Carotid Stenting – The CREST is Just Beginning

John R. Laird
Professor of Medicine
Medical Director of the Vascular Center
UC Davis Medical Center
RECONSTRUCTION OF INTERNAL CAROTID ARTERY
IN A PATIENT WITH INTERMITTENT ATTACKS OF HEMIPLEGIA
H. H. G. Eastcott
M.S. Lond., F.R.C.S.
ASSISTANT DIRECTOR OF SURGICAL UNIT, ST. MARY’S HOSPITAL
G. W. Pickering
F.R.C.P., Hon. M.D. Ghent
PROFESSOR OF MEDICINE IN THE UNIVERSITY OF LONDON
C. G. Rob
M.C., M.Chir. Camb., F.R.C.S.
PROFESSOR OF SURGERY IN THE UNIVERSITY OF LONDON
From the Medical and Surgical Units, St. Mary’s Hospital
London
Lancet 1954;267:994-6
Carotid Surgery

![Graph showing the number of carotid procedures per year with key events such as EC-IC, NASCET, and ACAS marked.]

**Stroke**
A Journal of Cerebral Circulation

Editorial

Carotid Endarterectomy Studies: A Glimmering of Science
Mark L. Dykons, M.D.
### Complications of CEA

- **Death or Stroke**: 5.8%
- **Cranial Nerve Palsy**: 7.6%
- **Wound Hematoma**: 5.5%
- **Wound Infection**: 3.4%
- **Cardiac**: 4.0%
In Search of a Less Invasive Approach
“High Risk” for CEA

“Hostile Neck”
Radiation Induced Carotid Stenosis
What is “High Risk”?  

- **Serious co-morbid medical condition**
  - Congestive heart failure (class III/IV) or severe left ventricular dysfunction LVEF <30%
  - Open heart surgery needed within 6 weeks
  - Recent MI (>24 hours and <4 weeks)
  - Unstable angina
  - Severe pulmonary disease
  - Age >80 years

- **Anatomic challenges**
  - Contralateral carotid occlusion
  - Contralateral laryngeal nerve palsy
  - Radiation therapy to neck
  - Previous CEA with recurrent stenosis
  - High cervical ICA lesions or CCA lesions below the clavicle
  - Severe tandem lesions
Improving Results Over Time in the High Risk Carotid Registries
Protected Carotid-Artery Stenting versus Endarterectomy in High-Risk Patients

Jay S. Yadav, M.D., Mark H. Wholey, M.D., Richard E. Kuntz, M.D., M.Sc., Pierre Fayad, M.D., Barry T. Katzen, M.D., Gregory J. Mishkel, M.D., Tanvir K. Bajwa, M.D., Patrick Whitlow, M.D., Neil E. Strickman, M.D., Michael R. Jaff, D.O., Jeffrey J. Popma, M.D., David B. Snead, Ph.D., Donald E. Cutlip, M.D., Brian G. Firth, M.D., Ph.D., and Kenneth Ouriel, M.D., for the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators*
SAPPHIRE STUDY
Cumulative % of MAE to 360 Days
All Randomized Patients – Kaplan Meier Analysis

<table>
<thead>
<tr>
<th>Time After Initial Procedure (days)</th>
<th>Cumulative Percentage of MAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5%</td>
</tr>
<tr>
<td>30</td>
<td>10%</td>
</tr>
<tr>
<td>60</td>
<td>15%</td>
</tr>
<tr>
<td>90</td>
<td>20%</td>
</tr>
<tr>
<td>120</td>
<td>25%</td>
</tr>
<tr>
<td>150</td>
<td>30%</td>
</tr>
<tr>
<td>180</td>
<td>35%</td>
</tr>
<tr>
<td>210</td>
<td>40%</td>
</tr>
<tr>
<td>240</td>
<td>45%</td>
</tr>
<tr>
<td>270</td>
<td>50%</td>
</tr>
<tr>
<td>300</td>
<td>55%</td>
</tr>
<tr>
<td>330</td>
<td>60%</td>
</tr>
<tr>
<td>360</td>
<td>65%</td>
</tr>
</tbody>
</table>

LR p = 0.04

CEA: 20.3%
Stent: 10.5%
Randomized Trials of CEA vs. CAS
“Standard” Risk Patients

Standard Risk
- EVA-3S [X]
- SPACE [X]
- ICSS [X]
- CREST
- ACT-1
Carotid Revascularization
Endarterectomy vs Stenting Trial

Grant Number: 2 R01 NS038384-07

Thomas G. Brott, MD, PI
Robert Hobson, II, MD, PI 1999-2007
CREST – A Refresher

• First patient enrolled – December 2000
• Enrollment completed – July 2008
  – 2,522 patients randomized at 108 community and academic hospitals across US and Canada
  – 1564 lead-in cases (5 - 20 per site, asx or sx, conventional or high risk)
• Conventional risk patients with symptomatic carotid stenosis (> or = 50% by angiography)
• Conventional risk patients with asymptomatic carotid stenosis (> or = 60% by angiography)
Enrollment of women – 37%
Enrollment of minorities – 9%
• Primary endpoint: Stroke, MI, and all cause mortality during 30-day peri-procedural period, and ipsilateral stroke over the follow-up period (extending up to 4 years)

• Secondary endpoints:
  – Efficacy of CAS and CEA in men and women
  – Restenosis rate of the two procedures
  – Health-related quality of life
  – Cost effectiveness of CAS and CEA
  – Evaluate subgroups of patients at differential risk for procedural morbidity and mortality after CAS and CEA
## CREST Results
### Peri-procedural period

<table>
<thead>
<tr>
<th>Event</th>
<th>CAS</th>
<th>CEA</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Death, Stroke, or MI</td>
<td>5.2%</td>
<td>4.5%</td>
<td>HR = 1.18; 95% CI:</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.82-1.68</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0.7%</td>
<td>0.3%</td>
<td>HR = 2.25; 95% CI:</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.69-7.30</td>
<td></td>
</tr>
<tr>
<td>All Stroke</td>
<td>4.1%</td>
<td>2.3%</td>
<td>HR = 1.79; 95% CI:</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.14-2.82</td>
<td></td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0.9%</td>
<td>0.6%</td>
<td>HR = 1.35; 95% CI:</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.54-3.36</td>
<td></td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>3.2%</td>
<td>1.7%</td>
<td>HR = 1.95; 95% CI:</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.15-3.30</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>1.1%</td>
<td>2.3%</td>
<td>HR = 0.5; 95% CI:</td>
<td>0.03</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0.26-0.94</td>
<td></td>
</tr>
<tr>
<td>Ipsilateral Stroke</td>
<td>2.0%</td>
<td>2.4%</td>
<td>HR = 0.94; 95% CI:</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.50-1.76</td>
<td></td>
</tr>
<tr>
<td>Cranial Nerve Palsy</td>
<td>0.3%</td>
<td>4.7%</td>
<td>HR = 0.07; 95% CI:</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.02-0.18</td>
<td></td>
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</tbody>
</table>
## Cranial Nerve Injury

<table>
<thead>
<tr>
<th>Cranial Nerve Injury</th>
<th>5.3% (62/1176)</th>
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<tbody>
<tr>
<td>Unresolved at Six Months</td>
<td>2.1% (25/1176)</td>
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</table>

<table>
<thead>
<tr>
<th>Cranial Nerve Injury</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial droop (VII)</td>
<td>8</td>
</tr>
<tr>
<td>Hoarseness (X)</td>
<td>7</td>
</tr>
<tr>
<td>Dysphagia (IX)</td>
<td>3</td>
</tr>
<tr>
<td>Tongue deviation (XII)</td>
<td>3</td>
</tr>
<tr>
<td>Facial numbness (V)</td>
<td>2</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
</tr>
</tbody>
</table>
Minor Stroke Neurological Deficit Assessed by NIH Stroke Scale

Overall neurological mayhem from minor stroke at 6 months is the same for CAS and CEA.

- 1 Month: 1.10% (n = 12) for CAS, 0.60% (n = 7) for CEA
- 6 Months: 0.62% (n = 7) for CAS, 0.60% (n = 7) for CEA

FDA Panel Presentation
Jan. 26, 2011
Minor Stroke and MI

- Control (N = 2183)
- MI (N = 56)
- Minor Stroke (N = 48)

Freedom From All Cause Mortality

Days: 0, 365, 730, 1095, 1460

- Control: 100% at 0, 94.8% at 1460 days
- MI: 100% at 0, 88.8% at 1460 days
- Minor Stroke: 100% at 0, 75.0% at 1460 days

FDA Panel Presentation
Jan. 26, 2011
Death and Stroke for CAS During CREST Enrollment

<table>
<thead>
<tr>
<th>Year</th>
<th>Frequency of Death or Any Stroke</th>
<th>N</th>
</tr>
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<tbody>
<tr>
<td>2000-2004</td>
<td>4.4%</td>
<td>160</td>
</tr>
<tr>
<td>2005</td>
<td>7.0%</td>
<td>201</td>
</tr>
<tr>
<td>2006</td>
<td>4.6%</td>
<td>308</td>
</tr>
<tr>
<td>2007</td>
<td>3.4%</td>
<td>298</td>
</tr>
<tr>
<td>2008</td>
<td>1.8%</td>
<td>164</td>
</tr>
</tbody>
</table>

FDA Panel Presentation
Jan. 26, 2011
Death and Major Stroke for CAS Symptomatic Patients

- 2000-2004: 2.5% (N=160)
- 2005: 3.6% (N=111)
- 2006: 0.8% (N=131)
- 2007: 0.0% (N=120)
- 2008: 0.0% (N=77)

Frequency of Death or Major Stroke

FDA Panel Presentation
Jan. 26, 2011
Death and Major Stroke for CAS Octogenarians

<table>
<thead>
<tr>
<th>Year</th>
<th>Frequency of Death or Major Stroke</th>
<th>N</th>
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<tbody>
<tr>
<td>2000-2004</td>
<td>6.5%</td>
<td>31</td>
</tr>
<tr>
<td>2005</td>
<td>5.0%</td>
<td>20</td>
</tr>
<tr>
<td>2006</td>
<td>0.0%</td>
<td>19</td>
</tr>
<tr>
<td>2007</td>
<td>0.0%</td>
<td>24</td>
</tr>
<tr>
<td>2008</td>
<td>0.0%</td>
<td>12</td>
</tr>
</tbody>
</table>
I’ll take the carotid stent
Continued Improvement in Carotid Stent Outcomes
Proximal Protection - MOMA Device

- Guiding Sheath integrating two highly compliant balloons
  - 6F I.D. fully usable Working Channel
  - 9F O.D. shaft
“Endovascular Clamping”

- Guiding sheath with 2 anchoring balloons
  - high system stability and back-up support
  - guide wire of choice to cross the lesion

- Lesion crossing under protection

- No need for suitable landing zone in the distal diseased ICA

- All type and size debris aspiration
Proximal Endovascular Occlusion for Carotid Artery Stenting

Results From a Prospective Registry of 1,300 Patients

Eugenio Stabile, MD, PhD, Luigi Salemme, MD, Giovanni Sorropago, MD, Tullio Tesorio, MD, Wail Nammas, MD, Marianna Miranda, MD, Grigore Popusoi, MD, Angelo Cioppa, MD, Vittorio Ambrosini, MD, Linda Cota, MD, Giampaolo Petroni, MD, Giovanni Della Pietra, MD, Angelo Ausania, MD, Arturo Fontanelli, MD, Giancarlo Biamino, MD, Paolo Rubino, MD
Mercogliano, Italy

Objectives

This single-center registry presents the results of proximal endovascular occlusion (PEO) use in an unselected patient population.

Background

In published multicenter registries, the use of PEO for carotid artery stenting (CAS) has been demonstrated to be safe and efficient in patient populations selected for anatomical and/or clinical conditions.

Methods

From July 2004 to May 2009, 1,300 patients underwent CAS using PEO. Patients received an independent neurological assessment before the procedure and 1 h, 24 h, and 30 days after the procedure.

Results

Procedural success was achieved in 99.7% of patients. In hospital, major adverse cardiac or cerebrovascular events included 5 deaths (0.38%), 6 major strokes (0.46%), 5 minor strokes (0.38%), and no acute myocardial infarction. At 30 days of follow-up, 2 additional patients died (0.15%), and 1 patient had a minor stroke (0.07%). The 30-day stroke and death incidence was 1.36% (n = 19). Symptomatic patients presented a higher 30-day stroke and death incidence when compared with asymptomatic patients (3.04% vs. 0.82%; p < 0.05). No significant difference in 30-day stroke and death rate was observed between patients at high (1.88%; n = 12) and average surgical risk (1.07; n = 7) (p = NS). Operator experience, symptomatic status, and hypertension were found to be independent predictors of adverse events.

Conclusions

The use of PEO for CAS is safe and effective in an unselected patient population. Anatomical and/or clinical conditions of high surgical risk were not associated with an increased rate of adverse events.
Proximal Occlusion During CAS

- Single center registry
- 1,300 patients treated from June 2004 – May 2009
- Procedural success in 99.7%
- 30-day stroke and death rate of 1.38%
Nitinol or ePTFE Membrane-Covered Stent Systems