LIFE AFTER STROKE: Discharge and Beyond

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TODAY’S SPEAKER HAS NO DISCLOSURE TO MAKE

### Epidemiology of Stroke in the United States

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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<tbody>
<tr>
<td>Prevalence</td>
<td>4.8 million ischemic stroke cases</td>
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<tr>
<td>Incidence</td>
<td>700,000 new or recurrent strokes each year</td>
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<tr>
<td>Morbidity/Mortality</td>
<td>Third leading cause of death&lt;br&gt;1 of every 15 deaths&lt;br&gt;(~273,000 deaths/yr*)&lt;br&gt;Every 3 minutes someone dies of a stroke&lt;br&gt;Stroke is a leading cause of long-term disability</td>
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Stroke Adjusted Death Rate - 1993

Stroke mortality rates by county, Mississippi, 1999-2001
Stroke Risk Factors for Jackson, MS

Acute Focal Neurological deficit

- Migraine
- Seizure
- Multiple sclerosis
- Hypoglycemia
- Radiculopathy

Stroke

- Acute Ischemic Stroke (82-85%)
- ICH
- IVH
- SAH (3-5%)

- Large vessel disease (35%)
- Small vessel disease (25%)
- Cardiogenic (15-20%)
- Hypertension, diabetes (5-10%)
- Cryptogenic (15%)

Hemorrhagic Stroke

- CVT
- AVM (1%)

- Hypercoag. states (5%)

Stroke Risk Factors

Primary Stroke Prevention

Nonmodifiable
- Age, Gender, Race, Heredity

Modifiable

Medical Conditions
- Hypertension
- Cardiac disease
- Atrial fibrillation
- Hyperlipidemia
- Diabetes mellitus
- Carotid stenosis
- Prior TIA or stroke

Behaviors
- Cigarette smoking
- Heavy alcohol use
- Physical inactivity
Non Modifiable Risk Factors

Age
- The risk of stroke doubles for each successive decade after age 55.

Sex
- More prevalent in men than women
- Female survivorship rates greater than male over age 85

Non Modifiable Risk Factors

- Low Birth Weight
  - Implications and causality being studied

- Race-Ethnicity
  - Higher general stroke rates in African Americans and some Hispanic American groups.
  - Possible reasons are higher prevalence of HTN, obesity and diabetes

- Genetic Factors
  - 5 fold increase in stroke prevalence among monozygotic
  - Gene therapy may move some of these factors into the modifiable category in the future.

CASE
Scenario #1

A 69 yr old gentleman brought to the ER with sub-acute onset of right sided weakness and slurred speech.

PMHx:
- Hypertension
- CABG x 2
- Diabetes
- Dyslipidemia

Examination:
- Awake
- Follows commands
- Right hemiparesis
- Dysarthria

Scenario #1

Rx:
- Aspirin 81mg
- Zocor
- Glipizide
- Hctz

Scenario #1

MRI brain shows a periventricular infarct in the left parietal region

MRA brain shows attenuation of signal on the cavernous portion of the right MCA

Carotid ultrasound: Bilateral high degree stenosis

Trans-thoracic Echocardiogram is normal
SCENARIO # 1

- Pt under goes cerebral angiogram
- Left ICA 72% stenosis 1 cm distal to bifurcation
- Right ICA 78% stenosis distal to CCA bifurcation
SCENARIO # 1

78% stenosis

Thrombus
SCENARIO # 1

What to do next?

- CEA vs. Stent placement? Side?
- Medical management?
- Choice of anti-platelets
- Choice of Statin therapy and goal?
- Blood pressure goals

Symptomatic Carotid Stenosis

- 85,000 strokes per year
- 20% of all ischemic stroke
- 26% risk of stroke in 2 years
- CEA reduces risk 4%/year
- Carotid Angioplasty

85,000 strokes per year
20% of all ischemic stroke
26% risk of stroke in 2 years
CEA reduces risk 4%/year
Carotid Angioplasty
Asymptomatic Carotid Stenosis

- There has been much debate about the cutoffs for surgical treatment of this condition.
- Patients with asymptomatic carotid stenosis should be screened for other treatable stroke causes.
- Patients should be intensively treated for all stroke risk factors including aggressive lipid lowering.
- The use of aspirin is recommended.
General Guidelines for Asymptomatic Carotid Stenosis

- Endarterectomy may be considered in selected patients with >60% and <100% carotid stenosis, when performed by a surgeon with morbidity/mortality rates <3%.
- Careful patient selection should be guided by co morbid conditions, life expectancy and patient preference.

GOALS: SCENARIO # 1

- Patient underwent Left CEA with plans for Right CEA in 4-6 weeks
- ASA was changed to Clopidogrel 75mg QD
- Lipitor 80mg to keep LDL < 70mg/dL
- Lisinopril to keep SBP <130mmHg
- Strict glycemic control
- Exercise 3x/wk and 1 alcoholic beverage

STROKE
5 year ARR of 2.2%
RRR 18%
Hypertension

- Meta-analysis has found that beta-blocker therapy and diuretics therapy can be effective in preventing stroke.
- Also, there are increasing data on ACE inhibitors and ARBs.
- Antihypertensive therapy is associated with a 35% to 44% reduction in stroke.
- Newer recommendations from JNC 7 recommend lower cut points for intervention.


Combination of ACE inhibitors and HcTz can reduce the risk of stroke by almost 40%
NEXT CASE

SCENARIO # 2

88 y o lady with 2 day history of left leg weakness and abulia brought to ER

History:
PVD
DM, HTN
Sleep Apnea
Cholesterol 256mg/dL
2 PPD smoker

SCENARIO # 2

MRI brain (DWI)
Right ACA territory IS
SCENARIO # 2

MRA brain flow gap Right ACA

SCENARIO # 2

TEE is negative for thrombus

All labs except lipid profile WNR

Intracranial Large Artery Stenosis

- High prevalence in African Americans, Asians, Hispanics
- Annual risk of stroke 7%-25%
- Under studied
- Lack of proven therapy
GOALS: SCENARIO # 2

Statins to keep LDL < 70mg/dL and cholesterol < 100mg/dL

Strict Glycemic control

ASA 325mg or Clopidogrel 75mg (never Dual)

SBP 120-140 mmHg range

Smoking cessation

Cigarette Smoke

- Doubles the risk of ischemic stroke
- Clearly for hemorrhagic stroke.
- Can clearly interact with oral contraceptives for young women.

Recommendations

1. OCs may be harmful in women with additional risk factors (eg, cigarette smoking, prior thromboembolic events) (Class III, Level of Evidence C).

RR for OC usage 1.3

RR for smoking 2.1

RR for BOTH 7.2!

Sleep Apnea

- Epidemiological study suggest habitual snoring associated with risk of ischemic stroke
- Associated with increase risk for MI and HTN

NEXT CASE

SCENARIO # 3

28 yo RH robust AA male

Acute onset of right ½ paresis and aphasia

Hx:
- Alcohol abuse
- Mild HTN
- Occasional palpitations
Paroxysmal A-fib on Rhythm strip

Hyperglycemic

TEE:
- Global hypokinesis
- EF 25%
- Left atrial thrombus
  0.5 x 0.5cm
Atrial Fibrillation

- 70,000 strokes per year
- Approximately 2.3 million Americans have atrial fibrillation
- 15% of ischemic stroke
- Annual risk 5%-25%
- Rhythm control does not appear to reduce stroke rates.

Atrial Fibrillation

- AF alone is associated with a 3 to 4 fold increased risk of stroke.
- 2% to 4% a year will have an ischemic stroke
- AF, like stroke, increases with age.
- Strokes from AF are especially large and disabling.
- Warfarin is effective.
ACCP 2012 RECOMMENDATIONS

Stroke Prevention for Patients with Cardioembolic Ischemic Events

- Long-term oral anticoagulation is recommended for prevention of stroke in patients with atrial fibrillation with a recent TIA or ischemic stroke - Grade 1a

- Recommended target INR is 2.5 (range 2.0 to 3.0).

- Oral anticoagulation for patients with other high risk conditions is acceptable (recent MI, left ventricular thrombus, dilated cardiomyopathy).

- Limited data is available to recommend anticoagulation of patients with low risk cardiac sources (mitral valve prolapse, mitral annular calcification, PFO, atrial septal aneurysm, calcific aortic stenosis).
WHAT ABOUT PFOs ????

Patent Foramen Ovale and the Risk of Ischemic Stroke in a Multiethnic Population
Marco R. Di Tullio, MD*; Ralph L. Sacco, MD†‡

Recommendations
1. ACC/AHA practice guidelines providing strategies to reduce the risk of stroke in patients with a variety of cardiac conditions, including valvular heart disease, unstable angina, chronic stable angina, and acute MI are endorsed.
2. Screening for cardiac conditions such as PFO in the absence of neurological conditions or a specific cardiac cause is not recommended (Class III; Level of Evidence A).

WHAT ABOUT CRYPTOGENIC STROKES ?

Therapeutic Strategies After Examination by Transesophageal Echocardiography in 503 Patients With Ischemic Stroke
Andreas Herrleff, MD; Michael Hardt, MD; Matthias Reinhart, MD; Amelie Grieb, MD; Andreas Hettler, MD

TEE strongly influences secondary stroke prevention
Consider TEE in patients in whom routine workup fails to reveal etiology

Metabolic Syndromes

- Cluster of metabolic conditions that increases the risk for atherosclerotic vascular diseases.
- Insulin resistance affects 50% of non-diabetic stroke and TIA patients

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Insulin resistance affects 50% of non-diabetic stroke and TIA patients
Obesity and Fat Distribution

- Each 5 kg/m² increase in BMI associated with 40% increase in Stroke mortality
- To date, no study looked at weight reduction to reduce Stroke risk
- BP reduction seen with weight loss

Diabetes

- Tight control of hypertension with ACEI or ARB treatment reduces stroke risk in diabetics (BP <130/80 mm Hg)
- Glycemic control reduces microvascular complications but is not as potent at stroke prevention
- Statin treatment of diabetic patients substantially decreases their risk of first stroke

Stroke

Effects of Admission Hyperglycemia on Stroke Outcome in Reperfused Tissue Plasminogen Activator–Treated Patients

Persistent Poststroke Hyperglycemia Is Independently Associated With Infarct Expansion and Worse Clinical Outcome
Acute Hyperglycemia Adversely affects Stroke Outcome: A Magnetic Resonance Imaging and Spectroscopy Study

Mark W. Parsons, FRACP, P. Alan Barber, PhD, FRACP, Patricia M. Desmond, MD, Tracy A. Baird, MRCP, Flavel D. Gray, PhD, FRACP, Graham Byrnes, PhD, Brian M. Tress, MD, FRACR, and Stephen M. Davis, MD, FRACP

Annals of Neurology 2002;52:20-8

Diffusion – Perfusion Mismatch

Diabetes

Glycosalated Hemoglobin

- HbA1c is independent risk factor for CVD.
- 20% relative increase in CVD for 1% point above the normoglycemia levels.
- HbA1c can help identify patient with high risk for recurrent vascular events.
Alcohol Consumption

- Excessive consumption of alcohol can lead to multiple medical complications including stroke
- Alcohol
- Light and high in aggregation and metabolism
- Heavy consumption: HTN, hypercoagulability, decrease cerebral perfusion and A-Fib

GOALS: SCENARIO # 3

- Started on Warfarin (INR 2.0-3.0 range)
- Statins and anti-HTN therapy
- Alcohols reduction / cessation
- Exercise and weight reduction
- Stroke risk factor stratification

NEXT CASE
SCENARIO # 4

67 yo RH lady found down with right ½ paresis and dysarthric speech (LKW 2hrs) Refused IV t-PA

No visual or cognitive deficits

BP: 180/111

SCENARIO # 4

Labs:
HbA1c: 5.7%
Homocystiene: 17.0 Umol/L
Lipid panel
cholesterol: 280 mg/dL
triglycerides: 162 mg/dL
LDL: 210 mg/dL
HDL: 38 mg/dL

MTHFR mutation detected
A1298C heterozygous
Lacunar syndromes

- Approx 125 different syndromes
- May be due to small hemorrhages
  - Pure motor LS
  - Pure sensory LS
  - Dysarthria clumsy hand syndrome
  - Ataxic-Hemiparesis

Lacunar Infarct in pons

Charcot-Bouchard aneurysm

- 0.8-1.0 mm in diameter
- Associated with long standing hypertension
- Commonly arise at the bifurcation of small arteries that lie deep within the brain
- Result from infiltration of the arterial walls by lipid and hyaline material - a process referred to as hypertensive lipohyalinosis.

Jean-Martin Charcot
French neurologist, born November 29, 1825 Paris; died August 16, 1893, Lac des Settons, Nièvre

Charles-Joseph Bouchard
French pathologist, born September 6, 1837, Moutiér en Der, département Haute-Marne; died 1915.

Lacunar Disease

- Overall good prognosis
- Stroke risk factor stratification
- Rx Antiplatelet agents
Hypercholesterolemia

- Not an established risk factor for Stroke
- Selected studies show an association between elevated LDL-C and atherosclerotic extra-cranial carotid disease

Dyslipidemia

- In general, increased levels of total cholesterol are associated with stroke
- Low HDL levels is a risk factor for ischemic stroke in men
- Patients with known CAD and hypertensive patients at high risk should be treated with lifestyle measures and a statin.

GOALS: SCENARIO # 4

Started on EC Aspirin 325mg Daily
(Check PFA in 96 hrs)
Lipitor: 80mg Daily
(LFTs / CK in 4-6 weeks)
Lisinopril 10mg daily & Hctz 12.5mg QD
(Target SBP < 130mmHg)
Strict Glycemic control and treat hyperhomocysteinemia
(Target BG < 125mg/dL and homocysteine < 10)
Hyperhomocysteinemia

- Serum maker and an independent risk factor for ischemia
- Increase events with levels above 15 μmol/L
- Treatment includes Folate, Vitamin B₁₂ and B₆
Transient Ischemic Attack

“brief episode of neurological dysfunction caused by focal disturbance of brain or retinal ischemia, with a clinical symptom typically lasting less than 1 hour, without evidence of ischemia”

Circulation 2006;113:409-449

200,000-500,000 Americans with TIAs / year
15% of Strokes with history of TIAs

5% stroke in 2 days
8.6% in 1 week
12% in 30 days
10% in 90 days
29% in 6 months

Timing of TIAs preceding stroke

Time window for prevention is very short

15-30% of patients reported preceding TIAs prior to a Stroke

NEUROLOGY 2005;64:817-820
TIA Workup

- Hospitalization
- At least a CT head
- Labs and EKG
- Consider MRI/A brain
- Carotid / Vertebral A. dopplers
- 2D Echocardiogram
- Aspirin 50-325mg/day OR (Aggrenox or PLAVIX)
- Anticoagulation in A-fib
- Consider CEA
carotid grade 70-99% stenosis vs angioplasty
- Target BP <140/90
- Tx Cholesterol <200 and LDL <70
- Alcohol: Limit to 1 drink/day
- Smoking cessation
- Diabetes: Tight control (<125mg/dl)
- Exercise: 3 times per week
- Harmful to continue OCP/HRT

Overlap of Atherosclerotic Disease

Patients with one manifestation often have coexistent disease in other vascular beds
An accumulating burden of Hypertension, Diabetes and smoking are important in the progression of atherosclerosis from the Coronary to the Carotid circulation.

Department of Stroke and Cerebrovascular Diseases, Emory University Hospital, Atlanta, Georgia
The Cleveland Clinic Foundation, Cleveland, Ohio
Neurology Specialist of Savannah, Savannah, Georgia

Anti-platelet Therapy for Acute Stroke

Aspirin and Beyond

Thrombosis in arteries is highly Platelet dependent unlike the Heart and the Veins
Aspirin Efficacy by Dose: Meta-Analyses in Patients With Stroke or TIA*

<table>
<thead>
<tr>
<th>Dose (mg/day)</th>
<th>Low Dose</th>
<th>Medium Dose</th>
<th>High Dose</th>
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<tbody>
<tr>
<td>50 – 100</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>300</td>
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<td>500 – 1500</td>
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</tr>
<tr>
<td>650 – 1500</td>
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* Endpoint: stroke, MI, or vascular death.
1. **No convincing evidence that benefit of aspirin is dose dependent**

2. **Enteric coating does not reduce likelihood; Require concomitant proton pump inhibitor**

3. **Antithrombotic Trialists' Collaboration: Meta-analysis of Antiplatelet Agents**
   - Collaborative meta-analysis of randomized trials of antiplatelet therapy for secondary risk reduction of vascular events (non-fatal MI, non-fatal stroke, or death from a vascular cause)
   - Reviewed 287 trials involving 135,000 patients
   - Trials that compared ASA vs placebo found a 23% RRR (P<0.0001)
CHARISMA
Clpidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance

Charipogel and Aspirin versus Aspirin Alone for the Prevention of Atherosclerotic Events

The New England Journal of Medicine

THE LANCET
Aspirin and clopidogrel compared with clopidogrel alone
after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial

Summary: Improved Relative Risk Reduction

ATTC
Aspirin vs placebo
provided an RR of 23%
in the combined end point
of myocardial infarction, stroke, or vascular death (PHIL6001)
as shown in the Antiplatelet
Trials Collaboration meta-analysis involving
135,000 high-risk patients

CAPRIE
PLAVIX (75 mg)
vs aspirin (325 mg)
provided an RR of 8.7%
in the combined end point of MI, stroke,
and vascular death seen in the
CAPRIE study (PHIL9002)

Relative Risk Reduction
Over Aspirin

23%
8.7%
**ASPIRIN resistance**

- Non responders or paradoxical increase (33% with 325mg dose)
- 8% of patients resistance
- Erythrocyte activation with higher doses
- Higher doses are better than lower doses?

**Oral Antithrombotic Therapies for Secondary Risk Reduction of Stroke: Separate Pathways**

**Noncardioembolic Stroke**

- Antiplatelet Therapy
- Clopidogrel
- Aspirin
- Ticlopidine
- Dipyridamole

**Cardioembolic Stroke**

- Anticoagulation
- Warfarin

**AHA/ASA Guideline**

Guidelines for Prevention of Stroke in Patients With Ischemic Stroke or Transient Ischemic Attack

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association Council on Stroke Co-Sponsored by the Council on Cardiovascular Radiology and Intervention

The American Academy of Neurology affirms the value of this guideline.

For patients with noncardioembolic ischemic stroke or TIA, antiplatelet agents rather than oral anticoagulation are recommended to reduce the risk of recurrent stroke and other cardiovascular events (Class I, Level of Evidence A). Aspirin (300 to 325 mg/d), the combination of aspirin and extended-release dipyridamole, and clopidogrel are all acceptable options for initial therapy (Class IIa, Level of Evidence B).
DVT PROPHYLAXIS

The efficacy and safety of enoxaparin versus unfractionated heparin for the prevention of venous thromboembolism after acute ischaemic stroke (PREVAIL Study): an open-label randomised comparison.

Compared with UFH, Enoxaparin was superior for reducing VTE risk in Acute ischemic stroke patients with similar bleeding risks.

ICR 0.4% 0.5% 0.69
ICH + ECH 0.9% 0.3% 0.73%

Lancet 2007; 369:1347-55
THAT’S MY TIME!