Carotid and Peripheral Interventions: Who, What, and When

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• Disclosures: Speakers Agreement Medtronic

• Learning Objectives: Discuss the screening and treatment of carotid and peripheral arterial disease
Carotid Interventions: Who, What, When?

• Who should be screened for carotid artery disease?
• What factors are associated with stroke risk?
• When is invasive treatment for carotid artery disease needed (vs. medical therapy)?
• When should CAS be the primary mode of revascularization (vs. CEA)?
Who should be screened for carotid artery disease?

- Prevalence: asymptomatic
  - Men and women age >65 (Cardiovascular Health Study, Framingham, Berlin Aging Study)
    - Stenosis >50%: 5-10%
    - Stenosis >80%: 1%
  - Screening of general populations for asymptomatic carotid stenosis is not recommended or cost effective
    - Bruits
    - Known cardiovascular or PAD
What factors are associated with stroke risk?

• Asymptomatic carotid artery stenosis
  – Annual stroke risk attributable to ipsilateral carotid stenosis >50% is 1% to 2%
  – Higher risk subgroups
    • Higher degree of stenosis
    • Plaque area
    • Progressive stenosis (>80%)
    • Plaque morphology
    • Contralateral ischemic symptoms
    • Silent embolic events by imaging
Plaque Area, Plaque Progression, and Microemboli

Spence, J. D. et al. Stroke 2002;33:2916-2922
When is invasive treatment for carotid artery disease needed (vs. medical therapy)?

- Asymptomatic
  - VA Coop, ACAS, ACST approx 50% risk reduction CEA c/w medical treatment
    - Dependent surgical risk (2.7-3.1%)
    - Benefits accrue after 1-2 yrs
    - Possibly less benefit in women (higher complication rates)
    - Medical therapy suboptimal for todays standards
Medical therapy for the treatment of asymptomatic carotid artery stenosis

1.7% fall in any-territory stroke rate is seen from 1986 to 2007

When is invasive treatment for carotid artery disease needed (vs. medical therapy)?

- Symptomatic TIAs/minor CVAs
  - Annual stroke risk 4-5%
  - NASCET, ECST, VA Coop
    - Stenosis >70% clear benefit, 50-70% uncertain, <50% stenosis and occlusions had no benefit
    - Greatest benefit in men, ≥75, recent event
    - Operators with peri-op complication rate less than 6%
    - Medical therapy suboptimal for today’s standards

- Operators with peri-op complication rate less than 6%
**Statin therapy for secondary prevention of stroke**

**SPARCL trial: 5 year outcomes**

<table>
<thead>
<tr>
<th>Event</th>
<th>Atorvastatin Events (%)</th>
<th>Placebo Events (%)</th>
<th>HR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>55 (11.2)</td>
<td>83 (16.1)</td>
<td>0.67</td>
<td>0.021</td>
</tr>
<tr>
<td>Without CS</td>
<td>210 (11.2)</td>
<td>228 (12.3)</td>
<td>0.90</td>
<td>0.256</td>
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<tr>
<td>Stroke or TIA</td>
<td>79 (16.0)</td>
<td>118 (23.0)</td>
<td>0.66</td>
<td>0.005</td>
</tr>
<tr>
<td>With CS</td>
<td>79 (16.0)</td>
<td>118 (23.0)</td>
<td>0.66</td>
<td>0.005</td>
</tr>
<tr>
<td>Without CS</td>
<td>296 (15.8)</td>
<td>358 (19.3)</td>
<td>0.80</td>
<td>0.005</td>
</tr>
<tr>
<td>Major Coronary Event</td>
<td>19 (3.9)</td>
<td>33 (6.4)</td>
<td>0.57</td>
<td>0.049</td>
</tr>
<tr>
<td>With CS</td>
<td>19 (3.9)</td>
<td>33 (6.4)</td>
<td>0.57</td>
<td>0.049</td>
</tr>
<tr>
<td>Without CS</td>
<td>62 (3.3)</td>
<td>87 (4.7)</td>
<td>0.69</td>
<td>0.024</td>
</tr>
<tr>
<td>Major Cardiovascular Event</td>
<td>70 (14.2)</td>
<td>108 (21.0)</td>
<td>0.64</td>
<td>0.004</td>
</tr>
<tr>
<td>With CS</td>
<td>70 (14.2)</td>
<td>108 (21.0)</td>
<td>0.64</td>
<td>0.004</td>
</tr>
<tr>
<td>Without CS</td>
<td>264 (14.1)</td>
<td>299 (16.1)</td>
<td>0.85</td>
<td>0.059</td>
</tr>
<tr>
<td>Carotid Revascularization</td>
<td>16 (3.2)</td>
<td>37 (7.2)</td>
<td>0.44</td>
<td>0.006</td>
</tr>
<tr>
<td>With CS</td>
<td>16 (3.2)</td>
<td>37 (7.2)</td>
<td>0.44</td>
<td>0.006</td>
</tr>
<tr>
<td>Without CS</td>
<td>13 (0.7)</td>
<td>7 (0.4)</td>
<td>1.83</td>
<td>0.199</td>
</tr>
<tr>
<td>Any Revascularization</td>
<td>38 (7.7)</td>
<td>76 (14.8)</td>
<td>0.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>With CS</td>
<td>38 (7.7)</td>
<td>76 (14.8)</td>
<td>0.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Without CS</td>
<td>56 (3.0)</td>
<td>87 (4.7)</td>
<td>0.61</td>
<td>0.005</td>
</tr>
<tr>
<td>Any Coronary Event</td>
<td>31 (6.3)</td>
<td>59 (11.5)</td>
<td>0.51</td>
<td>0.003</td>
</tr>
<tr>
<td>With CS</td>
<td>31 (6.3)</td>
<td>59 (11.5)</td>
<td>0.51</td>
<td>0.003</td>
</tr>
<tr>
<td>Without CS</td>
<td>92 (4.9)</td>
<td>145 (7.8)</td>
<td>0.61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any Cardiovascular Event</td>
<td>119 (24.1)</td>
<td>194 (37.7)</td>
<td>0.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>With CS</td>
<td>119 (24.1)</td>
<td>194 (37.7)</td>
<td>0.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Without CS</td>
<td>403 (21.5)</td>
<td>491 (26.5)</td>
<td>0.79</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Stroke. 2008;39:3297-3302*
When is invasive treatment for carotid artery disease needed (vs. medical therapy)?

- There is no conclusive evidence that medical therapy is an acceptable substitute for revascularization in patients with severe carotid artery stenosis with or without symptoms
  - Caveats
    - All patients should be treated with statins
      - Intensive lipid lowering for symptomatic patients (class I, level B)
    - Asymptomatic patients
      - The stenosis should be severe >70-80%
      - or there are high risk features
    - There are no RCT of medical therapy vs. CAS
    - RCT of CEA vs medical therapy are outdated
Who should have CAS (with EPD) as the primary intervention (vs. CEA)?

**SYMPTOMATIC**
- HIGH RISK
- SAPPHIRE (RCT)
- CAPTURE 2
- EXACT

**ASYMPTOMATIC**
- HIGH RISK
- SAPPHIRE (RCT)
- CATURE 2
- EXACT

**SYMPTOMATIC**
- STANDARD RISK
- EVA3s (RCT)
- SPACE 1 (RCT)
- CREST (RCT completed)

**ASYMPTOMATIC**
- STANDARD RISK
- ACT1 (RCT enrolling)
- SPACE 2 (RCT enrolling)
- CREST (RCT completed)
Protected Carotid-Artery Stenting versus CEA in High-Risk Patients (SAPPIRE)

- Inclusion Criteria
  - >50% stenosis Sx ≥80% stenosis Asx and comorbidity
- 747 Patients enrolled
  - 334 randomized (CEA vs. CAS)
  - 96 symptomatic
- Primary Outcome
  - Death, MI, stroke 30d
  - Death, ipsilateral stroke 31d-1yr

87.7%
79.9%
88.0%
79.9%
SAPPIRE 3-Year Outcomes

Death, MACE, stroke  Freedom from Target-Vessel Revascularization

- CAS and CEA are both durable procedures
- Similar Death, MACE, stroke

97%  92.9%
CAS for High Risk Patients

- EXACT and CAPTURE 2 registries
  - Prospective, multicenter (280 US sites, 672 operators), postmarket surveillance studies.
  - 2145 patients from the Emboshield and Xact Post Approval Carotid Stent Trial (EX)
  - 4175 patients from the Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events (C2).
  - Both studies had pre- and postprocedure neurological evaluation and independent adjudication of neurological events.

Grey, WA Circ CI 2009;2:159-166
CAPTURE 2 and EXACT: Thirty Day Outcomes

Composite endpoint of death and stroke

<table>
<thead>
<tr>
<th></th>
<th>EXACT (N=2145)</th>
<th>CAPTURE 2 (N=548)</th>
<th>Combined (N=761)</th>
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<tbody>
<tr>
<td>All</td>
<td>4.1</td>
<td>3.4</td>
<td>3.6</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>7.0</td>
<td>6.2</td>
<td>6.4</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>3.7</td>
<td>3.0</td>
<td>3.2</td>
</tr>
</tbody>
</table>

*The symptomatic status for one patient in EXACT could not be determined

Composite endpoint of death and major stroke

<table>
<thead>
<tr>
<th></th>
<th>EXACT (N=2145)</th>
<th>CAPTURE 2 (N=548)</th>
<th>Combined (N=761)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>1.5</td>
<td>1.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>2.8</td>
<td>2.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>1.4</td>
<td>1.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>
CAPTURE 2 and EXACT: Outcomes According to Age

Hierarchical Events – Includes only the most serious event for each patient and includes only each patient’s first occurrence of each event. Clinical Studies are not directly comparable by methodology presented.

EXACT: n=1620
CAPTURE 2: n=1523
EXACT: n=504
CAPTURE 2: n=464

Grey, WA presentation 2009
CAPTURE 2 and EXACT: Thirty Day outcomes in Subgroups

Patients <80 years old

Unfavourable anatomic factors


Circulation: Cardiovascular Interventions
CAS for Symptomatic Patients with Average Surgical Risk

Endarterectomy versus Stenting in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S)


P=0.01
CAS for Symptomatic Patients with Average Surgical Risk: SPACE

- Randomized, multicenter non-inferiority study of CEA vs. CAS in standard surgical risk symptomatic patients with 70% carotid stenosis
  - 1200 patients were randomly assigned (605 were randomly assigned to CAS and 595 were randomly assigned to CEA)
  - Primary endpoint 30-day ipsilateral stroke and death
  - Only 27% EPD use
  - Pre-specified secondary analyses include:
    - Age, Sex, Type of event, Side of intervention, Degree of stenosis, High-grade contralateral stenosis
Stent-protected angioplasty versus CEA in symptomatic patients (SPACE)

**Primary Endpoint**

30 day death and stroke (%)

<table>
<thead>
<tr>
<th></th>
<th>CEA</th>
<th>CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abs diff: 0.51, 90%CI 1.89-2.91, P=0.09 (non-inferiority)</td>
<td>6.34</td>
<td>6.84</td>
</tr>
</tbody>
</table>
### SPACE: Subgroups

<table>
<thead>
<tr>
<th></th>
<th>CAS n=132</th>
<th>Events (rate)</th>
<th>CAS p&lt;sup&gt;t&lt;/sup&gt;</th>
<th>CEA n=141</th>
<th>Events (rate)</th>
<th>CEA p&lt;sup&gt;t&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤62</td>
<td>138</td>
<td>3 (2.2%)</td>
<td>0.001 (trend 0.0002)</td>
<td>135</td>
<td>11 (8.3%)</td>
<td>0.417 (trend 0.401)</td>
</tr>
<tr>
<td>&gt;62-68</td>
<td>141</td>
<td>4 (2.8%)</td>
<td></td>
<td>141</td>
<td>6 (4.3%)</td>
<td></td>
</tr>
<tr>
<td>&gt;68-75</td>
<td>157</td>
<td>18 (10.8%)</td>
<td></td>
<td>127</td>
<td>5 (3.5%)</td>
<td></td>
</tr>
<tr>
<td>≥75</td>
<td>127</td>
<td>14 (11.0%)</td>
<td></td>
<td>160</td>
<td>9 (5.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>157</td>
<td>13 (8.3%)</td>
<td>0.457</td>
<td>162</td>
<td>9 (5.6%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Male</td>
<td>415</td>
<td>26 (6.3%)</td>
<td></td>
<td>401</td>
<td>22 (5.5%)</td>
<td></td>
</tr>
<tr>
<td><strong>Qualifying event</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occl.</td>
<td>91</td>
<td>3 (3.3%)</td>
<td>0.57</td>
<td>87</td>
<td>3 (3.4%)</td>
<td>0.358</td>
</tr>
<tr>
<td>TIA</td>
<td>169</td>
<td>14 (8.3%)</td>
<td></td>
<td>173</td>
<td>3 (1.8%)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>257</td>
<td>17 (6.6%)</td>
<td></td>
<td>241</td>
<td>18 (7.5%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>15</td>
<td>1 (6.7%)</td>
<td></td>
<td>7</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>41</td>
<td>4 (9.8%)</td>
<td></td>
<td>55</td>
<td>1 (1.8%)</td>
<td></td>
</tr>
<tr>
<td><strong>Contra-lateral stenosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>535</td>
<td>38 (7.1%)</td>
<td>0.50</td>
<td>524</td>
<td>26 (5.0%)</td>
<td>0.672</td>
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<tr>
<td>Yes</td>
<td>38</td>
<td>1 (2.6%)</td>
<td></td>
<td>39</td>
<td>5 (12.8%)</td>
<td></td>
</tr>
<tr>
<td><strong>Side of intervention</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>300</td>
<td>18 (6.0%)</td>
<td>0.567</td>
<td>297</td>
<td>18 (6.1%)</td>
<td>0.583</td>
</tr>
<tr>
<td>Right</td>
<td>273</td>
<td>21 (7.7%)</td>
<td></td>
<td>266</td>
<td>13 (4.9%)</td>
<td></td>
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<tr>
<td><strong>Stenosis grade</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60%</td>
<td>91</td>
<td>8 (8.8%)</td>
<td>0.20 (trend 0.057)</td>
<td>95</td>
<td>2 (2.1%)</td>
<td>0.377 (trend 0.050)</td>
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<tr>
<td>60-69%</td>
<td>123</td>
<td>4 (3.3%)</td>
<td></td>
<td>124</td>
<td>5 (4.0%)</td>
<td></td>
</tr>
<tr>
<td>70-79%</td>
<td>57</td>
<td>7 (12.3%)</td>
<td></td>
<td>57</td>
<td>4 (7.0%)</td>
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<tr>
<td>80-89%</td>
<td>195</td>
<td>14 (7.2%)</td>
<td></td>
<td>189</td>
<td>12 (6.6%)</td>
<td></td>
</tr>
<tr>
<td>≥90%</td>
<td>107</td>
<td>6 (5.6%)</td>
<td></td>
<td>104</td>
<td>8 (7.7%)</td>
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</tbody>
</table>
SPACE: Operator Volume

<table>
<thead>
<tr>
<th>Class</th>
<th>Centres (n)</th>
<th>Outcome event (n)</th>
<th>Total (n)</th>
<th>pOE rate (95% CI) in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS (ITT, pOE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥25 patients</td>
<td>9</td>
<td>18</td>
<td>370</td>
<td>4.9 (2.9–7.6)</td>
</tr>
<tr>
<td>10–&lt;25 patients</td>
<td>10</td>
<td>16</td>
<td>171</td>
<td>9.4 (5.4–14.7)</td>
</tr>
<tr>
<td>&lt;10 patients</td>
<td>15</td>
<td>8</td>
<td>66</td>
<td>12.1 (5.4–22.5)</td>
</tr>
<tr>
<td>CEA (ITT, pOE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥25 patients</td>
<td>8</td>
<td>21</td>
<td>337</td>
<td>6.2 (3.9–9.4)</td>
</tr>
<tr>
<td>10–&lt;25 patients</td>
<td>11</td>
<td>16</td>
<td>192</td>
<td>8.3 (4.8–13.2)</td>
</tr>
<tr>
<td>&lt;10 patients</td>
<td>15</td>
<td>1</td>
<td>60</td>
<td>1.7 (0.0–8.9)</td>
</tr>
</tbody>
</table>
## SPACE: 2-Year Outcomes

<table>
<thead>
<tr>
<th>Event</th>
<th>CAS</th>
<th>CEA</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipsilateral ischemic strokes within 2 years, including any periprocedural strokes or deaths</td>
<td>56 (9.5%)</td>
<td>50 (8.8%)</td>
<td>1.10 (0.75–1.61)</td>
</tr>
<tr>
<td>Any deaths between randomization and 2 years</td>
<td>32 (6.3%)</td>
<td>28 (5.0%)</td>
<td>1.11 (0.67–1.85)</td>
</tr>
<tr>
<td>Any strokes between randomization and 2 years</td>
<td>64 (10.9%)</td>
<td>57 (10.1%)</td>
<td>1.10 (0.77–1.57)</td>
</tr>
<tr>
<td>Ipsilateral ischemic stroke between 31 days and 2 years</td>
<td>12 (2.2%)</td>
<td>10 (1.9%)</td>
<td>1.17 (0.51–2.70)</td>
</tr>
</tbody>
</table>

- No differences between CEA and CAS for prevention of recurrent events
# SPACE: 2-Year Outcomes According to Subgroups

<table>
<thead>
<tr>
<th>Indicator event</th>
<th>CAS</th>
<th>CEA</th>
<th>Hazard ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>134157</td>
<td>102262</td>
<td>1.37 (0.80-2.32)</td>
<td>0.37</td>
</tr>
<tr>
<td>Men</td>
<td>406416</td>
<td>334401</td>
<td>1.38 (0.94-2.01)</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Age at randomisation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 years</td>
<td>137279</td>
<td>227296</td>
<td>0.57 (0.39-0.84)</td>
<td>0.005</td>
</tr>
<tr>
<td>≥65 years</td>
<td>40294</td>
<td>21217</td>
<td>2.00 (0.90-4.44)</td>
<td></td>
</tr>
<tr>
<td><strong>Indicator event</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneurysm, fusus and others?</td>
<td>9/106</td>
<td>3/94</td>
<td>2.31 (0.33-17.27)</td>
<td>0.09</td>
</tr>
<tr>
<td>TIA</td>
<td>180/163</td>
<td>142/73</td>
<td>1.38 (0.56-3.41)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>21/257</td>
<td>24/241</td>
<td>0.91 (0.44-1.87)</td>
<td></td>
</tr>
<tr>
<td>Multiple events</td>
<td>8/41</td>
<td>1/65</td>
<td>11.8 (1.32-103)</td>
<td></td>
</tr>
<tr>
<td><strong>Grade of treated stenosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70%†</td>
<td>18/214</td>
<td>13/228</td>
<td>2.44 (0.71-8.45)</td>
<td>0.59</td>
</tr>
<tr>
<td>70-99%†</td>
<td>35/350</td>
<td>209/345</td>
<td>2.33 (0.48-10.84)</td>
<td></td>
</tr>
<tr>
<td><strong>Side of treated stenosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>28/300</td>
<td>23/297</td>
<td>1.24 (0.70-2.17)</td>
<td>0.99</td>
</tr>
<tr>
<td>Right</td>
<td>25/273</td>
<td>20/255</td>
<td>2.23 (0.54-8.84)</td>
<td></td>
</tr>
<tr>
<td><strong>Status of contralateral carotid artery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70%†</td>
<td>50/535</td>
<td>35/421</td>
<td>2.45 (0.82-7.22)</td>
<td>0.18</td>
</tr>
<tr>
<td>70-99%†</td>
<td>2/21</td>
<td>5/24</td>
<td>0.20 (0.06-0.64)</td>
<td></td>
</tr>
<tr>
<td>Occluded</td>
<td>2/17</td>
<td>5/18</td>
<td>0.70 (0.31-1.60)</td>
<td></td>
</tr>
</tbody>
</table>
CAS in Symptomatic Patients

- AHA guideline limit 6%
CAS for Standard Risk Patients: Ongoing and Recently Completed Trials

- CREST
- ACT1
- SPACE 2
  - Asymptomatic
  - $\geq 70\%$ by ultrasound
  - Randomization
    - CEA vs. CAS vs. conservative
    - All with OMT up to 5 yrs
When should CAS be the primary mode of revascularization (vs. CEA)?

- Symptomatic High Risk Patients
- Symptomatic Standard Risk Patients
  - Age less than 68
- Asymptomatic High Risk Patients
  - Age less than 80
  - Patients with unfavorable surgical anatomy (prior CEA)
  - Enroll in PMS registry of CAS
- Asymptomatic Standard Risk Patients
  - Enroll in ACT1, Awaiting data CREST
- CAVEATS
  - By Experienced operators
  - With embolic protection devices
Recommendations for Interventional Approaches to Patients With Stroke Caused by Extracranial carotid disease*

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>For patients with recent TIA or ischemic stroke within the last 6 mo and ipsilateral severe (70%-99%) carotid artery stenosis, CEA is recommended by a surgeon with a perioperative morbidity and mortality of 6%.</td>
<td>Class I, Level A</td>
</tr>
<tr>
<td>For patients with recent TIA or ischemic stroke and ipsilateral moderate (50%-69%) carotid stenosis, CEA is recommended, depending on patient-specific factors such as age, gender, comorbidities, and severity of initial symptoms.</td>
<td>Class I, Level A</td>
</tr>
<tr>
<td>When degree of stenosis is 50%, there is no indication for CEA</td>
<td>Class III, Level A</td>
</tr>
<tr>
<td>When CEA is indicated, surgery within 2 wk rather than delayed surgery is suggested.</td>
<td>Class IIa, Level B</td>
</tr>
<tr>
<td>Among patients with symptomatic severe stenosis (70%) that are high risk for surgery CAS is not inferior to CEA and may be considered.</td>
<td>Class Iib, Level B</td>
</tr>
<tr>
<td>CAS is reasonable when performed by operators with established periprocedural morbidity and mortality rates of 4% to 6%, similar to that observed in trials of CEA and CAS.</td>
<td>Class IIa, Level B</td>
</tr>
<tr>
<td>Among patients with symptomatic carotid occlusion, bypass surgery is not recommended.</td>
<td>Class III, Level A</td>
</tr>
</tbody>
</table>

* ACC/ASA Guidelines  Circulation June 2006
Peripheral Interventions: Who, What, When?

- Who should be screened for PAD?
- When is endovascular treatment for PAD indicated for intermittent claudication (vs. medical therapy and surgery)?
- What devices should you have in your armamentarium for endovascular treatment of PAD?
PAD Epidemiology

• Estimated 27 million have PAD
  – Majority are asymptomatic
• Under diagnosed and undertreated
  – Several screening programs (POPADAD, Minnesota Regional screening Program, PARTNERS)
  – Prevalence in “at-risk” populations is 20-29%
• Prognosis
  – CAD equivalent
  – Poor quality of life
The 10-year Survival Rates (San Diego Artery Study)

Natural History of PAD

Limb Morbidity

- Stable Claudication 70-80%
- Worsening Claudication 10-20%
- Critical Limb Ischemia 1-2%

Cardiovascular Morbidity / Mortality

- Nonfatal CV Events 20%
- Mortality 15-30%

CV Causes 75%
Non CV Causes 25%
Who Should be screened for PAD?

- Age less than 50 years with diabetes, and one additional risk factor (e.g., smoking, dyslipidemia, hypertension, or hyperhomocysteinemia)
- Age 50 to 69 years and history of smoking or diabetes
- Age 70 years and older
- Leg symptoms with exertion (suggestive of claudication) or ischemic rest pain
- Abnormal lower extremity pulse examination
- Known atherosclerotic coronary, carotid, or renal artery disease
Medical treatment for PAD and revascularization considerations

- Antiplatelet agent
  - ASA or clopidogrel (Ia/b)
- Statin (Ib)
- HTN control (Ia)
  - ACE inhibitor (IIa)
- DM hA1c<7 (IIa)
- Smoking Cessation (Ia)
- Exercise
  - Supervised (1A)
  - Unsupervised (IIb)
- Cilostazol (1a)
  - No CHF

- Symptomatic?
- Typical claudication?
- Comorbidities limiting functional status?
- Favorable anatomy for percutaneous revascularization?
  - Inflow disease
- Procedural risk?
  - Endovascular
  - Surgical
- Procedural durability?
Efficacy of Supervised Exercise: 21-Study Meta-Analysis

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Exercise</th>
<th>Control</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain-Free Walking Distance</td>
<td>180% *</td>
<td>40%</td>
<td>2 blocks</td>
</tr>
<tr>
<td>Maximal Walking Distance</td>
<td>130% *</td>
<td>30%</td>
<td>3 blocks</td>
</tr>
</tbody>
</table>

Predictors of improvement:
- Exercise to a moderate level of claudication pain
- Walking exercise (vs. other modalities)
- > 3 (or 6) months exercise training
- Supervised exercise

RCT’s of Intervention vs. Exercise

- 2 RCT’s
- Edinburgh study showed better outcome in the angioplasty group\(^1\), but the Oxford study showing better results of exercise\(^2\)
- Edinburgh used home exercise, Oxford supervised exercise

Endovascular Treatment for Claudication

- Vocational or lifestyle-limiting disability due to typical intermittent claudication when
  - Response to exercise or pharmacologic therapy is inadequate, and/or
  - There is a very favorable risk-benefit ratio (e.g. focal aortoiliac occlusive disease)
- Endovascular intervention is recommended as the preferred revascularization technique for TASC type A (focal) iliac and femoropopliteal lesions
When is endovascular treatment for PAD indicated for intermittent claudication (vs. medical therapy)?

- The Adjuvant Benefit of Angioplasty in Patients with Mild to Moderate Intermittent Claudication (MIMIC)
  - PTA vs. OMT, All pts treated with supervised exercise
  - A total of 93 patients were randomized into the femoropopliteal trial (48 into PTA) and 34 into the aortoiliac trial (19 to PTA).
  - Stopped due to recruitment issues (10% eligible)
  - The primary outcome measure was AWD in meters at 24 months
MIMIC Outcomes

Geometric mean AWD at 24 months in the fem-pop trial was 1.38 after adjustment for baseline variables (p=.04)

Initial claudication distance at 12 and 24 months significantly greater in PTA group in the femoropopliteal trial

Eur J Vasc Endovasc Surg (2008) 36, 680e688
• Intervention for claudication is not proven to be better than supervised exercise
• Intervention is expensive and associated with short-term risk
• Exercise may have other benefits that are more important and long-lasting
Claudication: Exercise Vs. Endoluminal Revascularization

- prospective, multicenter, four-arm clinical trial
- Evaluate the relative efficacy and safety of major treatment strategies for aortoiliac disease
  - Optimal Medical Care (OMC) including cilostazol
  - OMC plus stenting
  - OMC plus supervised exercise training
  - OMC plus stenting plus supervised exercise training
The CLEVER Trial

Subjects w/ PAD & claudication: Men & women > 50 yrs
Resting ABI < 0.90
Aorto-iliac dz by non-invasive criteria

n=252

OMC (n = 42)
Angioplasty/stent (n = 84)
Supervised Exercise (n = 84)
PTA + SE (n = 42)

• Change in MWD at 6 mo.
• Change in MWD at 18 mo.
• Subjective QOL
• MACE, MAPE
• Health economics
• Risk Factors

Screening Evaluation

• Change in MWD
• Change in MWD
• Subjective QOL
• MACE, MAPE
• Health economics
• Risk Factors

PTA

Supervised Exercise

OMC

Angioplasty/stent

PTA + SE

Subjects w/ PAD & claudication:
Men & women > 50 yrs
Resting ABI < 0.90
Aorto-iliac dz by non-invasive criteria

--- 8 days ---

Supervised Exercise

OMC

Angioplasty/stent

PTA + SE

Subjects w/ PAD & claudication:
Men & women > 50 yrs
Resting ABI < 0.90
Aorto-iliac dz by non-invasive criteria
Aorto-iliac Disease

CASE: 59 y/o CAD/MI/CABG/low EF, progressive IC, ABI 0.46 left, 0.54 right
LE bypass: Indicated for stable patients with IC?

- Do any claudicants need open surgical bypass?
- 80% of procedures performed by vascular surgery and cardiology by 2006
Figure 2.8.2-C  Treatment of Claudication

Confirmed PAD Diagnosis

- No significant functional disability

  - No claudication treatment required.
  - Follow-up visits at least annually to monitor for development of leg, coronary, or cerebrovascular ischemic symptoms.

  Supervised exercise program

  Three month trial

  Pre- and post-program exercise testing for efficacy

  **Clinical improvement:** Follow-up visits at least annually

Pharmacological therapy

- Cilostazol
- Pentoxifylline

  Three month trial

  **Significant disability** despite medical therapy and/or inflow endovascular therapy, with documentation of outflow† PAD, with favorable procedural anatomy and procedural risk-benefit ratio

  Evaluation for surgical revascularization

Lifestyle limiting symptoms

Endovascular therapy (or surgical bypass per anatomy)

Lifestyle limiting symptoms with evidence of inflow disease *

Further anatomic definition by more extensive noninvasive or angiographic diagnostic techniques

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* Inflow disease should be suspected in individuals with gluteal or thigh claudication and femoral pulse diminution or bruit, and should be confirmed by noninvasive vascular laboratory diagnostic evidence of aorto-iliac stenoses.
† Outflow disease represents femoropopliteal and infrapopliteal stenoses, (the presence of occlusive lesions in the lower extremity arterial tree below the inguinal ligament from the common femoral artery to the pedal vessels).
Endovascular Treatment of Claudication: Summary

• The guidelines are subject to interpretation
  – Symptom severity
  – Response or desire to adhere to exercise or medical therapy

• Technology is rapidly advancing
  – Devices for treating total occlusions
  – Stents

• Research in PAD treatment is lacking
  – Efficacy intervention compared to OMC
  – Surgical versus percutaneous
  – Device versus device (PTA, stents, atherectomy)
What devices should you have in your armamentarium for endovascular treatment of PAD?

- PTA
- Stent
  - Balloon expandable
  - Nitinol (self expanding)
  - DES (Zilver paclitaxel)
  - Covered stents
- Drug eluting balloon
- Cryoplasty
- Cutting balloon
- Scoring balloon

- Debulking
  - Orbital atherectomy (Diamondback 360)
  - Directional atherectomy (Silverhalk)
  - Atherectomy/thrombectomy (Pathway)
  - Laser
- Thrombectomy
  - angiojet
- Reentry devices
  - Outback
  - Pioneer
Stents

Dutch Iliac Stent Trial

Kaplan-Meier survival curves for iliac patency measured with duplex US

The Femoral Artery Stenting Trial (FAST)

RCT PTA vs Nitinol Stents SFA

Klein W M et al. Radiology 2006;238:734-744
SFA disease

Case: 72-y/o male with chronic stable angina, laryngeal cancer, progressive claudication, ABI 0.53
Subintimal Angioplasty and Reentry Catheters

Case: 63-y/o male with an ischemic CMP, IC and non-healing ulcer, ABI 0.46

- Subintimal PTA Patency
  - 12 month 45%,
  - 36 month 25%

Revasc achieved 95% cases

Scott E. JVasc Surg 2008;48:878
Husmann JEVT 2009;16:206-212
Stent Grafts

- Viabahn vs fem-pop bypass (n=100 limbs)
  - Mean length 25.6cm
  - Patency DUS 3, 6, 9, 12 month
    - Stent graft 84% 82% 75.6% 73.5%
    - Surgery 90% 81.8% 79.7% 74.2%
- PTFE stent graft vs fem-pop (n=100 limbs)
  - Similar patency 24 months
  - Trend for decreased patency with higher TASC lesions
- PTFE vs PTA (n=197)
  - Technical success 95% vs 66% (P<.0001)
  - 1 year primary patency 65% vs 40% (p=.0003)
  - Benefit in lesions at least 3 cm long
- VIBRANT (Viabahn versus bare nitinol stent trial for treatment of long femoropop lesion)
  - 3 yr f/u DUS and angio
Stent Grafts
Orbital Atherectomy

- OASIS (n=124) Diamondback 360°
  - Multicenter non-randomized, prospective registry
  - 32% CLI, fem-pop/infrapop
  - Device success (<30% residual stenosis) 75%
  - Procedural Success 90% (with PTA±stent)
  - TLR 6 months 20%
## Orbital Atherectomy: Safety Profile

<table>
<thead>
<tr>
<th></th>
<th>OASIS Study</th>
<th>Post-Market Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>•124 patients</td>
<td>•358 patients</td>
</tr>
<tr>
<td>Dissection (minor)</td>
<td>10.5% (0 major)</td>
<td>2%</td>
</tr>
<tr>
<td>Perforation</td>
<td>2.4%</td>
<td>2%</td>
</tr>
<tr>
<td>Embolism</td>
<td>0.8%</td>
<td>2%</td>
</tr>
<tr>
<td>Spasm</td>
<td>18.5%</td>
<td>20%</td>
</tr>
</tbody>
</table>
Orbital Atherectomy for Calcified Stenosis
Drug-Eluting Balloons

• **Local Taxane with Short Exposure for Reduction of Restenosis in Distal Arteries (THUNDER) Trial**
  - 3 Arm randomized multicenter trial (n=154)
  - SFA and/or pop disease (mean 7.5cm)
  - Rutherford 1-5
  - 1:1:1
    • Standard balloon
    • Standard balloon with 17.1 mg paclitaxel/100ml contrast
    • Paclitaxel coated balloon 3ug/mm2
  - The primary end point was late lumen loss at 6 months.
THUNDER Trial

- 6 mo angiographic f/u
  - Less late lumen loss
    DEB (0.4 vs 1.7 mm)
  - Lower rate restenosis
    (17% vs 44% control)
- Lower TLR 12 and 24 mo with DEB
- No benefit of paclitaxel in contrast
Endovascular Treatment of PAD

- Proceed if there is a good indication
- Procedural success is high
  - Use of niche devices and stents as needed
- Primary patency remains an issue
  - Particularly for infrainguinal disease
  - Serial monitoring ABI, DUS
  - Await results of VIBRANT, DEB, DES