Stroke Prevention Guidelines

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Disclosures

Janssen:
Speaker

BMS:
Consultant, Speaker

Pfizer:
Consultant, Speaker

Merck:
Advisory Board

STROKE

- Approximately 795,000 people in the United States have a stroke each year
- ≈610,000 of whom have had first attacks, resulting in 6.8 million stroke survivors >19 years of age
- Stroke rate is falling. It was the No. 3 killer in the US, now No. 4 (Soon No. 5??)
**Stroke Types**

- **Ischemic**: 85%
- **Hemorrhagic**: 15%
  - Large Vessel: 35%
  - Cardioembolic: 25%
  - Lacunar: 20%
  - Other: 5%
  - ICH: 10%
  - SAH: 5%


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**AHA/ASA Guideline**

*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 offers the values of these guidelines as an educational tool for neurologists.

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

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Stroke 2014;45:00
Risk Factors

- Multifactorial
- Framingham Stroke Profile
- Independent stroke predictors: age, systolic blood pressure, hypertension, hypercholesterolemia, diabetes mellitus, current smoking
- Established cardiovascular disease: myocardial infarction, angina or coronary insufficiency, congestive heart failure, and intermittent claudication, atrial fibrillation (AF), and left ventricular hypertrophy

Targets for Stroke Prevention Are Aligned with the Life’s Simple 7’s

Non-modifiable Risk Factors

- **Age**: Incidence of both ischemic and ICH increases with age.
  Knodla BM. Neurology. 2012;79:1781

- **Low birth weight**: Odds of stroke doubled with birth weights <2.5 Kg (vs. 4.0 Kg).
  Lackland DT. J Clin Hypertens. 2003;5:133

- **Race/Ethnicity**: Blacks and some Hispanic/Latino Americans have a higher incidence of all stroke types and higher mortality rates compared with whites.
  Cruz-Flores S. Stroke. 2004;35:212

- **Genetic Factors**: A meta-analysis of cohort studies showed that a positive family history of stroke increases the risk of stroke by ≈30% (OR, 1.3; 95% CI, 1.2–1.5; P<0.00001)
  Flossman. Stroke 2004;35:212
Statins

- Treatment with statins reduces the risk of stroke in patients with or at high risk for atherosclerosis.

- One meta-analysis of 26 trials that included >90000 patients found that statins reduced the risk of all strokes by ≈21% (95% CI, 15–27)
  Amarenco P. Stroke. 2004;35:2902

- Another meta-analysis of randomized trials of statins in combination with other preventive strategies 165,792 individuals showed that each 39 mg/dL decrease in LDL cholesterol was associated with a 21% (95% CI, 6.3–33.5; P=0.009) reduction in stroke.
  Amarenco P. Lancet Neurol. 2009;8:453

Recommendations

- In addition to therapeutic lifestyle changes statins are recommended for the primary prevention of ischemic stroke in patients estimated to have a high 10-year risk for cardiovascular events (Class I; Level of Evidence A).

- Nonstatin lipid-lowering therapies such as fibric acid derivatives, bile acid sequestrants, niacin, and ezetimibe may be considered for patients with low HDL cholesterol or elevated, but its efficacy in preventing ischemic stroke is not established. Similarly for Fibric acid derivatives (Class IIb; Level of Evidence B).

Diabetes Mellitus

- Diabetes mellitus more than doubles the risk for stroke, and ≈20% of patients with diabetes mellitus will die of a stroke.
Diabetes Mellitus

- Diabetes mellitus more than doubles the risk for stroke, and ≈20% of patients with diabetes mellitus will die of a stroke.
- There is no evidence that improved glycemic control decreases short-term risk of macrovascular events, including stroke.

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Follow-up</th>
<th>Intensive vs Conventional</th>
<th>Effect on CVD/Stroke</th>
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</thead>
<tbody>
<tr>
<td>UKPDS</td>
<td>3277</td>
<td>5-yr</td>
<td>No difference</td>
<td>No difference</td>
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<tr>
<td>ACCORD</td>
<td>11430</td>
<td>5-yr</td>
<td>Intensive vs Conventional</td>
<td>No effect on CVD or stroke</td>
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<td>ADVANCE</td>
<td>11140</td>
<td>5-yr</td>
<td>Intensive vs Standard</td>
<td>No effect on CVD or stroke</td>
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<td>VA Diab Trial</td>
<td>7301</td>
<td>5-yr</td>
<td>Intensive vs Standard</td>
<td>No effect on CVD or stroke</td>
</tr>
</tbody>
</table>


**Substudy of 3577 patients with DM, ramipril led to a:**
- 25% (P=0.0004) reduction in the combined outcome of MI, stroke, and CV death.
- 33% (P=0.0074) reduction in stroke.


**Hypertension**

A Risk Factor for Cardiovascular Disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Men</th>
<th>Women</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary Disease</td>
<td>22.7</td>
<td>17.4</td>
<td>3.3</td>
<td>2.6</td>
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<tr>
<td>Stroke</td>
<td>21.5</td>
<td>2.8</td>
<td>9.9</td>
<td>7.1</td>
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<tr>
<td>Peripheral Artery Disease</td>
<td>6.2</td>
<td>6.3</td>
<td>13.9</td>
<td>13.9</td>
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<tr>
<td>Heart Failure</td>
<td>2.9</td>
<td>2.6</td>
<td>3.9</td>
<td>3.8</td>
</tr>
</tbody>
</table>

Biennial Age-Adjusted Rate per 1000 Patients

Kernel RR: JAMA 1999;282:1871-1878
Hypertension

- There is a strong, continuous, independent and predictive relationship between BP and risk of stroke.
  Chobanian AV. JAMA. 2003;289:2560

Treatment of HTN Reduces the Risk of Stroke

<table>
<thead>
<tr>
<th>Study name</th>
<th>Patients Anti-HTN</th>
<th>Patients Placebo</th>
<th>Risk Ratio Anti-HTN/Placebo</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>HOPE</td>
<td>1.04</td>
<td>1.01</td>
<td>1.02</td>
<td>0.12</td>
</tr>
<tr>
<td>SPRINT</td>
<td>1.10</td>
<td>1.01</td>
<td>1.11</td>
<td>0.12</td>
</tr>
<tr>
<td>ACCOS</td>
<td>0.99</td>
<td>1.00</td>
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<td>0.89</td>
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<td>COGENT</td>
<td>1.05</td>
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<td>ARIADNE</td>
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<td>1.00</td>
</tr>
</tbody>
</table>

22% reduction with anti-HTN vs. placebo (p<0.00001)
Sipahi I. Stroke. 2012;43:432

Atrial Fibrillation

- The risk of stroke is increased ~5-fold in NVAF patients versus those without NVAF.

Incidence of Stroke According to Presence of NVAF
(Framingham Heart Study)

- p<0.001
Sakemi N, et al. JACC. 2006;48:2279-2286
For patients with non-valvular atrial fibrillation, a CHA₂DS₂-VASc score of ≥2 and low risk for hemorrhagic complications, oral anticoagulants are recommended (Class I). Options include warfarin (INR, 2.0 to 3.0) (Level of Evidence A), dabigatran (Level of Evidence B), apixaban (Level of Evidence B), and rivaroxaban (Level of Evidence B).
Carotid Disease

- 10-15% of acute ischemic strokes are secondary to occlusion of ICA or artery to artery embolism
- Stroke secondary to ICA and MCA (“tandem”) occlusion is a strong predictor of mortality
- Current revascularization procedures to prevent carotid occlusion include Carotid Endarterectomy (CEA) and Angioplasty and Stenting (CAS)

Nogueira et al AJNR 2009
Linfante et al JNIS 2015

CEA/CAS

- Patients with symptomatic stenosis >50% should be considered for CEA or CAS (Class I; Level of Evidence A)

CEA/CAS

- It is reasonable to consider performing carotid endarterectomy in asymptomatic patients who have >70% stenosis of the internal carotid artery if the risk of perioperative stroke, myocardial infarction, and death is low (<3%). However, its effectiveness compared with contemporary best medical management alone is not well established (Class IIa; Level of Evidence A).
Any Stroke and Death Rates Within 30 Days for CAS Are Very Low And Within AHA Guidelines

<table>
<thead>
<tr>
<th></th>
<th>CREST</th>
<th>CAS</th>
<th>CEA</th>
<th>AHA Guidelines</th>
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<tbody>
<tr>
<td>Symptomatic</td>
<td>5.6%</td>
<td>2.6%</td>
<td>&lt; 6.0%</td>
<td></td>
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<tr>
<td>Asymptomatic</td>
<td>2.4%</td>
<td>1.5%</td>
<td>&lt; 3.0%</td>
<td></td>
</tr>
</tbody>
</table>

*Octogenarians excluded: 2294 Asymptomatic, and 1270 Symptomatic patients

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The Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Study

- NIH/NINDS. ClinicalTrials.gov: NCT02089217
- Multicenter, RCTs of carotid revascularization and intensive medical management versus medical management alone in patients with asymptomatic high-grade (>70%) carotid stenosis
- 2 simultaneous trials:
  - CAS Vs. Medical management
  - CEA Vs. Medical management

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Conclusions

- Great progress has been made in prevention of stroke now downgraded to No 4 cause of death in the USA
- The Life’s Simple 7’s are applicable to primary stroke prevention in the general public.
- Blood pressure control is particularly important in stroke prevention.
Thanks

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