Carotid Artery Stent: Is it ready for prime time?

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CAE and CAS

CAE 56 yrs old and the most studied vascular operation in history of medicine

CAS 15 yrs old and the most devated and scrutinized interventional procedure
Stroke

- Third most common cause of death
- 750,000 strokes each year in the US.
- Single most important cause of long term intellectual and physical disability.
- Huge economical burden on society.
- Approx 25% of strokes are related to extracranial carotid artery disease.
The **ONLY** reason for treating bifurcation carotid stenosis is:

**to reduce the risk of stroke**
INDICATIONS

The stroke risk associated with the intervention …should not exceed the stroke risk related to the natural history of the disease!

- **Symptomatic:** 10–15% next 6-9 months
- **Asymptomatic:** 2-3% per year
CAE for Carotid Stenosis

Risk of Stroke

- **NASCET**
  - ASA: 26.0%
  - Surgery: 9.0%

- **ACAS**
  - ASA: 10.6%
  - Surgery: 4.8%
CAROTID ENDARTERECTOMY INDICATIONS

GOAL: STROKE PREVENTION (IF BENEFIT > RISK)

SYMPTOMATIC: > 50%
- NASCET I and II and ECST

ASYMPTOMATIC: > 80%
- ACAS and ACST

If risk of surgery is less than 6%

If risk of surgery is less than 3%
Endarterectomy Trials: Exclusions

**NASCET and ACAS Exclusions**

- Age > 79
- Prior ipsilateral CEA
- Unstable coronary syndrome
- Myocardial infarct in previous 6 months
- Cardiac valvular or rhythm abnormality likely to cause embolic cerebrovascular symptoms
- Contralateral occlusion
- A more severe lesion cranial to the surgical lesion
- Contralateral CEA within previous 4 months
- Uncontrolled hypertension or diabetes
- Organ failure likely to cause death within 5 years
- Total occlusion
- Major surgical procedure in previous 30 days
- Prior severe CVA
- Progressing neurologic syndrome
Endarterectomy outcomes in high surgical risk patients

There are no randomized trials in high surgical risk patients to guide recommendations for therapy
FDA News
FOR IMMEDIATE RELEASE
August 31, 2004
Media Inquiries: (301) 827-6242
Consumer Inquiries: 888-INFO-FDA
FDA Approves Stent System as an option for patients at high risk for CAE
Carotid Artery Stenting: INDICATIONS

FDA approved CAS as an alternative to CAE in patients at high risk for surgery

1. ANATOMICAL:
   - Lesions too high or too low
   - Tandem lesions
   - Contralateral occlusion or stenosis
   - Restenosis post CAE
   - Post radiation or radical neck surgery
   - Neck too short, C-spine immobility
   - Contralateral laryngeal nerve palsy
Carotid Artery Stenting: INDICATIONS

2. PHYSIOLOGICAL (COMORBIDITIES):

- Older than 75
- CHF class III or IV
- EF less than 30%
- USA or recent MI
- Severe COPD
- Cardiac disease requiring surgery within 6 weeks
- Severe CAD (2 lesions > 70% stenosis or abn. Stress test in 2 territories or large defect)
- Renal failure requiring dialysis.
Diagnostic Algorithm for Extracranial Carotid Disease

Suspicion of Extracranial Carotid Disease

Carotid Duplex Ultrasonography

<50% Stenosis

50-99% Stenosis in Appropriate Clinical Scenario

Occlusion

<50% Stenosis → Appropriate F/U DUS

50-99% Stenosis in Appropriate Clinical Scenario → MRA/CTA → DUS/MRA/CTA Agree?

YES → CAS

NO → Angio

Appropriate F/U DUS

Occlusion → Appropriate F/U DUS

Surgery

Med Rx
CASE: High surgical risk

- 81 yr old, severe CAD with USA and needs CABG.
- Found to have an asymptomatic 90% R ICA stenosis
- Hypertension
- Hypercholesterolemia
Duplex US
Aortic Arch
Aortic Arch Types

Type I Arch

Type II Arch

Type III Arch
R ICA
Filter
After predilation
After Stent
Cerebral protection is necessary:
Filters Approved in US

- AngioGuard, Cordis
- EZ Filter, Boston Sci
- Spider Rx Filter, ev3
- Accunet Filter, Abbott
- Emboshield NAV6, Abbott
- Fibernet, Invatec
CASE: Multiple high risk features

- 80 yr old Tonsillar cancer 1988, s/p R radical neck dissection 1988 and RT
- Bilateral CAE 10 yrs ago
- Cardiomyopathy, ICD

- Asymptomatic, progressive R CCA stenosis by Duplex
L ICA

Prior L CAE
R Carotid Stenosis Post Neck radiation
Carotid Stenting
Balloon predilatation
Post Stenting
CASE: Post CAE restenosis

A 63-year-old diabetic with neuropathy, history of HTN and hypercholesterolemia, was s/p L CAE in Sep 2006 after TIA. He presented with a TIA/minor CVA in Dec 2008, and duplex revealed critical restenosis in R ICA and L ICA.
L ICA
Post CAE
restenosis
18 months later: Carotid Duplex
What about data?
Modern Randomized Trials

• **US TRIALS:**
  - Sapphire, NEJM 2004
  - CREST, on line NEJM 5/26/10

• **EUROPEAN**
  - EVA 3S, NEJM 2006
  - SPACE, Lancet 2006
  - ICSS, Lancet 2010
Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy

The SAPPHIRE Study

- U.S. Randomized, Multicenter trial in high-risk patients
- Symptomatic > 50% or asymptomatic > 80% stenosis
- Experienced Operators
SAPPHIRE: Trial Design

Integrated multi-specialty team
Surgeon, Interventionalist, Neurologist

- Surgical Refusal registry
  N=406

- Randomized
  N=310

- Interventional Refusal registry
  N=7

CAS 150
CEA 151

Primary end-point: Death, any CVA and MI at 30 days
# SAPPHIRE

## 30-Day Events

<table>
<thead>
<tr>
<th>Event</th>
<th>STENT (156 pts)</th>
<th>CEA (151 pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DEATH</strong></td>
<td>0.6%</td>
<td>2%</td>
</tr>
</tbody>
</table>
| **CVA:**
  Major:                      | 0.6%            | 2%            |
  Minor:                       | 3.8%            | 3.3%          |
| **MI**                       | 2.6%            | 7.3%          |
| **Death or CVA:**            | 4.5%            | 6.6%          |
| **Death/MI/CVA:**            | 5.8%            | 12.6%*        |

*p= 0.047*
SAPPHIRE: 1 year primary endpoint

- **STENT**
  - CEA: 19.9%
  - Stent: 11.9%
  - $P = 0.048$

Cumulative Percentage of MAE vs. Time after Initial Procedure (days)
SAPPHIRE Randomized Cohorts: CEA and CAS
30 day stroke and ipsilateral stroke 31-1080 days

No advantage of CEA over CAS in efficacy

<table>
<thead>
<tr>
<th>Time (Days)</th>
<th>CEA 3.0%</th>
<th>CAS 3.6%</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>3.0%</td>
<td>3.6%</td>
</tr>
<tr>
<td>360 Days</td>
<td>5.8%</td>
<td>4.9%</td>
</tr>
<tr>
<td>720 Days</td>
<td>6.7%</td>
<td>6.3%</td>
</tr>
<tr>
<td>1080 Days</td>
<td>6.7%</td>
<td>7.1%</td>
</tr>
</tbody>
</table>

p = 0.945
SAPPHIRE: Conclusions

• First randomized study comparing carotid stenting with emboli protection to CAE in high risk patients
• Major adverse cardiac events included MI unlike prior CAE trials
• Carotid artery stenting showed to be an option to CAE in high-risk patients
• Led to FDA approval in that group of patients
Carotid Revascularization
Endarterectomy Vs Stenting
Trial: CREST

Presented at the International Stroke Conference in San Antonio, Feb 26, 2010
Published online NEJM on May 26, 2010
CREST: FINAL ENROLLMENT

CREST Cumulative Randomizations
2000 through July 2008

# of Patients

2000 total
Mar-04
Jun-04
Sep-04
Dec-04
Mar-05
Jun-05
Sep-05
Dec-05
Mar-06
Jun-06
Sep-06
Dec-06
Mar-07
Jun-07
Sep-07
Dec-07
Mar-08
Jun-08

0
500
1000
1500
2000
2500
3000

Asx
Sx

1181
1321
CREST

- CREST is a decade long, multi-million dollar NIH study involving nearly 120 centers and 224 interventionalists.

- It is the largest (2500) randomized prospective study of CAS vs. CEA in both symptomatic and asymptomatic as well as low and high surgical risk patients.
CREST: Primary Endpoint*
Periprocedural period

CAS: 5.2
CAE: 4.5

*Death, any Stroke or MI

P = 0.38
CREST: Periprocedural

Major CVA: 0.9 vs 0.6%
Ipsilateral Stroke
After 30d and up to 4 yrs

\[ P = 0.85 \]
CREST: Symptom status
Any CVA or post procedural ipsilateral CVA

![Bar chart showing symptom status comparison between CAS and CAE](chart.png)
CREST: Age Influence

![Graph showing age influence on hazard ratio for primary end point with CAS.](image)

**Age 68**
CREST CONCLUSION

• CAS and CEA have similar global outcomes:
  – CAS caused more minor strokes than CEA
  – CEA caused more MIs and cranial nerve palsies
  – Symptomatic status: little more advantage for CEA

• AGE:
  – Younger patients slightly better with CAS
  – Older patients better with surgery
How about New Technology?

New stents

New Embolic Protection Devices:
New Filters

Proximal Protection
MGuard Stent

A stent wrapped with ultra-thin polymer mesh sleeve, knitted to the external surface.
EPIC FiberNet® EPS

No delivery system required with a crossing profile 1.7 to 2.9 F

Fiber-based filter conforms to asymmetrical vessels

**EPIC (30 days results)**
-
*All CVA: 2.1%
Death 0.4%
Mi 0.4%

Particle entrapment as small as 40 µm
30 Day Event Rates

All Stroke Clinical Trials Comparison

2000

SECURITY 6.9%
ARCHER II 5.5%
ARCHER III 5.4%
SAPPHIRE 4.9%
CREATE I 4.8%
CREATE II 4.4%
MAVERIC 4.0%
CABERNET 3.4%
EPIC 2.1%

2008
Proximal Cerebral Protection

Proximal Protection may be the “game changer” in Carotid Revascularization

Christopher White. Editorial
JACC 2010:55: 1668
EPD Categories

Distal protection (DEP)
- Filters, Antegrade Flow
- Distal Flow Blockage

Proximal protection (PEP)
- Flow Reversal
- A-V Shunt
The Concept: Flow Reversal
Applicable to the most complex anatomicies
PROXIMAL PROTECTION TRIALS

- **EMPIRE**: Gore Flow Reversal (WL GORE)
- **ARMOUR**: Mo.MA Device (InVatec).
- Italian Single Center Experience (1300 patients) using the MoMA Device
EMPIRE
GORE FLOW REVERSAL SYSTEM
MAJOR ADVERSE EVENT RATE AT 30 DAYS (N=245)

- Age > 80: 16%
- Symptomatic 32%
- Independent Neurology Eval.

Bar chart showing:
- MI: 0.8%
- Major Stroke: 0%
- Minor Stroke: 2%
- Death and Stroke: 2.9%
ARMOUR TRIAL
USING THE MO.MA PROXIMAL PROTECTION (N=257)

Death: 0.8%
Stroke: 2%
MI: 1.9%
MACCE*: 2.3%

* MACCE = Death + CVA + MI
ITALIAN REGISTRY: PROXIMAL PROTECTION USING THE MO.MA DEVICE
30-DAY OUTCOMES (N=1300)

- Age > 80: 10%
- High surgical risk: 50%
- Symptomatic: 28%
- Independent Neurology Eval.

Minor Strokes: 0.46
Major Strokes: 0.46
Death: 0.61
Any Stroke or death: 1.38%

CONCLUSION

• Optimal role of CAS Vs CAE continues to be debated…. but they are COMPLEMENTARY
• CAS is the procedure of choice in many high-surgical-risk patients (unstable cardiac disease, post CAE restenosis, post radiation and other anatomical risk factors).
• Favor CAE in elderly patients with symptoms especially with aortic arch disease (difficult access, calcified lesions and complex anatomies)
CONCLUSION

• Although safety of CAS in “low risk” patients (young, asymptomatic with favorable anatomy) is proven by current trials when done by experienced operators, the best approach at a given Institution should be based on a Team Approach.

• However, CMS reimbursement, financial and turf issues are currently the major obstacles for adoption of stenting and are some of the most important factors in the decision making today.
CONCLUSION

• Technology will continue to improve outcomes in CAS (i.e. new filters, stents, and proximal protection)

Thank you!