Carotid Stenting (Revascularization): 
A Review of the Current Data

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Disclosures

• In the past year, I have been on a scientific advisory board, worked as a consultant for, or conducted clinical research for:

  • Abbott Vascular, Cordis, Medtronic, and Covidien/EV3.

  • All of these companies produce endovascular products including carotid stents, proximal and/or distal filters, and guiding catheters
Stroke

- Carotid arterial disease accounts for a significant minority of CVA
- Consider other etiologies
- Rx has improved on all fronts

Medical Rx
Surgery- CEA
Endovascular- CAS
• Ulceration increases risk of stroke.
• 80% of pts with known carotid stenosis will not have warning TIA before stroke.
Carotid Artery Stenosis
What is the best treatment???

The controversy rages on…

Medical Therapy!

CEA!

STENTING!
Moving targets…
Medical Treatments That *Did Not Exist* During Revascularization Trials

- Modulators of Renin Angiotensin System
  - ACE inhibitors
    - Hope and PROGRESS
  - Angiotensin Receptor Blockers
    - Life
- Statins
  - HPS and SPARCL
  - CARDS
- Advanced antiplatelet therapies
ACE Inhibition Prevents Recurrent Stroke

The Progress Trial

6105 subjects with previous stroke randomly assigned to perindopril (n=3051) or placebo (n=3054)

PROGRESS Collaborative Group. Lancet 2001:358; 1033
SPARCL: High Dose Atorvastatin vs Placebo In Patients with Prior CVA/TIA

**Graph:**
- **Y-axis:** Stroke or Transient Ischemic Attack (%)
- **X-axis:** Years since Randomization
- **Lines:** Placebo and Atorvastatin
- **Statistics:** HR, 0.77 (95% CI, 0.67–0.88); P<0.001

**Table:**
- **No. at Risk**
  - Atorvastatin: 2365, 2148, 2023, 1933, 1837, 871, 119
  - Placebo: 2366, 2132, 1998, 1871, 1780, 803, 126

Asymptomatic carotid stenosis

**Medical Management**

- **SMART Study**
  - 221 patients with >50% carotid stenosis, 5 years
  - <0.5% stroke risk per year
  - Goessens et al. Stroke, 2007

- **Oxford Vascular Study**
  - 101 patients with >50% carotid stenosis, 3 years
  - <0.5% stroke risk per year
  - Marquardt et al. Stroke, 2010
Medical Treatment for Asymptomatic Carotid Stenosis

Asymptomatic Carotid Stenosis Clinical Trials

Patient with Asymptomatic Moderate-to-Severe Carotid Stenosis

• Overall annual risk of stroke was about 1% in more recent studies of medically managed asymptomatic carotid stenosis
• Follow up with carotid US 6 months initially then if stable annually
• If patients develop progressive stenosis despite maximum medical management, then consider CEA/CAS
• Lifestyle modification
• Aspirin or other antiplatelets as mono-therapy preferred over combination of ASA+Clopidogrel
• Aggressive cholesterol lowering with statins, as well as diet as discussed previously, target LDL <70
• For unilateral asymptomatic carotid stenosis (>70%), BP targets of <140/90 reasonable
Does Medical Therapy Prevent Progression of Carotid Artery Stenosis?

Carotid Endarterectomy

- Level 1 evidence.
- Most common major vascular operation.
- Index vascular procedure.
- Long-term stroke free survival.
- LOS, complications, and cost minimized.
- Established benchmarks.
Asymptomatic Carotid Surgery Trial
Early vs. Deferred CEA in 3120 Asymptomatic Pts with ICA Stenosis

Use of Medical Rx

ACST benefit of intervention with Med Rx over Med Rx alone

Lancet 2004;363
Macro-evolution in CEA outcomes over the past 4 decades

Symptomatic

Asymptomatic
Xact™ Carotid Stent
Tapered and Straight

- Crossing Profile: 5.7F
- Stent Matrix
  - Straight: 7, 8, 9, 10 X 20, 30 mm
  - Tapered: 10-8, 9-7, 8-6 X 30, 40 mm
- Stent Structure: Closed Cell
- Shortening: 5-8%
- Material: Nitinol
- 0.014” Wire compatible
- 6F sheath compatible
723 patients with high risk for CEA

- >50% stenosis in symptomatic patients
- >80% stenosis in asymptomatic patients
- >1 co-morbid condition
- Team of vascular surgeon, neurologist and interventionalist determined if patient was too high risk for randomization; these patients were entered in a registry and not randomized

**RANDOMIZED**

| Stenting with protection (n=156) | CEA (n=151) |

**REGISTRY**

| Surgical Refusal (n=409) | Stent Refusal (n=7) |

Primary Endpoint

30 day Death, Stroke or MI

Yadav et al, NEJM 2004
### SAPPHIRE

Randomized events at 30 days

<table>
<thead>
<tr>
<th></th>
<th>Stent (156)</th>
<th>CEA (151)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.6%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Stroke</td>
<td>3.8%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0.6%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>3.2%</td>
<td>3.3%</td>
</tr>
<tr>
<td>MI</td>
<td>2.6%</td>
<td>7.3%</td>
</tr>
<tr>
<td>Death/Stroke</td>
<td>4.5%</td>
<td>6.6%</td>
</tr>
<tr>
<td>Death/MI/Stroke</td>
<td>5.8%</td>
<td>12.6%</td>
</tr>
</tbody>
</table>

*Yadav et al, NEJM 2004*
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)
Carotid Stent Issues

- AHA guidelines for CEA:
  - Symptomatic pts: 6% risk of death or major stroke
  - Asymptomatic pts: 3% risk of death/major stroke

- High risk vs. low risk for CEA
- Symptomatic vs asymptomatic pts

- Initial strategy by multiple companies with various devices targeted CAS for the high risk CEA pt -
  - Clinical – USA, CHF(EF <30%), AS, MR, severe COPD, CABG w/in 6 wks, age >80 yrs.
  - Anatomic – prior CEA, high ICA lesion, prior neck XRT, contralateral occlusion, contralateral laryngeal nerve palsy, severe tandem lesions.
30 Day Event Rates (2000-->2013)

**All Stroke** - Stenting Trials for High Risk Surgical Patients

Factors: embolic protection, experience, case selection
### PROTECT: 30-day major adverse events

<table>
<thead>
<tr>
<th>EVENT</th>
<th>PROTECT (N=274)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, Stroke and MI*</td>
<td>1.8%</td>
</tr>
<tr>
<td>Death</td>
<td>0.4%</td>
</tr>
<tr>
<td>All Stroke</td>
<td>1.5%</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0.4%</td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>1.1%</td>
</tr>
<tr>
<td>MI</td>
<td>0.4%</td>
</tr>
<tr>
<td>All Stroke and Death</td>
<td>1.5%</td>
</tr>
<tr>
<td>Major Stroke and Death</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

**High Risk patients**
CREST: Study design

- Prospective, multicenter, randomized, controlled trial with blinded endpoint adjudication

- CAS vs. CEA in 2300 patients with symptomatic and asymptomatic stenosis

- 108 US and 9 Canadian sites

- Rigorous credentialing for CAS operators
  - 427 applicants/ 224 selected (52%) at 110 sites
  - ~1500 patients in lead-in phase
<table>
<thead>
<tr>
<th>Event</th>
<th>CAS</th>
<th>CEA</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periop death/stroke/MI</td>
<td>5.2%</td>
<td>4.5%</td>
<td>0.38</td>
</tr>
<tr>
<td>Periop stroke</td>
<td>4.1%</td>
<td>2.3%</td>
<td>0.01</td>
</tr>
<tr>
<td>Periop MI</td>
<td>1.1%</td>
<td>2.3%</td>
<td>0.03</td>
</tr>
<tr>
<td>Major periop stroke</td>
<td>0.9%</td>
<td>0.6%</td>
<td>0.52</td>
</tr>
<tr>
<td>Cranial nerve palsy</td>
<td>0.3%</td>
<td>4.7%</td>
<td>0.0001</td>
</tr>
</tbody>
</table>
Any material differences between CEA and CAS in CREST composite endpoints are in minor stroke and MI: PP FDA analysis

<table>
<thead>
<tr>
<th>Per protocol</th>
<th>CAS N = 1,131</th>
<th>CEA N = 1,176</th>
<th>Difference</th>
<th>Unadjusted p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Death, Stroke, or MI</td>
<td>5.8% (65)</td>
<td>5.1% (60)</td>
<td>0.7%</td>
<td>0.5200</td>
</tr>
<tr>
<td>Death</td>
<td>0.53% (6)</td>
<td>0.26% (3)</td>
<td>0.27%</td>
<td>0.3335</td>
</tr>
<tr>
<td>Any Stroke</td>
<td>4.1% (46)</td>
<td>1.9% (22)</td>
<td>2.2%</td>
<td>0.0019</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0.9% (10)</td>
<td>0.4% (5)</td>
<td>0.5%</td>
<td>0.2005</td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>3.2% (36)</td>
<td>1.5% (18)</td>
<td>1.7%</td>
<td>0.0088</td>
</tr>
<tr>
<td>MI</td>
<td>2.0% (22)</td>
<td>3.4% (40)</td>
<td>-1.5%</td>
<td>0.0387</td>
</tr>
</tbody>
</table>

* Fisher’s exact p-values were not adjusted for multiple comparisons; p-values for descriptive purposes only

CREST outcomes:
CEA and CAS are no different for the primary endpoint
Long-term mortality in CREST: No association with minor stroke but strong association with MI

<table>
<thead>
<tr>
<th>Comparison</th>
<th>HR</th>
<th>Confidence Interval</th>
<th>Log Rank P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI vs. Control</td>
<td>2.81</td>
<td>[1.53 - 5.17]</td>
<td>0.0005</td>
</tr>
<tr>
<td>Minor Stroke vs. Control</td>
<td>0.52</td>
<td>[0.13 – 2.09]</td>
<td>0.34</td>
</tr>
<tr>
<td>MI vs. Minor Stroke</td>
<td>5.18</td>
<td>[1.15 – 23.4]</td>
<td>0.02</td>
</tr>
</tbody>
</table>

No difference between CEA and CAS for the primary composite endpoint by symptomatic or octogenarian status in CREST.

Evolutionary outcome improvement for CAS within CREST (not seen with CEA within CREST): Death or any stroke in symptomatic patients

<table>
<thead>
<tr>
<th>Procedure related cranial nerve injury</th>
<th>CAS N = 1,131</th>
<th>CEA N = 1,176</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure related cranial nerve injury</td>
<td>0.0%</td>
<td>5.3% (62/1176)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unresolved at one month</td>
<td>0.0%</td>
<td>3.6% (42/1176)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unresolved at six months</td>
<td>0.0%</td>
<td>2.1% (25/1176)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CREST Spin

• Cardiologists:
  • CREST used obsolete technology.
  • Early in learning curve for CAS.
  • Cranial nerve injuries and MI’s are extremely morbid.

• Surgeons:
  • Strokes are more likely with CAS than CEA and patients care more about stroke than MI.
  • Most MI’s were minor.
  • Most cranial nerve injuries resolve.
### Multicenter randomized trials of CAS vs. CEA

<table>
<thead>
<tr>
<th><strong>Trial</strong></th>
<th><strong>30-Day Outcome (Death/Stroke)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>EVA-3S (30 days)</td>
<td>CEA: 3.9%  CAS: 9.6%</td>
</tr>
<tr>
<td>SPACE (30 days)</td>
<td>CEA: 6.3%  CAS: 6.8%</td>
</tr>
<tr>
<td>ICSS (120 days)</td>
<td>CEA: 4.7%  CAS: 8.5%</td>
</tr>
<tr>
<td>CREST (Symptomatic Only)</td>
<td>CEA: 5.4%  CAS: 6.7%</td>
</tr>
</tbody>
</table>
Endarterectomy vs. Angioplasty in Patients with Symptomatic Severe Carotid Stenosis trial

**EVA-3S**

- Stent-protected angioplasty vs. CEA in symptomatic pts with stenosis >60%

- Non-inferiority design, 872 pts to assess with 80% power with expected 30 d D/MI rate 5.6% after CEA and 4% after CAS, delta 2%

- 527 pts enrolled, DSMB stopped trial for safety and futility reasons

- Primary endpoint: 30 day CVA or Death
  - CEA 3.9% vs. CAS 9.6%
  - 6 month CVA/D – CEA 6.1% vs. 11.7%

- Concerns
  - Variable experience - >25 CEA in prior year vs. 5 prior CAS procedures
  - No plavix prior to CAS 17%
  - 91% received an embolic protection device

- **EVA-3S suggests pts with symptomatic carotid stenosis of >60% have lower rates of CVA and death at 1 and 6 mo than CAS.**

Mas et al. NEJM 355: 1660, oct 06
Critical trial construct and conduct issues *severely limit* the value of EU CEA and CAS outcomes

<table>
<thead>
<tr>
<th>Trial</th>
<th>EPD Use</th>
<th>MI Ascertainment</th>
<th>Operator Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVA-3S</td>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SPACE</td>
<td>½</td>
<td>0</td>
<td>++</td>
</tr>
<tr>
<td>ICSS</td>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CREST</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>
CAS achieves AHA guidelines in symptomatic patients
Large, prospective, multicenter neurologically-audited/independent adjudication single arm studies in high-surgical risk patients

N=589

EXACT/CAPTURE 2 (>180 sites and 400 operators):
30-day major adverse events symptomatic patients <80 years

 Hierarchical- Includes only the most serious event for each patient and includes only each patient first occurrence of each event.

Summary

• CAS and CEA are equivalent in primary outcomes and long-term stroke prevention in CREST
• Large, controlled single arm studies of high surgical risk patients achieve AHA guideline standards
  – European trials flawed and therefore interpretation of primary results limited
  – Significant rapid and continued improvement in outcomes in CAS over past decade; CEA outcomes excellent, plateau’d
  – More wound complication/re-op and cranial nerve injury with CEA

CEA vs. CAS in symptomatic patients
What role does CAS play in the standard surgical risk 
am
asymptomatic patient?
### Periprocedural outcomes in CREST:
No difference between CAS and CEA for Asx

<table>
<thead>
<tr>
<th>MI end point</th>
<th>CAS No. of Events (Proportion ± SE)</th>
<th>CEA No. of Events (Proportion ± SE)</th>
<th>Percent Absolute Treatment Effect (95% CI)</th>
<th>HR (95% CI)</th>
<th>P[</th>
<th></th>
<th>Treatment by Symptomatic Status Interaction P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>7 (1.2 ± 0.4)</td>
<td>13 (2.2 ± 0.6)</td>
<td>-1.0 (-2.5 to 0.4)</td>
<td>0.55 (0.22 to 1.38)</td>
<td>0.20</td>
<td></td>
<td>0.76</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>7 (1.0 ± 0.4)</td>
<td>15 (2.3 ± 0.6)</td>
<td>-1.2 (-2.6 to 0.1)</td>
<td>0.48 (0.18 to 1.11)</td>
<td>0.083</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Primary end point (any stroke, MI, or death within periprocedural period)**

| Asymptomatic | 21 (3.5 ± 0.8) | 21 (3.6 ± 0.8) | 0.0 (-2.2 to 2.1) | 1.02 (0.55 to 1.86) | 0.96 |
| Symptomatic  | 45 (6.7 ± 1.0) | 35 (6.4 ± 0.9) | 1.4 (-1.2 to 3.9) | 1.26 (0.81 to 1.96) | 0.30 |
CAS achieves AHA guidelines in asymptomatic patients

Large, prospective, multicenter neurologically-audited/independent adjudication single arm studies in high-surgical risk patients

N=4282

Hierarchical - Includes only the most serious event for each patient and includes only each patient's first occurrence of each event.

2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAPIP/SCAI/SIR/SNIS/SVM/SVS Guideline on the Management of Patients With Extracranial Carotid and Vertebral Artery Disease: Executive Summary


Developed in Collaboration With the American Academy of Neurology and Society of Cardiovascular Computed Tomography

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## 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><strong>70-99% stenosis</strong></td>
<td><strong>70-99% stenosis</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CEA</strong></td>
<td>Class I LOE: B</td>
<td>Class I LOE: B</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>Class IIb LOE: B</td>
</tr>
</tbody>
</table>
Managing patients with asymptomatic carotid stenosis: 

**Summary**

- Asymptomatic carotid stenosis is a risk factor for stroke
- Surgical revascularization therapy is proven beneficial vs. unmonitored (but probably real world) medical therapy
- CAS outcomes have demonstrated equivalent outcomes to CEA (CREST), achieved AHA guidelines, and now is Class 2b recommendation in asymptomatic patients (CEA Class 2a)
- The role of medical therapy remains a tantalizing but unproven alternative to revascularization in patients with established severe carotid stenosis.
  - Until such time as this benefit is demonstrated to be superior, the available randomized controlled data support revascularization in suitable patients
### TABLE V. Cumulative 1-Year Events, Resource Use, and Costs

<table>
<thead>
<tr>
<th>Cumulative to 1 year</th>
<th>MITT Population</th>
<th>Difference (95% CI)</th>
<th>P-value</th>
<th>Per-Protocol Population</th>
<th>Difference (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS (n=1212)</td>
<td>$16375.4 ± 7730.1</td>
<td>-$267.2 [13636.7] [13112.3] (-939.0, 404.6)</td>
<td>&lt;.0001</td>
<td>CAS (n=1136) $16380.9 ± 7527.8</td>
<td>-$197.8 [13600.1] [13126.7] (-875.8, 480.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>CEA (n=1193)</td>
<td>$16108.3 ± 9029.8</td>
<td></td>
<td></td>
<td>CEA (n=1184) $16183.0 ± 9022.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*MI was reported only when it occurred within 30 days of index procedure

---

**Prospective cost comparison: CEA and CAS**  
**SAPPHIRE**  
**CREST**
Carotid Artery Stenting in 2015

• Early 2000s - Device industry
  • Cordis, Guidant, Boston Scientific, EV3, Medtronic, Abbott Vascular.
  • Developed carotid stent systems including filters and nitinol stents
• Strategy for approval
  • Patients at high-risk or ineligible for CEA
• FDA-approved indication versus CMS-approved indications
• CMS-approved indications don’t match criteria in SAPPHIRE or high-risk registries
<table>
<thead>
<tr>
<th>Stent System</th>
<th>Filter System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott Acculink stent</td>
<td>Accunet filter</td>
</tr>
<tr>
<td>Abbott EXACT stent</td>
<td>Emboshield filter</td>
</tr>
<tr>
<td>Cordis Precise stent</td>
<td>Angioguard filter</td>
</tr>
<tr>
<td>BSC Next stent</td>
<td>EPI Filterwire</td>
</tr>
<tr>
<td>Medtronic/EV3 Protégé stent</td>
<td>Spider filter</td>
</tr>
</tbody>
</table>
Carotid Stent Approval

- **FDA**
  - Asymptomatic, high risk for CEA, ≥80% stenosis
  - Symptomatic, high risk for CEA, ≥50% stenosis

- **CMS**
  - Symptomatic, high risk for CEA, ≥70% stenosis
  - Must use cerebral protection device (filter)
  - Must use single stent
  - Must be Rankin 0-3
  - Must be qualified by CMS as a qualified center and enter all cases on CMS database
Carotid Stenting

Diagram showing the visibility over time with labeled stages:
- Technology Trigger
- Peak of Inflated Expectations
- Trough of Disillusionment
- Slope of Enlightenment
- Plateau of Productivity

Circles and dashed line indicating 2010 and 2015 points on the timeline.
Shuttle Select Introducer and Slip Cath
Baseline image

- 76 wm with mod AS
- Enrolled in Capture II registry
- Lateral or 45 degree ipsilateral oblique are best and/or working view
Cranial lateral and Towns views
Circle of Willis Anatomy

- Circle w/ aberrant anatomy
  - Right P-Com patent
  - Left P-Com ABSENT (Congenital)
  - A-Com patent
- When LICA occluded, L MCA territory ischemic supplied only by the RICA via A-Com
- Therefore, protecting flow in RICA paramount
Cerebral Perfusion Post RICA Stent
Aortic Arch Anatomy

Simple arch

Complex arch
Complex Aortic Arch and Vascular Anatomy

**CAS cases to avoid**

- Calcified aortic arch
- Elongated aortic root (Type III)
- Bovine arch
- Tandem lesions
- Tortuous common carotid
- Poor “landing zones” for EPD’s – think proximal protection
- Tortuous iliacs
Type 3 Arch

Vitek & Shuttle Select sheath
Carotid stent with EPD
Debris in filter 12 hr after 6Fr Perclose
EPDs/ Filters Dominate

- Scion
- BSX/FilterWire Gen I
- BSX/FilterWire Gen II
- MedNova
- BSX/Rubicon
- MDT/Interceptor
- Guidant AccuNet
- MicroVena - Trap
- MDT/PercuSurge
- Abbot/Rubicon - Guardian
- Kensey Nash

EPDs/ Filters Dominate
Emboshield NAV\textsuperscript{6}

- Wire moves independent of the filter
- Only other filter with this advantage is EV3 Spider filter
- Improved profile, deliverability
- Redesigned guide wires
- Enhanced radiopacity
- Filter used in the PROTECT Trial
Optimal case selection

- Age < 80
- Simple, non-calcified aortic arch
- Lack of lesion
  - Calcification
  - Thrombus
  - String sign
- No recent major stroke (< 4 weeks)
- Minimal tortuosity
Carotid Artery Stenting - Procedure

- Heparin to ACT >250 sec or bivalirudin
- Wire lesion and deploy filter
- Pre-dilate lesion to assess length and diameter – be ready with
  - Atropine…pre-treat if HR <50-60 pre-dilation
  - Neosynephrine 25-50 ug boluses and drip prn
- Deploy stent
- Post-dilate with 5-6 mm balloon
- Retrieve filter (if slow flow – aspirate filter with Export or long MPA2 prior to retrieval)
Carotid Artery Stenting - Procedure

- May give nitroglycerin if pressure can tolerate for spasm around filter
  - May Buddy wire to preserve lumen if needed when removing filter
- Neuro checks during and after the procedure ("squeeze ducky")
- Monitor blood pressure and HR
- Aggressive hydration
- Rx hypotension with Neosynephrine drip and po midodrine
Complications of Carotid Stenting

- Access site complications
- Hypotension/bradycardia
- Dissection
- Distal ICA spasm
- Slow-flow
- Cerebral embolism, stroke
- Hyperperfusion syndrome
Carotid body stimulation: procedural planning

- Recognition of carotid body stimulation aids in management.
- Occur more frequently at the bifurcation/ostial internal carotid artery in:
  - elderly
  - women
  - heavily calcified vessels
- Denervation from prior endarterectomy significantly reduces the likelihood of hemodynamic perturbation during stenting.
- Although not standard outside the cardiovascular laboratory setting, invasive hemodynamic and heart rate monitoring is essential during carotid stent procedures.
- Intermittent brachial cuff pressures are not satisfactory.
Management of carotid body stimulation: bradycardia

- Bradycardia is usually transient, even if profound (asystole), and usually resolves quickly with balloon depressurization.
  - Atropine (up to 2 mg) is occasionally required to support further balloon dilation
  - Temporary pacemaker placement---prophylactic or otherwise---is only rarely necessary.

- Although some operators prefer to pre-treat all patients with atropine, this may occasionally be problematic in the patient with significant coronary disease, and is generally unpleasant.
  - Clues to the need for atropine therapy can usually be discerned by observing the effects of pre-dilation balloon angioplasty
CAPTURE 3500: 30 Day Outcomes by Octogenarian Status

% of all Patients

≥ 80 (N=829)

8.9%

5.2%

4.7%

< 80 (N=2671)

2.2%

§ Denotes statistically significant difference at the 0.05 level

* Hierarchical Events – Includes only the most serious event for each patient and includes only each patient’s first occurrence of each event
What is the problem with octogenarians?

• Poor cerebrovascular reserve?
  • Atrophy, small vessel disease, cerebral autoregulation
  • Microembolization?, “silent” emboli on MRI
• Higher incidence of risky stenting anatomy.
  • Carotid tortuosity, bad arch, diffuse calcification
• More hemodynamic instability.
Alternatives for embolic protection
Proximal Occlusion

ASPIRATION
A-V SHUNT
CAS will only get better...

- Potential reduction in HITS and silent but worrisome (?) MRI defects seen in ICSS
- Extends capability of CAS
Proximal Protection in Practice

• Single-center registry
• 1300 patients
• Independent neurologic assessment
• Procedural success >99%
• 30 day stroke/death rate 1.4%

Stabile et al. J Am Coll Cardiol 2010;55:1661-1667
## Carotid Mesh Stent Designs

<table>
<thead>
<tr>
<th>Design</th>
<th>Aperture Size</th>
<th>Materials</th>
<th>(Min Guide Sheath/ Min Guide Cath)</th>
<th>Details</th>
</tr>
</thead>
</table>
| Gore Terumo Roadsaver CGuard™ Design        | 500µ          | PTFE mesh (Heparin coated) on nitinol stent     | 5F/7F                             | • Launched SCAFFOLD trial in Sept 2013  
• PI: Bill Gray, MD  
• Target 351 pts  
• Has enrolled 100 pts. FDA has stopped trial requesting 6 mo F/U on these 100 before proceeding |
|                                             | 375-500µ      | nitinol on nitinol                              | 5F/7F                             | • Data on first 11 pts presented at LINC (Max Amor, MD)  
• Flexibility, plaque coverage and ability to conform to any anatomy mentioned as key benefits  
• Easy to recross (tapered ends) |
|                                             | 150-180µ      | PET MicroNet™ on nitinol stent                  | 6F/8F                             | • Initial placements promising  
• 11 of 11 KOL’s (LINC) felt our aperture size a benefit over larger  
• Data on MGuard MicroNet a “plus” for CGuard  
• Ability to dilate MicroNet at external bifurcation a potential benefit |
CREST-2

Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis
CREST-2 Parallel Study Design (n = 1,240 in each trial)

Endpoint = all stroke & death in first 30 days and ipsilateral stroke thereafter up to 4 years.
Primary Aims

- In patients with ≥70% asymptomatic stenosis, to assess:
  - The treatment differences between medical management and CEA
  - The treatment differences between medical management and CAS
Secondary Aims

To assess:

- Differences in cognitive function in patients randomized to intensive medical management compared to those randomized to CEA or CAS at 4 years of follow-up.

- Differences in major stroke events at 4-years.

- Differences in primary outcomes affected by age, sex, severity of carotid stenosis, risk factor level, and duration of asymptomatic period.
≥70% Stenosis

PSV* ≥ 230 cm/second on DUS

plus one of the following 4 criteria:

• EDV** ≥ 100 cm/second on DUS or

• IC / CC PSV*** ≥ 4.0 on DUS or

• ≥ 70% stenosis on MR angiogram or

• ≥ 70% stenosis on CT angiogram

*peak systolic velocity
**end diastolic velocity
***internal carotid / common carotid artery peak systolic velocity
Stenosis Evaluation

NASCET Stenosis measurement protocol

- A is normal vessel diameter distal to stenosis
- B is diameter at greatest site of narrowing
- Percent stenosis = \( \frac{(A-B)}{A} \times 100 \)
Based on CREST:

- For ages 50-74 years, no favored procedure
- For ages <50 years, CAS is the favored procedure
- For ages >74 years, CEA is the favored procedure
- BUT, in CREST asymptomatic patients had few events, so there were wide confidence intervals

So, the choice of CEA or CAS cannot be mandated in CREST-2...

...and individual patient characteristics and preferences may supersede guidelines
Selected CAS Exclusions

- Excessive or circumferential calcification of the stenotic lesion
- Lesions >20 mm in length, sequential lesions, and narrow-mouth ulcers
- Inability to deploy or utilize an FDA-approved Embolic Protection Device (EPD)
Patients in both trials will take aspirin 325 mg per day for the entire follow-up period (CAS patients will also take clopidogrel per protocol).

Primary risk factors: systolic blood pressure and LDL cholesterol

- Managed by the study neurologist/internist
- Target systolic blood pressure <140 mmHg
- Target LDL <70 mg/dl
Medical Management

Secondary risk factor targets:

• Non-HDL cholesterol <100 mg/dl.
• Hemoglobin A1c <7.0%.
• Smoking cessation.
• Targeted weight management.
• > 30 minutes of moderate exercise 3 times a week.
Lifestyle management and cardiovascular disease risk reduction program.

Incorporates SAMMPRIS targets and national guidelines.

Provides individualized risk factor counseling telephone sessions at regular intervals:
- twice a month for 12 weeks.
- monthly thereafter.

Case Managers at INTERVENT call center, Savannah, GA.
BP Management Algorithm

- **At Enrollment:**
  - Is SBP < 140*?
    - **IN TARGET**
      - Return for Study visit and BP check in 30 days
    - **NOT IN TARGET**
      - Adjust meds per protocol
      - Return for BP check in 30 days

- **At 30 day visit**
  - Is SBP < 140*?
    - **IN TARGET**
      - Return for BP check at required 4 month visit
    - **NOT IN TARGET**
      - Adjust meds per protocol
      - Return for BP check in 30 days

- **At repeat 30 day blood pressure checks or at any study follow-up visit:**
  - Is SBP < 140*?
    - **IN TARGET**
      - Return for BP check at required 4 month visit
    - **NOT IN TARGET**
      - Adjust meds per protocol
      - Return for BP check in 30 days
Managing LDL

At enrollment:

1. If LDL $\geq 70$, start Atorvastatin 40* mg (if not already on a statin) OR increase dose of patient’s current statin, OR switch from current statin to Atorvastatin
2. If LDL < 70, leave on current statin at current dose
3. Send Baseline AST/ALT & CK (if not done already)

*starting dose 20 mg in Asians
Do NOT start Atorvastatin if:
- patient has documented allergy to Atorvastatin OR
- estimated creatinine clearance < 30 mL/min

CAS and CEA patients: Extra dose of Atorvastatin 80 mg or maximum dose of patient’s current statin night before procedure

Next visit at day 30

If enrollment LDL $\geq 70$ recheck LDL at 30 days:
- If LDL < 70, no change
- If LDL still $\geq 70$, increase Atorvastatin to 80 mg (40 mg in Asians) OR increase dose of patient’s other statin to maximum dose.
Selected Eligibility Criteria for Providers

Operators

• Operators must have done at least 50 total procedures. If they have done <50, they must have done at least 8 over the last 2 years

• Operators must have been reviewed and approved by the CREST-2 IMC. Regardless of the number of individual stenters at a center, each participating center will be subject to the overall enrollment restriction of 1:1 in the registry vs CREST-2
Final perspectives on CEA and CAS

- Outcomes in all are evolving to the positive, and most dramatically for CAS.
- The best data available support that the judicious, expert, and selective use of these therapies which can result in overall improved patient outcomes:
  - Fewer strokes, fewer MI’s
  - Less disability and less CV mortality
- The equivalence of outcomes of CEA and CAS in CREST bestow complementary, not competitive, roles in the patient requiring revascularization.
Conclusions

• Carotid stents are a less invasive alternative to CEA

• Hemodynamic perturbations are common in carotid stenting and should be anticipated in pre-procedural planning
  • Preparation of staff, pharmacologic, and mechanical solutions
  • Only rarely should result in a clinically relevant outcome

• Neurologic events are unusual, and evaluation of the specific syndrome directs management and aids in prognosis
Summary: *CAS should be applied selectively*

- **High risk factors for CAS:**
  - Advanced age
  - Recent symptoms
  - Challenging anatomy

- **CANOPY registry and CREST 2 will be revealing:**
  - Excludes octogenarians
  - Excludes high risk for CAS--protocol defined
  - Interventionalist criteria are strict and verified
  - Standardized protocol: routinely uses embolic protection, optimal medical therapy
Clinical Equipoise = Endovascular Superiority
## Asymptomatic Carotid Stenosis

**When to stent, when to operate and when to treat medically**

### Standard Risk

- **Stent**
  - Younger patients, those with heart problems, good anatomy for stent

- **CEA**
  - Older patients, low cardiac risk, bad anatomy for stent

- **Medical Alone**
  - 50-69% stenosis, women?

### High Risk

- **Stent**
  - Recurrence, high anatomic risk, some physiologic high risk

- **CEA**
  - None

- **Medical Alone**
  - Over 80 years, 50-69% stenosis, women, some physiologic high risk, bad anatomy for stent
## Symptomatic Carotid Stenosis

<table>
<thead>
<tr>
<th>Standard Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stent</td>
<td>• Stent</td>
</tr>
<tr>
<td>• Younger patients, those with heart problems, good anatomy for stent, 50-69% stenosis?</td>
<td>• Recurrence, high anatomic risk, physiologic high risk</td>
</tr>
<tr>
<td>• CEA</td>
<td>• CEA</td>
</tr>
<tr>
<td>• Older patients, low cardiac risk, bad anatomy for stent, more severe previous stroke, previous IC hemorrhage</td>
<td>• None</td>
</tr>
<tr>
<td>• Medical Alone</td>
<td>• Medical Alone</td>
</tr>
<tr>
<td>• None</td>
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</tr>
</tbody>
</table>