Carotid Artery Stenting
Current status and perspective
Natural Incidence of CVA in Carotid Stenosis

- Asymptomatic 80% carotid stenosis
  - 1.9%/year (ESCT registry)
  - 12%/5 year (ACAS, ACST)
- Symptomatic 50% carotid stenosis
  - 10%/year
  - 40%/5 years
Carotid Artery stenosis

Current guidelines
CEA vs. Medical Rx
Symptomatic Patients (DS ≥ 70%)

Death or Stroke (%)

ECST

VA

NASCET

CEA

Medical therapy

P<0.01

P=0.011

P<0.01

12.3

21.9

7.7

19.4

9

26
CEA vs. Medical Rx
Asymptomatic Patients (DS > 60%)

Death or Stroke (%)

- CASANOVA
  - CEA: 10.7
  - Medical therapy: 11.3
  - P=NS

- VA
  - CEA: 8
  - Medical therapy: 20.6
  - P<0.01

- ACAS
  - CEA: 5.1
  - Medical therapy: 11
  - P<0.001

- ASCT
  - CEA: 6.4
  - Medical therapy: 11.7
  - P<0.001
# Indications for carotid artery revascularization

<table>
<thead>
<tr>
<th>Indication level</th>
<th>Symptomatic stenosis</th>
<th>Asymptomatic stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Proven</strong></td>
<td>&gt; 60% stenosis</td>
<td>&gt; 60% stenosis</td>
</tr>
<tr>
<td></td>
<td>Periprocedural</td>
<td>Periprocedural</td>
</tr>
<tr>
<td></td>
<td>complication risk &lt;3%</td>
<td>complication risk &lt;3%</td>
</tr>
<tr>
<td></td>
<td>Life expectancy &gt; 5yrs</td>
<td>Planned CABG</td>
</tr>
<tr>
<td><strong>Acceptable</strong></td>
<td>50-69% stenosis</td>
<td>&gt; 60% stenosis</td>
</tr>
<tr>
<td></td>
<td>Periprocedural</td>
<td>Periprocedural</td>
</tr>
<tr>
<td></td>
<td>complication risk &lt;3%</td>
<td>complication risk &lt;3%</td>
</tr>
<tr>
<td></td>
<td>Planned CABG</td>
<td></td>
</tr>
<tr>
<td><strong>Unacceptable</strong></td>
<td>&lt;29% stenosis,</td>
<td>&lt; 60% stenosis</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td></td>
<td>Periprocedural</td>
<td>Periprocedural</td>
</tr>
<tr>
<td></td>
<td>complication risk &gt; 6%</td>
<td>complication risk &gt;3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No indication for CABG</td>
</tr>
</tbody>
</table>

*Asymptomatic stenosis*

*Symptomatic stenosis*

*Circulation 2006;113:2021-2030*
Carotid Stenting:

- NASCET-2 trial (2,226 pts, 50-69% stenosis) showed that a modest benefit in favor of surgery especially nondiabetics men with hemispheric ischemic stroke in patients with ≥ 50% stenosis.

- ESCT group (2,295 pts) showed that different stroke risk of asymptomatic stenosis; < 2% of <80% stenosis, 9.8% of 80-89% stenosis, 14.4% of 90-99% at 3 years.

Current guideline of carotid revascularization:

- Symptomatic stenosis ≥ 70%
- Asymptomatic stenosis ≥ 80%
Carotid Stenting:

• Currently, the only use of carotid stenting that has been approved by FDA is in **symptomatic patients with stenosis of the internal carotid artery exceeding 70%** who are at **high risk for complications after surgery**.

• The limited FDA approval of stenting is largely based on the results of SAPPHIRE trial, involving patients who had **symptomatic stenosis of the internal carotid artery exceeding 50% or asymptomatic stenosis exceeding 80%** and who were at **high surgical risk mainly owing to severe coronary artery disease**.
Current Goal of Carotid stenting based on NASCET\textsuperscript{1}, ECST\textsuperscript{2}, ACAS\textsuperscript{3}, ACST\textsuperscript{4}

Morbidity and mortality after carotid intervention should be…

Symptomatic < 6\%\textsuperscript{1,2}
Asymptomatic < 3\%\textsuperscript{3,4}
Carotid Artery stenosis

High risk group for surgery
High risk group for stenting
High Risk Features of Surgery vs. Stenting for Carotid Stenosis

**Surgery**
- Restenosis
- Prior radiation
- Cranial nerve palsies
- Previous OHS
- High and low lesion
- Contralateral occlusion
- Cardiovascular disease
- Pulmonary disease

**Intervention**
- Tortuosity
- Poor access
- Severe calcification
- Previous OHS
- Arch anatomy
- Intolerance to antiplatelet

**Elderly**
- String sign
- Thrombus
- Acute stroke
Who is High Risk Patient?

Clinical Criteria

- Age greater than 80
- Unstable angina CCS III-IV
- EF < 30%
- MI within past 6 wks
- Severe COPD (FEV1 < 30% predicted)
- Renarrowing after prior CEA (80% Asx; 50% Sx)
- Total occlusion of the contralateral ICA
- Two or more proximal or major coronary arteries with >70% stenosis
Who is High Risk Patient?

Anatomical Criteria

- Previous radiation treatment to neck
- Previous radical neck surgery
- Inability to extend neck
- Patient has a tracheostomy or tracheal stoma
- Laryngeal nerve palsy
- Lesion with difficult access
# Carotid End-Arterectomy

- 3,061 CEA during a 10-year period

<table>
<thead>
<tr>
<th></th>
<th>Stroke</th>
<th>Death</th>
<th>Stroke, MI, Death</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Risk Patients</strong></td>
<td>3.5%</td>
<td>4.4%</td>
<td>7.4%</td>
</tr>
<tr>
<td><strong>Low Risk Patients</strong></td>
<td>1.7%</td>
<td>0.3%</td>
<td>2.9%</td>
</tr>
</tbody>
</table>

*High risk patients*: severe coronary disease, COPD, renal insufficiency

### Features a/w increased procedural risks after carotid stenting

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
</tr>
<tr>
<td>Advanced age</td>
<td>Age ≥ 80 yrs</td>
</tr>
</tbody>
</table>
| Decreased cerebral reserve | - Dementia  
- Prior (remote) stroke  
- Multiple lacunar infarcts  
- Intracranial microangiopathy |
| **Angiographic** |          |
| Excessive tortuosity | ≥ 2 90° bends within 5 cm of the lesion |
| Heavy calcification | - Concentric circumferential calcification  
- Width ≥ 3mm |

*Circulation 2006;113:2021-2030*
Carotid Artery Stenting

Current status

Embolic protection device (EPD) ??
Why Embolic Protection?
Why Embolic Protection?

MCA (M1) embolic occlusion
Distal Occlusion Device

PercuSurge GuardWire™

Mean embolic count

Control

GuardWire

P < 0.001

P < 0.002

P < 0.004

Al-Mubarak et al, Circulation, 2001
Embolic Protection Device
Distal Occlusion

PercuSurge GUARDWIRE™
Embolic Protection Devices (EPD) Filter

- Guidant - ACCUNET
- BSC - FilterWire
- ABBOTT - Emboshield
- Cordis - Angioguard
- EV3 - Spider
Benefit of Distal Protection
Periprocedural Outcomes

% 10

- Minor stroke
- Major stroke
- Procedure death
- All events

P<0.05

Unprotected (n=6683)
- Minor stroke: 2.86
- Major stroke: 1.61
- Procedure death: 0.82
- All events: 5.29

Protected (n=4005)
- Minor stroke: 1.1
- Major stroke: 0.72
- Procedure death: 0.45
- All events: 2.27

AET 2003
Benefit of Distal Protection
Periprocedural Outcomes

All cause death, major & minor stroke

<table>
<thead>
<tr>
<th></th>
<th>Unprotected</th>
<th>Protected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic</td>
<td>6.97%</td>
<td>3.25%</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>4.78%</td>
<td>2.53%</td>
</tr>
</tbody>
</table>

P<0.05
Benefit of Distal Protection

30-Day Outcomes

- Without protection, n=2537
- With protection, n=896

- Minor stroke: Without protection 3.7%, With protection 0.5%
P<0.001

- Major stroke: Without protection 1.1%, With protection 0.3%
P<0.05

- Death: Without protection 0.8%, With protection 0.8%
P=NS

- Combined stroke and death: Without protection 5.5%, With protection 1.8%
P<0.001

Stroke 2003;34:813-819
Carotid Artery Stenting

Current status

Embolic protection device (EPD) is mandatory in CAS
Unended fight

Carotid Endarterectomy vs. Carotid Stenting
### Carotid Stent Trial Data

#### Pre-EPD
- Normal risk/randomized
  - WallStent trial-1999 (223)

#### Post-EPD
- Normal risk/symptomatic and asymptomatic/randomized
  - CREST, ACT 1
- Normal risk/symptomatic/randomized
  - EVA-3S, SPACE, CAVATAS 2
- Normal risk/non-randomized
  - CARESS-2003 (143)
- High risk/randomized
  - SAPPHIRE-2002 (334)
- High risk/registry
  - SAPPHIRE-2002 (406)
  - ARCHeR-2003 (581)
  - SECuRITY-2003 (305)
  - BEACH-2004 (408)
  - CABERNET-2004 (454)
  - CREATE-2005 (413)
US Carotid Stent Trials: pre-EPD

Schneider Carotid Wallstent trial

• First randomized trial to compare stent (non-dedicated, tracheobronchial, no embolic protection) with CEA in ~200 patients
• A “normal risk” trial in symptomatic patients
• Stopped early as DSMB determined continued enrollment would not meet pre-specified endpoints
<table>
<thead>
<tr>
<th>Event (1 year)</th>
<th>Stent (N=108)</th>
<th>Surgery (N=115)</th>
<th>Difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study-related death Or ipsilateral stroke</td>
<td>12% (12/98)</td>
<td>4% (4/91)</td>
<td>7.8%</td>
<td>0.067</td>
</tr>
<tr>
<td>Study-related death</td>
<td>6% (6/98)</td>
<td>2% (2/91)</td>
<td>3.9%</td>
<td>0.28</td>
</tr>
<tr>
<td>Ipsilateral stroke</td>
<td>7% (6/92)</td>
<td>3% (3/90)</td>
<td>3.2%</td>
<td>0.49</td>
</tr>
<tr>
<td>Major</td>
<td>2% (2/92)</td>
<td>1% (1/89)</td>
<td>1.1%</td>
<td>1.00</td>
</tr>
<tr>
<td>Minor</td>
<td>2% (2/92)</td>
<td>0% (0/89)</td>
<td>2.2%</td>
<td>0.49</td>
</tr>
<tr>
<td>Undetermined</td>
<td>2% (2/92)</td>
<td>2% (2/90)</td>
<td>-0.0%</td>
<td>1.00</td>
</tr>
</tbody>
</table>
No Phase I trial preceded this randomized effort

Trial design flawed:
- Power
- Endpoints

Operator training requirements were inadequate

Non-dedicated equipment without embolic protection

No PI or Executive Committee
- As a result, after Schneider acquisition by BSC, continuity of trial conduct was disrupted

Evolving technique and equipment represented a suboptimal environment for a randomized trial
Symptomatic high surgical & Asymptomatic high surgical
# CAVATAS

**CEA vs. Angioplasty without protection in Low and High Surgical Risk group**

<table>
<thead>
<tr>
<th></th>
<th>Angioplasty</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=251</td>
<td>N=253</td>
</tr>
<tr>
<td>30-day death &amp; stroke</td>
<td>6.4%</td>
<td>5.9%</td>
</tr>
<tr>
<td>Cranial neuropathy</td>
<td>0%</td>
<td>8.7%</td>
</tr>
<tr>
<td>1-year restenosis (&gt;70% DS)*</td>
<td>14%</td>
<td>4%</td>
</tr>
<tr>
<td>3-year death or disabling stroke</td>
<td>14.3%</td>
<td>14.2%</td>
</tr>
</tbody>
</table>

* Stenting = only in 26%

*Lancet 2001;357:1729-37*
CES vs. CAS with Filter
From August 2000 to July 2002

Carotid a stenosis with high risk (n=334)

Randomization (1:1)

Carotid Stenting with filter device (n=167)

Carotid endarterectomy (n=167)

Primary endpoint: composite of death, stroke, or myocardial Infarction within 30 days or death or ipsilateral stroke btw 31 days and 1 year

Yadav JS, et al. NEJM 2004;351:1493
CEA vs. CAS with Filter

30-Day Outcomes

Death /MI /Stroke

- CAS + Filter: 5.8%
- CEA: 12.6%

P = 0.047

Cranial nerve palsy

- CAS + Filter: 0%
- CEA: 5.3%

P < 0.001

Yadav JS, et al. NEJM 2004;351:1493
CEA vs. CAS with Filter

30-Day Outcomes

Symptomatic patients

Death /MI /Stroke

CAS + Filter: 2.1%
P = 0.18

CEA: 9.3%

Asymptomatic patients

Death /MI /Stroke

CAS + Filter: 5.4%
P = 0.20

CEA: 10.2%

Yadav JS, et al. NEJM 2004;351:1493
Primary endpoint: composite of death, stroke, or MI within 30 days or death or ipsilateral stroke between 31 days and 1 year

Yadav JS, et al. NEJM 2004;351:1493
1-Year Clinical Outcomes

Primary endpoint: composite of death, stroke, or MI within 30 days or death or ipsilateral stroke between 31 days and 1 year

Symptomatic patients

<table>
<thead>
<tr>
<th></th>
<th>%</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS + Filter</td>
<td>16.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEA</td>
<td>16.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Asymptomatic patients

<table>
<thead>
<tr>
<th></th>
<th>%</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS + Filter</td>
<td>9.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEA</td>
<td>21.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Yadav JS, et al. NEJM 2004;351:1493
CEA vs. CAS with Filter

1-Year TLR

\[ P = 0.06 \]

CAS + Filter: 0.6%

CEA: 4.0%

Yadav JS, et al. NEJM 2004;351:1493
Conclusion

• Among patients with severe carotid-artery stenosis and coexisting conditions, CAS with the use of an emboli-protection device is not inferior to CEA.

Yadav JS, et al. NEJM 2004;351:1493
CEA vs. CAS with or without EPD

30 days outcomes from 5 RCT (n=1269)
(CAVATAS, Kentucky A&B, Leicester, WALL STENT, SAPPHIRE)

Death / any stroke

OR, 1.33; CI, 0.86-2.04

Death / disabling stroke

OR, 1.22; CI, 0.61-2.41

CEA vs. CAS with or without EPD

Outcomes from 5 RCT (n=1269)
(CAVATAS, Kentucky A&B, Leicester, WALL STENT, SAPPHIRE)

Death /any stroke @ 1 year

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>13.5</td>
<td>13.3</td>
</tr>
</tbody>
</table>

OR, 1.01; CI, 0.71-1.44

Cranial nerve palsy

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>6.5</td>
<td>0</td>
</tr>
</tbody>
</table>

OR, 0.13; CI, 0.06-0.25

CES vs. CAS with Accunet

Multicenter, prospective, nonrandomized

Carotid a stenosis (n=581)

High-risk Sx & Asx patients

Carotid Stenting with Accunet (n=581)

Carotid endarterectomy (Historical control)

Primary endpoint: composite of perprocedural death, stroke, or myocardial Infarction within 30 days, plus ipsilateral stroke btw 31days and 1 year

CEA vs. CAS with Accunet

30-Day and 1-year Outcomes

30-day outcomes

1-year outcomes

CAS + Filter

Death/stroke/MI

0

12

15

Death/stroke

CAS+filter

0

5

10

15

20

CEA

CES vs. CAS with Filter

From 2001 to 2004

Carotid a stenosis (n=602)

Concurrent-risk matched group

Carotid Stenting with filter device (n=301)

Carotid endarterectomy (n=301)

Perioperative and midterm results of CAS vs. CEA

50% of CAS disabling strokes occurred during cannulation of epiaortic vessel

Death / disabling stroke

P = 0.4

P = 0.0004

CEA vs. CAS with Filter

30-Day Outcomes

A decreasing trend in 30-day stroke with expertise

Any stroke
All patients (n=301pts/arm)

% 10
8
6
4
2
0
CAS + Filter 2.3
CEA 7.9

P=0.001

Any stroke in
Last 201 pts/arm

% 10
8
6
4
2
0
CAS + Filter 1.9
CEA 5.4

P=0.1

CEA vs. CAS with Filter

36-Month restenosis

P=0.6

CAS + Filter: 6.4%

CEA: 7.9%

### Independent risk factors

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Disabling stroke/death</th>
<th>Any stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS</td>
<td>HR 3.6 [0.93-13.9], p=0.06</td>
<td>HR 3.9 [1.6-9.4], p=0.002</td>
</tr>
<tr>
<td>Urgency</td>
<td>HR 8.9 [1.71-46.4], p=0.009</td>
<td>HR 4.6 [1.2-18.6], p=0.03</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>HR 2.2 [1.01, 4.83], p=0.045</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td>HR 1.06 [1.01, 1.1], p=0.02</td>
</tr>
</tbody>
</table>

*Cao P, et al. Stroke 2006;37:1221-1226*
AMC Experience
Carotid Stenting in AMC

- From 04/2001’ to 04/2007’
- 103 consecutive patients (staged bilateral procedure in 5 patients)
- 108 lesions: bilateral stenting in 5 patients
- 103 severe (≥70%) ICA stenosis
- 4 moderate (50-70%) ICA stenosis
# Baseline Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>N=103</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>66.2±7.3</td>
</tr>
<tr>
<td>Sex, men</td>
<td>86 (79.6%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>53 (49.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>77 (71.3%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>32 (29.6%)</td>
</tr>
<tr>
<td>History of Smoking</td>
<td>65 (60.2%)</td>
</tr>
<tr>
<td>History of IHD</td>
<td>87 (80.6%)</td>
</tr>
<tr>
<td>Stable angina</td>
<td>31 (28.7%)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>48 (44.4%)</td>
</tr>
<tr>
<td>Recent or acute MI</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Old MI</td>
<td>9 (8.3%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>15 (13.9%)</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>8 (7.4%)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>12 (11.2%)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>10 (9.3%)</td>
</tr>
<tr>
<td>End stage renal failure</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>2 (1.9%)</td>
</tr>
</tbody>
</table>
### Neurologic Status / Underlying Coronary & Carotid Disease

<table>
<thead>
<tr>
<th>Variables</th>
<th>N=103</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior history of CVA (&gt;6months)</td>
<td>27/103 (26%)</td>
</tr>
<tr>
<td>History of TIA</td>
<td>6</td>
</tr>
<tr>
<td>History of stroke</td>
<td>21</td>
</tr>
<tr>
<td>Symptomatic (&lt;6months)</td>
<td>34/103 (33%)</td>
</tr>
<tr>
<td>Amaurosis fugax</td>
<td>3</td>
</tr>
<tr>
<td>TIA</td>
<td>11</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>1</td>
</tr>
<tr>
<td>Major stroke</td>
<td>19</td>
</tr>
<tr>
<td>Bilateral carotid stenosis (≥50%)</td>
<td>34/103 (33%)</td>
</tr>
<tr>
<td>Target lesion</td>
<td></td>
</tr>
<tr>
<td>Rt. ICA</td>
<td>59</td>
</tr>
<tr>
<td>Lt. ICA</td>
<td>47</td>
</tr>
<tr>
<td>Both ICA</td>
<td>5 (4.9%)</td>
</tr>
<tr>
<td>Severe CAD requiring revascularization</td>
<td>83/103 (81%)</td>
</tr>
</tbody>
</table>
30-day outcomes
Death/MI/Stroke

<table>
<thead>
<tr>
<th>Event</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor stroke</td>
<td>1.9%</td>
</tr>
<tr>
<td>Major stroke</td>
<td>1.0%</td>
</tr>
<tr>
<td>Death</td>
<td>1.0%</td>
</tr>
<tr>
<td>All events</td>
<td>3.9%</td>
</tr>
</tbody>
</table>
Long-term outcomes

Death/Stroke

Follow-up duration: mean 14.5 ± 13.7 months

No additional events

- Minor stroke: 1.9%
- Major stroke: 1%
- Death: 1%
- All events: 3.9%
30-Day Outcomes

Symptomatic (n=28)

- Death/Stroke: 3.8%

Asymptomatic (n=75)

- Death/Stroke: 4.0%
  - Minor stroke: 2.7%
  - Major stroke: 1.3%
  - Death: 1.3%
  - All events: 4.0%
30-Day Outcomes

High risk (n=93)

Death/Stroke

- Minor stroke: 2.2%
- Major stroke: 1.1%
- Death/Stroke: 4.3%

Normal risk (n=10)

Death/Stroke

- All events: 0%
30 Day Stroke/Death/MI in high risk Registry

<table>
<thead>
<tr>
<th>Study</th>
<th>30 Day Event Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPPHIRE 2002</td>
<td>6.9%</td>
</tr>
<tr>
<td>ARCHeR 2003</td>
<td>7.8%</td>
</tr>
<tr>
<td>SECuRITY 2003</td>
<td>7.2%</td>
</tr>
<tr>
<td>BEACH 2004</td>
<td>5.4%</td>
</tr>
<tr>
<td>MAVeRIC 2004</td>
<td>5.2%</td>
</tr>
<tr>
<td>CABERNET 2004</td>
<td>3.8%</td>
</tr>
<tr>
<td>AMC TCT 2005</td>
<td>4.3%</td>
</tr>
</tbody>
</table>
Symptomatic normal risk
&
Asymptomatic normal risk
CES vs. CAS with GuardWire

Multicenter, prospective, nonrandomized 1:2 ratio

Carotid a stenosis (n=397)

Normal-risk Sx & Asx patients

Carotid Stenting with GuardWire (n=143)

Carotid endarterectomy (n=254)

Primary endpoint: death and stroke at 30 days and a composite of death, stroke, or myocardial Infarction within 30 days and death or stroke btw 31 days and 1 year

CEA vs. CAS with GuardWire

30-Day and 1-year Outcomes

Death / stroke at 30 days

Death / stroke at 1 year

\[ P=NS \]

\[ P=NS \]

\[ 2.1 \] \[ 3.6 \] \[ 10 \] \[ 13.6 \]

CAS CEA CAS CEA

CEA vs. CAS
From November 2000 to September 2005

Symptomatic carotid stenosis of 60% or more

N=527

CEA (n=259)  CAS (n=261)

Primary end point: incidence of any stroke or death within 30 days after treatment

NEJM 2006;355:1660-71
Major eligibility Criteria

**Inclusion criteria**

- Age $\geq 18$yrs
- Hemispheric or retinal transient ischemic attack or nondisabling stroke (or retinal infarct) within 120 days before enrollment
- Stenosis $\geq 60\%$ in symptomatic carotid artery

**Exclusion criteria**

- Modified Rankin S $\geq 3$
- Severe tandem lesion
- Previous Hx. (CEA,CAS)
- Uncontrolled HT or DM
- Unstable angina
- Contra-Ix. of heparin, clopidogrel
- Hx. of bleeding disorder
- Life expectancy $< 2$yr
30-Day Outcomes

Relative risk: 2.5 (95% CI, 1.2 to 5.1)

P=0.01

NEJM 2006;355:1660-71
6 Months Events

<table>
<thead>
<tr>
<th></th>
<th>CEA</th>
<th>CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events: any stroke or death after treatment</td>
<td>6.1%</td>
<td>11.7%</td>
</tr>
</tbody>
</table>

P = 0.02

NEJM 2006;355:1660-71
Conclusion

In patients with symptomatic carotid stenosis of 60% or more, the rates of death and stroke at 1 and 6 months were lower with endarterectomy than with stenting.

NEJM 2006;355:1660-71
Limitation

- Early in the EVA-3S trial, protection from embolism was not used among patients who underwent stenting, and the incidence of stroke was 25% (5 of 20).
- Protection device was used in 91.9% of carotid stenting arm.
- Learning curve for carotid stenting; Involved center had a variable degree of experience in CAS.
- Five different stents, seven different protection devices, and experience with two procedures was required for any new device used.

NEJM 2006;355:1660-71
Limitation

- Although the angiographic appearance of the lesion was not an eligibility criterion, plaque morphology (length, degree of ulceration, and presence or absence of thrombus) could be related to complication rates for stenting.

- 42 and 36 patients who underwent stenting in the EVA-3S trial received only single (unspecified) antiplatelet therapy before and after the procedure, respectively.

*NEJM 2006;355:1660-71*
30 days results from **SPACE trial** in symptomatic patients

**Randomized non-inferiority trial**

1200 patients with severe CAD (>70%) and recent neurological symptoms (< 180 days)

- 567 treated with CAS
  - 18 not treated
  - 14 treated with CEA

- 565 treated with CEA
  - 12 not treated
  - 6 treated with CAS
  - 1 died before Tx.

1183 randomised patients included on an intention-to-treat basis for analysis

*Lancet 2006;368;1239-47*
Primary endpoint

Ipsilateral stroke (ischemic stroke or intracerebral bleeding or both, with symptoms lasting more than 24 hr) or death of any cause between randomization and 30 days after Treatment.

Null hypothesis

The difference between the events rates in CAS and CEA group was 2.5% or more.

Non-inferiority margin

defined as less than 2.5%
don the basis of an expected event rate 5%

*Lancet* 2006;368;1239-47
## Outcome events up to 30 days

<table>
<thead>
<tr>
<th>Event</th>
<th>Number (%)</th>
<th>Absolute diff.</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAS (n=599)</td>
<td>CEA (n=584)</td>
<td>CAS-CEA (90% CI)</td>
</tr>
<tr>
<td>Primary endpoint</td>
<td>41 (6.84%)</td>
<td>37 (6.34%)</td>
<td>0.51* (-1.89 to 2.91)</td>
</tr>
<tr>
<td>Ipsilateral ischemic stroke</td>
<td>39 (6.51%)</td>
<td>30 (5.14%)</td>
<td>1.26 (0.77 to 2.18)</td>
</tr>
<tr>
<td>Ipsilateral intra-cerebral bleeding</td>
<td>1 (0.71%)</td>
<td>5 (0.86%)</td>
<td>0.19 (0.004 to 1.74)</td>
</tr>
<tr>
<td>Death</td>
<td>4 (0.67%)</td>
<td>5 (0.86%)</td>
<td>0.78 (0.15 to 3.64)</td>
</tr>
</tbody>
</table>

*One-sided p value for non-inferiority is 0.09*
Conclusion

- SPACE failed to prove non-inferiority of CAS compared with CEA for the periprocedural complication rate.

- Results at 6-24 months are awaited

*Lancet* 2006;368;1239-47
Limitation of SPACE trial

Actual difference (90% CI) for primary endpoint in SPACE. Because upper CI is more than 2.5, study has failed to show non-inferiority for carotid angioplasty and stenting (CAS). However, because CIs cross zero, difference in primary outcome between carotid endarterectomy and carotid angioplasty and stenting was not statistically significant.

*Lancet* 2006;368;1239-47
Limitation of SPACE trial

• Only 27% (n=151) of patients used embolic protection devices

• The difference between the two treatments is very small and many people might feel that a difference of only four events in almost 600 patients per group is negligible

Lancet 2006;368;1239-47
Limitation of SPACE trial

• Despite SPACE being the biggest trial to date, one is left with the unavoidable conclusion that it was stopped prematurely.

• Notwithstanding funding issues, the planned margin of non-inferiority (<2.5%) was based on a power calculation of 1900 patients and this larger sample might have provided much tighter CIs and more robust statistical data.

_Lancet_ 2006;368;1239-47
Vascular Medicine Perspective: CEA versus Stent

- High risk symptomatic patient (>50%)
  - carotid stenting is preferred and reimbursed
- High risk asymptomatic patient (>80%)
  - carotid stenting is preferred and reimbursed
- Normal risk symptomatic patient (>50%)
  : CaRESS, SPACE, EVA-3S
  - More data are needed (CAVATAS-2, CREST)
- Normal risk asymptomatic patient (>80%)
  : CaRESS,
  - More data are needed (CREST, ACT1)
Suggested Treatment Algorithm

1. Carotid revascularization indicated
   - Yes
   - Evaluate carotid stent risk
     - Low
     - Carotid stenting
     - High
     - Evaluate CEA risk
       - Low
       - CEA
       - High
       - Consider medical therapy
   - No
   - Medical treatment

Evaluate carotid stent risk

- Age
- Cerebral reserve
- Tortousity
- Calcification

Evaluate CEA risk

Low

High
Patient Preference

Although all of us love our surgeons,

NOBODY loves surgery!
Now. Carotid Stenting

- Up to date, CS is at least equivalent results and a more preferred therapy to CEA with appropriate learning curve and the use of the protection device in symptomatic and asymptomatic high surgical risk group.

- Technical progress, advance in technical expertise and patients selection are important to reduce the risk of CS.

- CS may be extended to all patients subsets, such as symptomatic, asymptomatic, high risk, and low risk subgroups.