Will Mesh-covered Stents Help Reduce the Risk of Stroke?

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Disclosure

Peter A. Schneider

I have the following potential conflicts of interest to report:

- Scientific Advisory Board (non-paid): Cardinal, Abbott, Medtronic
- Royalty (modest): Cook
- Co-founder and Chief Medical Officer: Intact, Cagent
Both carotid endarterectomy (CEA) and carotid artery stenting (CAS) are effective at long-term stroke prevention. 

Restenosis:

CREST N Engl J Med 2010
SPACE Lancet, 2008

Freedom from Primary Endpoint:

No. at Risk
CAS: 1262, 1100, 787, 460, 162
CEA: 1240, 1099, 770, 430, 145
### Periprocedural Endpoints in CREST 1081 **Asymptomatic** Patients

<table>
<thead>
<tr>
<th></th>
<th>CAS Events (%)</th>
<th>CEA Events (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Stroke</td>
<td>3 (0.5)</td>
<td>2 (0.3)</td>
<td>0.66</td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>12 (2.0)</td>
<td>6 (1.0)</td>
<td>0.15</td>
</tr>
<tr>
<td>Stroke and death</td>
<td>15 (2.5)</td>
<td>8 (1.4)</td>
<td>0.15</td>
</tr>
<tr>
<td>MI</td>
<td>7 (1.2)</td>
<td>13 (2.2)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Silver et al. Stroke 2011;42:675
### Periprocedural Endpoints in CREST

#### 1321 Symptomatic Patients

<table>
<thead>
<tr>
<th>Event</th>
<th>CAS Events (%)</th>
<th>CEA Events (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Stroke</td>
<td>8 (1.2)</td>
<td>6 (0.9)</td>
<td>0.61</td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>29 (4.3)</td>
<td>15 (2.3)</td>
<td>0.042</td>
</tr>
<tr>
<td>Stroke and death</td>
<td>40 (6.0)</td>
<td>21 (3.2)</td>
<td>0.019</td>
</tr>
<tr>
<td>MI</td>
<td>7 (1.0)</td>
<td>15 (2.3)</td>
<td>0.083</td>
</tr>
</tbody>
</table>

Silver et al. Stroke 2011;42:675
CREST Trial

• The risk differential is in the first 30 days.
• The curves are parallel after that.

Areas of difference:
• CEA: Twice as many MIs plus cranial nerve injury
• CAS: Twice as many minor strokes
### ICSS MRI Subset

<table>
<thead>
<tr>
<th></th>
<th>Carotid stenting (n=124)</th>
<th>Carotid endarterectomy (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one new lesion</td>
<td>62 (50%)</td>
<td>18 (17%)</td>
</tr>
<tr>
<td>Single lesion</td>
<td>18 (15%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Multiple lesions</td>
<td>44 (35%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Location of lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral carotid circulation only</td>
<td>34 (27%)</td>
<td>14 (13%)</td>
</tr>
<tr>
<td>Ipsilateral carotid and non-ipsilateral (contralateral carotid or vertebrobasilar) circulations</td>
<td>22 (18%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Non-ipsilateral (contralateral carotid or vertebrobasilar) circulations only</td>
<td>6 (5%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

![Figure 3: Distribution of DWI lesion volumes on post-treatment scans according to whether or not focal neurological deficits occurred. DWI=diffusion-weighted imaging.](image)

Bonati et al. Lancet Neurology 2010;1016:1474
Most are temporary, not associated with neurologic deficits. Not clear if there is associated long-term cognitive deficit. Use as a surrogate end point for neurological risk.

**Recent meta-analysis**

**CAS 40.3%**

**CEA 12.2%**

Garguilo et al. Plos 2015;10:137
An amazing array of configurations

Vulnerable plaque with hemorrhage

What About the Stent?
Carotid Stent Design

We are asking much of carotid stents.

- Scaffolding
- Lesion containment
- Conformability
- Fatigue resistance
- Minimal fish-scaling for ease of re-crossing
- Visibility
- Ease of use
- Low profile
Plaque Prolapse Causes Events

Plaque prolapse between stent struts

deDonato et al. Eur J Vasc Endovasc Surg 2013;45:479

Plaque Prolapse
Open Cell: 61.5%
Closed Cell: 17.6%

Wholey J Endovasc Ther 2009;16:178
Increased DW-MRI Lesions with Open Cell Stents

Prospective RCT: MRI Hits Closed versus Open Cell Stents

<table>
<thead>
<tr>
<th>Closed cell (n=48)</th>
<th>Open cell (n=48)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.3%</td>
<td>51.1%</td>
<td>0.020</td>
</tr>
</tbody>
</table>

Park et al. J Neurosurg 2013;119:

Schnaudigel et al. Stroke 2008;39:911
# Neurologic Events with Open Cell Stents

**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>436</td>
<td>92</td>
<td>35</td>
</tr>
<tr>
<td>OE rate</td>
<td>5.5% (3.6–8.1%)</td>
<td>9.8% (4.6–17.8%)</td>
<td>14.3% (4.8–30.3%)</td>
</tr>
</tbody>
</table>

**SPACE Trial Olav J et al. Stroke 2009;40:841**

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Patients</th>
<th>All events</th>
<th>Post-procedural events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open cell</td>
<td>4.2%</td>
<td>3.4%</td>
<td></td>
</tr>
<tr>
<td>Closed cell</td>
<td>2.3%</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3179</td>
<td>2.83%</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

**Belgian-Italian Registry Bosiers et al. Eur J Vasc Endovasc Surg 2007;33:135**
# Neurologic Events with Open Cell Stents

The difference between open cell and closed cell stents is mainly in symptomatic patients.

## Table 5. P-values for the test that event rates differ between stents

<table>
<thead>
<tr>
<th>Population</th>
<th>Outcome</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>All events</td>
<td>0.018</td>
</tr>
<tr>
<td></td>
<td>Post-procedural events</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Symptomatic</strong></td>
<td>All events</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>Post-procedural events</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Asymptomatic</strong></td>
<td>All events</td>
<td>0.248</td>
</tr>
<tr>
<td></td>
<td>Post-procedural events</td>
<td>0.790</td>
</tr>
</tbody>
</table>

Bosiers et al. Eur J Vasc Endovasc Surg 2007;33:135
In symptomatic patients, the relative risk of stenting over CEA is highest with intervention in the first 7 days.

# Neurologic Events After 24 Hours

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Patients</th>
<th>All events</th>
<th>Post-procedural events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>3179</td>
<td>90</td>
<td>61</td>
</tr>
<tr>
<td>Open cell</td>
<td>4.2%</td>
<td>3.4%</td>
<td></td>
</tr>
<tr>
<td>Closed cell</td>
<td>2.3%</td>
<td>1.3%</td>
<td></td>
</tr>
</tbody>
</table>

2/3 of neuro events were delayed (1-30d)

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## CREST-Timing of Stroke After Carotid Stenting

<table>
<thead>
<tr>
<th>0-24 hours</th>
<th>1-30d</th>
<th>% of strokes that occurred after 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 events</td>
<td>19 events</td>
<td>40%</td>
</tr>
</tbody>
</table>

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Bosiers et al. Eur J Vasc Endovasc Surg 2007;33:135

Hill et al. Circulation 2012;126:3054
Mesh-Covered Stents
Roadsaver

Mesh coverage for sustained embolic prevention
Retrievable and repositionable
5Fr delivery
Closed cell, woven structure

– Roadsaver Italian Registry
  • 150 patients enrolled, MRI subset
  • 30 days: No stroke, death or TIA
  • 3 Italian centers, C Setacci

– Clear Road Trial
  • Enrolling 100 patients
    – (59 patients enrolled)
  • 12 European centers, M Bosiers

Microvention/Terumo
Mesh-Covered Stents
GORE Carotid Stent

- Open Cell Nitinol Frame
- Closed Cell 500 µ lattice on outside of Frame
- Permanently Bound CBAS Heparin on all device surfaces
Mesh-Covered Stents
SCAFFOLD Trial

Design-Prospective study comparing GORE® Carotid Stent to a performance goal developed from CEA outcomes

50 sites, 312 subjects.

Co-PIs: Bill Gray and Peter Schneider

Objective-Evaluate safety and efficacy of GORE® Carotid Stent in patients at increased risk for adverse events from carotid endarterectomy.

Primary endpoint-Death, stroke, or myocardial infarction through 30 days plus ipsilateral stroke between 31 days and 1 year.

200 patients entered so far

Courtesy: C. Schonholtz

Courtesy: C. Metzger
Mesh-Covered Stents

CGuard Prime EPS

Polyethylene Terephthalate (PET) 20µ wide fiber micronet on a nitinol stent
Attached to proximal and distal crowns of the stent

CARANET Study-30 patient trial
No stroke or death at 30 days
50% reduction in DW-MRI lesions
J Schoefer, LINC 2015

IRON-Guard Multicenter Italian Registry: 150 patients enrolled

InspireMD
Mesh Covered Stent Designs

<table>
<thead>
<tr>
<th>Design</th>
<th>Gore</th>
<th>Terumo Roadsaver</th>
<th>InspireMD CGuard™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aperture Size</td>
<td>500µ</td>
<td>300µ</td>
<td>180µ</td>
</tr>
<tr>
<td>Materials</td>
<td>PTFE mesh (Heparin coated) on nitinol stent</td>
<td>nitinol on nitinol</td>
<td>PET MicroNet™ on nitinol stent</td>
</tr>
<tr>
<td>CE Mark</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Mesh Covered Stents

**Conclusion**

Carotid lesions are the only application where an emboloegenic lesion has been treated with a non-covered stent.

Higher risk with open cell stents and occurrence of delayed events (>24h) suggest that non-covered stents are not adequate.

Mesh covered stents may provide better lesion containment with less potential for embolization through the stent.
Will Mesh-covered Stents Help Reduce the Risk of Stroke?

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