What's Hot in Neuro-Op Cerebrovascular Disease

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CEREBROVASCULAR DISEASE KEY POINTS

1. CLASSIFICATION OF TIAs
2. OCULAR SIGNS & SYMPTOMS OF CAROTID ATHEROSCLEROTIC DISEASE
3. WORK-UP FOR PATIENTS WITH CAD
4. MANAGEMENT OPTIONS

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Transient Ischemic Attacks

- Hemispheric
- Retinal
- Posterior circulation

Hemispheric TIAs (carotid artery TIA)
- Relatively “easy” to diagnose
- Any acute hemiparesis
- Hemi-sensory loss
- Aphasia
- Dysarthria
- Hemianopia (often described as non-specific vision loss)

Retinal TIAs (carotid artery & ophthalmic artery TIA)
- More difficult to diagnose
- Acute, monocular vision loss
- Partial (altitudinal) or complete
- “blackout” of vision (not “blurry” or “difficulty focusing)

Biousse V. NANOS 2014

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Posterior TIAs
(brainstem and occipital lobe TIA)

• Difficult to diagnose (high false positives)
• Acute vertigo, dizziness, gait instability, confusion, dysarthria
• Visual disturbance (including diplopia & binocular vision loss) particularly if multiple symptoms at the same time

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Risk Factors for CAD

• Older age
• Males
• African American
• Hypertension
• Diabetes mellitus
• Abnormal serum lipids
• Obesity
• Cigarette smoking

Pathophysioloogy

• Vessel wall shear stress (carotid artery bulb)
• Endothelial cell damage
• Fibrin/platelet aggregation
• Cellular proliferation
• Atheromatous plaque formation
• Plaque ulceration
• Vessel occlusion
Ocular Signs of CAD

- Retinal emboli
  - cholesterol
  - platelet-fibrin
- Retinal artery occlusion
- Ocular ischemic syndrome

Cholesterol Emboli (Hollenhorst Plaques)

- Yellow/copper-colored
- Refractile
- Arterial bifurcation
- “Pulse” @ CRA diastoly
- Originate from degenerating atheroma
  - carotid (common)
  - aorta (rare)

Hollenhorst RW. *JAMA* 1961

82 Y/O Asian Man

- C/o TMB OD
- BVA:
  - 20/20
  - 20/20
4 months later...

Platelet-Fibrin Emboli (Fisher Plugs)
- White-gray vascular casts (plugs)
- Dull
- Source:
  - carotid atheroma
  - heart (valves)

Fisher CM. Neurology 1959

Retinal Artery Occlusions
- Branch Retinal Artery Occlusion
- Central Retinal Artery Occlusion
Central Retinal Artery Occlusion

- Acute, painless vision loss
- FC to LP (slight improvement over time)
- Preceding TMB (+/-)
- Retinal emboli (+/-)
- +RAPD

47 y/o AA Woman

- C/o acute, painless vision loss OD x 3 days
- History of type 2 diabetes with retinopathy
- BVA = HM OD
67-y/o man
VA = HM x 18 hours
Evolution of CRAO - OCT

Management of CRAO

- Limited window of opportunity (0-6 hrs???)
- Conservative treatments don’t work!!!
- Paracentesis doesn’t work (some reports of embolic dislodgement)!!!

- ???
Etiology of CRAO

1. Embolic:
   - Carotids
   - Aorta
   - Cardiac

2. Inflammatory:
   - GCA

3. Localized thrombus

Thrombolytic Tx for CRAO

- t-PA, streptokinase, urokinase
- Intravenous v. intra-arterial (delay in Tx!!!)
- European trial (EAGLE Study) *discontinued...no difference in outcomes & 10% risk of intracranial bleed*

Thrombolysis in Acute Ischemic Stroke - NINDS 1995

Efficacy of IV tPA in CRAO: Report from a Randomized Controlled Trial (Chen C, et al. NANOS 2011)

- Australian study of 16 patients with acute (within 24 hrs.) CRAO randomized to IV tPA vs. placebo
- No difference in VA between placebo and tPA groups at 6 months
- Potential benefit if tPA administered *within 6 hours* of CRAO
- *Benefit of Tx does not justify the risk of IC bleed & stroke*

Branch Retinal Artery Occlusion

- “Sector” of vision loss
- Asymptomatic
- 80% improve to 20/40 or better
- Arterial bifurcation (posterior pole)
- 90% involve temporal retinal vessels

Brown GC, et al. *Arch Ophthmol* 1979
Evaluation of Elderly Patients with Retinal Artery Occlusions

- Carotid artery disease
- Cardiac disease
- Giant-cell arteritis (non-embolic CRAO)

- 63 y/o man
- + diabetes & hypertension
- + atrial fibrillation
- c/o loss of vision-superior hemifield, OD
- VA = 20/40, OD
Ocular Ischemic Syndrome

Manifestations of OIS
- Associated with severe, bilateral carotid atherosclerosis
- Retinal involvement
  - venous stasis retinopathy
- Choroidal ischemia
- Anterior segment involvement

Venous Stasis Retinopathy
- Dilated, non-tortuous veins (Brown - 1989)
- No disc swelling
- Mid-peripheral hemorrhage
- Neovascularization (NVD)
- Delayed A-V transit time (> 11 sec.)
- Other signs/symptoms of CAD:
  - TMB
  - light-induced amaurosis
  - orbital pain (improves while lying down)

Kearns & Hollenhorst Mayo Clin Proc 1963

68-y/o man
VA = 20/20, OU
Choroidal Ischemia

- Progressive vision loss
- "Purple vision" (NANOS-2008)
- Light-induced amaurosis
- No obvious clinical correlation
- Delayed & patchy choroidal filling

Brown & Magargal Int Ophthlmol 1988

72-y/o woman + light-induced TMB

Anterior Segment & Orbital Complications

- Mild A/C rxn ("ischemic uveitis")
- Orbital pain (improves when lying down)
  - trigeminal ischemia
- Cataract
- Dilated episcleral vessels
- Iris/angle neovascularization
  - neovascular glaucoma

Carter JE. Stroke 1985

Management of OIS

- Carotid Endarterectomy (CEA)
- Carotid angioplasty (stenting)
- PRP/anti-VEGF
Investigation of Carotid Artery Disease

- Auscultation for bruit
- Carotid duplex ultrasonography
- Magnetic resonance angiography (MRA)
- Computerized tomographic angiography (CTA)
- Carotid intima media thickness scan (CIMT)

Carotid Bruit

- Audible turbulence
- Carotid bifurcation
- Screening test for carotid stenosis
- 60-75% sensitivity & specificity for significant carotid stenosis

SauvC JS, et al. JAMA 1993

Non-Invasive/Minimally Invasive Carotid Imaging

- Duplex ultrasonography
- Magnetic resonance angiography (MRA)
- Computerized tomographic angiography (CTA)
- Intima Media Thickness (IMT)

Duplex Ultrasonography

- Combines:
  - B-mode ultrasound (2-d image)
  - Doppler ultrasound (quantitative hemodynamics of blood flow)
- 86% sensitive & 87% specific for > 50% carotid stenosis
- Low cost ($150-200)
**Magnetic Resonance Angiography (MRA)**
- Time-of-flight (visualization of arteries)
- Over 90% sensitive and specific for > 70% carotid stenosis
- $400-500

**Computerized Tomographic Angiography (CTA)**
- Contrast-enhanced CT
- 3-d image of intracranial and extracranial vasculature
- Simultaneous viewing of skull base and vasculature
- High-speed and creation of volumetric data set
- High resolution of plaque morphology

**72-y/o AA Man**
- C/o:
  - recent onset right-sided numbness & hemiparesis
  - Transient monocular blindness, OS

**CT Angio**

**DWI**

**ADC Map**

Restricted diffusion

Low ADC (acute infarct)
Carotid Intima Media Thickness (IMT) Ultrasonography

- Office-based screening tool for hemodynamically-significant stenosis & plaque formation (soft vs. calcified)
- Indirect assessment of coronary artery atherosclerosis (manufacturers claim of 96% agreement)
- Computed “risk score” for coronary artery atherosclerosis


Management of Carotid Stenosis

Symptomatic High-Grade Stenosis
Symptomatic Moderate Stenosis
Asymptomatic Carotid Stenosis
Symptomatic Low-Grade Stenosis

Carotid Endarterectomy

Clinical Trials

- North American Symptomatic Carotid Endarterectomy Trial (NASCET)
- European Carotid Surgery Trial (ECST)
- Asymptomatic Carotid Atherosclerosis Study (ACAS)
### NASCET 2 Year Results

- Study terminated early due to overwhelming benefit of CEA vs. best medical management for **symptomatic** patients with high-grade stenosis (70-99%)
  - 17% absolute risk reduction
  - 70% relative risk reduction

*NASCET N Engl J Med 1991*

### Symptomatic High-Grade Stenosis

**Surgery vs. Medical Management: NASCET & ECST Results**

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<thead>
<tr>
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<th>% Stroke @ 2 years</th>
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<tbody>
<tr>
<td><strong>NASCET</strong></td>
<td>24</td>
</tr>
<tr>
<td><strong>ECST</strong></td>
<td>17</td>
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</tbody>
</table>

ECST Lancet 1991*

### Asymptomatic Carotid Stenosis:

**ACAS data for > 60% stenosis**

<table>
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<th>% Stroke @ 5 years</th>
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<tr>
<td><strong>ACAS</strong></td>
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*ACAS JAMA 1995*

### Number Needed to Treat to Prevent One Stroke

- **Symptomatic High-Grade Stenosis**
  - NNT = 8
- **Asymptomatic High-Grade Stenosis**
  - NNT = 19

*Biller & Thies American Family Physician 2001*

### 2-Year Stroke Risk

**TMB vs. TIA**

- **TMB 17% (29%)***
- **TIA 44% (96%)***

*Easton & Wilterdink Ann Neurol 1994*
“Front-Loaded” Stroke Risk

• 50% of all strokes occur within 48 hours of resolution of TIA symptoms


Summary of Treatment

• Patients with symptomatic high-grade carotid stenosis should be recommended CEA if there are no other contraindications
• Patients with asymptomatic carotid stenosis may be recommended for CEA (particularly if > 80% stenosis) if surgeon complication rate < 3% and there are no other contraindications
• Mild - moderate stenosis should be managed medically

Kistler & Furie MGH data 2000

Carotid Stenting vs. Endarterectomy

EVA-3S Trial

• French study (20 academic medical centers)
• 527 patients with high grade stenosis (> 60%)
• 1-1 randomization (endarterectomy vs. stenting)
• Premature termination
• Results endarterectomy vs. stenting
  – 30 day mortality: 3.9% vs. 9.6%
  – 30 day disabling stroke: 1.5% vs. 3.4%
  – 6 month incidence of stroke/death: 6.1% vs. 11.7%

Mas JL, et al. NEJM 2006

International Carotid Stenting Study (ICSS)

• 1713 patients with symptomatic high grade stenosis
• 1-1 randomization (endarterectomy vs. stenting)
• Results endarterectomy vs. stenting
  – 120 day mortality/disabling stroke: 3.2% vs. 4.0%
  – 120 day stroke, death, procedural infarct: 5.2% vs. 8.5%

ICSS Study Group. Lancet 2010

Systematic Review of Stenting vs. Endarterectomy

• Stenting associated with higher risk of stroke
• Endarterectomy associated with higher risk of myocardial infarction
• Both stenting and endarterectomy may be viable based on patient selection characteristics

Cardiac Complications with Carotid Stenosis & Cerebral/Ocular Ischemia

- 30% risk of MI x 5 years
  - 18% mortality rate
- 1/2 to 2/3 of all deaths with CAD due to heart disease

Trobe JD. Ophthalmology 1987
Easton & Wilterdink, Ann Neurol 1994

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