Secondary Stroke Prevention

IM RESIDENT LECTURE 12/8/15

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Stroke Mechanism

- Large Artery (carotids, verts, medium sized vessels intracranially)
  - Atherosclerosis/stenosis
  - Other: Dissection, FMD, Vasculopathies
  - Risks are high with intracranial disease and procedures
- Small Vessel Disease
  - Refers to perforators, not everything is a lacune
  - Leukoariosis, lacunes, V-R Spaces, microhemorrhages
- Cardioembolic
  - AFIB/Flutter, recent ant MI, cardiomyopathy, PFO

Lifestyle and General Health

- Obesity is correlated with 1˚ stroke, but **not** clearly with 2˚ stroke
- Obesity **IS** associated CAD, mortality
  - Inflammation, DM, insulin resistance, dyslipidemia, HTN
- Interventions: behavioral, bariatic, drugs
  - Consider comprehensive physician driven programs
- Stroke Guidelines : Screen BMI, but weight loss effect uncertain
  3-4/week 40 minutes of vigorous exercise
  Perhaps BMI > 20, < 25

Lifestyle and General Health

- Mediterranean Diet
  - Mmmm
- OSA strong correlation
  - Consider screening
- Depression
  - Screen and treat
- Vitamins C, E, B12, Folate

Food	Meta-Analysis: First Author, Year, Reference	+ (Inverse Association With Stroke Risk)/ – (Association With Stroke Risk)
Fruits and vegetables	Hu et al, 2014[16]	+
Fish	Chowdhury et al, 2012[17]	+
	Xun et al, 2012[18]	+
	Larsson et al, 2011[19]	+
Olive oil	Martinez-Gonzalez et al, 2014[20]	+
Tree nuts and peanuts	Afshin et al, 2014[21]	Not statistically significant
Legumes	Afshin et al, 2014[21]	Not statistically significant
Red and processed meat	Kaluza et al, 2012[22]	–
White meat	Bernstein et al, 2012[23*]	+
Alcohol	Zhang et al, 2014[24]	–
Dairy	Soedamah-Muthu et al, 2011[25†]	Not statistically significant
	Hu et al, 2014[26‡]	+

Hypertension

- 78 million Americans, ~75% of Stroke patients
- 80% attributable risk for stroke

- When should we start meds post stroke and what level is acceptable acutely?
  - Guidelines suggest holding home BP meds for 24 post stroke, treat within days or before discharge
  - Rare patient can be harmed by quick correction
    - Usually Stenosis and large are occlusion patients
    - Guidelines allow **permissive HTN < 220/120 mmHg**

Hypertension

- **PATS** 1995 5000 pt with AIS or ICH over 2 years
  - Indapamide vs placebo **13%ARR** in recurrent stroke, mean ↓6 mmHg
- **PROGRESS** 2001 6000 pt AIS or ICH over 5 years
  - ACE-I vs ACE-I + diuretic **4% ARR** in recurrent stroke, ↓3 mmHg
- Conclusion: treating BP prevents recurrent stroke

Hypertension – How low?

- ACCORD 2010 DM with CVD patients
  - <120 vs <140
  - Primary outcome not significant
  - Stroke and Non-fatal stroke significant but very weak effect
- SPS3 2012 Small vessel stroke patients
  - <130 vs <150
  - No difference in ischemic stroke
  - Less ICH but small effect

Hypertension

- Overall: ↓5/2.5 mmHg ARR 1.3% over 3 years
  - 10/5 mmHg yields 66% percent RRR
- Guidelines: Treat to < 140/90 mmHg or patients >140/90
  - <130 mmHg SBP Goal reasonable in lacunar strokes
- Meta-analysis shows All BP Classes reduce risk
- Practical advice:
  - ACE-I and CCB for tolerability, less variability, cost
- SPRINT does not apply to stroke patients

Antiplatelet Therapy

- Overall vascular events are reduced by about 2-3% (20% RRR)
  - At the expense of 0.15% bleeding risk

  - Aspirin COX-1 irreversible inhibitor, effect within an hour
  - Clopidogrel (Plavix) thienopyridine ADP receptor inhibitor
    - Prodrug influenced by CYP activity, effect within 5 days
  - Aggrenox (Dipyridamole/ASA) PDE Inhibitor ↓cAMP

Antiplatelet Therapy

- ASA
  - CAST, IST trials
- PLAVIX
  - CAPRIE, PROFESS
- Aggrenox
  - ESPS, ESPS2, ESPIRIT

- Take Away: Stroke Patients should be on anti-platlet therapy
  - Choice of Drug can depend on patient

Aspirin Dose

- Acute dose is at least 325 mg daily – but 300 mg PR acceptable
- Long term secondary prevention dose is 50 mg- 325mg daily
- ASA 81 mg daily seems to have the best effect:tolerability ratio
- 325mg daily can be considered in AFIB, cardiomyopathy

Effect Testing and Switching

- No role at this time looking for resistance/function assays
  - Methods inconsistent and controversial
- How do you even know aspirin failed?
- No compelling evidence supports agent switching after clinical aspirin failure

Dual Antiplatelet Therapy

- Long term DAPT is no better than monotherapy and has higher bleeding risk
  - MATCH and CHARISMA trials
- Acute Intracranial Stenosis: ASA 325 mg + Plavix 75 mg daily x 3 months
  - SAMMPRIS Trial – Included high intensity statin
- Minor Stroke or TIA
  - CHANCE Trial ASA ~81mg + Plavix 75 x 21 days then Plavix alone ARR 3% at 90 days
  - POINT Trial Pending
- Weak argument in some AFIB cases, Dissection, and cervical large artery disease

Anticoagulation

- AFIB, Some Cardiomyopathy (EF <35%), Dissection (3-6 months)
- Mechanical Heart valves
- Bioprosthetic Heart valves with antiplatelet failure
- Not PFO unless DVT/PE Present

- Acutely using anticoagulation not proven helpful but used in selected cases (dissection, intra-lumenal thrombus, heart thrombus)
  - Stroke volume, BG, BP all dictate risk

Carotid Symptomatic Stensosis

- Symptomatic and > 70% Severe (CEA vs CAS) ARR 16%
  - 2 year life expectancy and <6% morbidity/mortality
- Symptomatic and 50-69% Moderate (CEA vs CAS) ARR 8%
  - Only in select cases

- Asymptomatic
  - No clear correlation with stenosis
  - Modern Trials are including medical management arms
  - Recurrent risk < prior acceptable morbidity/mortality <3%

Dyslipidemia

- High Intensity Statin therapy for ANY athero related stroke regardless of LDL without a target or otherwise per AHA/ACC guideline
- SPARKLE ~2% ARR at 5 years with atorvastatin 80 mg – excluded cardioembolic
- Statins increase A1c
- Don't use some ICH patients