Approach to Intervention in Carotid Artery Disease: The Interventionalist’s Perspective and Strategy

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Vascular Medicine and Intervention
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I am a Carotid Stentor, and do not perform CEA
THERAPY FOR CAROTID ARTERY STENOSIS

Stenting or CEA or Medical Therapy?

*What is the role of each??*

Remains a HOT topic
65 year old diabetic man with CAD and carotid bruit on good medical therapy. He asks—“Doc, what are my options?”

Proximal ICA PSV 490 EDV 263
Am I providing best therapy to prevent stroke, death, disability, and morbidity for my individual patient, and is this the therapy my patient prefers?"

Answer to these questions are not always clear, and certainly consensus is lacking.
**Carotid Artery Stenosis**

**Strategies for stroke prevention**

- Optimal medical therapy – this is a given for ALL patients at risk (Consensus!)

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**MRC Asymptomatic Carotid Surgery Trial (ACST): Medical RX**

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...and we need to do better!

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*ACST Collaborative Group. Lancet 2004; 363: 1491*
Medical Treatment for Asymptomatic Carotid Stenosis

CAS Landscape Today
Temporal Trends in Medicare CAS & CEA

Graph showing temporal trends in Medicare CAS & CEA

- Per 10,000 Endarterectomy
- Per 10,000 Stenting
Consensus:

- Revasc is indicated (on top of OMT) for symptomatic patients
- CEA has been existing standard
- Asymptomatic patients – threshold for revasc now needs to be re-evaluated

Where does CAS fit in?
Evidence base often derived from flawed trials, registries, databases – with variable methodologies:

- Comparisons made b/n patients who are fundamentally different (apples to oranges)
- Operators w/variable competency...differential skill level and procedural experience between those doing CAS vs. CEA
- Inconsistent neurologic assessment for stroke
- Utilization of equipment that is outdated for CAS
- Preponderance of Medicare age patients (commercial payors won’t allow investigational Rx)
“Characteristics of patients referred for CAS differ markedly from those referred for CEA. Because of extreme clinical disparities between these patients, …comparative effectiveness analyses of observational data will be difficult.”
### European trials: ICSS...RCT of Symptomatic Standard Risk

#### Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CAS (853)</th>
<th>CEA (857)</th>
<th>HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, stroke, MI</td>
<td>8.5%</td>
<td>5.2%</td>
<td>1.69</td>
<td>0.006</td>
</tr>
<tr>
<td>Any stroke</td>
<td>7.7%</td>
<td>4.1%</td>
<td>1.92</td>
<td>0.002</td>
</tr>
<tr>
<td>Any stroke or death</td>
<td>8.5%</td>
<td>4.7%</td>
<td>1.95</td>
<td>0.001</td>
</tr>
<tr>
<td>Disabling stroke or death</td>
<td>4.0%</td>
<td>3.2%</td>
<td>1.28</td>
<td>0.34</td>
</tr>
<tr>
<td>All-cause death</td>
<td>2.3%</td>
<td>0.8%</td>
<td>2.76</td>
<td>0.017</td>
</tr>
</tbody>
</table>
A minimum of 50 total stenting procedures, of which at least ten should be in the carotid artery; tutor-assisted procedures allowed for interventionalists with insufficient experience.

Metzger: “Are-You-Kidding-Me” Trial?
Ken Rosenfield in his first NASCAR race!
Physician Experience Dictates Outcomes

Data from CAPTURE 2

Source: JACC Interv 2011; Gray et al.
### RCT’s: CAS vs. CEA

<table>
<thead>
<tr>
<th>Symptomatic</th>
<th>Asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk</td>
<td>High-risk</td>
</tr>
<tr>
<td>Standard-risk</td>
<td>Standard-risk</td>
</tr>
</tbody>
</table>

**RCTs**:
- **SAPPHIRE**: completed
- **CREST**: ongoing
- **EVA3s, SPACE 1**: completed
- **ACT 1, SPACE 2**: ongoing
- **CREST**: completed

**None**
SAPPHIRE RCT: 1-Year Outcome
Sx and Asx high surgical risk

Cumulative Percentage of MAE – Stroke, death, MI

- **Stent**: 12.0%
- **Endarterectomy**: 20.1%

Time after Initial Procedure (days)
SAPPHIRE 3-Year Outcomes

Freedom from MAE

Declining Risk of Stroke, Death and MI with CAS

Catheterization and Cardiovascular Interventions 82:715–726 (2013)
Conditions qualifying pt at high surgical risk

*Per CMS (3/05), based on hi-risk studies*

<table>
<thead>
<tr>
<th>A. Anatomical Conditions</th>
<th>B. Co-morbid Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CCA lesion(s) below clavicle</td>
<td>• Clinically significant cardiac dz</td>
</tr>
<tr>
<td>• High cervical Internal Carotid Artery (ICA)</td>
<td>• Recent Myocardial Infarction (MI)</td>
</tr>
<tr>
<td>• Previous neck radiation</td>
<td>• LVEF &lt; 30%</td>
</tr>
<tr>
<td>• Prior neck surgery/radical neck dissection</td>
<td>• CHF NYHA Class III or IV</td>
</tr>
<tr>
<td>• Restenosis of prior CEA</td>
<td>• Abnormal stress test</td>
</tr>
<tr>
<td>• Tracheostomy</td>
<td>• Need for open-heart surgery</td>
</tr>
<tr>
<td>• Contralateral carotid occlusion</td>
<td>• Unstable angina: CCS III/IV</td>
</tr>
<tr>
<td>• Contralateral laryngeal nerve palsy</td>
<td>• Severe pulmonary disease</td>
</tr>
<tr>
<td></td>
<td>• Age ≥80</td>
</tr>
<tr>
<td></td>
<td>• ESRD on dialysis</td>
</tr>
</tbody>
</table>
CREST
Primary endpoint ≤4 years (mean 2.5)

Peri-procedural outcomes

MAE (%)

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7.2</td>
<td>6.8</td>
</tr>
</tbody>
</table>

P = 0.51

HR 1.11  95% CI: 0.81-1.51
CREST: Peri-procedural Stroke and MI

<table>
<thead>
<tr>
<th></th>
<th>CAS vs. CEA</th>
<th>Hazard Ratio 95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Stroke</td>
<td><strong>4.1 vs. 2.3%</strong></td>
<td>HR = 1.79; 95% CI: 1.14-2.82</td>
<td>0.01</td>
</tr>
<tr>
<td>MI</td>
<td><strong>1.1 vs. 2.3%</strong></td>
<td>HR = 0.50; 95% CI: 0.26-0.94</td>
<td>0.03</td>
</tr>
<tr>
<td>Major Stroke</td>
<td><strong>0.9 vs. 0.6%</strong></td>
<td>HR = 1.35; 95% CI: 0.54-3.36</td>
<td>0.52</td>
</tr>
</tbody>
</table>
Neurological Residual Deficit Rates Associated with Minor Strokes @ 6 Months

$\Delta = 0.50\%$

$\Delta = 0.02\%$

% of Per Protocol Population

1 Month

1.10%

n = 12

0.60%

n = 7

6 Months

0.62%

n = 7

0.60%

n = 7
Death or **Major** Stroke for CAS over CREST Enrollment (all pts)

- 2000-2004: 2.5% (N=160)
- 2005: 2.5% (N=201)
- 2006: 0.7% (N=308)
- 2007: 0.0% (N=298)
- 2008: 0.6% (N=164)

50% Trial Enrollment in August 2006
Conclusions

• Primary endpoint shows equivalence
• lower minor stroke with CEA and lower MI with CAS
• Significant liabilities of CEA (access cx, CN palsy, etc.) not captured in endpt
• Overall results of both are spectacular: Event rates lowest of any large RCT
• Issues:
  – Included both sx and asx: not powered to analyze independently
  – No Comparison to OMT alone
### ECVD Guidelines 2011 - Recommendations of 14 Specialties re: revascularization

<table>
<thead>
<tr>
<th></th>
<th>Symptomatic patients</th>
<th>Symptomatic patients</th>
<th>Asymptomatic patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>50-69% stenosis</strong></td>
<td>Class I LOE: B</td>
<td>Class IIb LOE: B</td>
<td></td>
</tr>
<tr>
<td><strong>CEA</strong></td>
<td>Class I LOE: B</td>
<td>Class I LOE: A</td>
<td>Class IIa LOE: A</td>
</tr>
<tr>
<td><strong>Stent</strong></td>
<td>Class I LOE: B</td>
<td>Class I LOE: B</td>
<td></td>
</tr>
</tbody>
</table>
Differences between CEA and CAS outcomes...no longer lies in the procedure choice, but rather:

- Operator
- Case selection
- Equipment and technique

Level I evidence and guidelines support offering CAS as (covered) option

Operators need appropriate training, experience, and judgement

Playing field should be level

- all patients with Carotid disease medical Rx or undergoing revasc should have closer oversight, independent neuro eval
CAROTID STENTING
Case Selection and Technical considerations

- Access to lesion – Arch type
- Tortuosity
- Lesion morphology
- EPD suitability
- Brain “reserve”
- Overall patient “protoplasm”
Aortic Arch Type I - Ideal

~70%-75% of patients
Aortic arch Type III – suboptimal
Likely not good candidates for CAS
Tortuous ICA:
• 90 degree take-off
• 120 degree prox. turn

XS Tortuosity - Higher Risk for CAS
“Look before you jump!”
Select appropriate patients to avoid this!
Filter/Frame Length and Landing Zones

Need enough parking space...

Ref: WLGore Website
Alternatives for embolic protection

Proximal Occlusion

- ASPIRATION
- A-V SHUNT
Profi – DW MRI lesions (embolic brain burden)
## Carotid Mesh Stent Designs

<table>
<thead>
<tr>
<th></th>
<th>Gore</th>
<th>Terumo Roadsaver</th>
<th>CGuard™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td>[Image of Gore stent design]</td>
<td>[Image of Terumo Roadsaver stent design]</td>
<td>[Image of CGuard™ stent design]</td>
</tr>
<tr>
<td>Aperture Size</td>
<td>500µ</td>
<td>375-500µ</td>
<td>150-180µ</td>
</tr>
<tr>
<td>Materials</td>
<td>PTFE mesh (Heparin coated) on nitinol stent</td>
<td>nitinol on nitinol</td>
<td>PET MicroNet™ on nitinol stent</td>
</tr>
<tr>
<td>(Min Guide Sheath/ Min Guide Cath)</td>
<td>5F/7F</td>
<td>5F/7F</td>
<td>6F/8F</td>
</tr>
<tr>
<td>Details</td>
<td>• Launched SCAFFOLD trial in Sept 2013</td>
<td>• Data on first 11 pts presented at LINC (Max Amor, MD)</td>
<td>• Initial placements promising</td>
</tr>
<tr>
<td></td>
<td>• PI: Bill Gray, MD</td>
<td>• Flexibility, plaque coverage and ability to conform to any anatomy mentioned as key benefits</td>
<td>• 11 of 11 KOL’s (LINC) felt our aperture size a benefit over larger</td>
</tr>
<tr>
<td></td>
<td>• Target 351 pts</td>
<td>• Easy to recross (tapered ends)</td>
<td>• Data on MGuard MicroNet a “plus” for CGuard</td>
</tr>
<tr>
<td></td>
<td>• Has enrolled 100 pts. FDA has stopped trial requesting 6 mo F/U on these 100 before proceeding</td>
<td></td>
<td>• Ability to dilate MicroNet at external bifurcation a potential benefit</td>
</tr>
</tbody>
</table>

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Procedural Selection:
Transcervical Approach With Flow Reversal

ENROUTE™ Transcarotid Stent and Neuroprotection System

- Blood flow is reversed from the common carotid artery
- Blood flow is returned to femoral vein
- Dynamic Flow Controller Hi / Low / Off
- Embolic filter (200µ)
- Shorter delivery system and wires for simplified setup and delivery

Silk Road Medical
Perspectives

Neurology
CMS & others

- Improved medical Rx may make revascularization obsolete
- “Need more data”
CREST-2 Registry: Objective

- The C2R CAS Registry (C2R) will promote rapid initiation and completion of enrollment in the CREST-2 trial
Perspective on CAS

• Widely divergent and strongly held opinions re: role and efficacy of CAS
• Well-conducted trials show CAS performed by experienced operators utilizing proper technique in appropriately selected pts is an excellent procedure
• Say “no” to high-risk CAS cases
• Prox. protection may extend utility to more patients
• CAS does NOT replace optimal medical Rx
• CAS does NOT replace CEA (ALL high-CAS risk, low CEA-risk pts best w CEA or med Rx)