Embolic Protection Devices for Transcatheter Aortic Valve Replacement

James M. McCabe, MD
Medical Director, Cardiac Cath Lab
University of Washington
Seattle, WA
Disclosures

• Proctoring and honoraria for Edwards LifeSciences and Medtronic Valve Programs
Explanted Porcelain Aorta
Risk of Stroke TAVR vs SAVR

PARTNER 1 trial reported a nearly two-fold increase in the incidence of TIA and stroke associated with TAVR compared to standard surgical aortic valve replacement (SAVR)

---

**Table 2. Clinical Outcomes at 30 Days and 1 Year in the Intention-to-Treat Population.***

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Transcatheter Replacement (N= 348)</th>
<th>Surgical Replacement (N= 351)</th>
<th>P Value</th>
<th>Transcatheter Replacement (N= 348)</th>
<th>Surgical Replacement (N= 351)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>From any cause</td>
<td>12 (3.4)</td>
<td>22 (6.5)</td>
<td>0.07</td>
<td>84 (24.2)</td>
<td>89 (26.8)</td>
<td>0.44</td>
</tr>
<tr>
<td>From cardiac causes</td>
<td>11 (3.2)</td>
<td>10 (3.0)</td>
<td>0.90</td>
<td>47 (14.3)</td>
<td>40 (13.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>Repeat hospitalization</td>
<td>15 (4.4)</td>
<td>12 (3.7)</td>
<td>0.64</td>
<td>58 (18.2)</td>
<td>45 (15.5)</td>
<td>0.38</td>
</tr>
<tr>
<td><strong>Stroke or transient ischemic attack</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Either</td>
<td>19 (5.5)</td>
<td>8 (2.4)</td>
<td>0.04</td>
<td>27 (8.3)</td>
<td>13 (4.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>3 (0.9)</td>
<td>1 (0.3)</td>
<td>0.33</td>
<td>7 (2.3)</td>
<td>4 (1.5)</td>
<td>0.47</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>3 (0.9)</td>
<td>1 (0.3)</td>
<td>0.34</td>
<td>3 (0.9)</td>
<td>2 (0.7)</td>
<td>0.84</td>
</tr>
<tr>
<td>Major</td>
<td>13 (3.8)</td>
<td>7 (2.1)</td>
<td>0.20</td>
<td>17 (5.1)</td>
<td>8 (2.4)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Reported Stroke Rates following TAVR

- Partner 1: 6.00%
- CoreValve Pivotal Trial: 5.00%
- Eurolntervention Meta-analysis: 4.00%
- ADVANCE Registry: 3.00%
- Sentinel Registry: 2.00%
- TVT: 1.00%

* 1 year rates

References:
Percent of Patients with new ischemic lesion on DWI-MRI

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Source</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rodes-Cabau</td>
<td>2011</td>
<td>JACC 2011</td>
<td>60</td>
</tr>
<tr>
<td>Ghanem</td>
<td>2010</td>
<td>JACC 2010</td>
<td>30</td>
</tr>
<tr>
<td>Arnold</td>
<td>2010</td>
<td>JACC Int</td>
<td>25</td>
</tr>
<tr>
<td>Kahlert</td>
<td>2010</td>
<td>Circulation</td>
<td>32</td>
</tr>
<tr>
<td>Astarci</td>
<td>2011</td>
<td>EJCTS 2011</td>
<td>80</td>
</tr>
</tbody>
</table>

Daneault et al, JACC 2011;58: 2143-50
Clinically overt stroke increases 30 day mortality following TAVR by 350%
No significant change in cognitive function pre vs post TAVR.
Silent Brain Infarcts and the Risk of Dementia and Cognitive Decline

Sarah E. Vermeer, M.D., Ph.D., Niels D. Prins, M.D., Tom den Heijer, M.D., Albert Hofman, M.D., Ph.D., Peter J. Koudstaal, M.D., Ph.D., and Monique M.B. Breteler, M.D., Ph.D.

- 1015 patients 60-90 years old

- Neuropsychological testing and MRI at base line in 1995 to 1996 and again in 1999 to 2000

- Mean follow up 3.6 years

- Silent brain infarcts at base line more than doubled the risk of dementia (hazard ratio, 2.26; 95 percent confidence interval, 1.09 to 4.70).
Microinfarcts increase the risk of dementia by >200%

Smith et al., Lancet Neurol 2012
Highest Risk of Stroke in TAVR is Peri-procedural

Timing of Cerebrovascular Events (CVE) in FRANCE-2 Registry (n=3,191)

Tchétché et al. J Am Coll Cardiol Intv 2014; 7(10)
CerebroEmbolic Material Origins Following TAVR

Cerebral embolic debris captured in TAVI patients (n=81)

Any debris > Acute or organizing thrombus > Valve leaflet = Endothelium > Undetermined collagenous > Myocardium > Foreign material

Valvular Calcification

13% of Surgically removed Aortic valves demonstrate mature lamellar bone with hematopoietic elements and active bone remodeling

Embolic Protection Technology Concepts
Cerebral Embolic Protection Devices

<table>
<thead>
<tr>
<th>Claret Sentinel™ Cerebral Protection System</th>
<th>Edwards Embrella™ Embolic Deflector</th>
<th>TriGuard™ Cerebral Protection Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filter capture</td>
<td>Deflector</td>
<td>Deflector</td>
</tr>
<tr>
<td>6F (radial)</td>
<td>6F (radial)</td>
<td>9F (femoral)</td>
</tr>
<tr>
<td>140 micron pore size</td>
<td>100 micron pore size</td>
<td>130 x 250 micron pore size</td>
</tr>
<tr>
<td>Brachiocephalic and LCC</td>
<td>Aortic arch position</td>
<td>Aortic arch position</td>
</tr>
<tr>
<td>CE marked and commercialized</td>
<td>CE marked</td>
<td>CE marked</td>
</tr>
</tbody>
</table>
Aims: To compare the extent of cerebral ischemic injury after transcatheter aortic valve replacement (TAVR) with the use of an Embrella Embolic Deflector System versus unprotected TAVR.

Study Design:
• 15 pts w/ severe AS underwent TAVR with use of the Embrella Embolic Deflector System for cerebral protection.

• Cerebral diffusion-weighted magnetic resonance imaging (DWI) was performed on day 4 after the procedure
• Images were retrospectively compared to 37 patients who had undergone TAVR without protection.
Edwards Embrella™ Embolic Deflector
Embrella Trial

More new lesions in the Embrella group
Mean lesion volume per patient tended to be smaller
TriGuard Deflector
A prospective randomized evaluation of the TriGuard™ HDH embolic DEFLECTion device during transcatheter aortic valve implantation: results from the DEFLECT III trial

Study Design:

• Prospective, multi-center, single-blind, randomized controlled trial (2014-15)
• 85 pts (randomized 1:1) undergoing TAVI at 13 sites in Europe and
• neurologic and cognitive evaluation at baseline, pre-discharge and 30 days;
• Cerebral DW- MRI performed pre-TAVI, 2 days post-TAVI and at 30 days.
## TriGuard Safety Outcomes MACCE

<table>
<thead>
<tr>
<th>Endpoint or event</th>
<th>TriGuard (N = 46)</th>
<th>Control (N = 39)</th>
<th>Relative risk [95% CI]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hierarchical composite in-hospital MACCE</td>
<td>21.7%</td>
<td>30.8%</td>
<td>0.71 [0.34, 1.46]</td>
<td>0.34</td>
</tr>
<tr>
<td>All-cause death</td>
<td>2.2% (1)</td>
<td>5.1% (2)</td>
<td>0.42 [0.04, 4.50]</td>
<td>0.46</td>
</tr>
<tr>
<td>All stroke</td>
<td>2.2% (1)</td>
<td>5.1% (2)</td>
<td>0.42 [0.04, 4.5]</td>
<td>0.46</td>
</tr>
<tr>
<td>Life-threatening bleeding</td>
<td>2.2% (1)</td>
<td>5.1% (2)</td>
<td>0.42 [0.04, 4.5]</td>
<td>0.46</td>
</tr>
<tr>
<td>AKI (Stage 2/3)</td>
<td>2.2% (1)</td>
<td>0.0% (0)</td>
<td>2.55 [0.11, 60.9]</td>
<td>0.91</td>
</tr>
<tr>
<td>Major vascular complications</td>
<td>15.2% (7)</td>
<td>15.4% (6)</td>
<td>0.99 [0.36, 2.7]</td>
<td>0.85</td>
</tr>
</tbody>
</table>
TriGuard vs Non-protected Controls
Freedom From Ischemic Brain Lesions

A

Freedom from ischemic brain lesions

<table>
<thead>
<tr>
<th>Percent of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
</tr>
<tr>
<td>50</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>0</td>
</tr>
</tbody>
</table>

- Intention To Treat
  - TriGuard: 21.2
  - Control: 11.5
  - +46%

- Per Treatment
  - TriGuard: 26.9
  - Control: 11.5
  - +57%

B

Single and maximum lesion volumes

<table>
<thead>
<tr>
<th>Median Lesion Volume (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250</td>
</tr>
<tr>
<td>200</td>
</tr>
<tr>
<td>150</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>50</td>
</tr>
<tr>
<td>0</td>
</tr>
</tbody>
</table>

- SLV Intention to Treat
  - TriGuard: 30.9
  - Control: 34.8
  - -11%

- MLV Intention to Treat
  - TriGuard: 68.5
  - Control: 68.3
  - -14%

- SLV Per Treatment
  - TriGuard: 19.6
  - Control: 34.8
  - -44%

- MLV Per Treatment
  - TriGuard: 35.5
  - Control: 68.3
  - -48%
Neuro-cognitive outcomes TriGuard Vs Control
Claret Embolic Protection Device
Sentinel CPS - Dual filters

Proximal Filter
(Innominate Artery)
9.0 – 15.0 mm

Distal Filter
(Left Common Carotid Artery)
6.5 – 10.0 mm

CAUTION:
Investigational device.
Limited to investigational use by United States law.
Case:

- 77 yo male with past medical history known AS presents w/ worsening functional status, c/o severe DOE, NYHA III symptoms.

- Past medical History:
  - CAD, w/ prior NSTEMI
  - Afib
  - PVD
  - Severe COPD (FEV1 37%, DLCO 31% predicted)
  - Esophageal stricture
TTE

- Global reduced systolic function, LVEF 42%. No regional WMA
- Aortic Stenosis
  - Jet Velocity 3.4 m/s
  - Mean gradient 30 mmHg
  - Calculated AVA 0.7 cm²
  - Mild AR
- Mild MR
• The patient was felt to be high risk for surgical aortic valve replacement (STS 11.7%)
  – Approved to undergo percutaneous aortic valve implantation
  – Edwards Sapien S3 valve via the transfemoral approach.
3D reconstruction of the aorta and great vessels
CT - Aortic valve annulus

<table>
<thead>
<tr>
<th>Annulus by CT</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short Annulus Diameter</td>
<td>22mm</td>
</tr>
<tr>
<td>Long Annulus Diameter</td>
<td>25.7mm</td>
</tr>
<tr>
<td>Annular Area</td>
<td>457 mm²</td>
</tr>
<tr>
<td>% Oversizing</td>
<td>14% (26mm)</td>
</tr>
<tr>
<td>Planned Valve Size</td>
<td>26mm</td>
</tr>
</tbody>
</table>
CT – Aortic Root

<table>
<thead>
<tr>
<th>Aortic Root by CT</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus of Valsalva Diameter</td>
<td>32 mm (mean)</td>
</tr>
<tr>
<td>Sinotubular Junction Diameter</td>
<td>28 x 30 mm</td>
</tr>
<tr>
<td>Left Coronary Height</td>
<td>12.9 mm</td>
</tr>
<tr>
<td>Right Coronary Height</td>
<td>18.1 mm</td>
</tr>
<tr>
<td>LVOT Calcification</td>
<td>Mild</td>
</tr>
<tr>
<td>Mitral Annular Calcification</td>
<td>None</td>
</tr>
</tbody>
</table>

Site Comments: Adequate sinuses and coronary heights.
• Successful TAVR via a left transfemoral percutaneous approach with a 26mm Sapien S3 valve

- No clinically evident neurological sequela

Hemodynamics: Baseline

Left ventricular pressure: 135/29 mmHg
Aortic pressure: 119/65/84 mmHg
Right atrial pressure: 10 mmHg
PA pressure: 48/26/35 mmHg
Cardiac Output: 3.5 L/min
Mean aortic valve gradient: 37 mmHg
Aortic Valve Area: 0.46 cm^2

Hemodynamics: Post-Valve Insertion

Left ventricular pressure: 139/31 mmHg
Aortic pressure: 141/66/91 mmHg
Right atrial pressure: 12 mmHg
PA pressure: 58/28/42 mmHg
Cardiac Output: 3.8 L/min
Mean aortic valve gradient: 6 mmHg
Aortic Valve Area: >2 cm^2
This Patient’s Post-Procedure MRI

- Multiple punctate foci of restricted diffusion involving the bilateral frontal lobes, right parieto-occipital lobes and left occipital lobes.

- Triangular area of restricted diffusion within the left cerebellar hemisphere, measuring approx 11 x 5 mm

- Findings are compatible with acute ischemia of embolic etiology
Conclusions

• Rates of clinically significant stroke following TAVR have improved but remain highly mortal.
• Silent infarcts appear to be ubiquitous and may play a role in long-term disability.
• Embolic protection devices may help reduce the number and size of peri-procedural infarcts but require further study.
Thank you

Jamie McCabe
jmmccabe@uw.edu