CAROTID STENOSIS: Diagnosis and Treatment . . . Where Are We Now?

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2015 Cardiovascular Symposium
Magnitude of the Problem

- Over **795,000 people** in the US have a stroke each year.
- Almost **130,000** are fatal (**1 out of every 19 deaths**)
- About **87%** of all strokes are ischemic strokes
- About **185,000 strokes**—**nearly one of four**—are in people who have had a previous stroke.
- Stroke costs the United States an estimated **$36.5 billion** each year.
Genesis of Stroke

Approximately 20% of strokes are related to carotid artery disease.
Carotid Duplex

- B-mode Imaging
- Color Flow
- Doppler Velocities
## Carotid Duplex - Interpretation

**TABLE 3**

Consensus Panel Gray-Scale and Doppler US Criteria for Diagnosis of ICA Stenosis

<table>
<thead>
<tr>
<th>Degree of Stenosis (%)</th>
<th>ICA PSV (cm/sec)</th>
<th>Plaque Estimate (%)</th>
<th>Additional Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;125</td>
<td>None</td>
<td>ICA/CCA PSV Ratio</td>
</tr>
<tr>
<td>&lt;50</td>
<td>&lt;125</td>
<td>&lt;50</td>
<td>&lt;2.0</td>
</tr>
<tr>
<td>50–69</td>
<td>125–230</td>
<td>≥50</td>
<td>2.0–4.0</td>
</tr>
<tr>
<td>≥70 but less than near occlusion</td>
<td>&gt;230</td>
<td>≥50</td>
<td>&gt;4.0</td>
</tr>
</tbody>
</table>

- Normal
- <50
- 50–69
- ≥70 but less than near occlusion
- Near occlusion
- Total occlusion

<table>
<thead>
<tr>
<th>ICA EDV (cm/sec)</th>
<th>ICA EdV (cm/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>&lt;40</td>
</tr>
<tr>
<td>40–100</td>
<td>40–100</td>
</tr>
<tr>
<td>&gt;100</td>
<td>&gt;100</td>
</tr>
</tbody>
</table>

- ICA/CCA PSV Ratio
- ICA EDV
- Variable
- Not applicable

* Plaque estimate (diameter reduction) with gray-scale and color Doppler US.
Carotid Duplex - Limitations

- Acoustic windows
  - Obesity
  - High Bifurcation

**Sensitivity and Specificity = 85-90%**

- Elevated velocities without obstruction
  - Contralateral occlusions
  - Significant tortuosity
  - Carotid stents

- Subtotal vs Complete Occlusion
Complimentary Imaging Modalities

- **CT Angiography**
  - **Advantages**
    - Widely available and reproducible
  - **Disadvantages**
    - Calcification ("Bloom artifact") and contrast exposure

- **MR Angiography**: Contrast Enhanced or Time of Flight
  - **Advantages**
    - Simultaneous brain imaging
  - **Disadvantages**
    - Cost
    - Claustrophobia / Motion artifact
    - Metallic implant limitations
    - Gadolinium (Nephrogenic Systemic Fibrosis)
Complimentary Imaging Modalities

• Catheter Based Angiography
  ▫ Gold Standard
  ▫ Advantages
    • High resolution
    • Flow and plaque characteristics
    • Can be performed with limited/dilute contrast
  ▫ Disadvantages
    • Invasive/Risk (0.3% stroke)
Carotid Stenosis - Treatment

- Optimal Medical Therapy
  - Antiplatelet Therapy
  - Lipid Lowering Therapy
  - Antihypertensive Therapy
  - Tobacco Cessation Strategies
  - Aggressive Glycemic Control

- Revascularization
  - Carotid Endarterectomy (CEA)
  - Carotid Stenting (CAS)
OMT - Antiplatelet Therapy

- 1996 **CAPRIE**: Clopidogrel > ASA

Conclusions

1. Clopidogrel is as effective (and currently cheaper than) ASA + ER-DP.

2. Both Clopidogrel and ASA + ER-DP appear to be superior to ASA alone.

3. There is no role for DAPT in primary or secondary prevention of stroke.

- 2004 **MATCH**: Copidogrel alone > DAPT

- 2006 **ESPRIT**: ASA + ER-DP > ASA

- 2006 **CHARISMA**: DAPT = ASA alone

- 2008 **PRoFESS**: Clopidogrel = ASA + ER-DP
OMT - Statin Therapy

- **SPARCL Trial**
  - RCT, Double Blind, Placebo controlled trial
  - Secondary prevention with Atorvastatin 80mg
  - 4.9 years follow-up
Carotid Revascularization

1. Which patients?
   ▫ Symptomatic vs Asymptomatic
   ▫ Lesion severity/characteristics

2. Which procedure?
   ▫ CEA versus CAS
   ▫ Defining operative risk
<table>
<thead>
<tr>
<th></th>
<th>After TIA</th>
<th>After Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>4% to 8%</td>
<td>3 to 10%</td>
</tr>
<tr>
<td>1 Year</td>
<td>12 to 13%</td>
<td>10% to 14%</td>
</tr>
<tr>
<td>5 Years</td>
<td>24% to 29%</td>
<td>25% to 40%</td>
</tr>
</tbody>
</table>

Lesion Severity and Risk for Stroke

“Higher” Risk Asymptomatic Subsets?

- More Complicated Than Simple Diameter Stenosis
  - Angiographic Criteria: Thrombus, Ulceration
  - Ultrasound Criteria (e.g. echolucency)
  - Silent microemboli by TCD
  - OCT/IVUS (e.g. virtual histology)
  - CT/MRI plaque characterization
  - Cerebrovascular Reserve
Carotid Endarterectomy - Background

- CEA experience dates back to the 1950's
- Major Clinical Trials (1980's, 1990's)
  - Symptomatic: NASCET and ESCT
  - Asymptomatic: ACAS and ACST
High Risk CEA: Stroke/Death

- Age > 75: 7-10%
- CHF: 8-9%
- CAD requiring CABG: 8-10%
- Contralateral Occlusion
  - ACAS – 2% worse than medical therapy
  - NASCET – 14.3%
- CEA Restenosis: 8-10%
- Chronic Kidney Disease
  - Cr > 1.5: 8.2%
  - Cr > 2.9: 43%

Wong et al. Stroke May 1997; 28(5), 891-98
Carotid Artery Stenting - Background

- First CAS device FDA approval 2004
  - Sapphire Trial (High Risk for CEA)
- Limited CMS reimbursement approval 2005
  - Symptomatic, High Risk Patients
- Further Randomized Controlled Trials (RCT's)
  - EVA 3-S (2006)
  - SPACE (2006)
  - ICSS (2010)
  - CREST (2010)
# Carotid Stenting Trials: Outcomes

## 30 to 120 Day Outcomes

<table>
<thead>
<tr>
<th>Trial</th>
<th>CEA: %</th>
<th>CAS: %</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVA 3S</td>
<td>3.9</td>
<td>9.6</td>
<td>0.01</td>
</tr>
<tr>
<td>SPACE</td>
<td>6.3</td>
<td>6.8</td>
<td>0.09</td>
</tr>
<tr>
<td>ICSS</td>
<td>4.7</td>
<td>8.5</td>
<td>0.001</td>
</tr>
<tr>
<td>CREST</td>
<td>4.5</td>
<td>5.2</td>
<td>0.38</td>
</tr>
</tbody>
</table>
CAS Trial Analysis: 3 Key Elements

1. Utilization of embolic protection
2. Myocardial infarction as a component of the endpoint
3. Operator experience
Embolic Protection Device (EPD)

- No randomized trials comparing stenting with versus without protection.
- Multiple retrospective analyses confirm significant reduction in procedural events.
- Particularly relevant in symptomatic patients or ulcerated/friable lesions with high embolic potential.
Perioperative MI and Vascular Surgery
Operator Volume Predicts Outcomes

Regression equation: \( \log(y) = 4.71 - 0.85 \times \log(x) \)

P-value of slope: <0.0001
R-square: 0.81

## Carotid Stent Trials: Outcomes

<table>
<thead>
<tr>
<th></th>
<th>EPD Use</th>
<th>MI Endpoint</th>
<th>Operator Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EVA 3S</strong></td>
<td>Not Originally Mandated</td>
<td>No</td>
<td>5 Lifetime CAS</td>
</tr>
<tr>
<td><strong>SPACE</strong></td>
<td>27%</td>
<td>No</td>
<td>Not formally described, except 25 “PTA’s”</td>
</tr>
<tr>
<td><strong>ICSS</strong></td>
<td>72%</td>
<td>No</td>
<td>10 Lifetime CAS Or 50 “stents”</td>
</tr>
<tr>
<td><strong>CREST</strong></td>
<td>&gt;95%</td>
<td>Yes</td>
<td>30 Lifetime CAS</td>
</tr>
</tbody>
</table>
CREST - CAS in Standard Risk Patients

<table>
<thead>
<tr>
<th>Event</th>
<th>CAS (%)</th>
<th>CEA (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.7</td>
<td>0.3</td>
<td>0.18</td>
</tr>
<tr>
<td>Any Stroke</td>
<td>4.1</td>
<td>2.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0.9</td>
<td>0.3</td>
<td>0.09</td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>2.9</td>
<td>1.4</td>
<td>0.009</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>1.1</td>
<td>2.3</td>
<td>0.03</td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1262</td>
<td>1240</td>
</tr>
</tbody>
</table>
The Lesser of Two Evils??

[Graph showing survival rates over time for different groups: Control (N = 2183), MI (N = 56), Minor Stroke (N = 48).]
CREST: Learning Curve

- **2000-2004**: 4.4% (N=160)
- **2005**: 7.0% (N=201)
- **2006**: 4.6% (N=308)
- **2007**: 3.4% (N=298)
- **2008**: 1.8% (N=164)

50% Trial Enrollment
August 2006

Frequency of Death or Any Stroke
CREST-2 Parallel Study Design

(n = 1,240 in each trial)

CAS + Medical
n = 620

Medical
n = 620

CEA + Medical
n = 620

Medical
n = 620
Case Presentation - HPI

- 84 year old white male
- Admitted to hospitalist service for SOB related to COPD and known diastolic HF
- Incidental finding of bilateral carotid bruits
- No history of TIA or stroke
- No recent focal neurologic symptoms
Case Presentation - PMH

- O2 dependent COPD
- Diastolic HF
- Chronic atrial fibrillation
- Hypertension
- Hyperlipidemia
- Obstructive Sleep Apnea
- CKD, stage III
Embolic Protection Device (EPD)
Distal Protection Filter
The Plot Thickens . . . 8 Months Later

Patient returns to the ER at the insistence of his daughter for evaluation of two overt episodes of amaurosis fugax (monocular blindness of the left eye) each lasting approximately 30 minutes.
Velocities 234/45 to 488/213 cm/s
L Dist ICA
PSV: -40.9 cm/s
EDV: -8.73 cm/s
Proximal Cerebral Protection

ARMOUR Trial
Parting Thoughts

• Ischemic stroke is a ubiquitous problem with marked morbidity/mortality and societal costs

• Symptomatic patients are at extremely high risk for recurrent events and benefit substantially from revascularization when possible

• Asymptomatic patients “likely” benefit from prophylactic revascularization when performed by experienced operators, but we need more data regarding the impact of modern OMT and novel risk stratification
  ▫ CREST 2 - Revascularization vs Modern Medical Management

• CEA currently remains the standard of care for high grade carotid disease with CAS representing a very effective alternative in appropriate subgroups
Loudermilk Heart and Vascular Center
John D. Archbold Memorial Hospital

Thomasville, Georgia