CEA, CAS and Best Medical Therapy
Alone: Which Treatment for Which Patient

R. Clement Darling, III, MD
Professor of Surgery
Chief, Division of Vascular Surgery
Director, Institute For Vascular Health and Disease
Albany, NY

Disclosures
None Pertaining to this Lecture

The Empirical Approach
NASCET 1991
ECST 1991
CASANOVA 1991
VA-Study 1993
ACAS 1995
EACST 2004
SAPPHIRE 2004
CREST

PROSPECTIVE RANDOMIZED STUDIES

<table>
<thead>
<tr>
<th>STUDY</th>
<th>NASCET</th>
<th>ECST</th>
<th>VA SYMPTOMATIC</th>
<th>ACAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEVERITY OF STENOSIS</td>
<td>70-99%</td>
<td>70-99%</td>
<td>70-99%</td>
<td>60-99%</td>
</tr>
<tr>
<td>FOLLOW-UP</td>
<td>MAX</td>
<td>20 MO</td>
<td>37.1%</td>
<td>21 MO</td>
</tr>
<tr>
<td></td>
<td>MEAN</td>
<td>18 MO</td>
<td>3.1%</td>
<td>12 MO</td>
</tr>
<tr>
<td>HOSPITAL MORTALITY</td>
<td>0.6%</td>
<td>0.6%</td>
<td>0.1%</td>
<td>-</td>
</tr>
<tr>
<td>STROKE RISK</td>
<td>SURG vs. MED</td>
<td>SURG vs. MED</td>
<td>SURG vs. MED</td>
<td>SURG vs. MED</td>
</tr>
<tr>
<td>LATE IPSILATERAL</td>
<td>9.0% vs. 26%</td>
<td>12% vs. 22%</td>
<td>7.9% vs. 24%</td>
<td>5.1% vs. 11%</td>
</tr>
<tr>
<td>P-VALUE</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
<td>&lt;0.004</td>
</tr>
</tbody>
</table>

NASCET Results 1991
Two year cumulative risk of ipsilateral stroke
- Medical group (331 patients): 26%
- Surgical group (326 patients): 9%*
*Includes perioperative morbidity/mortality of 5.8%

Two year cumulative risk of major or fatal stroke
- Medical group (331 patients): 13.1%
- Surgical group (326 patients): 2.5%**
**Includes perioperative morbidity/mortality of 2.1%

What Is “Asymptomatic” We Need To Know More
Unstable Plaques
Silent Infarcts
Medically Untreated Progressing Lesions
Asymptomatic Carotid Stenosis and Risk of Stroke

**ACSRS**

**HEMISPHERIC ISCHEMIC EVENTS**

**Patients:** 1,115
50 – 99% Stenosis
**F/U:** 6-84 (mean, 37) mos.

---

**Embolic Signals and Silent Cerebrovascular Events:**

Are They Really “Asymptomatic”

**Patients:** 467, > 70% Stenosis
**Centers:** 26
**TCD:** 0, 6, 12, 18 Months
**(+ TCD):** 77 (13%) (ACSRS)

---

**St. Georges U London, UK**

---

**CAROTID ARTERY DISEASE**

**Improvements in Medical Management**

- Antiplatelet Therapy
- **STATINS**
- ? Beta-Blockers

---

**RISK OF STROKE**

**Echolucent Plaque:**

HR 6.43, 95% CI 1.36-30.44, p= 0.019

**Both Echolucent Plaque & (+) TCD:**

HR 10.61, 95% CI 2.98-37.82, p= 0.0003

---

**Silent Infarcts & Cerebrovascular Events**

**Patients:** 821
- Carotid Duplex Scans
- **CT q 6 Mos x 8 Yrs**
**F/U:** 6 mos – 8 yrs (mean, 44.6 mos)

**STROKE-FREE RATE:**

---

**J Vasc Surg, 2009**

---

**Neurology, 2011**

---

**ACSRS**

**Patients:** 821
- Carotid Duplex Scans
- **CT q 6 Mos x 8 Yrs**
**F/U:** 6 mos – 8 yrs (mean, 44.6 mos)

**STROKE-FREE RATE:**

---

**Silent Infarcts:** 146 (18%)
**Ipsilateral Ischemic Events:**

- Amaurosis Fugax: 16
- TIs: 38
- CVAs: 47

---

**Ultrasound plaque echolucency and embolic signals predict stroke in asymptomatic carotid stenosis**

**Patients:** 435, (> 70% Stenosis)
- Echolucent Plaque: 164/435 (38%)
- (+) TCD: 23/428 (17%)
- Both: 27/428 (6.3%)

**RISK OF STROKE**

**Echolucent Plaque:** HR 6.43, 95% CI 1.36-30.44, p= 0.019

**Both Echolucent Plaque & (+) TCD:**

HR 10.61, 95% CI 2.98-37.82, p= 0.0003

---

**St. Georges U London, UK**

---

**Neurology, 2011**

---

**J Vasc Surg, 2009**

---

**Asymptomatic Carotid Artery Stenosis; When and Who To Treat**

- Risk Factor Modification
- Identification of Plaque
- Treatment/Stabilization of Plaque
- Ideal Treatment for Each Patient Should be individualized:
  - Medical Therapy
  - Endarterectomy
  - Stenting

---

**Asymptomatic Carotid Artery Stenosis;**

**When and Who To Treat**
**ASYMPTOMATIC CAROTID DISEASE**

**Improvements in Medical Management**

- Medical Therapy 3-8 times more cost effective than surgery (>50% stenosis)
- With BMT Stabilization of plaque and less progression
  Abbott et al Stroke 2005;36:1128-33

**BMT failed to prevent plaque prevention in 45% of patients**
  Conrad JVS 2013;58:128-138

**ACAS and Women**

<table>
<thead>
<tr>
<th></th>
<th>30 Day Event Rate</th>
<th>Observed 2.7 years</th>
<th>Estimated 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery (281 pts)</td>
<td>10 (3.6%)</td>
<td>15 (5.3%)</td>
<td>20 (7.3%)</td>
</tr>
<tr>
<td>Medical (287 pts)</td>
<td>0 (0%)</td>
<td>14 (4.9%)</td>
<td>25 (8.5%)</td>
</tr>
</tbody>
</table>

**Is It Statins or Are There Other Factors?**

- Statins
- Technique
- Anti Platelet Agents
- Plaque Morphology
- All Of The Above


**30-DAY RESULTS**

<table>
<thead>
<tr>
<th></th>
<th><strong>STATINS</strong> (n=657)</th>
<th><strong>NO STATINS</strong> (n=909)</th>
<th><em>p</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STROKE</strong></td>
<td>1.2%</td>
<td>4.5%</td>
<td>.002</td>
</tr>
<tr>
<td><strong>MORTALITY</strong></td>
<td>0.3%</td>
<td>2.1%</td>
<td>.002</td>
</tr>
<tr>
<td><strong>M.I.</strong></td>
<td>1.2%</td>
<td>2.1%</td>
<td>.191</td>
</tr>
</tbody>
</table>

- Reduced the Odds of Stroke: 3-Fold *(p= .019)*
- Reduced the Odds of Death: 5-Fold *(p=.049)*
The CREST PMA analysis shows *very low event rates* for both Asymptomatic CAS and CEA, lower than historical rates and within the AHA guidelines for 30-day event rates.

Management of Patients With Atherosclerotic Disease of the Carotid Arteries

**Primary Composite Endpoint for Asymptomatic Status**

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5.3%</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

Primary Endpoint= Death/Stroke/MI

**Recommendations for Selection of Asymptomatic Patients for Carotid Revascularization**

1. **Chao Hu**
2. It is reasonable to perform 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. 74 to 75.599:461–465 (Level of Evidence: A)
3. It is reasonable to choose CAS over CEA when revascularization is indicated in older patients, particularly when artery patency is unfavorable for endovascular intervention. 500:364–365 (Level of Evidence: III)
4. It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial surgery. 500:375 (Level of Evidence: III)

**Similar Freedom from Ipsilateral Stroke Day 31 to 4 Years CREST Data**

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>99.7%</td>
<td>99.7%</td>
</tr>
</tbody>
</table>

HR: 1.09 (95% CI 1.0-1.69)
Log Rank P-value: 0.89

**Results for ECA on Asymptomatic Patients**

<table>
<thead>
<tr>
<th></th>
<th>MALES</th>
<th>FEMALES</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>4856</td>
<td>3740</td>
</tr>
<tr>
<td>STROKE</td>
<td>0.44%</td>
<td>0.52%</td>
</tr>
<tr>
<td>Non-Fatal MI</td>
<td>0.20%</td>
<td>0.33%</td>
</tr>
<tr>
<td>DEATH</td>
<td>0.51%</td>
<td>0.52%</td>
</tr>
</tbody>
</table>

NO SIGNIFICANT DIFFERENCE
CEA in MARYLAND: 1994-2003
23,237 PATIENTS: 33-99 (Mean, 71) Yrs

85% Asymptomatic
47 Hospitals

Strokes 169 (0.73%)
Deaths 125 (0.54)

Stroke/Deaths 294 (1.3%)  JVS 2006

Which Procedure To Choose for CAS?

Do Trials Need to be Revisited? CREST II

Arguments for.....
“Best medical therapy” now even better!
(statins, Plavix™, BP control)
New Technology
Better Techniques

1) Relative RRs of 25% @ 5 years = ARR of 1.2.5% in compliant patients
2) Effect of CEA immediate
3) NNT for Plavix to prevent in Caprie Trial = 111 & NNT for simvastatin = 71
4) NNT in NASCET for 75 yr ♂ with 70-99% stenosis = 2

WHAT DOES THIS ALL MEAN?

THANK YOU!