Treatment of Carotid Artery Disease

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Objectives

- Stroke Epidemiology and risk factors
- Review indications for carotid revascularization
- Choosing between endarterectomy and stenting: outcomes
- Timing of revascularization

Stroke

- Ranks third as leading cause of death behind heart disease and cancer
- Annual stroke occurrence in the United States around 795,000
- Current American Heart Association data suggest that every 40 seconds someone in the United States is having a stroke

Stroke Epidemiology

- Significant gender and racial differences
- Strokes occur in 55,000 more women than men
- African-Americans have almost twice the stroke risk of whites
- Mexican Americans have also been shown to have an increased incidence of stroke


**Stroke Sequelae**

- 70% of stroke survivors do regain functional independence
- 15% to 30% become permanently disabled
- 3 months after stroke, up to 20% will continue to require long-term care


**Cost**

- In 2007, the total cost of stroke exceeded 40 billion dollars in U.S.
- Projections of future costs of stroke from 2005 to 2050
  - $1.52 trillion for whites
  - $313 billion for Hispanics
  - $379 billion for African-Americans


**Risk Factors**

- Modifiable risk factors for stroke mimic those for cardiovascular disease in general
- Smoking, diabetes and hypertension
- Atrial fibrillation independently increases the risk for stroke by a factor of 5


**Stroke Sequelae**

- Among ischemic strokes at 6 months after the initial insult for patients who are > 65 years old the following deficits exist:
  - 50% had some hemiparesis
  - 30% required some assistance with walking
  - 26% could not perform activities of daily living independently
  - 19% had aphasia
  - 26% were institutionalized

### Risk Factors

- **Age**
- **Gender**
  - women aged 45-84 have a lower risk than men
  - women aged greater than 85 have higher risk than men
- **Race**


### Risk Factors

- **TIA**
- 3% to 10% risk of stroke at 2 days following TIA
- 9% to 17% risk of stroke at 90 days after TIA
- TIA related mortality at 1 year is up to 25%


### Carotid Stenosis

- Stroke risk is directly related to the degree of carotid disease
- 1115 patients from the Asymptomatic Carotid Stenosis and Risk of Stroke (ACSRS) group
- Asymptomatic internal carotid artery stenosis greater than 50% followed for a mean of 37 months
- Linear relationship between stroke and degree of carotid stenosis

Carotid Stenosis

- 296 carotid arteries in 293 patients were followed for an average of 46 months
- Either less than 75% stenosis or greater than 75% stenosis
- Patients with greater than 75% stenosis were found to have higher risk of both TIA and stroke
- Plaque morphology


Carotid Artery Disease

- 20 to 30% of strokes are caused by atherosclerotic carotid artery disease
  - Carotid artery disease increases the risk for stroke:
    - by plaque or clot breaking off from the carotid arteries and blocking a smaller artery in the brain
    - by narrowing of the carotid arteries due to plaque build-up
    - by a blood clot becoming wedged in a carotid artery narrowed by plaque

Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for Asymptomatic Carotid Artery Stenosis. JAMA 1995;273:1421

Treatment Modalities

- Medical therapy
- Carotid endarterectomy
- Carotid artery stenting

Medical Treatment

- Advantages
  - Good option for those with short life expectancy (i.e. benefits of endovascular or surgical therapy does not outweigh the risks)
  - Does not require hospitalization
- Disadvantages
  - Risk of stroke may be higher
  - Risk of hemorrhage
  - Regular lab monitoring
Natural History of Asymptomatic Carotid Disease

- Asymptomatic Carotid Atherosclerosis Study (ACAS)
- European Asymptomatic Carotid Surgery Trial (ACST)
- Overall stroke risk in medically managed asymptomatic patients is about 2% per year

Indications

- Largely independent of method of revascularization
- Symptomatic disease
- Asymptomatic disease
- Vertebral or posterior fossa disease
- External carotid disease
- 3% rule (ACAS 2.3% stroke/death)

Results of Asymptomatic Trials

<table>
<thead>
<tr>
<th></th>
<th>Medical (%)</th>
<th>Surgical (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACAS (ipsilateral stroke risk)</td>
<td>11</td>
<td>5.1</td>
</tr>
<tr>
<td>ACST (any stroke risk)</td>
<td>11.8</td>
<td>6.4</td>
</tr>
</tbody>
</table>

Asymptomatic Disease

- > 60%
- ACAS 5 year follow up
  - 11% stroke risk in medical arm
  - 5.1% stroke risk in surgical arm
  - Lesser benefit in women
- Consider limiting to men, > 80%, contralateral occlusion or high grade stenosis, ulcerated lesions
- No increased benefit with increasing degrees of stenosis
<table>
<thead>
<tr>
<th>Symptomatic Disease</th>
<th>Vertebral Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 70 – 99%</td>
<td>• Carotid reconstruction first if there is concomitant carotid and vertebral disease in the presence of posterior fossa symptoms</td>
</tr>
<tr>
<td>• NASCET 2 year follow up</td>
<td></td>
</tr>
<tr>
<td>– 26% stroke risk in medical arm</td>
<td></td>
</tr>
<tr>
<td>– 9% stroke risk in surgical arm</td>
<td></td>
</tr>
<tr>
<td>– especially benefits males &gt; 75</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptomatic Disease</th>
<th>External Carotid Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 50 – 69%</td>
<td>• Ipsilateral hemispheric TIA (not amaurosis) in the setting of ipsilateral ICA occlusion and contralateral ICA stenosis – contralateral ICA revascularization</td>
</tr>
<tr>
<td>• NASCET 5 year follow up</td>
<td></td>
</tr>
<tr>
<td>– 22.7% stroke risk in medical arm</td>
<td></td>
</tr>
<tr>
<td>– 15.7% stroke risk in surgical arm</td>
<td></td>
</tr>
<tr>
<td>• Ipsilateral amaurosis in the setting of ipsilateral ICA occlusion and ipsilateral ECA stenosis – ipsilateral ECA revascularization</td>
<td></td>
</tr>
<tr>
<td>• Ipsilateral TIA in the setting of patent contralateral carotid system, ipsilateral ICA occlusion, and ipsilateral ECA stenosis – ipsilateral ECA revascularization</td>
<td></td>
</tr>
</tbody>
</table>
### Endarterectomy vs. Stenting

- High risk for endarterectomy – CMS criteria
- Endarterectomy outcomes
- Stenting outcomes

### High Risk for Endarterectomy

- COPD
- Anatomically inaccessible lesion
- Cervical immobility
- Prior neck dissection
- Tracheostomy
- Contralateral cranial nerve injury

### High Risk for Endarterectomy

- NYHA III or IV CHF
- EF < 30%
- Unstable angina
- Recent MI
- Contralateral occlusion
- Recurrent stenosis
- Radiation

### Endarterectomy Outcomes

- Symptomatic
  - 0.6 – 1% death
  - 5 – 7% stroke/death
- Asymptomatic
  - 2.3% stroke/death
Endarterectomy Outcomes

- Cranial nerve injury: 4 – 7%
- Hemorrhage: 3%
- MI: 1 – 2.6%
- Hyperperfusion syndrome/intracranial hemorrhage: 1%
- Restenosis: 3 – 6%
- Infection: 0.3 – 0.8%

Stenting Outcomes

<table>
<thead>
<tr>
<th>Trial</th>
<th>CEA Stroke/death</th>
<th>CAS stroke/death</th>
<th>CEA restenosis</th>
<th>CAS restenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAVATAS 2001</td>
<td>9.9%</td>
<td>10%</td>
<td>10.5%</td>
<td>30.7%</td>
</tr>
<tr>
<td>SAPPHIRE 2004</td>
<td>20.1%</td>
<td>12.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVA-3S 2006</td>
<td>3.9%</td>
<td>9.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPACE 2006</td>
<td>6.3%</td>
<td>6.8%</td>
<td>4.6%</td>
<td>10.7%</td>
</tr>
</tbody>
</table>

Stenting Outcomes

- Randomized trials plagued by
  - bias
  - operator inexperience
  - aberrant CEA outcomes
  - Non-standardized EPD
  - angioplasty without stent

ICSS (n = 1,713)

<table>
<thead>
<tr>
<th></th>
<th>Stroke</th>
<th>Stroke/death/MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>4.1%</td>
<td>5.2%</td>
</tr>
<tr>
<td>CAS</td>
<td>7.7%</td>
<td>8.5%</td>
</tr>
</tbody>
</table>
Carotid Revascularization Endarterectomy versus Stenting Trial (CREST)

- Only NIH sponsored, prospective, randomized, controlled, multi-center trial; normal risk patients
- Long enrollment period
- Rigorous operator training and credentialing
- Best medical therapy regimen used
- Independent neurologist evaluation
- Crossovers discouraged
- New devices now

CREST

- Primary endpoint of any stroke, MI or death during the periprocedural period or ipsilateral stroke for up to 4 years occurred in 7.2% of CAS patients and 6.8% of CEA patients
- Better outcomes were seen with patients aged < 70 who underwent CAS
- Patients aged > 70 did better with CEA

CREST sub analysis of MI and stroke

<table>
<thead>
<tr>
<th></th>
<th>CEA</th>
<th>CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>2.3%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.3%</td>
<td>4.1%</td>
</tr>
</tbody>
</table>

2502 patients
Symptomatic disease ≥50% by angiography, ≥70% by ultrasound, CTA or MRA,
Asymptomatic ≥60% stenosis by angiography, or >70% by ultrasound or >80% by CTA of MRA
Postprocedure analysis demonstrated greater impact on the patients who had suffered a stroke rather than an MI.

Timing of Revascularization

- Emergent
  - immediate thrombosis after CEA or CAS
- Urgent
  - crescendo TIA
  - stroke in evolution

Post-Procedural Stroke

- If patient awakens with neurologic deficit – return to OR
- Neurologic deficit within 24 hours – return to OR
- Neurologic deficit after 24 hours – head CT to rule out hemorrhage first

Timing of Revascularization

- 6 weeks
  - significant fixed deficit
  - large infarct volume
- 4 weeks
  - moderate fixed deficit
  - moderate infarct volume
- < 2 weeks
  - mild fixed deficit or no fixed deficit
  - small or undetectable infarct volume
Carotid Artery Disease

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Stent or Endarterectomy?

High Surgical Risk
Symptomatic high-grade stenosis
  – Stent
Asymptomatic high-grade stenosis
  – Stent (through a trial)
  – Continued Medical Management

Standard Risk Patients

Age < 70
CAS or CEA with equivalent composite stroke/MI/death rates
  – CAS: ↑ stroke risk ↓ MI risk
  – CEA: ↑ MI risk ↓ stroke risk

Standard Risk Patients

Age > 70
CEA (lower periprocedural stroke risk)
Medical management
1. Antiplatelet therapy
2. Statin
3. Management of hypertension
4. Smoking Cessation
National Coverage Determination for PTA (20.7)

- ONLY High-Risk, Symptomatic, >70% stenosis
- Otherwise has to be part of a trial
- Not covered if embolic protection not used
- Not covered if facility not Medicare approved

https://www.cms.gov/MedicareApprovedFacilitie/CASF/list.asp

Cardiac Complications

- MI is responsible for 25% to 50% of perioperative deaths
- Late deaths are due to myocardial infarction
- Surgically correctable CAD was identified in 20%

Preoperative Management

Eagle or Goldman / Detsky index used to determine need for further workup.
Minor predictors do not warrant cardiac testing.
No further workup:
  Recent coronary revascularization within 5 years
  Negative coronary angiography or cardiac stress testing within 2 years.
Anesthetic Choice

- General
  - Need to have monitoring of brain activity
  - Routinely shunt
- Local cervical block
**CN Injury**

**Hypoglossal Nerve**
- Tongue weakness and deviation to the affected side
- Unilateral hypoglossal nerve injury is rarely serious

**Vagus Nerve**
- Recurrent laryngeal branch - Paralysis of the ipsilateral vocal cord
- Hoarseness and loss of an effective cough mechanism
- **Superior Laryngeal Nerve** - loss of tensioning of the ipsilateral vocal cord

**Facial Nerve: Marginal Mandibular Branch**
- Drooping of the ipsilateral lower lip
- Injury is usually due to excessive stretch

Hewitt R M, Stewart G E J Neurol Neurosurg Psychiatry 2011;82:376-377
CN Injury

**Glossopharyngeal and Spinal Accessory Nerves**
- Exceedingly rare
- Glossopharyngeal - mild dysphasia to recurrent aspiration
- Spinal accessory nerve - shoulder droop, scapular winging, and difficulty abducting the shoulder

Hyperperfusion

- Related to loss of cerebral autoregulation
- Usually acute but may present delayed
- Risks:
  - Hypertension and recent contralateral carotid
  - Very tight stenosis preop
  - Headaches and Hypertension
  - May result in cerebral hemorrhage / death

Recurrent Stenosis

- Meta-analysis - 6% to 14%
- 10% within the first year, 3% in the second, and 2% in the third year
- Usually from intimal hyperplasia
- Some regress over time
- Closure with a patch reduces recurrent stenosis
### Follow-Up Schedule for Duplex

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Schedule</th>
</tr>
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<tbody>
<tr>
<td>20-49%</td>
<td>An annual study</td>
</tr>
<tr>
<td>50-79%</td>
<td>Every six months</td>
</tr>
<tr>
<td>80-99%</td>
<td>Every 6 months if surgery not performed</td>
</tr>
</tbody>
</table>

### Filter Wires

- Set wires and catheters
- Cross lesion before protected

### Follow-Up Schedule for Duplex

After carotid endarterectomy

- Ipsilateral/unilateral examinations
  - At six weeks
  - Six months
  - One year

Bilateral study

- Symptoms or previously disease in the contralateral carotid

### Flow Reversal

- Closer to how it is done in CEA
- Can use different wire and catheters
- “Belt and Suspenders” with filter in ICA
Complications

- Hyperperfusion syndrome
  - Headache and hypertension
  - Focal motor seizures and intracerebral hemorrhage
    1.1% incident
- Myocardial infarction
  1 to 4%

Complications

- Renal dysfunction
  - Contrast-induced nephropathy
  - Atheroemboli
  - Hypoperfusion
  - Risk greatest in moderate to severe renal insufficiency and diabetes
### Complications

**Access-related complications**
- Hematoma
- Bleeding
- Pseudoaneurysm
- Atheroembolization
  - Purple discoloration of the toes or gangrene
  - Marbled pattern (livedo reticularis)
  - Extremely Painful

**Carotid restenosis**
- Acute thrombosis in 0.5 to 2%
- Early restenosis due to neointimal hyperplasia, 6% 1 year
- Stent fracture
  - As high as 29 percent
  - Clinical significance unknown as of yet

### Follow Up

- Dual Antiplatelet Therapy
  - Aspirin 325mg for life
  - Plavix 75mg 6 weeks or longer
- Statin
- Smoking Cessation
- BP control

### Carotid Duplex

- Normal criteria probably overestimate degree of stenosis
- Related to decreased compliance from stent
- Those in trials will have defined follow up
- Otherwise similar to CEA for ultrasound