 mechanical devices with FDA clearance: Merci Retrieval System (2004), the Penumbra System (2007), the Solitaire Flow Restoration Device (2012), and the Trevo Retriever (2012)

• Devices are cleared as mechanical means for recanalization of acutely occluded arteries based on studies without noninterventional control groups
Acute Management: endovascular thrombolysis

- 3 endovascular thrombectomy trials were highlighted at the 2013 International Stroke Conference
  - IMS III
  - MR RESCUE
  - SYNTHESIS Expansion
Acute Management: endovascular thrombolysis

• All 3 trials failed to show a statistically significant difference between the endovascular therapy group and the best medical management group (which could include IV-tPA) as measured by an mRS of 2 or less
LANDMARK ACUTE ISCHEMIC STROKE ENDOVASCULAR TRIALS

MR CLEAN
ESCAPE
EXTEND IA
SWIFT -PRIME

N Engl J Med 372;1/1, 2015
April 17, 2015DOI: 10.1056/NEJMoa1415061
MR CLEAN: A Randomized Trial of Intra-arterial Treatment for Acute Ischemic Stroke

- Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands
- Published January 1, 2015
- 500 patients with large vessel occlusion (LVO) confirmed by CTA were randomized to intra-arterial treatment (n=233) or medical management (n=267) within 6 hours of symptom onset
- 32.6% of patients who received endovascular treatment achieved a good functional outcome (mRS 0-2) compared to 19.1% of patients who received medical management

MR CLEAN: A Randomized Trial of Intra-arterial Treatment for Acute Ischemic Stroke

Age and mortality/dependency after treatment and no treatment
ESCAPE: Randomized Assessment of Rapid Endovascular Treatment Ischemic Stroke

- Published February 11, 2015
- Trial was stopped early because of efficacy
- 316 patients with proximal large vessel occlusion (LVO) and good collateral circulation confirmed by CTA were randomized to endovascular intervention (n=165) or medical management (n=150) within 12 hours of symptoms onset
- Rates of functional independence (mRS 0-2) at 90 days was statistically significant for the endovascular intervention group compared to the control group (53.0% vs. 29.3%; p< 0.001)
- Endovascular intervention was associated with reduced mortality (10.4% vs 19.0%; p=0.04)

DOI: 10.1056/NEJMoa1414905
ESCAPE: Randomized Assessment of Rapid Endovascular Treatment Ischemic Stroke

Effect size for Intervention is Large

common OR* ("shift") 3.1 (2.0-4.7)

mRS 0-2 29.3% → 53.0% NNT = 4

Death HR* 19.0% → 10.4% 0.4 (0.2-0.8)

*Adjusted for age, sex, baseline NIHSS score, baseline ASPECTS score, IV alteplase use, baseline occlusion location
Unique Features of ESCAPE

- Excluded poor collaterals (mCTA) and large core (ASPECTS >6)
- Time target
- Consent deferral
mCTA gives:
1. Easy and reliable assessment of collaterals
2. Very fast acquisition and fully automated image reconstruction
3. Less sensitive to patient motion
4. Easy to learn and interpret
EXTEND-IA: Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

- Published February 11, 2015
- Trial was stopped early due to efficacy
- 70 patients with internal carotid or middle cerebral artery occlusion, salvageable brain tissue, and ischemic core < 70 ml confirmed by CTP were randomized to endovascular thrombectomy with the Solitaire FR stent retriever (m=35) or alteplase alone (n=35) within 4.5 hours of symptom onset
- The endovascular reperfusion group achieved greater reperfusion at 24 hours (median, 100% vs. 37%; p<0.001) and increased early neurologic improvement at 3 days (80% vs. 37%, p=0.002) as measured by the NIHSS
- No significant difference in mortality or symptomatic ICH

SWIFT PRIME

- Results presented at ISC on February 11, 2015
- Trial was stopped early due to efficacy
- 196 patients with large vessel occlusion (LVO) confirmed by CTA or MRA were randomized to endovascular treatment with the Solitaire FR stent retriever (n=98) or alteplase alone (n=98) within 6 hours of symptom onset
- The OR for mRS shift at 90 days in the endovascular treatment group compared to the alteplase alone group was statistically significant (p=0.0002), and good functional outcome (mRS 0-2) was achieved in 60.2% of the patients in the endovascular treatment group compared to 35.5% of the patients in the control group (p=0.0008)

SWIFT PRIME: Secondary Endpoints

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Endovascular Treatment</th>
<th>Control</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRS score of 0 - 2 at 90 d (%)</td>
<td>60.2</td>
<td>35.5</td>
<td>.0008</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>9.2</td>
<td>12.4</td>
<td>.50</td>
</tr>
<tr>
<td>Mean improvement in NIHSS score at 27 h (points)</td>
<td>8.5</td>
<td>3.9</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>
## Comparing Interval Times

<table>
<thead>
<tr>
<th></th>
<th>ESCAPE</th>
<th>MR CLEAN</th>
<th>IMS III</th>
<th>SYNTHESIS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset→ Randomization</strong></td>
<td>171 min (IQR 118-285)</td>
<td>204 min (IQR 152-251)</td>
<td>~135 min</td>
<td>~146 min</td>
</tr>
<tr>
<td><strong>Onset→ IV tPA</strong></td>
<td>114 min (IQR 82-160)</td>
<td>85 min (IQR 67-110)</td>
<td>~111 min</td>
<td>165 min (IQR 140-200)</td>
</tr>
<tr>
<td><strong>Onset→ Groin Puncture</strong></td>
<td>200 min (IQR 144-315)</td>
<td>260 min (IQR 210-313)</td>
<td>~196 min</td>
<td>~225 (?200) min**</td>
</tr>
<tr>
<td><strong>Onset→ Reperfusion</strong></td>
<td>241 min (IQR 176-359)</td>
<td>---</td>
<td>~321 min</td>
<td>---</td>
</tr>
</tbody>
</table>

**Onset-to-treatment (eg. infusion of intra-arterial tPA)**
Impact on acute stroke treatment

- All 4 trials showed statistically significant evidence of endovascular treatment in select acute ischemic stroke patients
- Selection of patients should be confirmed by vascular imaging
- IV rt-PA should always be the first line treatment for eligible acute ischemic stroke patients
- On average approximately 5% of stroke patients receive acute stroke treatment
- We need to continue to improve community and physician awareness
STROKE PREVENTION
Guidelines for the Primary Prevention of Stroke

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

The American Academy of Neurology affirms the value of these guidelines as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons, the Congress of Neurological Surgeons, and the Preventive Cardiovascular Nurses Association

James F. Meschia, MD, FAHA, Chair; Cheryl Bushnell, MD, MHS, FAHA, Vice-Chair; Bernadette Boden-Albala, MPH, DrPH; Lynne T. Braun, PhD, CNP, FAHA; Dawn M. Bravata, MD; Seemant Chaturvedi, MD, FAHA; Mark A. Creager, MD, FAHA; Robert H. Eckel, MD, FAHA; Mitchell S.V. Elkind, MD, MS, FAAN, FAHA; Myriam Fornage, PhD, FAHA; Larry B. Goldstein, MD, FAHA; Steven M. Greenberg, MD, PhD, FAHA; Susanna E. Horvath, MD; Costantino Iadecola, MD; Edward C. Jauch, MD, MS, FAHA; Wesley S. Moore, MD, FAHA; John A. Wilson, MD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Functional Genomics and Translational Biology, and Council on Hypertension

Abstract—The aim of this updated statement is to provide comprehensive and timely evidence-based recommendations on the prevention of stroke among individuals who have not previously experienced a stroke or transient ischemic attack. Evidence-based recommendations are included for the control of risk factors, interventional approaches to atherosclerotic disease of the cervicophepatic circulation, and antithrombotic treatments for preventing thrombotic and thromboembolic stroke. Further recommendations are provided for genetic and pharmacogenetic testing and for the prevention of stroke in a variety of other specific circumstances, including sickle cell disease and patent foramen ovale.  (Stroke. 2014;45:3754-3832.)

Key Words: AHA Scientific Statements ▪ atrial fibrillation ▪ diabetes mellitus ▪ hyperlipidemias ▪ hypertension ▪ intracranial aneurysm ▪ ischemia ▪ prevention and control ▪ smoking ▪ stroke
Estimated 10-year stroke risk in adults 55 years of age according to levels of various risk factors (Framingham Heart Study).

<table>
<thead>
<tr>
<th>Blood Pressure*</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cigarette Smoking</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Prior AF</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Prior CVD</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* - Closest ranges for women are: 95-104 and 115-124.
Stroke Rates by Blood Pressure Level

Source: Framingham Heart Study, 1980
Distribution of Blood Pressures in Adults in the United States

Source: NHANES II
Population-Based Strategy

Reduction in SBP mmHg

<table>
<thead>
<tr>
<th>Reduction in SBP mmHg</th>
<th>% Reduction in Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stroke</td>
</tr>
<tr>
<td>2</td>
<td>-6</td>
</tr>
<tr>
<td>3</td>
<td>-8</td>
</tr>
<tr>
<td>5</td>
<td>-14</td>
</tr>
</tbody>
</table>

SBP Distributions

Before Intervention

After Intervention

Reduction in BP

Lifestyle interventions

- JNC VII recommends therapeutic lifestyle change only for most people with pre-hypertension
  - Weight reduction
  - DASH diet
  - Dietary sodium reduction
  - Physical Activity
  - Moderate alcohol consumption

http://www.nhlbi.nih.gov/guidelines/hypertension/
JNC VII Medication Recommendations*

- **Pre-hypertension**
  - Lifestyle interventions

- **Stage 1 Hypertension**
  - (SBP 140–159 or DBP 90–99 mmHg) Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination

- **Stage 2 Hypertension**
  - (SBP ≥160 or DBP ≥100 mmHg) 2-drug combination for most (usually thiazide-type diuretic* and ACEI, or ARB, or BB, or CCB)

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI</td>
<td>ace inhibitors</td>
</tr>
<tr>
<td>ARB</td>
<td>angiotensin receptor blockers</td>
</tr>
<tr>
<td>BB</td>
<td>beta blockers</td>
</tr>
<tr>
<td>CCB</td>
<td>calcium channel blockers</td>
</tr>
</tbody>
</table>

*JNC-VII includes chlorothalidone among thiazide-type diuretics.
ASA RECOMMENDATIONS
HYPERTENSION CONTROL

Regular blood pressure screening and appropriate treatment of patients with hypertension including life style modification and pharmacological therapy, are recommended (Class I; Level of Evidence A).

Annual blood pressure screening for high blood pressure and health-promoting lifestyle modification are recommended for patients with prehypertension (systolic blood pressure of 120-139 mmHg or diastolic blood pressure of 80-89 mmHg) (Class I; Level of Evidence A).

Successful reduction of blood pressure is more important in reducing stroke risk than the choice of a specific agent, and treatment should be individualized on the basis of other patient characteristics and medication tolerance (Class I; Level of Evidence A).

Self-measured blood pressure monitoring is recommended to improve blood pressure control (Class I; Level of Evidence A).
Role of the Provider

- Patients may be able to lower the required dose of blood pressure medicines through reduced sodium intake
- Patients with normotension or prehypertension may reduce or prolong their risk for developing hypertension through sodium reduction
  - Referral to a Registered Dietitian for Counseling
  - Education during BP screenings
  - Downloadable CDC resource: Reducing Sodium in Your Diet to Help Control Your Blood Pressure
  - Advise consumption of fresh fruits and vegetables, frozen fruits and vegetables without sauce, and no salt added canned vegetables
  - Advise limiting processed foods high in sodium
Patient Education – It’s Not the Salt Shaker, It’s the Food Choices!

www.cdc.gov/salt
Medication Adherence

- Clinician empathy increases patient trust and motivation
- Physicians should consider their patients’ cultural beliefs and individual attitudes in formulating therapy
- Team-based care (pharmacy medication therapy management, physician assistants, nurse practitioners, etc.)
- Consider the Morisky Medication Adherence questionnaire for your hypertensive patients
SUMMARY

Stroke is Progressive

Stroke is an EMERGENCY

Stroke is Preventable