Evolving Role of Carotid Intervention

Peter A. Schneider, MD
Hawaii Permanente Medical Group
Honolulu, Hawaii

Kaiser National Surgical Symposium
April, 2012

Disclosure

- Scientific Advisory Board: AbbottVascular (non-paid)
- Educational Programs: Cordis, Medtronic, Terumo
- Royalties: Cook (modest)
- Board of Directors: VIVA Physicians

CAS: A list of “firsts”

- First time that a new treatment had to beat the old treatment at the time of introduction to be approved for use.
- Divergence between FDA and CMS rulings.
- MI as an endpoint.
- Opposite of traditional open vs endo comparisons: Long term results of CAS and CEA are similar but short term morbidity of the endo option is higher.

CAS: A list of “firsts”

- First time that a new treatment had to beat the old treatment at the time of introduction to be approved for use.
- Divergence between FDA and CMS rulings.
- MI as an endpoint.
- Opposite of traditional open vs endo comparisons: Long term results of CAS and CEA are similar but short term morbidity of the endo option is higher.

Vote:
On Question 1, the panel voted 6-4-1 that the data show that there is reasonable assurance that the RX Acculink Carotid Stent System is safe for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication.
On Question 2, the panel voted 8-2-1 that there is reasonable assurance that the RX Acculink Carotid Stent System is effective for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication.
On Question 3, the panel voted 7-3-1 that the benefits of the RX Acculink Carotid Stent System for use in the prespecified patient population do outweigh the risks of the RX Acculink Carotid Stent System for use in standard surgical risk patients outlined in the proposed indication.

Any periprocedural stroke or death or postprocedural ipsilateral stroke:

<table>
<thead>
<tr>
<th>Symptoms?</th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic patients</td>
<td>(2.5±0.6)</td>
<td>(1.4±0.5)</td>
</tr>
<tr>
<td>Symptomatic patients</td>
<td>(6.0±0.9)</td>
<td>(3.2±0.7)</td>
</tr>
</tbody>
</table>

CAS: A list of “firsts”

- First time that a new treatment had to beat the old treatment at the time of introduction to be approved for use.
- Divergence between FDA and CMS rulings.
- MI as an endpoint.
- Opposite of traditional open vs endo comparisons: Long term results of CAS and CEA are similar but short term morbidity of the endo option is higher.

Vote:
On Question 1, the panel voted 6-4-1 that the data show that there is reasonable assurance that the RX Acculink Carotid Stent System is safe for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication.
On Question 2, the panel voted 8-2-1 that there is reasonable assurance that the RX Acculink Carotid Stent System is effective for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication.
On Question 3, the panel voted 7-3-1 that the benefits of the RX Acculink Carotid Stent System for use in the prespecified patient population do outweigh the risks of the RX Acculink Carotid Stent System for use in standard surgical risk patients outlined in the proposed indication.

Any periprocedural stroke or death or postprocedural ipsilateral stroke:

<table>
<thead>
<tr>
<th>Symptoms?</th>
<th>Stroke/Death Threshold Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>3%</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>6%</td>
</tr>
</tbody>
</table>

CAS: A list of “firsts”

- First time that a new treatment had to beat the old treatment at the time of introduction to be approved for use.
- Divergence between FDA and CMS rulings.
- MI as an endpoint.
- Opposite of traditional open vs endo comparisons: Long term results of CAS and CEA are similar but short term morbidity of the endo option is higher.
FDA CREST Analysis

Areas of difference:
- Minor stroke: twice as many with CAS
- MI: twice as many with CEA
- Cranial nerve injury

FDA CREST Analysis

Minor Stroke Neuro Deficit by NIH Stroke Scale

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

MI: With Us as an Endpoint

Blackshear et al. Circulation 2011;123:2571

Cranial Nerve Injury

<table>
<thead>
<tr>
<th>Cranial Nerve Injury</th>
<th>Unresolved at Six Months</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>

Freedom from Primary Endpoint After Repair

Both CEA and CAS are effective at long-term stroke prevention.
FDA CREST Analysis

- The curves are parallel after periop period.
- The risk is in the first 30 days.
  - Specific risks of each procedure.

Latest devices and their data

- Lumen/Invatec Fibernet
  - 30 day MAE: 3.0%
- Gore Flow Reversal System
  - 30 day MAE: 3.7%
- Abbott Vascular Next Gen Emboshield
  - 30 day MAE: 1.8%

During the eight years that CREST enrolled, we were learning how to make CAS safer.

Was this improvement in CAS results also happening in CREST?

FDA CREST Analysis

CAS Death/Major Stroke Symptomatic Patients

Physiologic
- Age >80

Anatomic
- Tortuous arch
- Calcified arch
- Diseased great vessels
- Tortuous carotid artery
- Pre-occlusive lesion
- Heavy plaque burden
- Circumferential calcification
- Echolucent plaque
- Thrombus in lesion
- Isolated cerebral hemisphere
CAS Improved Over Time
We were exploring the limits of the technology

• Better patient selection
  – Arch and great vessel anatomy
  – Carotid bifurcation anatomy
  – Lesion issues
• Routine performance of more cases
• Would results improve even more if we had choice of equipment and better technology?

CAS: Select Protection Devices

<table>
<thead>
<tr>
<th>Method of Protection</th>
<th>Approach</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filtered flow</td>
<td>Fixed wire filter system</td>
<td>Most experience, most patients can be treated</td>
<td>Incomplete filtration, less versatile for crossing lesion</td>
</tr>
<tr>
<td></td>
<td>Free wire filter system</td>
<td>Versatile for crossing lesions</td>
<td>Incomplete filtration</td>
</tr>
<tr>
<td>Cessation of flow</td>
<td>Distal occlusion</td>
<td>Lowest profile for crossing lesion</td>
<td>Intolerance, vessel damage at balloon site</td>
</tr>
<tr>
<td></td>
<td>Proximal occlusion</td>
<td>No need to cross lesion, can treat bad ICA lesion</td>
<td>Adds risk in a bad arch, intolerance</td>
</tr>
<tr>
<td>Reversal of flow</td>
<td>PAES catheter</td>
<td>Better removal of embol, simple, avoid arch</td>
<td>Adds risk in a bad arch, intolerance</td>
</tr>
<tr>
<td></td>
<td>Direct cervical</td>
<td>Better removal of embol, simple, avoid arch</td>
<td>Neck incision, no good in hostile neck, intolerance</td>
</tr>
</tbody>
</table>

DW-MRI

Failure of cerebral protection!

CAS: up to 70%
CEA: up to 27%

Pushing the Limits
Select Protection Devices

Dangerous lesion-consider proximal occlusion

Pushing the Limits
Select Protection Devices

Bad arch/tortuous pathway-consider direct cervical CAS
Pushing the Limits: Select Protection Devices

Anatomical characteristics
Patient characteristics

Lesion

Choice

Elderly

Young

Proximal occlusion

CAS: Select Protection Devices

Anatomical characteristics

Cerebral collaterals

Good

Bad

Good

Bad

Choice

Good

Bad

Proximal occlusion

Choice

Direct Cervical CAS

Proximal

Distal

Bersin TCT 2008

Pushing the Limits: Carotid Stent Design

<table>
<thead>
<tr>
<th>Proximal</th>
<th>Radiant-Link (Tapered, 8-mm)</th>
<th>RX ACCULINK™ (Tapered, 8-mm)</th>
<th>WALLSTENT® (Straight, 8-mm)</th>
<th>Precise® (Straight, 8-mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pore diam. (mm)</td>
<td>1.08</td>
<td>1.06</td>
<td>0.96</td>
<td>1.12</td>
</tr>
<tr>
<td>Pore size (mm²)</td>
<td>1.80</td>
<td>10.78</td>
<td>2.23</td>
<td>2.43</td>
</tr>
<tr>
<td>Cell area (mm²)</td>
<td>4.48</td>
<td>10.78</td>
<td>2.23</td>
<td>7.39</td>
</tr>
</tbody>
</table>

Pushing the Limits
Different Than Other Pathologies We Treat

- Primarily an embolizing disease, connected to an embolus-sensitive organ
- Variable plaque morphology
- Carotid bifurcation is often tortuous
- Artery tapers and has a branch

Vulnerable plaque with hemorrhage

An amazing array of configurations
Pushing the Limits
Carotid Stent Design

We are asking carotid stents to do many things at once.
• Scaffold and constrain plaque
• Conformability
• Fatigue resistance
• Minimal fish-scaling for deployed stent
• Visible
• Easy to use

Delayed Neurologic Events 1-30d
Especially with Open Cell Stents

<table>
<thead>
<tr>
<th></th>
<th>Total population</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>All events</td>
<td>Post-procedural events</td>
</tr>
<tr>
<td>Open cell</td>
<td>937</td>
<td>39</td>
<td>32</td>
</tr>
<tr>
<td>Closed</td>
<td>2345</td>
<td>44</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>3179</td>
<td>83</td>
<td>64</td>
</tr>
</tbody>
</table>

Failure of the stent!

More Neuro Events With Open Cell Stents
SPACE Trial

Table 4. Influence of Different Stent Types on OE Rate

<table>
<thead>
<tr>
<th>Stent</th>
<th>Wallstent</th>
<th>Acculink</th>
<th>Precise</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>439</td>
<td>92</td>
<td>35</td>
</tr>
<tr>
<td>Pat. with OE</td>
<td>24</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>OE rate (95% CI)</td>
<td>5.6% (3.6-8.1%)</td>
<td>9.8% (4.6-17.8%)</td>
<td>14.3% (4.8-30.3%)</td>
</tr>
<tr>
<td>Combined OE rate: 11.0% (5.2-17.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

New Brain Lesions After Carotid Stenting Versus Carotid Endarterectomy: A Systematic Review of the Literature

Pushing the Limits
Covered Stent Systems

Government financing

• Last coverage change: March, 2005
  – Opened and kept the same twice
• Current coverage:
  – High risk symptomatic >70%
  – Clinical trial
• What next?
Change in demographics
Statins
• Lower the risk of stroke
• Decrease progression of carotid disease
• Plaque more stable

Result:
Fewer symptomatic carotid presentations

Pushing the Limits
Asymptomatic Carotid Stenosis

LEADING ARTICLE
Who Benefits Most from Intervention for Asymptomatic Carotid Stenosis: Patients or Professionals?
A.R. Naylor 1,*, P.A. Gatters 2, P.M. Rothwell 1

1 The Department of Vascular Surgery at Leicester Royal Infirmary, Leicester, UK
2 The Oxford Vascular Service, John Radcliffe Hospital, Oxford, UK

Submitted 16 January 2001; accepted 31 January 2001
Available online 6 April 2001

ACST: Repair Decreased Risk By 50% at 5 Years

ACST: Effect of statins on stroke or perioperative death

Medical Treatment for Asymptomatic Carotid Stenosis
Is the current annual risk really less than 1%?

Medical Treatment for Asymptomatic Carotid Stenosis
SMART Study (Goessens et al. Stroke, 2007)
• 223 patients with >50% carotid stenosis
• PSV >250 cm/sec; only 96 pts had PSV >310
• Stroke 2.7% over 3.6yrs; deaths not assessed
• 7% had carotid repair

Oxford Vascular Study (Marquardt Stroke, 2010)
• 101 patients with >90% carotid stenosis, 3 years
• Only 32 patients had 70-99%
• <0.5% stroke risk per year
• 1.8% TIA, vascular death 7.7%


5 year risk of stroke
An inflection point at a PSV >250

Pushing the Limits
Going Back to Imaging

- Brain imaging
  - Anatomic imaging
  - Functional imaging
- Plaque evaluation
  - Duplex
  - MR

Pushing the Limits
Proximal Occlusion for Intracranial Intervention

Pushing the Limits
Less Common but Lots of Opportunity

- Intracranial intervention
  - Acute carotid syndrome
  - “Door to balloon time”
- Arch, great vessel, carotid trauma
- Internal carotid dissection
- Carotid aneurysm
- Fibromuscular disease

Pushing the Limits on Carotid Disease
Conclusion

- We have been pushing the limits of technology.
- Need customized stents and protection devices with ability to individualize to the patient.
- Better understand asymptomatic stenosis.