Ischemic stroke: management, prevention and follow up

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Providence Stroke Center
Providence Brain and Spine Institute
Quotes

• **Benjamin Franklin:**
  – “All would live long, but none would be old.”

• **Abraham Lincoln:**
  – “And in the end, it’s not the years in your life that count. It’s the life in your years.”
Ischemic stroke: management and prevention

• Epidemiology
• Acute management
• Prevention and follow up
Epidemiology

• Lifetime risk for incident stroke at 65 years has decreased to
  - 14.5% from 19.5% in men
  - 16.1% from 18% in women
• Number of incident strokes is expected to more than double by 2050
• Majority in aged ≥75 years
• Cost increase - $71.6 billion to $184.1 billion
Prevalence of stroke by age and sex


Heart Disease and Stroke Statistics—2014 Update: A Report From the American Heart Association
Mortality in 1 year after the stroke

Recurrent stroke within 5 years of first stroke
Disabilities after stroke

in more >65 years old

• 50% hemiparesis
• 30% unable to walk without some assistance
• 46% cognitive deficits
• 35% depressive symptoms
• 19% aphasia
• 26% dependent in activities of daily living
• 26% institutionalized in a nursing home
The most FAQs to stroke neurologists

• What is the appropriate anti platelet management when my patient has a stroke or TIA on aspirin?

• What is the appropriate diagnostic work up for a patient admitted with a TIA or stroke?  
  MRI or CT? Carotid ultrasound, CTA or MRA? TTE or TEE?  
  When do I order a hypercoaguuable panel?

• What do I do if echocardiography shows a patent foramen ovale (PFO)?

• How long should I monitor a patient to assess for paroxysmal atrial fibrillation (PAF)?
• If patient has afib and an acute stroke, how soon do I start anticoagulation?

• Are the new anticoagulants superior to warfarin for stroke prevention with afib?

• What is the recommendation for blood pressure management in the hours and days after stroke?
• Carotid stenosis, symptomatic vs asymptomatic, when to treat?
The most frequent sites of arterial and cardiac abnormalities causing ischemic stroke. Ischemic stroke etiologies

- Intracranial Atherosclerosis
- Penetrating Artery Disease
- Carotid Plaque with Arteriogenic Emboli
- Flow Reducing Carotid Stenosis
- Aortic Arch Plaque
- Atrial Fibrillation
- Cardiogenic Emboli
- Valve Disease
- Left Ventricular Thrombi
Stroke Subtypes and Incidence

Ischemic stroke 85%
Cryptogenic 30%
Cardiogenic embolism 20%
Atherosclerotic cerebrovascular disease 20%
Small vessel disease “lacunes” 25%
Cryptogenic 30%
Hemorrhagic stroke 15%
Other 5%

Albers et al. Chest 2004; 126 (3 Suppl): 438S–512S.
Acute stroke management- Intravenous thrombolytic

- IV tpa up to 3 hours (NINDS trial)
- IV tpa up to 4.5 hours (ECASS III trial)
  - Age < 80
  - Not on anti coagulation
  - NIHSS < 25
  - No h/o DM and stroke combined
Intra arterial treatment and mechanical thrombectomy

- IA therapy 6 hours (Class I; level of evidence B)
- Various FDA approved devices; SOLITAIRE FR, MERCI, PENUMBRA, TREVO
- Multiple case series of positive outcome
- Class IIa; level of evidence B
- ‘MR CLEAN’, SWIFT PRIME, ESCAPE and EXTEND –IA, 2014-2105
Case

- 75 yr female came with acute left side of weakness, NIHSS 18
- Stroke team paged 7 pm
- Confusion about time of onset 11 am vs 3 pm
- More detailed history- time of onset 3 pm
- Out of tpa window
Follow up at 1, 4 months

• Full recovery in 4 months
• Patient found to have a fib; started on newer anticoagulation
• Able to drive, no need for PT/OT after 2 months, no cognitive deficits
“It’s an experimental procedure. Every time I sneeze, it unclogs my arteries!”
Atrial Fibrillation and stroke

Prevalence
- 5% of people over age 65
- 10% of people over age 80
- 50% of all patients with a fib are over age 80

Detection with tele monitoring
- PAF detection over average hosp LOS: ~3%
- 48 holter 2-3%
- 30 day monitor 11-16%
- 6 month monitor 22%
- 12 month 25%
- 36 months 30%
75 Y/F with HTN, HPL, right sided weakness and mod left atrial enlargement. Telemetry neg during 2 days hospitalization, no large vessel occlusion or carotid stenosis

- Start anticoagulation
- Aspirin and no further work up
- 48 hour holter monitoring on discharge
- 30 days or longer holter monitoring
When to suspect cardioembolic stroke?

- Peripheral cortical wedge shaped infarct or multi focal infarcts
- Enlarged left atrium on TTE
- No significant stenosis/irregular ulcerated plaques in carotid arteries or in intracranial circulation
What are we worried about?

• Risk of fall
• Risk of ICH
• Other major bleeds
• Which anti coagulation to choose
• When to restart after ICH
• What to do if patient has MCI or dementia
Stroke and bleeding risk stratification with A fib

Table 1: Stroke and bleeding risk stratification with the CHA\textsubscript{2}DS\textsubscript{2}-VASc and HAS-BLED schemas

<table>
<thead>
<tr>
<th>CHA\textsubscript{2}DS\textsubscript{2}-VASc</th>
<th>Score</th>
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<tr>
<td>Congestive heart failure/LV dysfunction</td>
<td>1</td>
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<tr>
<td>Aged ≥75 years</td>
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<td>1</td>
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<tr>
<td>Vascular disease [prior MI, PAD, or aortic plaque]</td>
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<td>Age (e.g. &gt;65)</td>
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<td>Aged 65-74 years</td>
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<td>1</td>
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<tr>
<td>Sex category [i.e. female gender]</td>
<td>1</td>
<td></td>
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<tr>
<td>Maximum score</td>
<td>9</td>
<td></td>
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Case

- 79 year male with new a fib, h/o of HTN, MI (score 3)
- But he was alcoholic with altered renal function and with uncontrolled HTN (HAS-BLED 5)
- Not started on anticoagulation

Table 1: Stroke and bleeding risk stratification with the CHA₂DS₂-VASc and HAS-BLED schemas

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After 6 months, new ischemic stroke
Now risk score is 5
Discussed better control of BP and alcohol abstinence
Goal to bring HAS BLED score from 5 to 3
Started on Warfarin
Bleeding risk with anticoagulation

<table>
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<th>GI bleed</th>
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<tr>
<td>• Debigatran 0.3%/year to</td>
<td>• Debigatran 1.5%/year to</td>
</tr>
<tr>
<td>warfarin 0.74%/year</td>
<td>warfarin 1.02%/year</td>
</tr>
<tr>
<td>• Rivaroxaban 0.5%/year to</td>
<td>• Rivaroxaban 2.8%/year to</td>
</tr>
<tr>
<td>warfarin 0.7%/year</td>
<td>warfarin 2.3%/year</td>
</tr>
<tr>
<td>• Apixaban 0.33%/year to</td>
<td>• Apixaban 0.76%/year to</td>
</tr>
<tr>
<td>warfarin 0.8%/year</td>
<td>warfarin 0.86%/year</td>
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Newer anticoagulation reversal agent

- FDA approved Praxbind under “accelerated approval program” in October, 2015
- In patient requiring emergent surgery who received Praxbind, 89% patients had decrease in blood concentration of Pradaxa within 4 hours
- In 283 healthy volunteers, immediate decrease in Pradaxa concentration that lasted for 24 hours
- Need to see practical effectiveness
When to start anticoagulation after ischemic stroke

- Standard answer within 2 weeks
- Would favor starting earlier if patient has small embolic infarct
- Would favor at 2 weeks if large hemispheric infarct where risk of hemorrhagic transformation is high
- In some cases with large infarct and petechial hemorrhages, CT scan head is advised before starting anticoagulation
Long term cardiac monitoring for suspected cardioembolic stroke

**EMBRACE trial** - 15% AF detection at 30 days

**CRYSTAL AF** - 13% AF detection at 1 year


75 Y/F with HTN, HPL, right sided weakness and mod left atrial enlargement. Telemetry neg during 2 days hospitalization, no large vessel occlusion or carotid stenosis

- Start anticoagulation
- Aspirin and no further work up
- 48 hour cardiac monitoring on discharge
- 30 days or longer cardiac monitoring
Risk of falls and bleeding on anti coagulation

- Not many studies
- Published study in 2012
- Prospective, 515 patients, 308 patients (59%) at high risk of falls
- Follow up for 12 months
- 35 patients with first major bleed
- No difference between high risk and law risk group

What AAN says

- Clinicians might offer anticoagulation in patients with mild dementia and occasional falls. Risk benefit ratio is uncertain in patients with frequent falls and mod to severe dementia.


Amyloid angiopathy and microbleeds

- Anticoagulation contraindicated
- Increase the chances of microbleeds and large lobar hemorrhage
- Anti platelets would be a safer option particularly with h/o of ischemic stroke, CAD and stent placement
- In case of recurrent microbleeds, even anti platelets are not a safe alternative
- Role of procedure/device?
Cardiac procedure/devices for patients with contraindication to anticoagulation

- Future promise -
  - Left atrial appendage closure devices
    - WATCHMAN device
    - LARIAT closure procedure
- Not FDA approved yet
- Investigational use and research trial use only
Anticoagulation after ICH

- Individualized to each patient
- High risk of recurrent ICH (lobar ICH or probable amyloid angiopathy) antiplatelets may be considered
- Risk of ICH - 9.3% in patients with microbleeds compared with 1.3% without microbleeds
- Optimal timing to restart uncertain
- Wait time to start 4 weeks or longer
Case

• 82 years with h/o of HTN, a fib, lupus anticoagulant disorder, h/o of bladder and prostate cancer
• Large rt cerebellar hemorrhage. He received FEIBA And FFP to reverse his INR.
• Managed with osmolar therapy for raised ICP. Fortunately, he did not require surgery for large ICH.
• Partial code/no intubation/no CPR/no life saving surgery
• F/up at 6 months- imbalance, mild cognitive dysfunction, on aspirin
Antiplatelet agents after ischemic stroke/TIA

65 Y/M with uncontrolled HTN, HPL and DM who is on ASA on 81 mg and with new mild rt sided symptoms

- Increase ASA to 325 mg daily
- Change to Clopidogrel
- Change to Aggrenox
- Keep ASA 81 mg, add high intensity statin, intensive control of DM, HTN, diet and lifestyle modifications
Antiplatelet agents after ischemic stroke/TIA

- Aspirin, Clopidogrel, Aspirin- Dypiridamole combination, Ticlopidine (rarely used)
- Aspirin or Aggrenox should be initiated for secondary stroke prevention
- Clopidogrel is a reasonable alternative
- No clear data to show effectiveness of increasing dose of aspirin after having stroke on low dose aspirin
Antiplatelet agents after ischemic stroke/TIA

• Combination of Aspirin and Clopidogrel might be considered for 21 days after minor ischemic stroke
• Our practice is to look for optimal control of stroke risk factors (HTN, HPL, DM, sleep apnea, obesity, physical activity etc.) before making decision on changing anti platelet agent
• No difference between Clopidogrel and combination of Aspirin-Dypiridamole (CHARISMA trial)
Antiplatelet agents after ischemic stroke/TIA

- **CHANCE trial**- Combination of Aspirin and Clopidogrel for 21 days initiated within 24 hours may be more effective in secondary stroke prevention

- **SPS 3 and MATCH trial**- Combination of aspirin and Clopidogrel for longer duration like 2-3 years initiated within 6 months of lacunar stroke increases the risk of ICH and GI bleed without any significant additional benefit

- **POINT trial (On going)**- Aspirin vs aspirin plus Plavix for 90 days in patients with high risk TIA or minor ischemic stroke
Dual antiplatelet agents after ischemic stroke/TIA

- SAMMPRIS trial - For symptomatic intracranial stenosis (>70%), combination of Aspirin plus Clopidogrel for 90 days along with aggressive risk factors modification is more effective and less harmful than stenting

- Caveat - there was no single anti platelet agent arm in that trial
Antiplatelet agents after ischemic stroke/TIA

65 Y/M with uncontrolled HTN, HPL and DM who is on ASA on 81 mg and with new mild rt sided symptoms
  • Increase ASA to 325 mg daily
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Prevention of stroke in carotid stenosis

• Symptomatic and asymptomatic
• Stroke/TIA within last 6 months, carotid stenosis is defined as symptomatic

• Optimum medical management
• CEA
• CAS
Prevention of stroke in carotid stenosis

- 74 year old male with CAD, HTN and HPL with sudden dizziness, near syncope episode. Work up showed 50-69% narrowing of rt carotid artery, CTA shows 65-70% stenosis with calcified regular plaque. Patient is on Plavix, 20 mg of simvastatin and partially controlled blood pressure.

- CAS
- CEA
- Continue same management
- Change to high intensity statin, better control of HTN, exercise, diet and follow up carotid duplex
Management of symptomatic carotid stenosis

- CEA for ipsilateral severe (70%–99%) carotid artery stenosis if the perioperative morbidity and mortality risk is estimated to be <6%
- Proven in multiple trials, NASCET, ECST and VACS
- Standard of care

Management of symptomatic carotid stenosis

- For 50-69% stenosis, CEA is recommended depending on patient-specific factors, such as age, sex, and co morbidities
- For > 70% stenosis, CAS is a reasonable alternative to CEA
- EC-IC bypass is not recommended
- Should be done within 2 weeks of TIA/stroke
Management of symptomatic carotid stenosis

Favoring CEA (usually first line)
• > 70 years
• ? Medical co morbidities

Favoring CAS
• Radiation induced stenosis
• Non favorable anatomy like high cervical bifurcation
• Contra lateral carotid occlusion
Management of asymptomatic carotid stenosis

- 3% per year stroke risk with 80-99% (previous trials)
- 5% per year with 90-99% (previous trials)
- Recent data shows stroke risk of 0.5% to 1% per year when carotid stenosis > 50%.
- A recent meta analysis showed decrease stroke rates 2.83% before 2000 to 1.13% per year after 2000.

Management of asymptomatic carotid stenosis: Pearls

- Benefit of CEA in women is not clear
- Benefit in men > 75 years is not clear
- Medical management is a first line of management in mod degree stenosis
- Carotid revascularization may be indicated in selected group of high risk/high degree stenosis
- CREST-2 trial will have medical therapy arm along with stenting and CEA
Management of asymptomatic carotid stenosis: Pearls

- Ill-defined dizziness
- Generalized weakness
- Syncope or near-syncope
- “Blurry vision,” or transient positive visual phenomena
- Life expectancy of less than 5 years are unlikely to benefit from the modest risk reduction afforded by surgery
Management of asymptomatic carotid stenosis: Pearls

High risk group among asymptomatic patients

• Embolic signals on TCD
• Stenosis progression rate
• Plaque morphology
• Serum biomarker
• Cerebrovascular reserve

Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial (CREST-2)

• Intensive medical management vs carotid revascularization in asymptomatic patient with >70% carotid stenosis
• Medical management vs stenting
• Medical management vs CEA
Prevention of stroke in carotid stenosis

- 74 year old male with CAD, HTN and HPL with sudden dizziness, near syncope episode. Work up showed 50-69% narrowing of rt carotid artery, CTA shows 65-70% stenosis with calcified regular plaque. Patient is on Plavix, 20 mg of simvastatin and partially controlled blood pressure.

- CAS
- CEA
- Continue same management
- Change to high intensity statin, better control of HTN, exercise, diet and follow up carotid duplex
PFO and stroke

RESPECT trial

• In the primary intention-to-treat analysis, there was no significant benefit associated with closure of a patent foramen ovale in adults who had had a cryptogenic ischemic stroke.

• However, closure was superior to medical therapy alone in the prespecified per-protocol and as-treated analyses, with a low rate of associated risks.
PFO and stroke

CLOSURE trial

• In patients with cryptogenic stroke or TIA who had a patent foramen ovale, closure with a device did not offer a greater benefit than medical therapy alone for the prevention of recurrent stroke or TIA.
PFO and stroke

- In patient with cryptogenic stroke and PFO, closure of PFO is not recommended routinely.
- In the presence of PFO and venous source of embolism, anticoagulation is indicated.
- If anticoagulation is not possible then IVC filter should be considered.
- In patient with PFO and recurrent venous thrombosis, PFO closure can be considered depending on the risk of recurrence.
Statin therapy and risk of ICH

- Conflicting reports about statin use and risk of ICH
- SPARCL trial reported an increased risk of ICH among patients with high dose of atorvastatin and with h/o ICH
- Might have resulted from high crossover rates in the SPARCL trial itself
- Likely that many clinicians have been wary of prescribing statins to patients with ICH
Statin therapy and risk of ICH

• A meta analysis of 31 RCT
• More than 91000 patients in statin and non statin arm
• No increased risk of ICH in statin arm
• Decrease in stroke rate and all cause mortality rate in statin arm
Effect of Statin Use During Hospitalization for Intracerebral Hemorrhage on Mortality and Discharge Disposition

RESULTS Among patients hospitalized for ICH, inpatient statin users were more likely than nonusers to be alive 30 days after ICH (odds ratio [OR], 4.25 [95% CI, 3.46-5.23]; P < .001) and were more likely than nonusers to be discharged to their home or an acute rehabilitation facility (OR, 2.57 [95% CI, 2.16-3.06]; P < .001). Patients whose statin therapy was discontinued were less likely than statin users to survive to 30 days (OR, 0.16 [95% CI, 0.12-0.21]; P < .001) and were less likely than statin users to be discharged to their home or an acute rehabilitation facility (OR, 0.26 [95% CI, 0.20-0.35]; P < .001). Instrumental variable

JAMA Neurol. doi:10.1001/jamaneurol.2014.2124
Published online September 22, 2014.
Statin therapy and risk of ICH

Risk Factors, Stroke Prevention Treatments, and Prevalence of Cerebral Microbleeds in the Framingham Heart Study
José Rafael Romero, Sarah R. Preis, Alexa Beiser, Charles DeCarli, Anand Viswanathan, Sergi Martinez-Ramirez, Carlos S. Kase, Philip A. Wolf and Sudha Seshadri

*Stroke.* 2014;45:1492-1494; originally published online April 8, 2014;

**Conclusions**—We observed the expected association of hypertension with deep CMB and low cholesterol and APOE ε4 with lobar CMB. In addition, statin use was independently associated with CMB risk. This potential adverse effect of statin use needs to be examined in other cohorts. (*Stroke.* 2014;45:1492-1494.)

Statin Use and Microbleeds in Patients With Spontaneous Intracerebral Hemorrhage
Diogo C. Haussen, Nils Henninger, Sandeep Kumar and Magdy Selim

*Stroke.* 2012;43:2677-2681; originally published online July 24, 2012;

**Results**—Sixty-four percent had lobar ICH. Overall, 53% had microbleeds and 39% had csMB. Statin users were older, had significantly lower cholesterol and low-density lipoprotein levels, and higher prevalence of hypertension, diabetes, dyslipidemia, and antiplatelet use. The prevalence and number of other MB were similar in statin-treated and statin-untreated individuals. However, more statin-treated patients had csMB (57% vs 33%; *P* = 0.007), with almost twice as many lesions (4.6±11.3 vs 2.4±8.0; *P* = 0.007) compared with untreated patients. Age and statin use were independently associated with both the presence and increased number of MB (odds ratio [OR], 1.03; 95% confidence interval [CI], 1.00–1.05; *P* = 0.01 and OR, 2.72; 95% CI, 1.02–7.22; *P* = 0.04, respectively) and csMB (OR, 1.03; 95% CI, 1.00–1.06; *P* = 0.01 and OR, 4.15; 95% CI, 1.54–11.20; *P* < 0.01) in multivariate analyses.

**Conclusions**—Statin use in patients with ICH is independently associated with MB, especially csMB. Future studies are needed to confirm these findings and to investigate whether csMB are associated with increased risk of ICH.
Statin therapy and risk of ICH

Use caution…
- In patients with unexplained lobar bleeds
- When high degree suspicion of amyloid angiopathy
- MRI shows cortical micro bleeds

Statin is ok if…
- No micro bleeds on MRI s/o of probable amyloid angiopathy
- ICH is secondary to hypertensive bleed
- High risk of recurrent infarcts and small vessel disease
Arterial dissection and stroke prevention

- Antiplatelet or anticoagulation
- CADISS trial, published in Lancet Neurology
- 250 patients, carotid and VA dissection
- 126 received antiplatelet, 124 anticoagulation
- 4 patients with stroke or death over follow up - 2%
- No difference between 2 group

- Antiplatelet is being used more
- Anticoagulation when burden of overlying thrombus and risk of thromboembolism is high (subjective - no clear criteria to define)
- Anticoagulation when vessel diameter is compromised significantly with long segment dissections
Post stroke depression

• Prevalence after stroke 29 percent (95% CI 25-32 percent).*
• Major predictors of depression
  - disability
  - depression pre-stroke
  - cognitive impairment
  - stroke severity
  - anxiety.
• In a study with mean age of 74, at 1 year post stroke
  - 51% impairment of ADL
  - 33% clinically significant levels of depression.**
• Depression screening is important in post stroke clinic follow up.

*Natural history, predictors and outcomes of depression after stroke: systematic review and meta-analysis: Br J Psychiatry. 2013 Jan;202:14-21
**Predictors of depression at one year post-stroke in older adults: Brain Impairment. 2013; 14: 381-391
Other things to control for secondary stroke prevention

• Blood pressure goal: Usually less than 140/90; lacunar- Less than 130/85; Will SPRINT trial result change these goals?
• Good glycemic control with goal of HBA1C less than 7
• Screen for sleep apnea
• Screen for metabolic syndrome
• Diet and exercise
Primary prevention of stroke (AHA/ASA Oct 28, 2014, published guideline)

- BP goal less than 140/90
- Home monitoring of blood pressure
- Migraine with aura- avoid estrogen containing contraception, smoking cessation
- NOAC reasonable option with high risk AF
- ASCVD risk calculator reasonable to use but with limitations
- Mediterranean diet with nuts, DASH style diet
Complex cases which require follow up

- Cryptogenic stroke
- Recurrent strokes
- Stroke due to hypercoagulopathy
- Arterial dissection
- A fib and high risk of bleed
- Venous sinus thrombosis
- Stroke in young
- Complex carotid stenosis
...And it's as simple as that!
Thank you

Providence Stroke Center
West Campus (PSVMC), East Campus (PPMC)