Contemporary Management of Carotid Bifurcation Disease

Anthony J. Comerota, MD, FACS, FACC
Director, Jobst Vascular Institute
Adjunct Professor of Surgery, University of Michigan

Disclosures
1. I am a Vascular Surgeon
2. Seek best outcome for patients

Carotid Artery Disease

• Symptomatic vs. Asymptomatic
• How to select asymptomatic patients for CEA
• CEA vs. CAS

Have advances in medical Rx changed the natural course of carotid disease?
Can this be avoided?
What are the data?

Carotid Artery Disease
Symptomatic

Carotid Artery Disease
What does it look like?
Is symptomatic disease different from asymptomatic disease?
Carotid Artery Disease
Symptomatic
- Ulcer
- Subintimal Hemorrhage
- Luminal Thrombus (platelet-rich)

Carotid Artery Disease
Symptomatic

Carotid Artery Disease
Asymptomatic
- Atherosclerosis
Carotid Artery Disease

<table>
<thead>
<tr>
<th>Asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neointimal Fibroplasia</td>
</tr>
</tbody>
</table>

Asymptomatic

Symptomatic

Urgent CEA for Symptomatic Carotid Disease
Recurrent Stroke

Risk of Stroke After TIA or Minor Stroke

![Graph showing risk of stroke](image)

- 70% of strokes after symptomatic disease occurred within 14 days
- 80% of those...within 4 days

Strokes clustered soon after TIA/Stroke

Log rank P<0.05

Early Carotid Endarterectomy

Acute Stroke

When is the patient at higher risk for recurrence?

Soon After The Initial Event!

Symptomatic Carotid Disease

Acute Stroke

Why are there proponents of delayed intervention?

- Fear...
- Hemorrhagic conversion...
- Procedure related stroke...

Any Data to Justify this Fear?
Early Carotid Endarterectomy

Early vs. Late Days to CEA Stroke Rate

<table>
<thead>
<tr>
<th>Study</th>
<th>Days to CEA</th>
<th>Stroke Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whittemore et al</td>
<td>11</td>
<td>0%</td>
</tr>
<tr>
<td>Rosenthal et al</td>
<td>&lt;3 weeks</td>
<td>3%</td>
</tr>
<tr>
<td>Sbarigia et al</td>
<td>1.5 days</td>
<td>0%</td>
</tr>
<tr>
<td>Alesic et al</td>
<td>4 days</td>
<td>6%*</td>
</tr>
<tr>
<td>Ballotta et al</td>
<td>&lt;30 days</td>
<td>2%</td>
</tr>
<tr>
<td>Paty et al</td>
<td>1 week</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

No increased morbidity from early CEA

Early Carotid Endarterectomy: 21 Year Review

228 patients with acute stroke having CEA within 4 weeks

**Results**

<table>
<thead>
<tr>
<th>Interval (weeks)</th>
<th>Op stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1*</td>
<td>2.8%</td>
</tr>
<tr>
<td>1-2</td>
<td>3.4%</td>
</tr>
<tr>
<td>2-3</td>
<td>3.4%</td>
</tr>
<tr>
<td>3-4</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

*71% op strokes due to thrombosed ICA
*Only one hemorrhage
*Significantly greater NIHSS score

Symptomatic Carotid Disease

Consistent Observations

- Delaying therapy expose patient to unnecessary risk!
- No increased risk of early CEA...
  - Stroke
  - Intracranial hemorrhage

However...

...has risk of delayed CEA or benefit of early CEA been quantified? **YES!**
CEA for Symptomatic Carotid Stenosis

Timing of Procedure

Pooled data from NASCET and ECST

- 5,893 patients
- 33,000 patient years of follow-up

**Benefit of CEA**

| Males | \(P = 0.003\) |
| Age \(\geq 75\) | \(P = 0.03\) |
| <2 weeks from event | \(P = 0.009\) |

Rothwell PM et al
Lancet. 2004;363:915

ARR of Ipsilateral Ischemic Stroke at 5yrs by CEA
Stratified by Time to Randomization

**Symptomatic Carotid Disease**

All 50-99% Stenosis

<table>
<thead>
<tr>
<th>Time to Randomization</th>
<th>ARR</th>
<th>NNT</th>
<th>CVA/1000*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 Weeks</td>
<td>18</td>
<td>5</td>
<td>185</td>
</tr>
<tr>
<td>Waiting ≥ 4 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>reduces benefit by 70%</td>
<td></td>
<td></td>
<td>98</td>
</tr>
<tr>
<td>&gt; 12 Weeks</td>
<td>0.8</td>
<td>125</td>
<td>8</td>
</tr>
</tbody>
</table>

waiting ≥ 4 weeks reduces benefit by 70%

Naylor AR
Eur J Vasc Endovasc Surg. 2008;35:383

ARR of Ipsilateral Ischemic Stroke at 5yrs by CEA
Stratified by Time to Randomization

**Symptomatic Carotid Disease**

All 70-99% Stenosis

<table>
<thead>
<tr>
<th>Time to Randomization</th>
<th>ARR</th>
<th>NNT</th>
<th>CVA/1000*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 Weeks</td>
<td>23</td>
<td>4</td>
<td>230</td>
</tr>
<tr>
<td>Waiting ≥ 4 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>reduces benefit by 66%</td>
<td></td>
<td></td>
<td>159</td>
</tr>
<tr>
<td>&gt; 12 Weeks</td>
<td>7.4</td>
<td>14</td>
<td>74</td>
</tr>
</tbody>
</table>

waiting ≥ 4 weeks reduces benefit by 66%

Naylor AR
Eur J Vasc Endovasc Surg. 2008;35:383
### CEA for Symptomatic Carotid Stenosis

**Timing of Procedure**

Pooled data from NASCET and ECST

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA &lt; 2 weeks</td>
<td>5</td>
</tr>
<tr>
<td>Age ≥75</td>
<td>5</td>
</tr>
<tr>
<td>Males</td>
<td>9</td>
</tr>
<tr>
<td>Age &lt;65</td>
<td>18</td>
</tr>
<tr>
<td>Women</td>
<td>36</td>
</tr>
<tr>
<td>CEA at 6 weeks</td>
<td>62</td>
</tr>
<tr>
<td>CEA ≥12 weeks</td>
<td>125</td>
</tr>
</tbody>
</table>

No signal that hemorrhage occurred…

…only benefit to early CEA!

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### Symptomatic Carotid Disease

61 yo. man with nondisabling stroke and carotid stenosis (NASCET patient)

How long would you wish to wait after a stroke to have this lesion removed?

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### Symptomatic Carotid Disease

Symptomatic carotid artery disease should be treated as a

**Vascular Emergency!**
Patients to “Avoid” Early CEA

**Avoid Early CEA**

- Recent carotid occlusion
- Rankin score ≥ 3
- Infarct > 2/3 MCA territory
- Fluctuating consciousness
- Intracranial hemorrhage

…based upon available literature

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**Symptomatic Carotid Disease**

**Non Disabling Stroke/TIA**

Carotid Duplex → CT/MRI Brain → ≥50% Carotid Stenosis → ≤67% MCA Territory Infarct

**URGENT CEA PROTOCOL**

- ASA 81mg
- Clopidogrel 600mg
- Atorvastatin 80mg
- Glucose ≤ 120
- BP ≤ 135/85

**URGENT CEA**

---

**Carotid Artery Disease**

**Asymptomatic**

*Have recommendations changed?*
Carotid Artery Disease
Fact

97% of carotid etiology strokes occur in patients with **symptomatic** disease!

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Carotid Artery Disease
Fact

**Current preoccupation...**
Treat vast number of ASX patients

**Assume that...**
- All 60-99% ASX carotid stenosis identified
- All Rx’ed with ≤ 2.3% procedure risk

**...Outcome...**
Will do *little* to reduce overall burden of stroke
...97% of strokes will still occur!!

---

Asymptomatic Carotid Artery Disease
Principles of Care!

**Caveat #1**
Any procedure offered to patients should reduce the risk of a stroke...
... compared to best medical care.

**Caveat #2**
If procedure related-stroke/death is not *less than* best medical care...
... procedure should not be performed.

**Seems reasonable!**
ACAS: Asymptomatic Atherosclerosis
Procedure Related Stroke/Death and Stroke to 5 Years

Randomized
42 Days 5 Years

Treated an average of 25 years ago

Asymptomatic Carotid Disease

Carotid Endarterectomy
- The Interventional Gold Standard -

Operative Stroke/Death

<table>
<thead>
<tr>
<th>Procedure</th>
<th>ACAS (JAMA 1995)</th>
<th>CREST (NEJM 2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/Death</td>
<td>1.5%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

3% Procedure related event rate is not acceptable!

Considering outcomes with current medical care, a 1.5% procedure related event rate is not acceptable!

Asymptomatic Carotid Disease

Patient Implications

1000 CEA's with procedural risk - 2.3%

...will prevent 59 ipsilateral strokes in 5 years (according to medical risk 15-20 years ago)

11% - Ipsilateral stroke
12-17% - Any stroke
Asymptomatic Carotid Disease

Observation

If it were possible to identify and operate on all asymptomatic 60-99% stenoses…

…with a procedural risk of 2.3%

…fewer than 5% of all strokes would be prevented

Naylor A R
Surgeon 2007; 5:23
Hankey G J

Asymptomatic Carotid Disease

Randomized Trials

ACAS
Relationship of severity of carotid stenosis to stroke
None

Benefit to women
None

JAMA 1995
Lancet 2004

Randomized Trials: Asymptomatic Disease
Risk of Stroke: Medical Care

- Medical Treatment -

• No definition of "best medical care"

• No defined pharmacotherapy

• No treatment targets

Therefore … this was not "best" medical Rx …

… and probably not good medical Rx!
Has the risk of stroke and death from atherosclerotic carotid artery disease **decreased** in the past 25 years?

...If yes, we cannot accept historical medical controls (ACAS) for comparators to today’s procedures.

...leading to the current controversy

**Asymptomatic Carotid Disease**

**Risk of Stroke and Medical Rx**

Is there evidence that improvement in medical therapy is reducing the annual stroke risk?
Asymptomatic Carotid Disease

Randomized Trials

Best Medical Care

ACAS - No data re: Changing trends in therapy, compliance or medical outcome

ACST - Considerable data on changes in medical Rx during the 10 year trial

ie: Statins...

- 17% - 1996
- 58% - 2000
- 70% - 2003
- 90% - 2008

Temporal changes in the 5-year risk of “any” stroke and “ipsilateral” stroke

<table>
<thead>
<tr>
<th>Trial</th>
<th>Years</th>
<th>Pub Year</th>
<th>‘Any’</th>
<th>‘Ipsilateral’</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACAS</td>
<td>1 - 5</td>
<td>1995</td>
<td>17.5%</td>
<td>11.0% (2.2)</td>
</tr>
<tr>
<td>ACST</td>
<td>1 - 5</td>
<td>2004</td>
<td>11.8%</td>
<td>5.3% (1.1)</td>
</tr>
<tr>
<td>ACST</td>
<td>6 - 10</td>
<td>2009</td>
<td>7.2%</td>
<td>3.6% (0.7)</td>
</tr>
</tbody>
</table>

10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicentre randomised trial

Antihypertensives

- 69% increase BP meds
- 11% reduction DBP

Lipid Lowering Drugs

- Immediate
- Deferred

Randomized Trials

JAMA 1995

Lancet 2004

Halliday A et al

Lancet 2010; 376:1074

Naylor A R

Nature 2012; 9:116
SPARCL Trial
Risk Reduction with Statin

- 4731 stroke / TIA patients
- Randomized: atorvastatin 80mg vs. placebo

Results at 4.9 years

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>RRR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke (any)</td>
<td>16%</td>
<td>.03</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>23%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Any CV event</td>
<td>26%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Major CV event</td>
<td>35%</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

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Stroke and Blood Pressure
Importance of Diastolic Blood Pressure

<table>
<thead>
<tr>
<th>Diastolic BP</th>
<th>Risk of Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>75 vs. 90 mmHg</td>
<td>0.33</td>
</tr>
<tr>
<td>75 vs. 105 mmHg</td>
<td>0.12</td>
</tr>
<tr>
<td>(420,000 patients)</td>
<td></td>
</tr>
<tr>
<td>6 mmHg reduction with Rx:</td>
<td>0.60</td>
</tr>
<tr>
<td>(Rx with diuretic)</td>
<td></td>
</tr>
<tr>
<td>Mc Mahon et al Lancet 1990</td>
<td></td>
</tr>
<tr>
<td>Collins et al Lancet 1980</td>
<td></td>
</tr>
</tbody>
</table>

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Carotid Intervention in the USA

Asymptomatic Disease

Should cost be a concern?
**Carotid Intervention in the USA**

Extrapolating ACST Medical Risk to 2005
(5 last 5 years of the Study)

- Cost of CEA

122,986 Procedures
(2.3% Procedural Risk)

2,371 Strokes Prevented at 5 Years
...but Conversely

120,615 Unnecessary Procedures!

- $374,145 \text{ to prevent any stroke in } 5 \text{ years}
- $870 million dollars on unnecessary procedures

Modified from:
McPhee J T et al
J Vasc Surg 2005; 48:1442

---

**Second Manifestation of ARTerial Disease**

The SMART Study
(2007)

- Prospective
- 2684 consecutive patients
- Clinical manifestations of arterial disease, or
- Type II diabetes
- No history of cerebral ischemia
- Carotid duplex
- 221 (8%) ≥50% carotid stenosis
- Follow-up to 5 years (mean 3.6 years)
- Evaluated for ischemic events

Bertine M B et al
Stroke 2007; 38:1470

---

**The SMART Study**
Asymptomatic Carotid Stenosis

Risk of Stroke*

<table>
<thead>
<tr>
<th>Degree of Stenosis</th>
<th>Ischemic Stroke</th>
<th>All Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 - 49%</td>
<td>0.7</td>
<td>1.0</td>
</tr>
<tr>
<td>50 - 69%</td>
<td>0.6</td>
<td>1.4</td>
</tr>
<tr>
<td>70 - 99%</td>
<td>0.7</td>
<td>1.4</td>
</tr>
<tr>
<td>Occlusion</td>
<td>2.6</td>
<td>1.5</td>
</tr>
</tbody>
</table>

* vs. no stenosis

Bertine M B et al
Stroke 2007; 38:1470

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Asymptomatic Carotid Disease

SMART Study

Annual risk of "ipsilateral" or "any" stroke with 50 - 99% stenosis was <0.7%

Asymptomatic Carotid Stenosis

- Oxford Vascular Study -

301 Patient Year Follow-Up
• 1 minor stroke
• 5 TIs

The highest risk asymptomatic patient!

Annual Event Rate

- Ipsilateral stroke - 0.34%
- Disabling ipsilateral stroke - 0%
- Ipsilateral TIA - 1.78%

Carotid Artery Disease

Asymptomatic

Some patients with asymptomatic carotid disease will have a stroke…
…can they be identified?
Asymptomatic Carotid Artery Disease

Patient Evaluation

- Identify “High Risk Plaque” –

- Plaque characteristics
  - Plaque type (heterogeneous/homogeneous)
  - Gray-Scale Median
  - Juxta-Luminal Black Area

- Embolization
- Cerebral infarction

...identify carotid lesion that is likely to become symptomatic

From the Society for Vascular Surgery

Asymptomatic internal carotid artery stenosis and cerebrovascular risk stratification

Andrew N. Nicolaides, MS, FRCS, PhD (Hon.), Stewart H. Kakkas, MD, MSc, PhD, DHC
Effy Lyritis, PhD, MS, FRCS, PhD
Barry G. Griffin, BSc, FRCS, PhD
Michael S. Sileni, MD, FRCS, PhD, DHC
Hyde J. Thomas, MD, PhD, FRCR
Thomas Tjora, MD, PhD, George Konstantakos, MD, PhD
Nicole L. Groat, PhD, MSc, MMSc, Radha C. Doshi, MD, FRCR
Tom P. Mearns, MS

J Vasc Surg 2010; 57:1486

Asymptomatic internal carotid artery stenosis and cerebrovascular risk stratification

ACRS Study

- Prospective, multicenter, cohort study
- Asymptomatic ICA stenosis 50-99% (ECST)
- Medical Rx only (not standardized)
- Features correlated with ipsilateral cerebrovascular or retinal ischemia (CORI)
- Statistical analysis
  - Univariate
  - Proportional hazards model

Nicolaides AN et al
J Vasc Surg 2010; 57:1486
Asymptomatic internal carotid artery stenosis and cerebrovascular risk stratification

ACSRS Features Studied

Clinical
• Hx contralateral stroke/TIA
• % Stenosis

Plaque Characteristics
• Plaque area (mm²)
• Plaque type
• Juxta-Luminal Black Area (mm²)
• Gray-Scale Median

Asymptomatic Carotid Artery Disease

Plaque Characteristics
– Echolucent, Type 1 Plaque –

Can contrast arteriography improve upon this?

Asymptomatic Carotid Artery Disease

Echolucent Plaque

– High Risk Plaque –
(GSM <25)
Asymptomatic Carotid Artery Disease

Echogenic, Type 4 Plaque

– Low Risk Plaque –

Nicolaides AN et al
J Vasc Surg 2010; 57:1486

Annual Risk of Ipsilateral Stroke

– Univariate Analysis –

<table>
<thead>
<tr>
<th>Plaque Type</th>
<th>Annual Stroke Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0.4%</td>
</tr>
<tr>
<td>3</td>
<td>0.8%</td>
</tr>
<tr>
<td>1 &amp; 2</td>
<td>3.0%</td>
</tr>
</tbody>
</table>

Asymptomatic internal carotid artery stenosis and cerebrovascular risk stratification

Juxtaluminal Black Area

– High Risk Plaque –
Asymptomatic Carotid Artery Disease

Juxtaluminal Black Area

– High Risk Plaque –

Asymptomatic internal carotid artery stenosis and cerebrovascular risk stratification

**Annual Risk of Ipsilateral Stroke**

<table>
<thead>
<tr>
<th>JBA (mm²)</th>
<th>Annual Stroke Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4</td>
<td>0.4%</td>
</tr>
<tr>
<td>4-8</td>
<td>1.4%</td>
</tr>
<tr>
<td>8-10</td>
<td>3.2%</td>
</tr>
<tr>
<td>&gt;10</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plaque Area (mm²)</th>
<th>Annual Stroke Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>0.6%</td>
</tr>
<tr>
<td>15-30</td>
<td>1.6%</td>
</tr>
<tr>
<td>&gt;30</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

Multi-Regression Analysis:

*Develop an Individualized Annual Risk of Stroke Using:*

- Stenosis severity
- Contralateral symptoms
- Plaque area
- Gray-scale median
### Asymptomatic internal carotid artery stenosis and cerebrovascular risk stratification

#### 80-99% NASCET Stenosis

<table>
<thead>
<tr>
<th>Plaque Area mm²</th>
<th>Annual Stroke Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;80</td>
<td>&gt;4%</td>
</tr>
<tr>
<td>40-80</td>
<td>3.0-3.9%</td>
</tr>
<tr>
<td>&lt;40</td>
<td>2.0-2.9%</td>
</tr>
<tr>
<td>≥30</td>
<td>1.0-1.9%</td>
</tr>
<tr>
<td>&lt;15</td>
<td>&lt;1.0%</td>
</tr>
</tbody>
</table>

#### Asymptomatic Carotid Artery Disease

#### High Risk Plaque

- **Other Questions**
  - Is it embolizing?
  - Has it caused cerebral infarction?
### Results

**– Ipsilateral Stroke –**

<table>
<thead>
<tr>
<th>Time (Days)</th>
<th>Embolic signals present</th>
<th>Embolic signals absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5.57</td>
<td>0.006</td>
</tr>
</tbody>
</table>

- **Absolute Annual Risk**: 3.62%
- **Absolute Annual Risk**: 0.7%


---

**Silent embolic infarcts on computed tomography brain scans and risk of ipsilateral hemispheric events in patients with asymptomatic internal carotid artery stenosis**

- Steven K. Kakkor, MD, MSc, PhD, FVCS
- Michael Sibbest, MD, FRCSC
- Thomas Tigges, MD, PhD
- Julie Sweeney, MB, BCh. (University of Toronto, MA, MD, FRCP; Mississauga, ON, PhD)**
- George Gomeschino, FRCSC, PhD**
- and Andrew N. Nicolaides, HIS, FRCSC, PhD (Ecole)** for the Asymptomatic Carotid Stenosis and Risk of Stroke (ACSSS) Study Group.**

*Leeds, United Kingdom*


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**Silent embolic infarcts and risk of ipsilateral hemispheric stroke with asymptomatic internal carotid artery stenosis**

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>No Infarct</th>
<th>Infarct*</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60%</td>
<td>1.1%</td>
<td>0.48%</td>
<td>NS</td>
</tr>
<tr>
<td>60–99%</td>
<td>1.0%</td>
<td>3.6%</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*CT Scans*

**Carotid Artery Disease**

**Conclusions**

1. Symptomatic carotid artery disease is a vascular emergency
2. Asymptomatic carotid disease is best treated with intensive medical care
3. High risk plaques can be identified…
   A. Ultrasound plaque characteristics
   B. Embolization detected by TCD
   C. Asymptomatic cerebral infarction on brain imaging

**Carotid Bifurcation Disease**

How best to treat symptomatic and asymptomatic atherosclerotic disease

**Carotid Angioplasty/Stenting vs. Carotid Endarterectomy:**
**Randomized Trials**
Critical Question

Are there any data showing that CAS reduces the risk of stroke vs. best medical care?

NO!

Carotid Artery Disease: Ultimate Data

Symptomatic

It is possible to pass guide wires and catheters through these lesions without causing distal emboli?

CEA vs. CAS for Symptomatic Disease

Independently funded, investigator initiated, randomized trials

The GOLD Standard!
CAS vs. CEA: Symptomatic Disease

Randomized Trials

- Symptomatic Atherosclerotic -

<table>
<thead>
<tr>
<th>Trial/Funding</th>
<th># Patients</th>
<th>Primary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPACE</td>
<td>1200</td>
<td>Symptomatic Stroke/Death</td>
</tr>
<tr>
<td>EVA-3S</td>
<td>527</td>
<td>Symptomatic Stroke/Death</td>
</tr>
<tr>
<td>ICSS</td>
<td>1713</td>
<td>Symptomatic Stroke/Death</td>
</tr>
<tr>
<td>CREST</td>
<td>2502</td>
<td>Symptomatic (N=1321) Stroke/Death</td>
</tr>
</tbody>
</table>

- Procedure Related Outcomes -

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CAS (N=2381)</th>
<th>CEA (N=2353)</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>7.1%</td>
<td>4.2%</td>
<td>1.69</td>
</tr>
<tr>
<td>Disabling Stroke</td>
<td>2.2%</td>
<td>1.7%</td>
<td>1.29</td>
</tr>
<tr>
<td>Death</td>
<td>1.2%</td>
<td>0.6%</td>
<td>2.00</td>
</tr>
<tr>
<td>Stroke/Death</td>
<td>7.8%</td>
<td>4.8%</td>
<td>1.63</td>
</tr>
<tr>
<td>Disab. Stroke/Death</td>
<td>3.4%</td>
<td>2.3%</td>
<td>1.48</td>
</tr>
</tbody>
</table>

Conclusion: No difference in primary outcome – CEA vs. CAS!
Study Finds Stents Effective in Preventing Strokes

It is unethical for physicians to allow this perception!

**CAS vs CEA**

**CREST**

**The New York Times**

Expect the World

Study Finds Stents Effective in Preventing Strokes

By RONI CARYN RABIN

Published: February 26, 2010

This captures the attention of the lay-public!

It is unethical for physicians to allow this perception!

**CAS for Symptomatic Disease**

**CREST** (N=1321)

- Symptomatic -

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CAS (N=668)</th>
<th>CEA (N=653)</th>
<th><em>p</em>-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/Death or Post. Ipsilat Stroke</td>
<td>6.0%</td>
<td>3.2%</td>
<td>0.02</td>
</tr>
<tr>
<td>Proc. Stroke and Post. Ipsilat. Stroke</td>
<td>5.5%</td>
<td>3.2%</td>
<td>0.04</td>
</tr>
</tbody>
</table>

*Brott T et al*  *NEJM* 2010; 363(1):11

This is the key outcome!

Randomized trials do not support CAS; and outcomes are generally better in trials than community practice!

...what are community practice results?
Stroke and death after carotid endarterectomy and carotid artery stenting with and without high risk criteria

**National Inpatient Sample**
- Largest All Payor Inpatient Database in US -

- 2004 – 2007
- 538,958 patients
  - CEA – 482,394
  - CAS – 56,564
- Outcome stratified by risk

<table>
<thead>
<tr>
<th>High Risk</th>
<th>CAS</th>
<th>CEA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/Death</td>
<td>11.8%</td>
<td>4.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>7.5%</td>
<td>4.2%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

These are community results!

---

Carotid Interventions in the Post-CREST Era: Contemporary Outcomes in the State of Michigan
Charles J. Shanley, MD, Michael J. Borov, MD, Yeo J. Park, PhD, Hitinder S. Gurm, MD, Paul M. Grossman, MD, Jeffrey R. Rubin, MD and Peter K. Henke, MD

38th Annual Meeting
Carotid Interventions in the Post-CREST Era:
Contemporary Outcomes in the State of Michigan

30 Day Outcomes Study

- Consecutive carotid interventions
- Prospective, statewide quality improvement registry
- 3,136 carotid interventions
  - 2,482 CEAs
  - 654 CAS
- Outcomes: in-hospital
  - Any TIA/stroke
  - Ipsilateral stroke
  - MI
  - Death
  - Composite: stroke/death
  - Composite: MI/stroke/death

Outcomes

- In-Hospital –

<table>
<thead>
<tr>
<th>All Patients</th>
<th>CAS</th>
<th>CEA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA/Stroke</td>
<td>1.9%</td>
<td>5.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke/Death</td>
<td>2.3%</td>
<td>6.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MI/Stroke/Death</td>
<td>2.7%</td>
<td>6.7%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Propensity matched samples gave same results

Outcomes

- In-Hospital –

<table>
<thead>
<tr>
<th>TIA/Stroke</th>
<th>CAS</th>
<th>CEA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>1.5%</td>
<td>5.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>2.7%</td>
<td>6.0%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Carotid Interventions in the Post-CREST Era: Contemporary Outcomes in the State of Michigan

Symptomatic Patients
– CAS vs. CEA –

CAS Associated with:
• 6X increased death
• 7X increased TIA/stroke
• 4X increased death >70 years
• 3X increased stroke/death in women

CAS: Symptomatic Disease

Asymptomatic MI is argued to be a primary endpoint in randomized trials…

...what about asymptomatic stroke?

Especially since there is a major difference on QOL!!

New Brain Lesions After Carotid Stenting Versus Carotid Endarterectomy
A Systematic Review of the Literature
Sonja Schmiedgel, MD; Klaus Grünche, MD; Sara M. Pilgrim, MD; Andreas Kastrup, MD

32 Studies

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipsilateral</td>
<td>37%</td>
<td>10%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Contralateral</td>
<td>15%</td>
<td>0.1%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total</td>
<td>52%</td>
<td>10%</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Silent Brain Infarcts and the Risk of Dementia and Cognitive Decline

Results
- Silent Brain Infarcts -

At Baseline
• More than doubled risk of dementia (HR 2.26)
• Worse performance on neuropsych. tests

New Infarcts $p=0.025 – 0.005$
• Decline in global cognitive function
• Decline in memory
• Decline in psychomotor speed

Carotid Bifurcation Disease

Conclusions
1. Symptomatic disease is a vascular emergency
2. Urgent CEA is the recommended procedure
3. PreOp statin and platelet inhibition
4. CAS is associated with an increased stroke/death rate in both symptomatic and asymptomatic disease
5. Majority of patients with asymptomatic disease should be treated with best medical care
6. If patients with asymptomatic disease are operated, they should be carefully selected
Preoperative symptom type influences the 30-day perioperative outcomes of carotid endarterectomy and carotid stenting in the Society for Vascular Surgery Vascular Registry

Geraghty P J et al

J Vasc Surg 2014; 60:639-44

30 Day Outcomes

- Retrospective review
- Contemporary vascular practice
- 2004 – 2011
- CEA or CAS
- Discrete preprocedural symptom type
  - Ipsilateral stroke
  - TIA
  - Transient monocular blindness
  - Asymptomatic

Presentation — Ipsilateral Stroke

<table>
<thead>
<tr>
<th>30 Day Outcome</th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>1.8%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Stroke</td>
<td>4.6%</td>
<td>8.6%</td>
</tr>
<tr>
<td>MI</td>
<td>0.8%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Death/Stroke/MI</td>
<td>6.7%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Death/Stroke</td>
<td>6.2%</td>
<td>11.0%</td>
</tr>
</tbody>
</table>
## – Presentation –
### Ipsilateral TIA

<table>
<thead>
<tr>
<th>30 Day Outcome</th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.8%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Stroke</td>
<td>3.3%</td>
<td>7.9%</td>
</tr>
<tr>
<td>MI</td>
<td>1.6%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Death/Stroke/MI</td>
<td>5.0%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Death/Stroke</td>
<td>4.0%</td>
<td>8.4%</td>
</tr>
</tbody>
</table>

## – Presentation –
### Ipsilateral TMB

<table>
<thead>
<tr>
<th>30 Day Outcome</th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.0%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.6%</td>
<td>3.2%</td>
</tr>
<tr>
<td>MI</td>
<td>0.9%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Death/Stroke/MI</td>
<td>2.5%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Death/Stroke</td>
<td>1.6%</td>
<td>3.2%</td>
</tr>
</tbody>
</table>

## – Presentation –
### Asymptomatic

<table>
<thead>
<tr>
<th>30 Day Outcome</th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.8%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.6%</td>
<td>3.2%</td>
</tr>
<tr>
<td>MI</td>
<td>1.2%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Death/Stroke/MI</td>
<td>3.1%</td>
<td>4.9%</td>
</tr>
<tr>
<td>Death/Stroke</td>
<td>2.2%</td>
<td>4.3%</td>
</tr>
</tbody>
</table>
New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: a substudy of the International Carotid Stenting Study (ICSS)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Censored</th>
<th>Treated</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-randomized studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic &amp; stroke</td>
<td>41</td>
<td>21</td>
<td>62</td>
<td>0.006</td>
</tr>
<tr>
<td>Non-stroke</td>
<td>15</td>
<td>2</td>
<td>17</td>
<td>0.005</td>
</tr>
<tr>
<td>Symptomatic &amp; TIA</td>
<td>8</td>
<td>12</td>
<td>20</td>
<td>0.030</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>21</td>
<td>46</td>
<td>67</td>
<td>0.001</td>
</tr>
<tr>
<td>Randomized studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (N=1200)</td>
<td>200</td>
<td>600</td>
<td>800</td>
<td>0.001</td>
</tr>
</tbody>
</table>
| p<0.00001

Asymptomatic infarcts are serious!