Stroke in Family Medicine

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Speaker Disclosure

- Dr. Moquist has disclosed that he has no actual or potential conflict of interest in relation to this topic.
Learning Objectives

By the end of this activity, the participant should be better able to:

- Discuss the impact of cerebrovascular disease.
- Recognize and implement treatment of acute stroke.
- Recognize and treat Transient Ischemic Attacks (TIA).
- Identify and prescribe treatment for primary stroke prevention.
- Identify and prescribe treatment for secondary stroke prevention.
- Discuss the impact of atrial fibrillation on stroke.
Outline

Background
Acute Stroke
TIA
Risk Factor Reduction
Atrial Fibrillation
Other Issues
Summary
Background

Impact
Causes
Small Vessel
Large Vessel
Cardioembolic
ARS Question

In what percentage of ischemic strokes is no cause identified?

1. 10%
2. 20%
3. 35%
4. 50%
5. 70%
Impact of Cerebrovascular Disease

- Leading cause of disability and death in older adults
- 795,000 new strokes each year
- 6.8 million stroke survivors
- Incidence doubles with each decade
- Six months after stroke in older adults
  - 26% dependent in ADLs
  - 46% measurable cognitive deficits
- Fatality rate within 1 month is 20-30%
Causes of Strokes

- Ischemic: 80-85%
  - Small Vessel: 17%
  - Large Vessel: 19%
  - Cardioembolic: 27%
  - Cryptogenic – No identifiable cause: 35%
- Hemorrhagic: Will not discuss
  - Intracerebral
  - Subarachnoid
  - Subdural
Small Vessel Disease

- Occlusion of small penetrating vessels
- Supply internal capsule, basal ganglia, thalamus, and pons
- Well-defined clinical syndromes
  - Pure Motor Hemiplegia
  - Pure Hemisensory Stroke
  - Ataxic Hemiparesis
  - Dysarthria – Clumsy Hand Syndrome
- Strokes < 1 cm: Lacunar
- Risk Factors: Hypertension, diabetes, and smoking
Large Vessel Disease

- Atherosclerosis: Progressive occlusion of anterior & posterior circulation
- Emboli from atherosclerotic lesion
- Stroke syndromes consistent with anatomy
- Internal Carotid Artery: Amaurosis fugax or hemispheric deficit
- Posterior circulation causes dysfunction
  - Cranial nerves
  - Descending motor or ascending sensory
  - Cerebellar and vestibular
  - Visual cortex
Cardioembolic

- Potential preventable cause
- Atrial Fibrillation is most common cause
- 4-5 fold increase with thrombus in L atrial appendage
- Accounts for 25-30% of all ischemic strokes
- Similar for persistent and paroxysmal
- Multiple cerebral infarcts in more than one vascular area
- Often occur without TIA
Acute Stroke

Presentation
Risk Factors
Immediate Treatment
NIHSS
Immediate Studies and Imaging
Acute Care
Recombinant Tissue Plasminogen (rt-PA)
ARS Question

What percentage of ischemic strokes are caused by 5 modifiable factors: HTN, current smoking, obesity, unhealthy diet, and physical inactivity?

1. 20%
2. 40%
3. 60%
4. 82%
5. 100%
ARS Question

The AHA recommends what window of time for treatment of an acute stroke with rt-PA in patients \( \leq 80 \) years of age who have NIHSS scores of \( \leq 25 \) and no prior history of stroke and diabetes?

1. One hour
2. Two hours
3. Three hours
4. Four and half hours
5. Six hours
Acute Stroke

- Most common historical feature is awakening with or acute onset of symptoms
- Most common physical findings are unilateral weakness and speech disturbance

<table>
<thead>
<tr>
<th>Symptom or Sign</th>
<th>Prevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Onset</td>
<td>96</td>
</tr>
<tr>
<td>Arm Weakness</td>
<td>63</td>
</tr>
<tr>
<td>Leg Weakness</td>
<td>54</td>
</tr>
<tr>
<td>Speech Disturbance</td>
<td>53</td>
</tr>
<tr>
<td>Facial Weakness</td>
<td>23</td>
</tr>
<tr>
<td>Arm Paresthesias</td>
<td>20</td>
</tr>
<tr>
<td>Leg Paresthesias</td>
<td>17</td>
</tr>
<tr>
<td>Headache</td>
<td>14</td>
</tr>
<tr>
<td>Dizziness (Not Ortho)</td>
<td>13</td>
</tr>
<tr>
<td>Arm Paresis</td>
<td>69</td>
</tr>
<tr>
<td>Leg Paresis</td>
<td>61</td>
</tr>
<tr>
<td>Dysphasia/Dysarthria</td>
<td>57</td>
</tr>
<tr>
<td>Ataxic Gait</td>
<td>53</td>
</tr>
<tr>
<td>Facial Paresis</td>
<td>45</td>
</tr>
<tr>
<td>Abnormal Eye Movement</td>
<td>27</td>
</tr>
<tr>
<td>Visual Field Defect</td>
<td>24</td>
</tr>
</tbody>
</table>
Acute Stroke Risk Factors

- Five modifiable risk factors: 82% of strokes
  - Hypertension
  - Current Smoking
  - Obesity
  - Unhealthy Diet
  - Physical Inactivity

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio of Cerebral Ischemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>2.64</td>
</tr>
<tr>
<td>Current Smoking</td>
<td>2.09</td>
</tr>
<tr>
<td>Increased W to Hip</td>
<td>1.65</td>
</tr>
<tr>
<td>High Alcohol Intake</td>
<td>1.51</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1.36</td>
</tr>
<tr>
<td>Unhealthy Diet</td>
<td>1.35</td>
</tr>
<tr>
<td>Psychosocial Stress</td>
<td>1.30</td>
</tr>
<tr>
<td>Regular Physical Activity</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Posterior Circulation Stroke

<table>
<thead>
<tr>
<th>Symptom or Sign</th>
<th>Prevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>47</td>
</tr>
<tr>
<td>Unilateral Limb Weakness</td>
<td>41</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>31</td>
</tr>
<tr>
<td>Headache</td>
<td>28</td>
</tr>
<tr>
<td>Nausea or Vomiting</td>
<td>27</td>
</tr>
<tr>
<td>Unilateral Limb Weakness</td>
<td>38</td>
</tr>
<tr>
<td>Gait Ataxia</td>
<td>31</td>
</tr>
<tr>
<td>Unilateral Limb Ataxia</td>
<td>30</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>28</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>24</td>
</tr>
</tbody>
</table>

- Dizziness can be challenging to diagnose
- Uncommon for stroke
- One fourth have stroke
  - Vertigo > 1 hour
  - Gaze-evoked nystagmus
  - Nausea and vomiting
  - Head motion intolerance
  - New gait unsteadiness
Immediate Treatment of Acute Ischemic Stroke

- **Quickly use head CT imaging** to determine whether the patient is suffering from an ischemic or hemorrhagic event.
- **Assess the severity and pattern** of neurologic deficits, such as by using the NIH Stroke Scale.
- **Identify non-stroke causes** of acute neurologic dysfunction, such as migraine, seizure, and drug intoxication.
NIHSS

- 15 item scale
- Can be performed in 5 minutes
- Can help distinguish stroke from stroke mimics
- Chief use to evaluate stroke severity
- Used to predict prognosis
NIH Stroke Scale (NIHSS)

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of consciousness</td>
<td>0–7</td>
</tr>
<tr>
<td>Best gaze</td>
<td>0–2</td>
</tr>
<tr>
<td>Visual fields</td>
<td>0–3</td>
</tr>
<tr>
<td>Facial palsy</td>
<td>0–3</td>
</tr>
<tr>
<td>Motor: arms</td>
<td>0–8</td>
</tr>
<tr>
<td>Motor: legs</td>
<td>0–8</td>
</tr>
<tr>
<td>Limb ataxia</td>
<td>0–2</td>
</tr>
<tr>
<td>Sensory</td>
<td>0–2</td>
</tr>
<tr>
<td>Best language</td>
<td>0–3</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>0–2</td>
</tr>
<tr>
<td>Extinction and inattention</td>
<td>0–2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>0–42</strong></td>
</tr>
</tbody>
</table>

Greater score reflects increased impairment:

<5 suggests very good prognosis
>20 suggests very poor prognosis, high risk of major complications

Details about scoring each item are at [https://www.mdcalc.com/nih-stroke-scale-score-nihss#next-steps](https://www.mdcalc.com/nih-stroke-scale-score-nihss#next-steps)

Accessed on April 24, 2017

Available as an App on Smart Phone Via Mdcalc
Immediate Diagnostic Studies

- Noncontrast Brain CT or Brain MRI
- Blood Glucose
- Oxygen Saturation
- BMP
- CBC
- Cardiac Markers
- Prothrombin Time/INR
- ECG
- Echocardiogram
- Carotid Ultrasound
Urgent Imaging

- Distinguish ischemic and hemorrhagic stroke
- Presence of nonischemic CNS lesions
- Multimodal MRI
  - Better resolution
  - Greater sensitivity for acute ischemic stroke
  - Lower rate of misdiagnosis in < 55 years of age
- CT Scan
  - Faster
  - More available
  - Less expensive
  - Performed in patients with implantable devices
  - Performed in patients with claustrophobia
Acute Care

- Optimize hydration
- Control BP while avoiding hypotension
  - Should NOT lower < 160
  - Treat if BP is > 220/120
- Preventing DVT
- Detecting and treating coronary ischemia, heart failure and cardiac arrhythmias
- Start long-term RX with antiplatelet agents or oral anticoagulation
- Normalize glucose and body temperature
- Formal dysphagia evaluation
- Carotid Doppler ultrasound
Recombinant Tissue-Plasminogen Activator (rt-PA)

- Consider when:
  - Patient presents within 3 hours of neurologic deficit
  - CT confirms absence of intracranial hemorrhage
- AHA recommendation: Increase the window to 3-4.5 hours for patients ≤80 years old who have NIHSS score ≤25 and no prior history of stroke or diabetes
- Use requires careful assessment by a clinician experienced in treatment of stroke
- Carries a 6% risk of intracerebral hemorrhage, usually among patients with severe strokes
Regions of Cerebral Hypoperfusion Following Acute Ischemic Stroke

MRI indicates magnetic resonance imaging. A, Schematic representation of regions of hypoperfused brain tissue following acute occlusion of the middle cerebral artery. The ischemic core is an area of irreversible ischemia and cell death; ischemic penumbra, potentially salvageable tissue with prompt reperfusion; benign oligemia, decreased perfusion but no infarction risk regardless of treatment. The infarct core can enlarge into the penumbra if reperfusion is not successful. B, Top, Axial diffusion-weighted MRI (DWI) showing a hyperintensity consistent with irreversible ischemia (ischemic core) in the deep perforating territory of the right middle cerebral artery affecting the caudate, internal capsule, and lentiform nucleus. Bottom, Axial perfusion-weighted MRI (PWI) at the same level as the DWI showed a much larger area of diminished perfusion consistent with prolonged ischemia compared with the DWI. The region of prolonged ischemia is the ischemic penumbra in which reperfusion could salvage some of the tissue. Perfusion-weighted imaging uses contrast material to estimate cerebral blood flow. The color scale represents mean transit time of a contrast bolus; blue indicates normal transit time and shades of green, yellow, orange, and red indicate delay in transit time (ischemia). The region of the ischemic core as defined in the DWI shows areas of no contrast (black) in the ischemic core. The area with abnormal transit time surrounding the core is considered the ischemic penumbra.

These images are from a 49-year-old patient who presented with sudden onset of dysarthria and left hemiparesis. The MRI images were obtained following intravenous recombinant tissue plasminogen activator administered approximately 50 minutes after symptom onset to assess eligibility for mechanical thrombectomy.
Contraindications to rt-PA

- Major surgery within the previous 2 weeks
- Previous intracranial hemorrhage
- Systolic BP >185 or diastolic BP >110 mmHg
- Symptoms of subarachnoid hemorrhage
- Recent uncontrolled bleeding
- Coagulopathy
- Thrombocytopenia
- INR >1.7
More on IV rt-PA

- Meta-analysis of 2775
- Confirmed *time dependency* of thrombolytic therapy
- Odds ratios of good outcomes
  - 0-90 Minutes: 2.55
  - 91-180 Minutes: 1.64
  - 181-270 Minutes: 1.34
  - No net benefit beyond 4.5 hours (270 minutes)
Rt-PA & Endovascular Thrombectomy

- 4 recent randomized studies
- Endovascular thrombectomy in proximal large vessel occlusions of the anterior cerebral circulation showed significant benefit when treatment began within 6 hours
- Most patients received IV rt-PA before thrombectomy
- Benefits:
  - 50% reduction in NIHSS score at 24 hours
  - Improved functional outcomes at 90 days
- Increased risk of new ischemic stroke within 90 days: 5.6%
Transient Ischemic Attack

Definition
TIA Mimics
Clinical Symptoms
Stroke Risk After TIA
Definition of TIA

- In 1960’s, sudden focal neurologic deficit for less than 24 hours
- Using classic definition many had infarct on MRI
- Evidence of stroke on MRI redefined as a stroke not TIA
- Defined as a brief episode of neurologic dysfunction caused by focal ischemia to the brain or spinal with NO infarction
- Newer Imaging: Typically lasts < 1-2 hours
TIA Mimics

- More likely gradual onset of symptoms
- Nonspecific symptoms
- Seizures
- Migraines
- Metabolic disturbances
- Syncope
- Drug intoxication

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Odds TIA Mimic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory Loss</td>
<td>9.17</td>
</tr>
<tr>
<td>Headache</td>
<td>3.71</td>
</tr>
<tr>
<td>Blurred Vision</td>
<td>2.48</td>
</tr>
<tr>
<td>Unilateral Paresis</td>
<td>0.35</td>
</tr>
<tr>
<td>Amaurosis Fugax</td>
<td>0.15</td>
</tr>
<tr>
<td>Diplopia</td>
<td>0.14</td>
</tr>
</tbody>
</table>
## Clinical Symptoms of TIA vs. Mimics

<table>
<thead>
<tr>
<th>Clinical Symptom</th>
<th>% TIA Mimics</th>
<th>% TIAAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral Paresis</td>
<td>29.1</td>
<td>58</td>
</tr>
<tr>
<td>Memory Loss</td>
<td>18 to 26</td>
<td>2-12</td>
</tr>
<tr>
<td>Headache</td>
<td>14.6-23</td>
<td>2-36</td>
</tr>
<tr>
<td>Blurred Vision</td>
<td>21.8</td>
<td>5.2</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>12.7</td>
<td>20.6</td>
</tr>
<tr>
<td>Hemianopia</td>
<td>3.6</td>
<td>3.6</td>
</tr>
<tr>
<td>Transient Monocular Blindness</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Diplopia</td>
<td>0</td>
<td>4.8</td>
</tr>
</tbody>
</table>
## Differential Diagnosis of TIA

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Key Findings</th>
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</thead>
<tbody>
<tr>
<td>Brain Tumor</td>
<td>Severe Unilateral HA with N&amp;V</td>
</tr>
<tr>
<td>CNS Infection</td>
<td>Fever, HA, Confusion, Neck Stiffness, N&amp;V, Photophobia, Change in Mental Status</td>
</tr>
<tr>
<td>Falls/Trauma</td>
<td>HA, Confusion, Bruising</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Confusion, Weakness, Diaphoresis</td>
</tr>
<tr>
<td>Migraines</td>
<td>Severe HA w or w/o Photophobia, Younger Age</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>Diplopia, Limb Weakness, Paresthesia, Urinary Retention, Optic Neuritis</td>
</tr>
<tr>
<td>Seizure Disorder</td>
<td>Confusion w or w/o Loss of Consciousness, Urinary Incontinence, Tongue Biting, Tonic-Clonic Movements</td>
</tr>
<tr>
<td>Subarachnoid Hemorrhage</td>
<td>Severe HA with Sudden Onset and Photophobia</td>
</tr>
<tr>
<td>Vertigo (Central or Peripheral)</td>
<td>Generalized Dizziness &amp; Diaphoresis With or Without Hearing Loss</td>
</tr>
</tbody>
</table>
Management of TIA

- TIA symptoms should be evaluated emergently
- Brain imaging, ideally with MRI, is important to determine whether there has been an acute stroke and, if one is found, its location and type
- Noninvasive imaging of the carotid arteries, EKG, and echocardiography are important to determine the most likely cause of ischemia
- Initiate treatment for secondary stroke prevention based on the results of the evaluation
Stroke Risk After TIA

- ABCD2 used to determine stroke risk
- Highly predictive of severity of stroke
- Higher scores correlate with higher disability
- Highly predictive of stroke within 24 hours
- 76% of recurrent stroke had a score of 5 or greater
- One study from an emergency room
  - Score of 0-3 – Discharge with imaging within 2 days
  - Score of 4-5 – Imaged in ER
  - Score > 5 – Admitted
  - Lower rates of admission and lower recurrent stroke rate
## ABCD2 Scoring System

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age $\geq$ 60 Years</td>
<td>1</td>
</tr>
<tr>
<td>Blood Pressure: Systolic $\geq$ 140 or Diastolic $\geq$ 90</td>
<td>1</td>
</tr>
<tr>
<td>Unilateral Weakness</td>
<td>2</td>
</tr>
<tr>
<td>Speech Impairment w/o Weakness</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1</td>
</tr>
<tr>
<td>TIA Duration $\geq$ 60 Minutes</td>
<td>2</td>
</tr>
<tr>
<td>TIA Duration 10-59 Minutes</td>
<td>1</td>
</tr>
<tr>
<td>Stroke Risk at 2 Days: 1-3 Points 1%</td>
<td>4-5 Points 4.1%; 6-7 Points 8.1%</td>
</tr>
</tbody>
</table>
RISK FACTOR REDUCTION

- Hypertension
- Current Smoking
- Obesity
- Unhealthy Diet
- Physical Inactivity
- Dyslipidemia
- Antiplatelet Agents
Hypertension

- Continuous association with both systolic and diastolic
- BP Control after TIA: 30-40% reduction in stroke
- Reduction in strokes, MI, heart failure and all vascular events
- Annual screening for high BP
- Goal of Treatment: 140/90
- Successful reduction of BP is more important than the choice of a specific treatment
- Self-measured BP monitoring is recommended
Current Smoking

- Increases BP and augment atherosclerosis
- Increase the risk of stroke 2-4 fold than nonsmokers
- Dose-response to cerebral ischemia
- Risk of stroke decreases after quitting
- Most effective RX is combination of behavioral therapy, nicotine replacement, and social support
- Abstention from smoking recommended for non-smokers
Obesity

- Defined as BMI >30
- Associated with increased risk of death
- Increased waist-to-hip ratio: Increased risk of stroke
- Mediterranean Diet
  - Control body weight
  - Reduce risk of stroke
  - Reduce risk of MI
Diabetes Mellitus

- DM is a clear risk factor
- Newly diagnosed DM doubles risk
- Risk factor reduction is imperative
- Control BP to a target of 140/90
- Treatment with a statin is recommended to reduce risk
- ADA recommends HgbA1C goal of <7.0%
- From available clinical trials there is no evidence that reduced glycemia decreases the short-term risk of macrovascular events in DM2
Unhealthy Diet

- Reduced intake of sodium and increased intake of potassium is indicated by US Dietary Guidelines
- Dash Diet which emphasizes fruits, vegetables and low-fat dairy products recommended to lower BP
- Diet rich in fruits and vegetables may lower the risk of stroke
- A Mediterranean Diet supplemented with nuts may be considered in lowering risk of stroke
Physical Inactivity

- Physical activity associated with a reduction in the risk of stroke
- 2008 Physical Aerobic Activity Guidelines
  - > 150 min/wk of moderate intensity (fast walking)
  - Or 75 min/wk of vigorous intensity (running)
- 2013 AHA/ACC Guidelines: Healthy adults should perform at least moderate-to-vigorous intensity aerobic physical activity at least 40 min/d 3 to 4 days per week
- Some physical activity is better than none
- Any amount of physical activity gain some health benefits
Dyslipidemia

- Independent risk factor for stroke
- Statin therapy recommended for primary and secondary
- Primary: >7.5% 10-year risk for cardiovascular events as recommended in the 2013 ACC/AHA Guidelines on the Treatment of Blood Cholesterol to Reduce Risk in Adults
- Secondary: Intensive statin therapy among patients with ischemic stroke or TIA to be of atherosclerotic origin and an LDL-C ≥ 100 with or without clinical ASCVD
# Intensity of Statin Therapy

<table>
<thead>
<tr>
<th>High Intensity</th>
<th>Moderate Intensity</th>
<th>Low Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Dose Lowers LDL-C on Average $\geq$ 50%</td>
<td>Daily Dose Lowers LDL-C on Average 30 to &lt;50%</td>
<td>Daily Dose Lowers LDL-C on Average &lt; 30%</td>
</tr>
<tr>
<td>Atorvastatin 40-80 mg Rosuvastatin 20-40 mg</td>
<td>Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin 40 mg BID</td>
<td>Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg</td>
</tr>
</tbody>
</table>
Antiplatelet RX for Noncardioembolic

- For **noncardioembolic** ischemic strokes or TIA, antiplatelet agents rather than oral anticoagulation to reduce strokes
- Aspirin doses > 325 mg do not add therapeutic benefit
- Aspirin as monotherapy or aspirin 25 mg + ER dipyridamole 200 mgm BID is indicated as initial therapy after TIA or ischemic stroke
- Clopidogrel 75 mg is reasonable for monotherapy in patients allergic to aspirin
- Individualized selection of antiplatelet agent on basis of risk factors, cost, tolerance and relative known efficacy
More on Antiplatelet RX

- Combination of aspirin and clopidogrel might be initiated within 24 hours of minor stroke or TIA and for continuation for 90 days.
- Combination of aspirin and clopidogrel initiated days to years after a minor stroke or TIA, increases risk of hemorrhage relative to either agent alone.
- For patients having an ischemic stroke or TIA while taking aspirin, no evidence of increasing dose provides benefit.
- For patients with ischemic stroke or TIA, AF, and CAD the usefulness of adding antiplatelet therapy to VKA is uncertain for purposes of reducing the risk of ischemic cardiovascular and cerebrovascular events.
- For noncardioembolic ischemic stroke or TIA, antiplatelet agents rather than oral anticoagulation is recommended.
Update on AHA/ACC Primary Prevention

- Assess the risk of first stroke using a risk assessment tool such as the AHA/ACC Cardiovascular Risk Calculator
- Encourage lifestyle habits promoting physical activity, low sodium diet, and smoking cessation
- Treat patients with a $\geq 7.5\%$ 10-year risk of CV events as in the 2013 ACC/AHA Guidelines of treatment of blood cholesterol to reduce atherosclerotic CV risk in adults
- Use of aspirin for CVD prophylaxis is reasonable for people who have a 10-year risk of a CV event $>10\%$
- Aspirin is NOT useful in preventing stroke in people at low risk
More on Primary Prevention Update

- Patients with nonvalvular AF and a CHA2DS2-VASc score of ≥ 2 and low risk of complications anticoagulation with either
  - Warfarin
  - Or Dabigatran, Apixaban, or Rivaroxaban

Atrial Fibrillation

Background
Mechanisms
Risk Stratification
Bleeding Risk
Oral Anticoagulation
Primary and Secondary Prevention
AF Background

- AF increases stroke risk 5-fold
  - Age 50-59: 4.6%
  - Ages 80-89: 20.2%
- Outcome of strokes from AF:
  - Higher mortality
  - Greater disability
  - Longer hospital stay
  - Poorer functional outcome
  - Lower chance of being discharged home
- Risk of stroke reduced by antithrombotic therapy
Case Question

- 84-year-old man with newly diagnosed nonvalvular AF comes to the office for FU. History includes HTN, DM, HL, and CKD. Meds include metformin, lisinopril, atorvastatin, and aspirin. No history of Stroke.

- On exam, HR is 86 and irregularly irregular and BP is 130/75. He has decreased proximal muscle strength when he arises from a chair. Recent ECHO shows no atrial clot and normal systolic and diastolic function.
Which of the following is most appropriate RX for reducing his risk of stroke?

1. Continue aspirin
2. Stop aspirin and begin warfarin
3. Stop aspirin and begin apixaban
4. Continue aspirin and add warfarin
Case Question

- 86 year-old woman comes to the ER because she has arm pin that began when she picked up her granddaughter. No history of HTN, HF, DM, or arrhythmia. A year ago she had an episode of Amaurosis Fugax in her L eye that completely resolved.
- On exam, BP is 130/82 and HR is 62-102 beats per minute. There is no heart murmur, JV distention, rales, or peripheral edema. EKG shows new AF with no ischemia. Echo confirms NL LV systolic function and no abnormal valves.
Which one of the following is the next step in her care?

1. Electrical cardioversion
2. Heart rate control
3. Anticoagulation
4. Pharmacologic cardioversion
Case Question

- A 72 year-old man comes to the office because earlier in the day he had difficulty speaking for several hours; his aphasia has since resolved. History includes well-controlled HTN & HL. Meds include lisinopril, HCTZ, atorvastatin, and ASA 81 mg.

- On exam, vitals are NL and other findings are unremarkable. MRI shows scattered micro hemorrhages involving the cortex. Ultrasound reveals < 50% stenosis in both carotid arteries.
Which one of the following is the most appropriate next step in management?

1. Increase aspirin dosage to 325mg/d
2. Stop aspirin
3. Stop aspirin and start clopidogrel 75mg/d
4. Stop aspirin and start dipyridamole/aspirin
Mechanism of Stroke

- Stasis in left atrium causing flow abnormalities
- Structural heart and vascular disease
  - Mitral stenosis
  - Abnormal vessel wall
- Abnormal coagulation and fibrinolysis
Risk Stratification

- CHADS2 validated in hospitalized patients with AF
- Does not include many of the stroke risk factors
  - Increasing age
  - Vascular disease
  - Female sex
  - Asymptomatic L ventricular dysfunction
- Those with prior stroke and no other risk factors would only score a 2 and classified as moderate risk
CHADS2

- Congestive Heart Failure History: 1 point
- Hypertension History: 1 point
- Age ≥ 75: 1 point
- Diabetes Mellitus History: 1 point
- Stroke or TIA or TE: 2 points

<table>
<thead>
<tr>
<th>CHADS2 Score</th>
<th>Stroke Risk %</th>
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</thead>
<tbody>
<tr>
<td>0</td>
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<td>1</td>
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<td>3</td>
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<td>4</td>
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<tr>
<td>5</td>
<td>12.5</td>
</tr>
<tr>
<td>6</td>
<td>18.2</td>
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</table>
CHA2DS2-VASc

- Validated in many studies
- Significantly predictive of stroke
- Best at identifying “truly low risk”
- The C stands for:
  - L ventricular dysfunction < 40%
  - Recent decompensated HF irrespective of EF
  - Includes HF with low EF and preserved EF
- Does not include amyloid heart disease and ESRD
- CHA2DS2-VASc is now the recommended risk score by Europe, US, and NIH
### CHA2DS2VASCc

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
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<tbody>
<tr>
<td>CHF</td>
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<tr>
<td>Hypertension</td>
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</tr>
<tr>
<td>Age ≥ 75</td>
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<tr>
<td>Diabetes Mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/TE</td>
<td>2</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>1</td>
</tr>
<tr>
<td>Age 65-74</td>
<td>1</td>
</tr>
<tr>
<td>Female Sex</td>
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</table>

<table>
<thead>
<tr>
<th>CHA2DS2VASCc</th>
<th>Stroke Risk %</th>
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<td>8</td>
<td>12.5</td>
</tr>
<tr>
<td>9</td>
<td>15.2</td>
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</tbody>
</table>
Risk Factors for Bleeding

• Three have been validated in AF populations
  • HEMORR2HAGES
  • HAS-BLED
  • ATRIA

• HAS-BLED is preferred
  • Validated in multiple independent cohorts
  • Outperforms other bleeding risk scores
  • Validated in New Oral Anticoagulants (NOACs)
  • Validated in untreated and aspirin treated patients
  • Predictive of intracranial hemorrhage risk
  • Predicts bleeding during bridge therapy
HAS-BLED

<table>
<thead>
<tr>
<th>Maximum Score</th>
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<tbody>
<tr>
<td>Hypertension: Systolic &gt;160</td>
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</tr>
<tr>
<td>Abnormal Renal and Liver Function</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding Tendency/ Predisposition</td>
<td>1</td>
</tr>
<tr>
<td>Labile INRs (TTR&lt;60%)</td>
<td>1</td>
</tr>
<tr>
<td>Elderly</td>
<td>1</td>
</tr>
<tr>
<td>Drugs or Alcohol</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Low Risk (0-2)</td>
<td>High Risk (≥3)</td>
</tr>
</tbody>
</table>

- High risk NOT a reason to withhold Oral Anticoagulants (OAC)
- Can be used to highlight potential risk
- More regular visits
- Falls evaluation
- Avoid high risk activities
Clinical Benefit of Oral Anticoagulants (OAC)

- Vitamin K Antagonists
  - Absolute RR of 2.7%/year (NNT 37) for no history of stroke
  - Absolute RR of 8.4%/year (NNT 12) for prior history of stroke
- Efficacy of aspirin is much weaker
- Aspirin for those deemed inappropriate for OAC
- Quality of Control Critical: Time in Therapeutic Range (TTR)
- With INRs >3.0 increase in bleeding
- With INRs <2.0 increase in thromboembolisms
BAFTA Study

- Prospective randomized open-label
- Only people over age 75
- Compare warfarin vs. aspirin
- INR target of 2.5 and aspirin 75 mg/d
- Primary Outcome: Stroke or Embolism
  - 1.8% in warfarin group
  - 3.8% in aspirin group
  - NNT for 1 year 50
- No significant differences in secondary outcomes – death, hospitalization, hemorrhage
SAMe-TT2R2

- Newly diagnosed AF
- No previous anticoagulation
- Score 0-2
- TTR >65%
- Good candidate for VKA
- Score > 2 poor candidate for VKA: Initially NOAC

New Oral Anticoagulants (NOACs)

- Offer efficacy, safety, and convenience
- Two Broad Classes
  - Direct Thrombin Inhibitor: Dabigatran
  - Oral Factor Xa Inhibitors: Rivaroxaban, Apixaban, & Edoxaban
- Advantages compared to warfarin
  - Reduced stroke/systemic embolism: 19%
  - Reduction in hemorrhagic stroke
  - Reduced all-cause mortality
  - Reduced intracranial hemorrhage
- Increased GI tract bleeding compared to warfarin
- Dabigatran 150 mg BID reduces ischemic and hemorrhagic
<table>
<thead>
<tr>
<th>Situation</th>
<th>VKA, Warfarin</th>
<th>Direct Thrombin Inhibitors</th>
<th>Factor X Inhibitors</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
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</thead>
<tbody>
<tr>
<td>Recurrent stroke or TIA despite treatment VKA&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>150 mg of dabigatran, 2/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate or severe renal impairment&lt;sup&gt;b&lt;/sup&gt;</td>
<td>✔️</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔️</td>
</tr>
<tr>
<td>GI tract symptoms or dyspepsia&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td>✔️</td>
<td></td>
<td>✔️</td>
</tr>
<tr>
<td>High risk of bleeding&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td>75 mg dabigatran, 2/d (US); 110 mg dabigatran, 2/d (rest of world)</td>
<td></td>
<td></td>
<td>✔️</td>
<td>✔️&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Preference for 1 dose per day</td>
<td>✔️</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔️</td>
</tr>
</tbody>
</table>

Abbreviations: GI, gastrointestinal; TIA, transient ischemic attack; VKA, vitamin K antagonist.

<sup>a</sup> Superior efficacy for preventing both stroke and hemorrhage.

<sup>b</sup> For creatinine clearance of <15 mL/min use VKA.

<sup>c</sup> Also has an increased risk of bleeding.

<sup>d</sup> High risk of bleeding is defined by a HAS-BLED score of 3 or higher. Use agent with the lowest incidence of bleeding, especially for GI tract bleeding.

<sup>e</sup> Awaiting approval.
Dabigatran vs. Rivaroxaban

- No randomized head-to-head comparisons of NOACs
- Retrospective new-user cohort study of 118,891
- Nonvalvular AF 65 years of age or older
- Rivaroxaban showed reduction in stroke
- Rivaroxaban statistically significant increases in
  - Intracranial Hemorrhage: Exceeded reduction in embolic stroke
  - Major Extracranial Bleeding
  - Including GI Bleeding
  - Increase in Mortality
- In patients >75 or CHADS2 >2, Rivaroxaban had a statistically significant increase in mortality compared to Dabigatran
Approaching the Patient

- **Initial Step: Identify the low risk patient – No therapy**
  - Younger than age 65
  - Score of 0 for males
  - Score of 1 for females
- Patients with at least one additional stroke risk factor offered effective OAC
  - VKA
  - Or NOACs
- Use SAMe-TT2R2 to aid initial decision between VKA and NOAC
Algorithm for Risk Stratification and Selection of Anticoagulation Therapy for Stroke Prevention in Atrial Fibrillation

See Table 1 footnotes for abbreviation expansions; SAMe-TT$_2$R$_2$ is explained in Table 5.

*Consider NOAC or VKA. If considering VKA, calculate SAMe-TT$_2$R$_2$ first before deciding on optimal OAC therapy.
For patients with nonvalvular AF, a CHA2DS2-VASc score of > 2 and acceptable low risk for hemorrhagic CX, OAC are recommended. Options include Warfarin, Dabigatran, Apixaban & Rivaroxaban. Selection of agent should be individualized:

- Risk Factors – Risk for Intracranial Hemorrhage
  - Cost
  - Tolerability
  - Patient Preference
  - Potential Drug Interactions
  - Renal Function
  - Time in INR Therapeutic Range
More on 2014 Primary Prevention

- Patients with **valvular** AF at high risk for stroke (score ≥ 2) and acceptable low risk for hemorrhagic CX, long-term OAC with warfarin at a target INR of 2.0-3.0 is recommended.
- Patients with **nonvalvular** AF and CHA2DS2-VASc score of 0, it is reasonable to omit antithrombotic therapy.
- Patients with **nonvalvular** AF and score of 1 and acceptable low risk for hemorrhagic CX, no thrombotic therapy, anticoagulant therapy, or aspirin therapy may be considered.
2014 AHA/ACC Guideline on Secondary Prevention in AF

- Prolonged rhythm monitoring for patients with acute ischemic stroke or TIA with no other apparent cause
- Combination of OAC with platelet therapy is NOT recommended for ALL patients after a stroke or TIA – reasonable in apparent CAD: ACS or stent placement
- Patients unable to take OAC, aspirin alone recommended
- Usefulness of closure of the L Atrial Appendage with the WATCHMAN device in patients with Stroke/TIA and AF is uncertain
More on Secondary Prevention in AF

- VKA Therapy, Apixaban, Dabigatran, and Rivaroxaban are ALL indications for prevention or recurrent stroke in patients with nonvalvular AF, whether paroxysmal or permanent. Selection should be individualized:
  - Risk Factors
  - Cost
  - Tolerability
  - Patient Preference
  - Potential Drug Interactions
  - Renal Function
  - Time in INR Therapeutic Range
New Recommendations in 2014

- For most patients with a stroke or TIA with AF, reasonable to start OAC with 14 days after neurological symptoms
- Presence of high risk for hemorrhagic conversion, it is reasonable to delay start OAC beyond 14 days
  - Large Infarct
  - Hemorrhagic Transformation
  - Uncontrolled HTN
  - Hemorrhagic Tendency
Other Issues

- Acute MI & LV Thrombus
- Cardiomyopathy
- Valvular Heart Disease
- Prosthetic Valves
- Asymptomatic Carotid Stenosis
- Symptomatic Carotid Stenosis
Acute MI & LV Thrombus

- Treatment with VKA (INR 2.0-3.0) for 3 months is recommended in most patients with ischemic stroke or TIA in the setting of Acute MI with LV mural thrombus
- Same recommendation for anterior STEMI with LV mural thrombus but with anterior apical dyskinesis
- Patients with ischemic stroke or TIA with Acute MI and LV mural thrombus or LV EF <40% who are intolerant of VKA, treatment with LMWH, Dabigatran, Rivaroxaban, or Apixaban for 3 months is recommended
Cardiomyopathy

- Usefulness of anticoagulation is not well established in patients with HF who do not have AF or thromboembolism.
- Patients with ischemic stroke or TIA in sinus rhythm who have L atrial or LV thrombus by echo anticoagulant therapy with VKA is recommended for ≥3 months.
- With ischemic stroke or TIA with mechanical LVAD, treatment with VKA is reasonable with absence major CX.
- In patients without L atrial or LV thrombus, the effectiveness of anticoagulation compared with antiplatelet therapy is uncertain.
Prosthetic Valves

- All mechanical valves require VKA
- For patients with a mechanical aortic valve and history of TIA or ischemic stroke before insertion, VKA therapy is recommended with an INR of 2.0-3.0.
- For patients with a mechanical mitral valve and history of TIA or stroke before insertion, VKA therapy is recommended with an INR of 2.5-3.5. (NEW)
- For patients with a mechanical mitral or aortic valve with history of stroke or TIA & low risk for bleeding, the addition of aspirin 75-200 mg/day is recommended
Valvular Heart Disease

- For patients with ischemic stroke or TIA who have rheumatic mitral valve disease with or without AF, long-term VKA therapy with an INR target of 2.0-3.0 is recommended.
- Antiplatelet therapy should not be routinely added after an ischemic stroke or TIA.
- Patients with rheumatic mitral valve disease who have an ischemic stroke or TIA while being treated adequately with VKA, the addition of aspirin might be considered.
- Patients with mitral valve prolapse who have ischemic stroke or TIA who do not have AF, antiplatelet rx is recommended.
More on Prosthetic Valves

- Patients with a mechanical heart valve who have an ischemic stroke or systemic embolism despite adequate VKA, it is reasonable to increase dose of aspirin or target INR.

- Patients with a bioprosthetic aortic or mitral valve, history of TIA or stroke before insertion and no other indication for OAC beyond 3-6 months, long-term therapy with aspirin 75-100 mg/d is recommended to long-term OAC.

- Patients with a bioprosthetic aortic or mitral valve who have a TIA, ischemic stroke, or systemic embolism despite adequate antiplatelet RX, the addition of VKA with a target of 2.0-3.0 may be considered.
Asymptomatic Carotid Stenosis

- Prescribe daily aspirin and a statin. Screen for other treatable risk factors and appropriate therapies instituted.
- Patients who undergo CEA, aspirin is recommended perioperatively and postoperatively.
- Reasonable to consider CEA who have >70% stenosis of the internal carotid artery if the risk of perioperative stroke, MI and death is low (<3%). Effectiveness compared to medical management is not well established.
- Reasonable to repeat duplex US annually.
- Prophylactic CAS might be considered in highly selected patients (minimum 60% by angiogram), its effectiveness compared with medical RX is not well established.
Symptomatic Carotid Stenosis

- Patients with a TIA or ischemic stroke within the past 6 months and ipsilateral severe (70-99%) carotid stenosis by noninvasive imaging, CEA is recommended if the perioperative M&M is estimated to be <6%.
- With recent TIA or ischemic stroke and ipsilateral moderate (50-69%) carotid stenosis, CEA is recommended depending on patient-specific factors and operative M&M is estimated to be <6%.
- When the degree of stenosis is <50%, CEA and CAS are not recommended
More on CAS

- CAS is an alternative to CEA for patients at average or low risk of complications associated with endovascular intervention when the diameter of the ICA is reduced by >70% when rate of stroke or death is <6%.

- Among patients with severe carotid stenosis with radiation-induced stenosis or restenosis after CEA, CAS is reasonable.

- For patients > 70%, CEA may be associated with improved outcomes compared to CAS. For younger patients, CAS is equivalent to CEA in terms of CX and stroke.
FREE Apps for Smart Phone

- Developed by American College of Cardiology
- Anticoag Evaluator
  - Calculates CHA2DS2-VASc
  - Calculates HAS-BLED
  - Calculates risk reduction with treatment chosen
- BridgeAnticoag
  - Calculates CHA2DS2-VASc & HAS-BLED
  - Determines the need for bridging anticoagulation
- Can send an email report
SUMMARY

• Cerebrovascular disease is a leading cause of disability and death among older patients
• Acute stroke treatments can effectively improve outcomes in patients, especially when care is provided soon after stroke symptoms begin and in a multidisciplinary stroke center
• Primary and secondary stroke prevention can significantly decrease the burden of cerebrovascular disease in older populations
• Remember to evaluate risk for stroke in Atrial Fibrillation with CHA2D2s-VACs validated scoring system
SUMMARY

- Remember to evaluate for risk of bleeding with HAS-BLED in Atrial Fibrillation. This has been validated in NOACs, aspirin, and untreated patients.
- May want to use the SAMe-TT2Re scoring system to help deciding to use VKA or NOAC when OAC is indicated.
- Remember to address the modifiable risk factors in your patients with TIA or ischemic stroke.
## Medications

<table>
<thead>
<tr>
<th>Generic Name</th>
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<tbody>
<tr>
<td>Apixaban</td>
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<tr>
<td>Dabigatran</td>
<td>Pradaxa</td>
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<tr>
<td>Rivaroxaban</td>
<td>Xarelto</td>
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<tr>
<td>rt-PA</td>
<td>Alteplase</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Savaysa</td>
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</table>
Resources


Resources

- Graham D. Stroke, Bleeding, and Mortality Risks in Elderly Medicare Beneficiaries Treated With Dabigatran or Rivaroxaban for Nonvalvular Atrial Fibrillation. *JAMA*. Published online October 3, 2016.