Carotid Stenting: Unanswered Questions and Future Directions

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Potential Conflicts

Consultant & research support:
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Financial interests:
Boston Scientific EPI, Cordis, J&J, Micrus, Endotex, Access Closure Inc
I. Current Results…Ongoing Trials
II. Will proximal embolic protection find a niche?
I. Manpower
II. Training
V. When will patients get full access?
New Results

- Endarterectomy versus Stenting in Patients with Symptomatic Severe Carotid Stenosis
- EVA-3S Trial
- New England Journal of Medicine
- October 19, 2006

- Off The Chart !!!!
EVA-3S Trial: Design

- Prospective, Multicentered, Randomized
- Sponsored by French Ministry of Health
- Inclusion:
  - Symptomatic Carotid Stenosis > 60%
  - Patients equal candidate for either option
- Primary endpoint:
  - Any stroke or death within 30 days- (Not MI)
- Stopped prematurely by safety monitoring committee after 527 patients were enrolled
EVA-3S Trial: Results

- **30 Day rate of any stroke or death**
  - Endarterectomy = 3.9%
  - Carotid Stent = 9.6%
  - Relative Risk of 2.5 (95% CI 1.2 to 5.1)

- **30 Day rate of disabling stroke or death**
  - Endarterectomy = 1.5%
  - Carotid Stent = 3.4%
  - Relative Risk of 2.2 (95% CI 0.7 to 7.2)***
    - Not statistically significant
EVA-3S Trial: Results

- 6 month rate of any stroke or death
  - Endarterectomy = 6.1%
  - Carotid Stent = 11.7% \( (p = 0.02) \)

- **Conclusion:**
  - For symptomatic patients (>60%) with acceptable surgical risk, rates of death and stroke were lower with CEA than with stenting
EVA-3S Trial: Limitations

- Distal protection was only “[strongly] recommended” after February 2003 (50% trial duration)
  - 30 day stroke or death
    - Without DEP = 25% (5 of 20)
    - With DEP = 7.9% (18 of 227)

- If 7.9% rather than 9.6% is used:
  - Relative Risk = 2.0 (p = 0.07)
EVA-3S Trial: Limitations

• Rates of MI were not assessed
  – (Reduced rate of MI was one source of benefit identified in the SAPPHIRE Trial)

• Only 30 day and 6 month follow up
  – (Despite trial ongoing since 2000)
EVA-3S Trial: Limitations

• Experience bias
  – Vascular surgeons:
    – Required 25 CEAs in the year prior to study entry
  – Endovascular physicians:
    – Required 12 carotid stents or 35 “supra-aortic stents” with at least 5 carotid stents
    – Or, Allowed to receive training and credentialing “under supervision” as they enrolled patients in the trial
    – Allowed to use new stents after only two cases
EVA-3S Trial: Limitations

• Enrollment Bias…?
  – Total CEA case volumes were not discussed
  – Estimated <<10 of all patients randomized
    – Thirty hospitals
    – Assuming only 1 vascular surgeon per hospital with the enrollment criteria minimum 25 cases/yr
    – 4.75 years of enrollment = 3562.5 patients
  – 5 pts taken to OR (bailout)….2 strokes
CAPTURE 2500
Age & Symptoms

- DSMI overall  \( Sx \ 12.2 \quad \text{Asx} \ 5.3 \ (.0001) \)
- DS (F Worse)  \( Sx \ F <80 \ \text{vs} \ \text{Sx M} <80 \ (.03) \)
CREATE High Risk Registry

**EV3 Stent + Spider Filter**

30 Day Results

- **30 day death, stroke and MI** 6.2%
- **Major Stroke** 3.5%
- **Hemorrhage** 1.3%

- **Risk Factors**
  - Symptomatic carotid stenosis
  - Renal failure
  - Duration of filter deployment
**SPACE Trial**

**RPCT (Sx)  N=1200**

*Death, Stroke and MI - 30 day*

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Event Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS</td>
<td>6.8%</td>
</tr>
<tr>
<td>CEA</td>
<td>6.3%</td>
</tr>
</tbody>
</table>

*p = 0.09*

*CEA better in older patients*
CAS Risk Factors

1) Symptomatic lesion
2) Sx > age 80
3) Renal Failure
4) Multiple stents
5) Duration Filter deployment
6) Pre dilitation
7) Corkscrew/calcified arteries
CAS
Non Predictors of Risk

1. Sex
2. Calcification
3. Residual stenosis
4. Filter
5. Contralateral occlusion
6. Smoking
7. Diabetes
8. Statins
Complementary Techniques

- Most evidence shows Stents are not inferior in efficacy and safety to CEA. – ARCHeR, CaRESS, SAPPHIRE
- We know which pts are not suited for CEA…from EXPERIENCE!
- We are learning which pts are not suited for CAS…from trials and from experience
NASCET Exclusion Criteria

Poor Candidates for CEA

- Age > 79
- Previous ipsilateral endarterectomy
- Intracranial stenosis > carotid lesion
- Lung, liver, or renal failure
- Unstable angina
- MI < 6 months
- Uncontrolled hypertension or diabetes
- Contralateral CEA < 4 months
- Progressive neurologic dysfunction
- Major surgery < 30 days
Low Risk Sx Patients

- NASCET Surgical risks (30 day peri-op M&M)
- Symptomatic with ≥ 70% stenosis
  - 5.8% total
  - 3.7% minor stroke,
  - 1.5% major stroke
  - 0.6% death
- How about “moderate risk” ??
- Symptomatic ≥ 70% and Contralateral Occlusion
  - 14.3% total
Long Term Durability

• Major events at 3 years
  – Stent 25.5% vs. CEA 30.3% (p=0.231)

• Death at 3 years
  – Stent 20.0% vs. CEA 24.2% (p=0.280)

• Ipsilateral stroke at 3 years (All stroke 30 days)
  – Stent 7.1% vs. CEA 6.7% (p=0.945)

• Need for same vessel revascularization
  – Stent 3.0% vs. CEA 7.1% (p=0.084)
Long Term Durability

- Need for revascularization
  - 2.2% at 1 year

Doppler Ultrasound Follow Up

<table>
<thead>
<tr>
<th></th>
<th>1mo</th>
<th>1yr</th>
<th>2yr</th>
<th>3yr</th>
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</thead>
<tbody>
<tr>
<td>n =</td>
<td>504</td>
<td>437</td>
<td>166</td>
<td>86</td>
</tr>
<tr>
<td>&lt;50% Stenosis</td>
<td>80%</td>
<td>65%</td>
<td>70%</td>
<td>70%</td>
</tr>
<tr>
<td>&gt;70% Stenosis</td>
<td>1%</td>
<td>5%</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>
What will CREST teach us that we don’t already know?

- Differences from EVA-3S
  - Distal Embolic Protection in most patients
  - Vetting of all surgeons & interventionalists
  - MI rates are monitored
  - Dual antiplatelet therapy in all patients
  - Long term follow up
  - More rigorous interventionalist credentialing

- CREST is now **more important** than ever
  - Challenges to Recruitment are present
Conclusions

• CAS and CEA are complementary

• High-risk CEA patients should be treated by CAS: proven efficacy with less risk

• Asymptomatic patients deserve treatment…we don’t know which is best yet

• Low-risk patients should be enrolled in further trials! CREST, ACT 1…
Clinical Equipoise = Endovascular Superiority
Will proximal embolic protection find a niche?

- Low GSM score
- Perilesional Kinks
- Distal Tortuosity
- No landing zone
- Complete occl
- Luminal thrombi

- Ok arch
- Ok CCA
In all FDA studies on CAS with embolic protection, visible debris was collected in over 50% of cases.
## CAS With and Without Protection

<table>
<thead>
<tr>
<th>Event</th>
<th>Without DEP</th>
<th>With DEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor stroke</td>
<td>3.7% (94/2537)</td>
<td>0.5% (5/896)</td>
</tr>
<tr>
<td>Major stroke</td>
<td>1.1% (28/2537)</td>
<td>0.3% (3/896)</td>
</tr>
<tr>
<td>Death</td>
<td>0.3% (8/2537)</td>
<td>0.8% (8/896)</td>
</tr>
<tr>
<td>Any stroke or death</td>
<td>5.5% (40/2537)</td>
<td>1.7% (16/896)</td>
</tr>
</tbody>
</table>

Kastrup et al *Stroke* 2003
Carotid Stenting with Flow Reversal
Illustrative Case

- 82 year old woman
  - Three episodes of dysarthria, paucity of speech
  - One episode with right upper extremity weakness
- Neurological exam normal – NIHSS 0
61% Symptomatic Stenosis
Flow Reversal

• Ischemic time - 6 minutes
• Patient became less arousable and developed expressive aphasia
• Rapidly normalized with return of antegrade flow
Carotid Stent Evolution

10 year history

Initial results discouraging … High M&M
- Technology evolution
- Embolic protection
- Better patient selection
- Large clinical experience

Evolution of Trial Results
How much will CAS cost?

• Costs are already within the range of other preventative strategies
  – Highly effective, Small NNT
  – Shorter ICU stay and hospitalization

• The materials cost will improve with more market competition

• Carotid stenting may become one of the most cost effective stroke prevention strategies
When will patients’ get full access?

• Low Risk Trials are underway…

• **EVERYONE** is watching

There is no stopping CAS…more data and technology evolution will make CAS mainstream

Best Guess…. 2010 ?
What Effect Will Subspecialty “Standards” and Lobbying Have on Cardiologists and Carotid Stenting?
OPPORTUNITY

You’ll always miss 100% of the shots you don’t take.
Who Will Treat Acute Stroke?

- 750,000 CVAs per year and growing
- ~250 neurointerventionalists
- ~60 endovascular neurosurgeons
- ~5 endovascular neurologists
- 8,000 interventional cardiologists
How Do We Get There?

• Training
• Collaborating
Collaboration

Subspecialty Strengths

- Neurology
- Radiology
- Vascular surg
- Vascular med
- Cardiology

- End organ cognitive
- Imaging/cath skills
- Own CEA market
- Cognitive/imaging
- Cath/angioplasty skills
- Clinicians
- Industry partners
- Clinical research
Simulator Training Model

Commercial Pilot
- Mandatory yearly training
- 60 hours *simulated* instrument training
- 60 hours *actual* instrument training
“Virtual Reality Training Improves Operating Room Performance”

- Seymour, Gallagher, et al.
- Randomized, Double-Blinded Study
- 16 surgical residents
- Assessment during laparoscopic cholecystectomy by surgeon-investigator blinded to the resident’s training status.
Learn Angiography with No Patient Risk
Scan In Tomorrow’s Case and Practice Before You Treat
• 27 year old female
• Cesarean delivery 8 weeks prior
• Ground level fall and head impact
• No LOC, No seizure
• Acute onset right neck and head pain
• Left upper extremity weakness
• Slurred speech
Illustrative Case

• Meds: Oral contraceptives

• In ED: NIHSS = 11
• Left facial weakness, dysarthria, left upper extremity weakness, left sided anesthlesia

• Head CT: no acute trauma
• Head CT perfusion…
Original CT Perfusion

Time to Peak
Emergent Angiogram
Acute RICA occlusion

- Heparin 4000
- ACT > 250
Microcatheter Injections

Nautica microcatheter
Transcend exchange microwire
Carotid Stent

BMW wire to supraclinoid ICA
Xpert stent 4 x 40
Still occluded proximally
Xpert stent 5 x 40
No overlap
Xpert stent 5 x 30
Acute MCA Occlusion
Merci Clot Retrieval

... Integrilin
Neuroform Stent for Failed Merci

• Neuroform 3.5 x 20
  – Friction from 3 ICA stents caused difficulty and premature deployment
  – Pulled into CCA and advanced with cook shuttle into ECA
Neuroform Stent for Failed Merci

- Renegade microcatheter

- Neuroform (4 x 20) loaded into microcatheter
Follow Up CT perfusion
Post Procedure MRI