Carotid Stenosis and Stroke
5th Annual Upstate Stroke Symposium:
A Comprehensive Review of Stroke Care

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Disclosures

• None
Carotid Disease

Looking at the Numbers

- Currently 500,000 new strokes annually
- 3rd Leading cause of Death in North America
- Cost = $ 30 billion / year
- Population of USA = 294,451,985
- # of Baby boomers = 76,000,000 (60 yo in 2006)
- # of Baby boomers with Carotid dz = 5,776,000 (7.6%*)

* AVA 2004 Carotid Screening Data
Carotid Stenosis and Stroke

Prevalence of Stroke by Age and Sex: NHANES 1999-2002

% of Population

Source: CDC/NCHS and NHLBI
Carotid stenosis and stroke risk?

Diagnosis of Carotid Disease

• A bruit does not automatically indicate a significant carotid stenosis nor does absence of a bruit rule out carotid stenosis

• Only 20% with a bruit will have > 60% stenosis
Asymptomatic Carotid Artery Stenosis
Risk of Stroke

• General pop. has 3-9% rate of ICA stenosis
• 20 – 35% of pts w/ PVD have >50% stenosis
• ACAS- 11% - 5 year stroke risk with >60%
• Of patients suffering CVA >50% will not have preceding TIA’s
Stroke Risk for >50% Asymptomatic Carotid Stenosis with Best Medical Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Annualized Any Stroke</th>
<th>Annualized Ipsilateral Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACAS</td>
<td>1995</td>
<td>3.5%</td>
<td>2.2%</td>
</tr>
<tr>
<td>ACST</td>
<td>2004</td>
<td>2.4%</td>
<td>1.1%</td>
</tr>
<tr>
<td>ACRSR</td>
<td>2005</td>
<td>2.1%</td>
<td>1.7%</td>
</tr>
<tr>
<td>ASED</td>
<td>2005</td>
<td>2.2%</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

Best Medical Therapy:
Smoking cessation, control of lipids, hypertension, diabetes, and use of antiplatelet therapy
Carotid Stenosis
Symptoms and Signs

- **TIA** = a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than 1 hour and without evidence of acute cerebral infarction.
  - **Amaurosis fugax** = transient monocular blindness, lasts around one minute, curtain comes down

- **CVA** = **STROKE** = term used when the neurologic ischemic symptoms begin abruptly and persist > 24 hours, as a result of either inadequate blood flow (ischemic stroke) or hemorrhage into brain tissue or surrounding subarachnoid space.
Symptomatic Carotid Artery Stenosis & Risk of Stroke

- Framingham data - 5yr recurrent CVA rate = 42% (9% per yr)
- NASCET – 2 year stroke rate w/ >70% ICA stenosis = 26%
- Symptomatic pts warrant imaging
Imaging and Diagnostics

- Duplex Ultrasound

- No radiation

- Inexpensive

- “Risk free”
• Duplex Ultrasound
  – For stenosis >50% US has a sensitivity of 91% and a specificity of 93%
  – PPV of 90% and accuracy of 92%
  – For stenosis >60% US has a reported sensitivity of 100% and specificity of 98% and PPV 99%
## GHS Carotid Duplex Criteria

### Modified S.R.U. Consensus Criteria

Stenosis criteria derived similar to NASCET method

<table>
<thead>
<tr>
<th>Degree of Stenosis %</th>
<th>Primary Parameters</th>
<th>Additional Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICA PSV cm/sec</td>
<td>% Plaque Estimate, Gray Scale and Color</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt; 140</td>
<td>None</td>
</tr>
<tr>
<td>&lt; 50</td>
<td>&lt; 140</td>
<td>&lt; 50 Mild to moderate plaque</td>
</tr>
<tr>
<td>50 - 69</td>
<td>140 - 230</td>
<td>&gt; 50 Moderate to severe plaque</td>
</tr>
<tr>
<td>70 - 99</td>
<td>&gt; 230</td>
<td>&gt; 50 Severe plaque</td>
</tr>
<tr>
<td>Occlusion</td>
<td>Undetectable</td>
<td>Visible, no detectable Lumen</td>
</tr>
</tbody>
</table>
Imaging and Diagnostics

- MRA

- No radiation

- Processing required

- Can over call
Imaging and Diagnostics

• CT Angiography
• Noninvasive
• Provides 3D info
• Readily available
CTA Bloom Artifact
Imaging and Diagnostics

• Carotid Angiography

• “Gold Standard”

• Excellent resolution

• Rarely performed today
Evaluation of Symptomatic Patients

- CT
- Duplex
- MRI
- CTA
CEA vs CAS
## Carotid Endarterectomy Trials

<table>
<thead>
<tr>
<th>Symptomatic</th>
<th>Asymptomatic</th>
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<tbody>
<tr>
<td>NASCET</td>
<td>CASANOVA</td>
</tr>
<tr>
<td>ECST</td>
<td>ACAS</td>
</tr>
<tr>
<td>ACST</td>
<td>ACST</td>
</tr>
<tr>
<td>VA Cooperative</td>
<td></td>
</tr>
</tbody>
</table>
Trials

- Asymptomatic
  - ACAS
    - 1662 patients randomized over 6 years – reported in 1995
    - First major study looking at CEA in asymptomatic
    - Asymptomatic with >60% stenosis by angiography
    - Aggregate risk of ipsilateral stroke over 5 years and perioperative stroke or death was 5.1% in CEA group versus 11% in medical management
    - Relative risk reduction of 53% with CEA
Trials

• Asymptomatic
  – ACST – Asymptomatic Carotid Surgery Trial
    • Lancet May 2004 – reported 5 year results
    • Compared immediate CEA (60-99% stenosis) v MM in asymptomatic
    • 5 year stroke/death risk was 6.4% v 11.8% (CEA v MM)
    • 46% relative risk reduction
    • 3.5% v 6.1% for fatal or debilitating stroke
    • Men over 75 had 8.2% RR reduction at 5 years
    • Women had 4.1% RR reduction at 5 years
Trials

• Symptomatic
  – NASCET
    • 2885 randomized over 9 years
    • Ipsilateral stenosis 70-99%
    • CEA + Medical Management (MM) reduced stroke from 26% to 9% compared to MM alone
    • Fatal stroke reduced from 13.1% to 2.5%
    • Excluded: heart failure, recent MI, debilitating CVA
    • Surgical morbidity has to be less than 6% and the surgeon must perform 3 or more CEA every 2 yrs
Trials

- Symptomatic
  - ECST – European Carotid Surgery Trial
    - Enrolled 3024 patients with a stroke or TIA within the prior 6 months
    - Patients were randomized into CEA or MM (regardless of degree of disease)
    - Risk of death or major stroke did not differ
    - ICA stenosis of 80% or more, there was a lower event rate with CEA v. MM (14.9% v. 26.5%)
Carotid Artery Stenting Trials
Carotid Stenting Trials

• SAPPHIRE Trial
  – Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy
  – Published October 7, 2004 NEJM
  – Multi-center trial that randomized patients with asymptomatic >80% lesions or symptomatic with >50% lesions
  – Primary End Points = stroke, death, MI
Carotid Stenting Trials

• SAPPHIRE Trial
  – Primary End Points
    • Stents – 12.2%
    • CEA – 20.1%
    • $p = 0.004$
Carotid Stenting Trials

- SAPPHIRE Trial
  - Conclusion: “carotid stenting with the use of an emboli-protection device is not inferior to carotid endarterectomy”
Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis

Thomas G. Brott, M.D., Robert W. Hobson, II, M.D.*, George Howard, Dr.P.H., Gary S. Roubin, M.D., Ph.D., Wayne M. Clark, M.D., William Brooks, M.D., Anare Medley, M.D., Michael D. Hill, M.D., Pierre P. Leimgruber, M.D., Alice J. Sheftell, Ph.D., Virginia J. Howard, Ph.D., Wesley S. Moore, M.D., Jennifer H. Voels, Ph.D., L. Nelson Hopkins, M.D., Donald E. Cutlip, M.D., David J. Cohen, M.D., Jeffrey J. Popma, M.D., Robert D. Ferguson, M.D., Stanley N. Cohen, M.D., Joseph L. Blackshear, M.D., Frank L. Silber, M.D., J.P. Mohr, M.D., Brajesh K. Lal, M.D., and James F. Meschia, M.D., for the CREST Investigators†

ABSTRACT

BACKGROUND
Carotid-artery stenting and carotid endarterectomy are both options for treating carotid-artery stenosis, an important cause of stroke.

METHODS
We randomly assigned patients with symptomatic or asymptomatic carotid stenosis to undergo carotid-artery stenting or carotid endarterectomy. The primary composite end point was stroke, myocardial infarction, or death from any cause during the periprocedural period or any ipsilateral stroke within 4 years after randomization.

RESULTS
For 2502 patients over a median follow-up period of 2.5 years, there was no significant difference in the estimated 4-year rates of the primary end point between the stenting group and the endarterectomy group (7.2% and 6.6%, respectively; hazard ratio with stenting, 1.11; 95% confidence interval, 0.81 to 1.51; P = 0.51). There was no differential treatment effect with regard to the primary end point according to symptomatic status (P = 0.84) or sex (P = 0.34). The 4-year rate of stroke or death was 6.4% with stenting and 6.7% with endarterectomy (hazard ratio, 1.50; P = 0.03); the rates among symptomatic patients were 8.0% and 6.4% (hazard ratio, 1.37; P = 0.14), and the rates among asymptomatic patients were 4.5% and 2.7% (hazard ratio, 1.65; P = 0.07), respectively. Periprocedural rates of individual components of the end point differed between the stenting group and the endarterectomy group: for death (0.7% vs. 0.3%, P = 0.18), for stroke (4.1% vs. 2.3%, P = 0.02), and for myocardial infarction (1.1% vs. 2.3%, P = 0.03). After this period, the incidences of ipsilateral stroke with stenting and with endarterectomy were similarly low (2.0% and 2.4%, respectively; P = 0.85).

CONCLUSIONS
Among patients with symptomatic or asymptomatic carotid stenosis, the risk of the composite primary outcome of stroke, myocardial infarction, or death did not differ significantly in the group undergoing carotid-artery stenting and the group undergoing carotid endarterectomy. During the periprocedural period, there was a higher risk of stroke with stenting and a higher risk of myocardial infarction with endarterectomy. (ClinicalTrials.gov number, NCT00004732)

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*Deceased.
†The Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) Investigators and committee members are listed in the appendix.
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<tr>
<th></th>
<th>CAS (%)</th>
<th>CEA (%)</th>
<th>HR</th>
<th>95% CI</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Procedural CVA</td>
<td>4.1</td>
<td>2.3</td>
<td>1.79</td>
<td>1.14-2.82</td>
<td>0.01</td>
</tr>
<tr>
<td>Major CVA</td>
<td>0.9</td>
<td>0.7</td>
<td>1.35</td>
<td>0.54-3.36</td>
<td>0.52</td>
</tr>
<tr>
<td>No Significant Difference in CEA vs CAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>CNI</td>
<td>0.3</td>
<td>4.8</td>
<td>0.07</td>
<td>0.02-0.18</td>
<td>&lt;0.0001</td>
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<tr>
<td>Late CVA</td>
<td>2.0</td>
<td>2.4</td>
<td>0.94</td>
<td>0.50-1.76</td>
<td>0.85</td>
</tr>
<tr>
<td>Combined CVA &amp; CNI</td>
<td>4.4</td>
<td>7.1</td>
<td></td>
<td></td>
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</tr>
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</table>

Roadster Trial
Roadster Set-up
### High Surgical Risk Demographics

<table>
<thead>
<tr>
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<th>Roadster Results n=141 pts</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>72.9 (40-90)</td>
</tr>
<tr>
<td>Age &gt; 80</td>
<td>28%</td>
</tr>
<tr>
<td>Female</td>
<td>35%</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>26%</td>
</tr>
<tr>
<td>Local Anesthesia</td>
<td>53%</td>
</tr>
<tr>
<td>Reverse flow time</td>
<td>10 minutes</td>
</tr>
<tr>
<td>Procedural success</td>
<td>96%</td>
</tr>
</tbody>
</table>

### Results

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/D/MI</td>
<td>5</td>
<td>3.5%</td>
</tr>
<tr>
<td>Major DVA</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Minor CVA</td>
<td>2</td>
<td>1.4%</td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
<td>1.4%</td>
</tr>
<tr>
<td>MI</td>
<td>1</td>
<td>0.7%</td>
</tr>
<tr>
<td>CVA &amp; death</td>
<td>4</td>
<td>2.8%</td>
</tr>
<tr>
<td>Cranial NI</td>
<td>1</td>
<td>0.7%</td>
</tr>
<tr>
<td>CNI @ 6 m</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Safer CAS

Procedural Stroke

Archer: 8.3
Sapphire: 6.9
SeCurity: 7.5
Capture: 6.1
Exact: 4.1
Capture2: 3.5
Choice: 3.9
Protect: 2.3
Roadster: 1.4
Safer Surgery

Procedural Stroke

- VA Trial: 4.2
- ACST: 2.8
- ACAS: 2.3
- CREST Surg: 1.4
Carotid Artery Stenting

- CMS currently only reimburses CAS for
  - “High Risk” Symptomatic patients
  - Asymptomatic patients enrolled in clinical trials
CREST-2
Guiding Treatments for Asymptomatic Carotid Disease

Examining stenting and endarterectomy in the context of intensive medical management.

Figure 1. CREST-2 parallel study design. Endpoint = stroke and death in first 30 days and ipsilateral stroke thereafter up to 4 years. S, screening; R, randomization.
Summary

• Stroke
  – 3rd leading cause of death in NA
  – We have Level 1 evidence for therapy of carotid disease

• Carotid Studies
  – CEA
    • Symptomatic – NASCET, ECST
    • Asymptomatic – ACAS, ACST
  – Stent
    • Sapphire
    • CREST
Summary

- Treatment is based on clinical situation
  - Asymptomatic vs TIA vs CVA
  - Diagnostic tests - % stenosis, plaque location
  - Patient comorbidities and medical status
  - Surgeon and Center experience
Factors to Consider for the Symptomatic Patient

- **Favors CEA**
  - Recently symptomatic patient (<2 weeks)
  - Age > 75 years
  - Tortuous or heavily calcified aorta
  - Long lesion, heavily calcified lesion

- **Favors CAS**
  - Contralateral carotid occlusion
  - Recurrent carotid stenosis
  - Presence of significant cardiac disease
  - Presence of significant lung disease
Timing of Treatment

• Historically wait 6 weeks
• Currently treat sooner
  – Smaller strokes
  – Stable neurologic status
Early endarterectomy for severe carotid artery stenosis after a nondisabling stroke: Results from the North American Symptomatic Carotid Endarterectomy Trial

Andrew P. Gacecki, MD, Gary G. Ferguson, MD, Michael Eliaasz, PhD, G. Patrick Clagett, MD, Allan J. Fox, MD, Vladimir Hachinski, MD, and Henry J. M. Barnett, MD, London, Ontario, Canada, and Dallas, Texas

Purpose: The timing of carotid endarterectomy (CE) after a recent nondisabling stroke remains controversial. Delaying surgery in such cases may needlessly place patients at risk for a recurrent stroke that may be major and disabling. This study examines the prognostic implications of performing early endarterectomy compared with delayed endarterectomy in patients from the North American Symptomatic Carotid Endarterectomy Trial.

Method: This retrospective, subgroup analysis involved 100 surgical patients with severe (70% to 99%) angiographically defined carotid artery stenosis, who were diagnosed with a nondisabling hemispheric stroke at entry into the trial. Forty-two CEs were performed within 30 days (early group, ranging 3 to 30 days), and 58 were performed beyond 30 days (delayed group, range 33 to 117 days) after stroke. The risk of subsequent stroke after CE was compared between the two groups.

Results: Baseline clinical characteristics were comparable in both the early and delayed groups. In the delayed group more lesions were identified ipsilateral to the symptomatic side on the preoperative computed tomography scans. The postoperative (30 days after endarterectomy) stroke rate was 4.8% in the early group and 5.2% in the delayed group, yielding a relative rate of 0.92 (95% confidence interval, 0.16 to 5.27; \( p = 1.00 \)). No deaths occurred after operation in either group. At the end of 18 months, the rates of any stroke or death were 11.9% and 10.3% for the early and delayed groups, respectively, resulting in a relative rate of 1.15 (95% confidence interval, 0.38 to 3.52; \( p = 1.00 \)). No association was found between an abnormal preoperative computed tomography scan result and the subsequent risk of stroke when early operation was used.

Conclusion: Early CE for severe carotid artery stenosis after a nondisabling ischemic stroke can be performed with rates of morbidity and mortality comparable to those who receive delayed endarterectomy. Delaying the procedure by 30 days for patients with symptomatic high-grade stenosis exposes them to a risk of a recurrent stroke, which may be avoidable by earlier surgery. (J VASC SURG 1994;20:288-95.)
Carotid Endarterectomy

- “Gold Standard” Tx
- Asymptomatic >60% Stenosis “Good Risk” pt
- Symptomatic >50% Stenosis
- Currently provided by a limited group of surgeons
- GHS stroke/death rate of 1.6%
Trials

- Asymptomatic
  - CASANOVA - Carotid Artery Surgery Asymptomatic Narrowing Operation versus Aspirin Trial
    - asymptomatic pts with CAS of 50 to 90%
    - Randomized 410 patients to CEA v. MM
    - After 30 days 3.6% of CEA pts suffered stroke or death
    - Showed no statistically significant difference between CEA and MM