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Secondary Stroke Prevention: A global issue that needs a global solution

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Disclosure

I have no actual or potential conflicts of interest in relation to this presentation.

I have no relevant relationships with any commercial interests.

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Just Imagine

• You are a 40 year old male with no significant medical history that you know of but you don’t really go see physicians because you’re your own doctor

• You were playing outside with your 10 year old and suddenly fell and couldn’t move your right side
In the Emergency Room

• You arrived to the ED via EMS
• Your blood pressure was found to be 205/96
• Your blood sugar was 275
• The doctors rushed you to the cat scan and thankfully there was no evidence of blood on your brain
• You can now move your right side off the bed and you start thinking that you are “out of the woods”
• The ED gave a little hydralazine to get the blood pressure down.

• About 2 hours later you now cannot move your right side at all
Introduction

- Over 900,000 Strokes per year in the US
  - every 40 seconds in the US
  - 87% are ischemic
- About 250,000 second strokes per year in the US
- One of the leading causes of death
  - 4\textsuperscript{th} (down from 3\textsuperscript{rd} until 2 years ago) in the US
    - 1994-2004, 7% decrease in mortality
  - 3\textsuperscript{rd} in Western Europe
  - 2\textsuperscript{nd} worldwide (WHO)
- 4.5 million stroke survivors
  - Leading cause of adult disability in the USA and WE
  - Recurrent stroke markedly increases disability
Burden of Stroke

• In 2015 the total cost in the US was approximately $66.3 billion

• Projected to increase to $143 billion by 2035

• Burden of stroke is on both the stroke survivor and the family/caregiver

OBJECTIVES

• Review up to date secondary stroke prevention guidelines based on stroke etiology

• Discuss barriers preventing appropriate risk factor management amongst different ethnic groups

• Introduce interventions that may increase better risk factor control
Carotid Stenosis
CREST: Carotid Revascularization Endarterectomy Versus Stenting Trial

- Randomized
- >50% symptomatic stenosis
- >50% asymptomatic stenosis
Bottom line

• Based on CREST: Overall safety and efficacy largely the same for CAS and CEA
  • no difference for MAJOR strokes

• Younger (< 69) patients did better with stent
• Older (> 70) patients did better with surgery
• MI greater concern with CEA
• Stroke greater concern with CAS
• No significant sex differences
Cardiogenic Emboli

• Responsible for ≈20% of ischemic strokes
• Common sources of emboli
  – Non-valvular atrial fibrillation (~50%)
  – Valvular heart disease (~25%)
  – Left ventricular mural thrombus

• Congestive Heart Failure increases stroke risk by 2 or 3 fold
Atrial Fibrillation

• AF affects > 2.7 million Americans
• It becomes more prevalent with age
• Stroke is the principal adverse consequence
• In the US, AF is responsible for >70,000 stroke each year (10%-12% of all ischemic strokes)
Warfarin therapy

• Multiple clinical trial established warfarin as the preferred choice for primary stroke prevention in patients with AF
• RR rate of 68%
• 32 ischemic stroke will be prevented each year for every 1000 patients treated
New oral anticoagulants

• **RE-LY (2009)**: direct thrombin inhibitor **dabigatran** 110mg and 150mg twice daily vs. adjusted-dose warfarin (open-label) in 18,113 patients.

• **AVERROES (2011)**: factor Xa inhibitor **apixaban** 5mg twice daily vs. aspirin (double-blind) in 5,599 patients.

• **ROCKET AF (2011)**: factor Xa inhibitor **rivaroxaban** 20mg daily vs. adjusted-dose warfarin (double-blind) in 14,264 patients.

• **ARISTOTLE (2011)**: factor Xa inhibitor **apixaban** 5mg twice daily vs. adjusted-dose warfarin (double-blind) in 18,201 patients.
Detection of occult AF

• 10% of patients with acute ischemic stroke or TIA have new AF during hospital admission

• In additional 10-15%, AF is detected within 30 days with MCOT

• Pacemaker interrogation identified 28% incidence of occult AF

• Implantable cardiac rhythm devices identify 10-28% occult AF
ASA/AHA Guidelines

- For patients with no other cause of stroke, prolonged cardiac monitoring (about 30 days) is reasonable within 6 months of the event (new recommendation)

- VKA therapy (Class I; Level of Evidence A), apixaban (Class I; Level of Evidence A), and dabigatran (Class I; Level of Evidence B) are all indicated for the prevention of recurrent stroke in patients with nonvalvular AF

- Rivaroxaban is reasonable for the prevention of recurrent stroke in patients with nonvalvular AF (Class IIa; Level of Evidence B). (New recommendation)

- Target INR of 2.5 is recommended (range, 2.0–3.0) (Class I; Level of Evidence A).
Small Vessel Disease

• Most common cause of small vessel (lacunar) strokes in Hypertension

• Other causes
  • Hypercholesterolemia
  • Diabetes
  • Smoking
HYPERTENSION

• Several patients have undiagnosed hypertension (about 70 million Americans have HTN)
• Treatment of HTN is the most important intervention for secondary prevention of ischemic stroke
• Blood pressure management is associated with a risk reduction of 30-40%
AHA/ASA GUIDELINES

1. Initiation of BP therapy is indicated for previously untreated patients with ischemic stroke or TIA who, after the first several days, if BP $\geq 140$ mm Hg systolic or $\geq 90$ mm Hg diastolic
   (Class I; Level of Evidence B).

2. Resumption of BP therapy is indicated for previously treated patients with known hypertension for both prevention of recurrent stroke and prevention of other vascular events in those who have had an ischemic stroke or TIA and are beyond the first several days
   (Class I; Level of Evidence A). (Revised recommendation)

3. Goals for target BP level or reduction from pretreatment baseline are uncertain and should be individualized, but it is reasonable to achieve a systolic pressure $<140$ mm Hg and a diastolic pressure $<90$ mm Hg
   (Class IIa; Level of Evidence B).

4. For patients with a recent lacunar stroke, it might be reasonable to target an SBP of $<130$ mm Hg
   (Class IIb; Level of Evidence B). (Revised recommendation)
Hypertension (cont’d)

• Life Style Modification:
  • Diet
    • Fruits
    • Vegetables
    • Nuts
    • Low-fat dairy
  • Exercise
  • Limited alcohol consumption
Dyslipidemia

- Modification of LDL is an important component of secondary stroke prevention.
- Low LDL levels are associated with increased risk of ICH.
- In multiple clinical trials, statins were efficacious in reducing risk of first stroke without significant ICH risk.
- SPARCL was the only statin trial focusing on secondary stroke prevention.
Effects of High-dose Atorvastatin After Stroke or TIA

HR, 0.77 (95% CI, 0.67–0.88); P<0.001

SPARCL = Stroke Prevention by Aggressive Reduction in Cholesterol Levels.

Impact of Statin therapy

It has been shown that pre- and post-stroke treatment with statins have a 24% reduction in mortality

High intensity treatment (atorvastatin 40mg or 80mg) – in high risk patient

Low intensity treatment (atorvastatin 10mg) – in low risk patients

DIABETES/PRE-DIABETES

• Burden of diabetes is increasing both in developed and developing countries

• Prevalence in the US
  • 3.7% age 20-44
  • 27% >65

• Higher in Hispanics and Blacks

• Diabetes – defined as HgA1c >6.5% or 2hr GTT sugar >200

• Pre-diabetes
  • Impaired fasting glucose (100-125)
  • Impaired glucose tolerance (2hr GTT with sugar >140-199)
  • Fluctuating Glycated HgA1c between 5.7% and 6.4%
Diabetes

• Diabetes and Hypertension –
  – American Diabetes Association recommends using an ACE-I or ARB\(^1\)

• Diabetes and Hyperlipidemia –
  – LDL-cholesterol should be less than 70\(^2\)
    – Heart Protection Study showed that diabetics with total cholesterol >135 that were treated with simvastatin had a 28% reduction of ischemic stroke compared to 4.7% in placebo

• Goal HgA1c <7%\(^3\)

Obstructive Sleep Apnea

- Present in about 50-75% of patients with stroke or TIA
- About 70-80% of the patients with sleep apnea are neither diagnosed or treated
- American Academy of Sleep Medicine Adult OSA Task force recommends that stroke or TIA patients with symptoms undergo sleep study
- Multiple RCTs have been done with mixed results but trends towards treatment with CPAP showing improvement in outcomes in stroke patients
- The newer recommendations is that stroke and TIA patients undergo sleep study
  And treatment with CPAP might be considered in this population
Secondary Prevention
Antiplatelet Agents

The BIG debate for years was
Aspirin vs Plavix vs Dipyridamole

However recent studies show benefit of dual antiplatelet therapy
Both studies looked at treatment with Aspirin and Clopidogrel vs Aspirin alone

Included were patients with minor strokes (NIHSS \( \leq 3 \) or TIA with ABCD^2 score \( \geq 4 \))

Conclusion - benefit of DAPT for 21 days.

Recommendation – load patient with 300mg clopidogrel and then 75mg daily with aspirin 81mg daily for 21 days then aspirin alone

Pooled analysis of the studies showed a higher rate of hemorrhage after 90 days with DAPT and net clinical benefit occurred within the first 21 days

Pan, Y et al. Outcomes associated with clopidogrel-aspirin use in Minor Stroke or TIA, a pooled analysis. Jama Neurology August 19, 2019
Back to our initial case

• That patient was started on an ACE-inhibitor while in the hospital but decided they didn’t need it at home because they were going to “watch their diet”

• They were also found to have a HgA1c of 7.4% but thought that had to be a mistake and was only elevated due to the acute stress of having a stroke
Challenges in Secondary Stroke Prevention

• Factors that have played a role in health disparities for stroke prevention

  • Race and Ethnicity
  • Socioeconomic status
  • Level of Education
  • Access to Health Care
Blood Pressure Control

• Only about 40-50% of patients have good blood pressure control

• Some suggested factors that may play a role in good blood pressure control are the following:
  • Biological, social and cultural differences
  • Differences in health care provider and health care systems
  • Types of medications given
  • Insufficient attention by health care providers
  • Adherence to medications
  • Lack of resources to make recommended lifestyle changes
Other factors

• Age – elderly were less likely to get Anticoagulation for Afib and stroke prevention

• Swedish study showed that antihypertensive meds for stroke prevention and outpatient follow-up was less in university based centers

• Australian study showed that increased incidences of CVD events in less educated population

1. Diagnostic Procedures, Treatments, and Outcomes in Stroke Patients Admitted to Different Types of Hospitals
2. Socioeconomic Inequalities in the Prescription of Oral Anticoagulants in Stroke Patients With Atrial Fibrillation
3. Socioeconomic variation in incidence of primary and secondary major cardiovascular disease events: an Australian population-based prospective cohort study
How to Improve Secondary Stroke Prevention: Old fashion education?

• Inner-city New York study
  – Blacks and latinos from low income families
  – Attended peer-led (stroke survivors), community-based, stroke prevention self-management group workshop
  – Found better control of blood pressure but not other risk factors in this group compared to control group
  – Control group was a group of individuals who were handed pamphlets about stroke prevention and had to do it on their own
Can Smart Phones Help?

• Several Apps are available to help patients monitor blood pressure, physical activity, weight changes etc.

• We should use technology if we can
Functional and Integrative Medicine

• New branch of medicine

• Use of Primary care physician, dietician, psychiatrist (psychologist), chiropractors, acupuncture, supplementary medicine

• Some of the neurological diseases this has been used for are Parkinson patients, ALS, Fibromyalgia, Chronic pain (headache) and are now considering patients with recurrent strokes who are having a hard time getting risk factors under control
CONCLUSION

• Secondary Prevention should focus on the primary etiology of ischemic stroke

• Large Vessel Atherosclerosis: CEA or Stenting and antiplatelet + risk reduction

• Cardioembolic: A-fib - Warfarin, NOAC

• Small Vessel Disease: Antiplatelet agent + Control of HTN, DM, and ↑ Lipids (DAPT for 21 days)

• Cryptogenic stroke ( ~30%) – may use long-term event monitoring if suspect paroxysmal a-fib + antiplatelet agent
Ischemic Stroke Prevention

It Takes A Team To Prevent Further Ischemic Strokes:

• Neurology
• Neurosurgery
• Neuro-Interventional Radiologists
• Cardiologists
• Primary Care Physician
Conclusion

• Newer techniques are being tested to help with getting better control of risk factors for stroke

• Life style changes and alternative medicine may make a significant difference in reducing the 25% of secondary strokes
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THANK YOU