STROKE AND MULTIPLE SCLEROSIS

2016 ACOI Internal Medicine Review Course
Renaissance Resort at SeaWorld
Orlando, Florida

Scott Spradlin D.O. FACP,FACOI
I have no relevant financial or nonfinancial relationships in the products or services described, reviewed, evaluated or compared in this presentation.
Stroke and Multiple Sclerosis

Stroke or Brain Attack

5th Leading cause of Death for men
4th leading cause of Death for women
Acute brain injury due to a vascular etiology
Sudden onset
Persist at least 24 hours
Neurological deficit

TIA

Neurological deficits lasting less than 24 hours
Stroke Imaging
STROKE

• 795,000 Strokes Occur each year

• 87 percent of those strokes are ischemic

• Stroke kills 130,000 Americans/year

• Stroke costs the US an estimated 34 billion/yr

• Leading cause of serious long term disability
STROKE

- Race/Sex/Geography
  - Black risk of death is 1.49X Whites
  - Males greater risk than females
  - Hispanics higher risk for lacunar infarcts
  - Southeastern US has higher risk

- Age
  - Stroke occurs in all ages
  - Stroke increases with age
  - Age >64 is where 75% of occurrence
STROKE RISK FACTORS

- **Non-modifiable Risk Factors**
  - Age
  - Race
  - Sex
  - Ethnicity
  - History of Migraine
  - Sickle Cell Disease
  - Fibromuscular Dysplasia
  - Heredity
STROKE RISK FACTORS

- Laboratory Monitoring Risk
  - Glucose and Electrolytes
  - CBC with Platelets
  - Prothrombin Time/ Partial Thromboplastin Time
  - Cholesterol/LDL/HDL
  - ANA/RF/Homocysteine/ESR
  - Protein C/ Protein S/ Antithrombin III/ Leiden
  - Anticardiolipin Antibody
  - Lupus Inhibitor/ Antiphospholipid Antibodies
VASCULAR RISK FACTORS

• Modifiable conditions and lifestyle characteristics identified as a risk factors for stroke:

- High blood pressure
- Atrial fibrillation
- Diabetes mellitus
- Carotid artery disease
- Myocardial infarction
- High Cholesterol
- Hyperhomocysteinemia
- Smoking
- Heavy alcohol use
- Physical inactivity
- Obesity
CIGARETTE SMOKING

- **Background**
  - Independent risk factor for ischemic stroke in men and women
  - 2-3 fold increased risk compared to non-smokers\(^1\)
  - Spousal cigarette smoking may be associated with an increased stroke risk\(^2\)
  - 50% risk reduction by 2 years after stopping smoking\(^3\)

ALCOHOL CONSUMPTION

- **Background**
  - Increased risk for both ischemic (RR 1.69) and hemorrhagic stroke (RR 2.18) with heavy alcohol consumption (>60g/day)
  - BP elevation might be a reasonable explanation
  - Light alcohol consumption (<12g/day) associated with reduced ischemic (RR 0.80) and hemorrhagic stroke
  - Red wine consumption carries the lowest risk

PHYSICAL ACTIVITY

- Background
  - Regular exercise (at least 3x30min/week) is associated with a decreased risk of stroke
  - Physically active individuals have a lower risk of stroke or death than those with low activity (RR 0.73)\(^1\)
  - This is mediated, in part, through beneficial effects on body weight, blood pressure, serum cholesterol, and glucose tolerance\(^2\)

---

BODY WEIGHT, DIET, NUTRITION

• Background
  • High body mass index (BMI ≥25) increases risk of stroke in men and women¹
  • Abdominal adiposity is a risk factor for stroke in men but not women²
  • A randomized trial in women found no effect of dietary interventions to reduce the incidence of stroke³
  • Tocopherol and beta carotene supplementation do not reduce the risk of stroke. Vitamin E might increase mortality when used at high-dose (≥400 IU)

• Background

• Stroke rates rise rapidly in women after the menopause
• Hormone replacement therapy in postmenopausal women is associated with an 44% increased risk of stroke

1: Gabriel S et al.: Cochrane Review (2005) CD002229
Background

- In low risk persons low dose aspirin reduced coronary events, but not stroke\(^1\)
- In women over 45 years aspirin reduces the risk of ischemic stroke (OR 0.76; 95%CI 0.63-0.93) \(^2\)
- Aspirin reduces MI in patients with asymptomatic carotid artery disease\(^3\)

VITAMINS

- Background
  - Beta carotene increased the risk (RR 1.10) of cardiovascular death\(^1\)
  - Antioxidant supplements may increase mortality\(^2\)
  - Folate, B12, B6 vitamins given to lower homocysteine levels may not reduce stroke recurrence and may increase vascular events\(^3\)

SLEEP-DISORDERED BREATHING

- Background
  - Sleep-disordered breathing (SDB) is both a risk factor and a consequence of stroke
  - More than 50% of stroke patients have SDB, mostly in the form of obstructive sleep apnoea (OSA).
  - SDB is linked with poorer long-term outcome and increased long-term stroke mortality
  - Continuous positive airway pressure is the treatment of choice for OSA.

MANAGEMENT OF COMPlications

- Falls
  - Are common in every stage of stroke treatment
  - Risk factors include cognitive impairment, depression, polypharmacy and sensory impairment\(^1\)
  - A multidisciplinary package focusing on personal and environmental factors might be preventive\(^2\)
  - Exercise, calcium supplements and bisphosphonates improve bone strength and decrease fracture rates in stroke patients\(^3,4\)

Dysphagia and feeding

- Dysphagia occurs in up to 50% of patients with unilateral hemiplegic stroke and is an independent risk-factor for poor outcome\(^1\)

- For patients with continuing dysphagia, options for enteral nutrition include NG or PEG feeding

- PEG does not provide better nutritional status or improved clinical outcome, compared to NG\(^2,3\)

REHABILITATION

- Early rehabilitation
  - More than 40% of stroke patients need active rehabilitation

- Active rehabilitation should start early, providing the patient is clinically stable

- Passive rehabilitation should be given if the patient is unconscious or paralyzed

- Rehabilitation should be continued as long as perceptible recovery is taking place
Multidisciplinary stroke team for rehabilitation

- Stroke physician
- Nurses experienced in stroke management
- Physiotherapist trained in stroke rehabilitation
- Occupational therapist skilled in stroke
- Speech therapist familiar with speech problems in stroke patients
- Neuropsychologist accustomed to stroke rehabilitation
- Social worker familiar with the problems of stroke patients
Calculating Risk

**ABCD2**

To identify individuals at high early risk of stroke after transient ischemic attack.

A (Age); 1 point for age $\geq$60 years,

B (Blood pressure $\geq$140/90 mmHg); 1 point for hypertension at the acute evaluation,

C (Clinical features); 2 points for unilateral weakness, 1 for speech disturbance without weakness,

D (symptom Duration); 1 point for 10–59 minutes, 2 points for $\geq$60 minutes.

D (Diabetes); 1 point Total scores ranged from 0 (lowest risk) to 7 (highest risk).

**Scale:**

Stroke risk at 2 days, 7 days, and 90 days:

Scores 0-3: low risk
Scores 4-5: moderate risk
Scores 6-7: high risk
Stroke and Multiple Sclerosis

Types of Stroke

**Ischemic** - most common >70%
- Thrombotic
  - Atherosclerosis
- Embolic
  - Emboli form the Heart or Vessels

**Hemorrhagic** -
- Intracerebral
  - Hypertension or Amyloid Angiopathy
- Subarachnoid
  - Berry Aneurysms
Stroke and Multiple Sclerosis

Thrombotic Strokes

Atherosclerosis
  - Internal Carotid
  - Middle Cerebral
  - Vertebrobasilar

Symptoms
  - Slow stepwise progression of symptoms
  - Usually preceded by TIA’s

Other Causes
  - Lupus anticoagulant
  - Polycythemia
  - Syphilis
  - Thrombocytosis
  - Dissecting Aortic Aneurysm
Stroke and Multiple Sclerosis

Embolic Stroke

Not usually preceded by TIA

Emboli
- Heart
- Large Blood vessel
  Usually effects middle>posterior>anterior cerebral

Symptoms
- Neurodeficits worst at onset
- Weakness is greater in distal extremities
Stroke and Multiple Sclerosis

Stroke Symptoms By Region

Middle cerebral
Anterior cerebral
Posterior cerebral
Single Hemisphere
Vertebrobasilar
Lateral Medullary syndrome
Lacunar-small vessel
Stroke and Multiple Sclerosis

Middle Cerebral Artery Occlusion

Contralateral hemiplegia
Contralateral hemianesthesia
Homonymous hemianopsia
Impaired conjugate gaze in opposite direction
Impaired spatial- nondominant
Impaired language-dominant
If lesion high- loss face/upper ext
If it is in the main trunk- same throughout
Stroke and Multiple Sclerosis

Anterior Cerebral Artery Occlusion

Most affected in distal contralateral leg
Urinary incontinence
Gait abnormalities
If includes corpus callosum the patient will have tactile anomia (cannot name what they touch)
Stroke and Multiple Sclerosis

Posterior Cerebral Artery Occlusion

Contralateral homonymous hemianopsia
Usually upper quadrantanopsia
Mild contralateral hemiplegia/anesthesia
Color anoma= corpus callosum damage
Memory loss
If occlusion bilateral memory will be severe/persistent
Stroke and Multiple Sclerosis

Single Hemisphere injury
Does not affect paraspinal muscles
Does not affect pharynx
Does not affect jaw
Does not affect the forehead
If any or all of the above are affected think:
  Bilateral hemispheric infarct
  Brainstem infarct
Stroke and Multiple Sclerosis

Vertebrobasilar Artery Occlusion
Associated with brain stem strokes
Bilateral extremity motor/sensory dysfunction
Quadraplegia in severe cases
Crossed motor and sensory deficits
Horner syndrome
Cerebellar signs/stupor/coma
Cranial nerve dysfunction
Stroke and Multiple Sclerosis

Lateral Medullary Syndrome

Also called *Wallenberg Syndrome*

Nausea

Vomiting

Nystagmus

Ipsilateral Horner Syndrome

Ipsilateral palate and vocal cord weakness

Ipsilateral face hemianesthesia

Contralateral body hemianesthesia
Stroke and Multiple Sclerosis

Lacunar Strokes

Due to hypertension
Occlusion of very small arterioles
Over time they form cysts in the brain
Pure hemiplegia
Pure hemisensory
Multiple bilateral frontal lobe “lacunes” can cause pseudobulbar palsy
Stroke and Multiple Sclerosis

Work up:

- History
- Computerized Tomography Brain
- CBC with platelets
- Troponin
- Electrolytes, Glucose, Bun, Cr,
- Coagulation profiles
- EKG
- Trans-thoracic Echocardiogram
- Carotid Ultrasound/Trans-cranial Doppler
- MRI/MRI Diffusion/Angiography
Stroke and Multiple Sclerosis

Ischemic Stroke Treatment

Thrombolysis-Alteplase

>18 yrs old with an ischemic stroke Dx

Onset time – 3 hours (3-4.5 with caveats)

Oxygen

Treat BP-gradually

Aspirin/Antiplatelets

Surgical Intervention-

-mechanical thrombectomy
Stroke and Multiple Sclerosis

- **CONTRAINDICATIONS TO ALTEPLASE (tPA)**
  
  **Absolute**-
  - Intracranial hemorrhage on CT
  - Clinical Presentation suggests subarachnoid hemorrhage
  - Neurological surgery, serious head trauma, or previous stroke past 3 months
  - Uncontrolled hypertension (>185 mmHg SBP or >110 mm Hg DBP)
  - History of intracranial hemorrhage
  - Seizure at stroke onset
  - Known AVM, neoplasm, or aneurysm
  - Active internal bleeding
  - Suspected/confirmed endocarditis
  - Known bleeding diathesis: plts <100,000, heparin with elevated PTT, oral anticoagulants and INR >1.7, thrombin inhibitors
  - Abnormal blood glucose (<50 or >400 mg/dl)

  **Relative** –
  - Only minor or rapidly improving stroke symptoms
  - Patient has had major surgery or serious trauma excluding head trauma in previous 14 days
  - History of GI/Urinary hemorrhage in last 21 days
  - Recent arterial puncture at a noncompressible site
  - Recent lumbar puncture
  - Post myocardial infarction pericarditis
  - Pregnancy

**Additional WARNINGS to tPA > 3 hr onset**-

- Age >80
- History of prior stroke and diabetes
- Any active anticoagulant use (even with INR <1.7)
- NIHSS>25
Stroke and Multiple Sclerosis

• Post Acute Care Therapy

Antiplatelets

ASA (50-325 mg)/Aggrenox/Ticlodipine
Clopidogrel
Coumadin
Dabigatran, Apixaban, Rivaroxaben- (non valvular Atrial Fibrillation)

Manage underlying causes

Cardiac- ACC
HTN- JNC guidelines
Diabetes- HbA1C <6.5-7.0
Tobacco abuse
Hyperlipidemia- LDL <70
If >70% carotid stenosis- surgical evaluation/discussion
Stroke and Multiple Sclerosis

• **CHADS2**

Score for Atrial Fibrillation Stroke Risk

- Congestive Heart Failure: 1pt
- Hypertension: 1pt
- Age>75: 1pt
- Diabetes Mellitus: 1pt
- Stroke or TIA Symptoms: 2pt

Score >2: **High**  
oral anticoagulant

Score >1 <2: **Moderate**  
oral anticoagulant or ASA

Score 0: **Low**  
ASA 75-325mg
Stroke and Multiple Sclerosis

Intracerebral Hemorrhage

Amyloid Angiopathy

Commonly causes recurrent bleeds

>65 yrs old

Subcortical, rarely affects deep structures

Can cause multiinfarctional dementia

Also found in alzheimers patients- unclear association

Occasionally can be associated with subarachnoid
Stroke and Multiple Sclerosis

Intracerebral Hemorrhage

Hypertension
Gradual and smooth onset of symptoms
Putamen > Thalamus > Pons > Cerebellum

Putamen
- Contralateral hemiparesis/sensory loss/hemianopsia
- Acts just like a middle cerebral infarct

Thalamus
- Contra hemiplegia/hemianesthesia/sensory > motor

Pons
- Coma/pinpoint pupils/complete paralysis
- Can have decerebrate posturing bilaterally

Cerebellum
- Acute dizziness/ataxia/vomiting
- No mentation change or loss of consciousness
Stroke and Multiple Sclerosis

Subarachnoid Hemorrhage

Cerebral saccular aneurysm bleed
   Usually Circle of Willis
   IC=40%/AC=35%/MC=20%

Hypertensive hemorrhages with ventricular rupture

A-V Malformations

Symptoms
   Acute/Severe headache (thunderclap)-unresponsive to meds
   May be alert/confused/comatose
   No focal neurological signs
   Neck stiffness is classic- but not always present
Stroke and Multiple Sclerosis

• **Hemorrhagic Stroke Work Up**
  
  Computerized Tomography
  (CT misses 10% of Bleeds)
  Lumbar Puncture
  Xanthochromic supernatent is diagnostic
  If LP (-) can be hours before blood gets in CSF
  Cerebral Angiography
  Can rebleed in 24 hours/Vasospasm

  **Treatment**
  
  Neurosurgery consult/Intervention
  ABC’S
  Hemodynamic and edema management/Nimodipine/Mannitol/Glycerol/Saline
Stroke and Multiple Sclerosis

**Multiple Sclerosis**

Myelin deterioration
- Brain-
- Spinal Cord-
- Optic Nerve -

**Pathophysiology**
- 10x more common in northern latitudes
- May be viral in origin— Female 2:1 Males
- Autoimmune but does have genetic components
- Onset 20-50 yrs of age

**Plaques**
- Cause a mononuclear inflammation
- Demyelination with axonal sparing
- Oligodendroglial cell loss and astrocyte proliferation
- Long standing lesion Astrogliosis
Stroke and Multiple Sclerosis

Symptoms

- Mononeuropathy +/- multiplex
- Optic neuritis
- Ophthalmoplegia
- Intermittent Diplopia
- Extremity weakness
- Tremors
- Lhermitte sign-
  (Paresthesias radiating down the spine into extremities on neck flexion)
Multiple Sclerosis - H&E STAIN
Stroke and Multiple Sclerosis

• Types of Multiple Sclerosis

Clinically Isolated Syndrome (CIS)
  No occurrence after initial

Relapsing-remitting
  Most common
  Has attacks followed by none then reoccurs

Primary-Progressive
  Men
  Gradual decline few plateaus

Secondary-progressive
  Stage II relapsing-remitting. No periods of remission

Progressive-relapsing
  Rare. Progressive form until the end

Malignant (Marburg Variant)
  Very rare. Decline to death in few months
Stroke and Multiple Sclerosis

- Diagnostic Tests
  - MRI – TEST OF CHOICE - Brain/Spinal Cord
    - White plaques
  - Evoked Action Potentials
    - Silent lesions
  - Lumbar Puncture
    - Increased IgG / Oligoclonal IgG bands in CSF
    - Elevated protein
Stroke and Multiple Sclerosis
Stroke and Multiple Sclerosis
Stroke and Multiple Sclerosis

**Treatment**

**Acute Phase/Initial**
- Steroids  500mg daily x 5 days
- Plasma exchange for severe deficits with poor response to steroids

**Oral Immunomodulator-**  Fingolimod(Gilenya), Ampyra,Aubagio,Tecfidera

**Relapsing-Remitting**
- Beta-interferons(1-a,1-b)-
  - Avonex/Rebif/Betaseron/Extavia/Plegridy
- **Monoclonal Antibodies-**
  - Tysarbi-
  - Alemtuzumab (Lemtrada)- HIV negative
- **Copolymer-**
  - Copaxone/Glatoba

**Chronic/Advanced**
- Novantrone(mitoxantrone)
Stroke and Multiple Sclerosis

• 34 yr old with history of ataxia, ophthalmoplegia and paresthesia of the legs intermittently with a massive weight loss over the past few months.
• His history is significant for HIV and has been on gancyclovir and protease inhibitors and T-cell counts have remained <200.
• His mentation is going quickly and he has no memory and has stopped eating.

• What is your diagnosis?
PML

Progressive Multifocal Leukencephalopathy

PML is caused by the JC Virus but there are some drugs that can create a reversible leukencephalopathy.
Stroke and Multiple Sclerosis

Central Pontine Myelinolysis

Occurs in patients with severe hyponatremia
Their sodium is corrected too aggressively
- Quadraparesis
- Mutism
- Pseudobulbar palsy
- Swallowing dysfunction

Treatment

Correct Na slowly and treat underlying cause