Objectives

- Evaluation of carotid disease:
  - Who do we treat?
  - When do we treat?

- Review interventions:
  - Carotid Endarterectomy
  - Stenting Procedures

- Review relevant Trials and Guidelines:
  - Historical trials
  - CREST Trial
  - Guidelines
Carotid Endarterectomy
## Effect of operative risk on stroke prevention based on ACAS, ECST, and NASCET data.

<table>
<thead>
<tr>
<th>Operative risk (%)</th>
<th>ACAS 60–99%</th>
<th>NASCET 50–69%</th>
<th>ECST 80–99%</th>
<th>NASCET 70–99%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ARR at 5 years</td>
<td>NNT at 5 years</td>
<td>ARR at 3 years</td>
<td>NNT at 3 years</td>
</tr>
<tr>
<td>0</td>
<td>8.2%</td>
<td>12</td>
<td>13%</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>6.2%</td>
<td>16</td>
<td>11%</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>4.2%</td>
<td>24</td>
<td>9%</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>2.2%</td>
<td>45</td>
<td>7%</td>
<td>14</td>
</tr>
<tr>
<td>8</td>
<td>0.2%</td>
<td>500</td>
<td>5%</td>
<td>20</td>
</tr>
<tr>
<td>10</td>
<td>n/a</td>
<td>n/a</td>
<td>3%</td>
<td>33</td>
</tr>
<tr>
<td>Trial risk</td>
<td>2.3%</td>
<td>6.5%</td>
<td>4.8%</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

Carotid Stenting
Carotid Stents

Xact/CLOSED
Precise/OPEN
Acculink/OPEN
Cristallo Ideale/Hybrid
Embolic Protection

- Distal Balloons
- Filterwires:
  - Angioguard (Cordis)
  - Accunet (Abbott)
  - Emboshield (Abbott)
  - Spyder (EV3)
- Flow reversal Systems
  - Gore
  - Mo.MA (Medtronic/Invatec)
CAS Surveillance Strategy

- One month
- At 6 months
- At 12 months
- Yearly thereafter
Trials and management recommendations for carotid occlusive disease.
History of Carotid Surgery

- 1798 carotid artery ligation (Abernathy)
- 1856 Relation to neurologic symptoms (Savory)
- 1927 cerebral angiography (Moniz)
- 1951 L ECA to distal ICA bypass with resection of proximal ICA. (Carrea)
- 1954 carotid resection with primary anastomosis (Eastcott and Robb)
- 1953 carotid endarterectomy (DeBakey)
Rise, Fall, and Rise of Carotid Endarterectomy

**Table 1. Net Benefits of Carotid Endarterectomy Demonstrated in Randomized, Controlled Trials Involving More Than 500 Patients.**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Degree of Stenosis</th>
<th>Recent Symptomatic</th>
<th>Absolute Reduction in Risk</th>
<th>Rate of Surgical Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>Yes</td>
<td>% PERCENT</td>
<td>P VALUE</td>
</tr>
<tr>
<td>NASCET4</td>
<td>&gt;70</td>
<td>Yes</td>
<td>16.5 at 2yr</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ECST8</td>
<td>&gt;60</td>
<td>Yes</td>
<td>11.6 at 3yr</td>
<td>0.001</td>
</tr>
<tr>
<td>NASCET6</td>
<td>15–69</td>
<td>Yes</td>
<td>10.1 at 5yr</td>
<td>0.005</td>
</tr>
<tr>
<td>NASCET6</td>
<td>&lt;50</td>
<td>Yes</td>
<td>0.8 at 5yr</td>
<td>0.97</td>
</tr>
<tr>
<td>ECST9</td>
<td>&lt;40</td>
<td>Yes</td>
<td>Surgery group worse at 3yr</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ACAS5</td>
<td>&gt;60</td>
<td>No</td>
<td>6.3 at 5yr</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*Figure 1. Numbers of Carotid Endarterectomies Performed in the United States, 1980–1996.*

Data for 1980–1989 were obtained from Hsieh et al.,1 data for 1990–1995 were obtained from the National Center for Health Statistics,2 and data for 1996 were obtained from the National Center for Health Statistics (Graves E: personal communication).
1662 Pts, 39 centers: Asymptomatic Carotid Stenosis > 60%
Best Med vs. Best Med plus CEA.
Outcomes: ipsilateral CVA or any CVA or death

- Over half periop events related to angiogram
- Conclusion: CEA for ASX stenosis > 60% justified
- Recurrent stenosis (≥60%) at 5 years: 12%

Asymptomatic Carotid Stenosis: ACAS Trial
Symptomatic Carotid Stenosis: NASCET Trial

659 Pts, 50 centers: TIA, Afx, Non-Disabling CVA within 6 months:

- 70-99%: Ipsi CVA @ 2 yr (p<0.001) - Med 26%, CEA 9%
- 70-99%: Maj/Fatal CVA @ 2 yr (p<0.001) - Med 13%, CEA 3%
- 50-69%: Ipsi CVA @ 5 yrs (p<0.045) - Med 22%, CEA 16%
- 30-49%: Ipsi CVA @ 5 yrs (NS) - Med 19%, CEA 15%

Perioperative stroke/death rate = 5.8%
Carotid Stenting Trials

- MAVErIc: III Evaluation of the Medtronic AVE Self-Expanding Carotid Stent System With Distal Protection In the Treatment of Carotid Stenosis
- PASCAL Performance And Safety of the Medtronic AVE Self-Expandable Stent in Treatment of Carotid Artery Lesions
- ARCHeR ACCULINK for Revascularization of Carotids in High-Risk Patients
- BEACH Boston Scientific EPI-A Carotid Stenting Trial for High Risk Surgical Patients
- CAPTURE 2 Registry Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events
- CAPTURE Carotid RX ACCULINK/ACCUNET Post-Approval Trial to Uncover Unanticipated or Rare Events
- CREST: Carotid Revascularization Endarterectomy vs Stent Trial
- EVA-3S Endarterectomy versus Angioplasty in Patients with Severe Symptomatic Carotid Stenosis
- EXACT Emboshield and Xact Post Approval Carotid Stent Trial
- ICSS (CAVATAS-2) International Carotid Stenting Study
- SAPPHIRE Stenting and Angioplasty with Protection in Patients and High Risk for Endarterectomy
- SHELTER Stenting of High risk patients Extracranial Lesions Trial with Emboli Removal
- SPACE Stent-protected Percutaneous Angioplasty of the Carotid vs. Endarterectomy
CREST Study Design

• Prospective, multicenter, randomized, controlled trial with blinded endpoint adjudication.

• Comparing CEA and CAS in participants with symptomatic and asymptomatic stenosis

• 108 US and 9 Canadian sites

• Team included neurologist, interventionalist, surgeon, and research coordinator at each center.

• NEJM May, 2010.
<table>
<thead>
<tr>
<th></th>
<th>CAS  (n=1262)</th>
<th>CEA  (n=1240)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>69</td>
<td>69</td>
</tr>
<tr>
<td><strong>Female - %</strong></td>
<td>36</td>
<td>34</td>
</tr>
<tr>
<td><strong>Asymptomatic - %</strong></td>
<td>47</td>
<td>47</td>
</tr>
<tr>
<td><strong>Hypertension - %</strong></td>
<td>86</td>
<td>86</td>
</tr>
<tr>
<td><strong>Diabetes - %</strong></td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td><strong>Dyslipidemia - %</strong></td>
<td>82</td>
<td>85</td>
</tr>
<tr>
<td><strong>Current smoker - %</strong></td>
<td>26</td>
<td>26</td>
</tr>
</tbody>
</table>
CREST Primary Endpoint

- Peri-procedural (a composite of):
  - any Clinical Stroke
  - Myocardial infarction
  - Death

- Post-procedural
  - Ipsilateral stroke up to 4 years
CREST: Stroke

- An acute neurological ischemic event of at least 24 hours duration with focal signs and symptoms.
- Adjudicated by at least two neurologists blinded to treatment.
CREST: Myocardial Infarction

• Combination:
  • Elevation of cardiac enzymes (CK-MB or troponin) to a value 2 or more times the individual clinical center's laboratory upper limit of normal. **Plus**
  • Chest pain or equivalent symptoms consistent with myocardial ischemia, **or**, ECG evidence of ischemia including new ST segment depression or elevation > 1mm in 2 or more contiguous leads
  • Not enzyme-only
  • Adjudicated by two cardiologists blinded to treatment
Primary Endpoint: peri-procedural
(any death, stroke, or MI within peri-procedural period)

<table>
<thead>
<tr>
<th>CAS vs. CEA</th>
<th>Hazard Ratio, 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.2% vs. 4.5%</td>
<td>HR = 1.18; 95% CI: 0.82-1.68</td>
<td>0.38</td>
</tr>
</tbody>
</table>
### Peri-procedural Stroke and MI

<table>
<thead>
<tr>
<th>Condition</th>
<th>CAS vs. CEA</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>4.1 vs. 2.3%</td>
<td>HR = 1.79; 95% CI: 1.14-2.82</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>1.1 vs. 2.3%</td>
<td>HR = 0.50; 95% CI: 0.26-0.94</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>
# Peri-procedural Stroke

<table>
<thead>
<tr>
<th>All Stroke</th>
<th>CAS vs. CEA</th>
<th>Hazard Ratio 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Stroke</td>
<td>4.1 vs. 2.3%</td>
<td>HR = 1.79; 95% CI: 1.14-2.82</td>
<td>0.01</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0.9 vs. 0.6%</td>
<td>HR = 1.35; 95% CI: 0.54-3.36</td>
<td>0.52</td>
</tr>
</tbody>
</table>

“The quality of life analysis among survivors at one year in our trial indicate that stroke had a greater adverse effect on a broad range of health-status domains than did myocardial infarction.”
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Hazard Ratio, 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS vs. CEA</td>
<td>HR = 0.94; 95% CI: 0.50-1.76</td>
<td>0.85</td>
</tr>
</tbody>
</table>
CREST Conclusions

- CEA and CAS have similar net outcomes though the individual risks vary, lower stroke with CEA and lower MI with CAS.
Multispecialty Guidelines: 2011

- **Recommendations for Selection of Patients for Carotid Revascularization** *(CAS and CEA) Class I*

- **CAS is indicated as an ALTERNATIVE to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by more than 70% as documented by noninvasive imaging or more than 50% as documented by catheter angiography and the anticipated rate of periprocedural stroke or mortality is less than 6% (Level of Evidence: B).*
Multispecialty Guidelines: 2011

- **Recommendations for Selection of Patients for Carotid Revascularization** (CAS and CEA)

  **Class I**

  - Selection of asymptomatic patients for carotid revascularization should be guided by an assessment of co-morbid conditions, life expectancy, and other individual factors and should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences. (Level of Evidence:C)
• **Recommendations for Selection of Patients for Carotid Revascularization*** (CAS and CEA)

**Class IIa**

• *CEA in asymptomatic patients who have more than 70% stenosis of the internal carotid artery if the risk of perioperative stroke, MI, and death is low. (Level of Evidence: A)*

• *Choose CEA over CAS in older patients, particularly when arterial pathology and anatomy is unfavorable for endovascular intervention. (Level of Evidence: B)*

• *Choose CAS over CEA in patients with unfavorable neck anatomy. (Level of Evidence: B)*
Recommendations for Selection of Patients for Carotid Revascularization (CAS and CEA)

Class IIb

- Prophylactic CAS might be considered in highly selected patients with asymptomatic carotid stenosis (minimum 60% by angiography, 70% by validated Doppler ultrasound), but its effectiveness compared with medical therapy alone in this situation is not well established (Level of Evidence: B).
“The term “Alternative” may easily be misinterpreted as “equivalent” to justify the widespread use of CAS”

August 2011

SVS invited response:

– agree that CAS is not equivalent to CEA in symptomatic patients.
– Endorse the multispecialty guidelines as a high quality document on all of cerebrovascular disease.
– believes the document should not be held for one word in the entire document.
Updated SVS Guidelines: Sept. 2011

- Updates the SVS 2008 Guidelines, not the multispecialty one.
- It is in concordance with the multispecialty document except for minor differences in the recommendations for either CAS or CEA.
- Differences are mostly due to emphasis on stroke and death as endpoints and not MI.
- They took into consideration another 20 publications that appeared between the two sets of guidelines.

Current SVS Position

- The SVS endorses both sets of Guidelines
- For CEA vs. CAS choice it supports the terminology in the updated SVS guidelines published in the JVS in September of 2011.
• In the majority of patients with carotid stenosis who are candidates for intervention, **CEA is preferred to CAS** for reduction of all cause stroke and periprocedural mortality (Grade 1, level of evidence B).

• **Asymptomatic** patients with > 60% diameter stenosis, should be considered for **CEA** if the patient has a 3- to 5-year life expectancy and perioperative stroke/death rates can be equal to or < 3% (Grade 1, level of evidence A).
• **CEA** is preferred over **CAS** in patients > 70 years of age, with long (15 mm) lesions, preocclusive stenosis, or lipid-rich plaques that can be completely removed safely by a cervical incision in patients who have a virgin, nonradiated neck (Grade 1, level of evidence A).

• **CAS** is preferred over **CEA** in **symptomatic** patients and prior ipsilateral operation, tracheal stoma, and other anatomic high risk situations (Grade 2, level of evidence B).
• **CAS** is preferred over CEA in symptomatic patients and severe uncorrectable CAD, CHF, or COPD (Grade 2, level of evidence C).

• **There are insufficient data to recommend CAS as primary therapy for asymptomatic patients.** In properly selected patients, CAS in the hands of experienced interventionalists and combined stroke and death rate below 3% can be used (Grade 2, level of evidence B).
SURGICAL MANAGEMENT

Patient Selection

Asymptomatic

• 70 to 99% in surgically fit patient
• Consider in >60% range if unfavorable plaque.

Symptomatic

• 50% or higher
• Implies ideal surgical results and optimum surgical risk.

Recurrent Disease /High Risk

• If symptomatic
• Stent v. Surgical Reconstruction
Summary

• In appropriately selected patients, CEA remains a safe and effective treatment of cervical carotid occlusive disease.

• CAS is an effective therapy in selected patients, and with technical advances and innovation in stent design and embolic protection, hopefully patient outcomes will improve.

• Must be aware of potential long term effects of silent embolic events.