TAVR vs. SAVR

- TAVR=Trans-vascular aortic valve replacement
- SAVR=Surgical aortic valve replacement
- Sapien=TAVR device manufactured by Edwards LifeSciences
- CoreValve/SURTAVI/EVOLUT= TAVR device manufactured by Medtronic
- Prospective Randomized Trials

TAVR History/Timeline

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Partner 1</th>
<th>Partner 2</th>
<th>FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>TAVR Concept</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>Percutaneous Valve Technologies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td>First TAVR Cribier</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>Edwards Acquires PVT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>Partner 1 and CoreValve High Risk/Inoperable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>Partner 2 and SURTAVI Intermediate Risk</td>
<td></td>
<td>High Risk/Inoperable</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>FDA Approval: High Risk/Inoperable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>FDA approval: Intermediate Risk</td>
<td></td>
<td>Intermediate Risk</td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td>FDA Approval: Low Risk</td>
<td></td>
<td>FDA approval:</td>
<td>Partner 3 and Evolute Trials</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1987-2019
TAVR History/Timeline

- **2007**: Partner 1 and CoreValve (High Risk / Inoperable)
- **2011**: Partner 2 and SURTAVI (Intermediate Risk)
- **2011**: FDA Approval: High Risk / Inoperable
- **2016**: FDA approval: Intermediate Risk
- **2019**: Partner 3 and Evolute Trials (Low Risk)

---

**TAVR vs. SAVR**

DEBATE: ALL PATIENTS WITH SEVERE AORTIC STENOSIS SHOULD NOW UNDERGO TAVR
TAVR vs. SAVR

DEBATE: **ALL** PATIENTS WITH SEVERE AORTIC STENOSIS SHOULD NOW UNDERGO TAVR

Partner 3: Inclusion/Exclusion Criteria

- **Inclusion criteria:**
  - Symptomatic high-gradient aortic stenosis
  - Suitable for transfemoral access
  - Society of Thoracic Surgeons (STS) risk of 30-day mortality: <4.0%

- **Exclusion criteria:**
  - Frailty
  - Bicuspid aortic valve
  - Anatomical features that increased the risk of complications
  - Left ventricular ejection fraction <50%
  - Myocardial infarction within the last month
  - Stroke or transient ischemic attack within the last 90 days
  - Severe aortic or mitral regurgitation
  - Moderate mitral stenosis
  - Pre-existing mechanical or bioprosthetic valve in any position
  - Complex coronary artery disease including unprotected left main disease
  - Symptomatic carotid or vertebral artery disease
  - Anemia/thrombocytopenia or high risk for bleeding
  - Severe lung disease or severe pulmonary artery hypertension
  - Body mass index >50 kg/m²

20% = All? 80%
TAVR vs. SAVR

DEBATE: **ALL** PATIENTS WITH SEVERE AORTIC STENOSIS SHOULD NOW UNDERGO TAVR

WHICH PATIENTS ARE CANDIDATES FOR SAVR?

Low Risk Trials:

- **Low Risk** = TAVR for “all comers”
- **Low Risk** = TAVR Risk Stratification is now obsolete
TAVR History/Timeline

2007
2011
2011
2016
2019

TAVR Valve Iteration

- Efficacy
- Mortality
- Stroke
- Para-valvular leak
- TAVR related Permanent Pacemaker
- Durability
TAVR vs. SAVR

- Efficacy
- Mortality
- Stroke
- Para-valvular leak
- TAVR related Permanent Pacemaker
- Durability
TAVR vs. SAVR

Efficacy

- Medtronic CoreValve to Evolute PRO
- EOA
- Mean Gradient

TAVR vs. SAVR

- Efficacy
- Mortality
- Stroke
- Para-valvular leak
- Permanent Pacemaker
- Durability
Patients at Extreme Surgical Risk

Foundational trials tested new TAVR therapy in patients without the option for a surgical aortic valve replacement

US CoreValve Pivotal Trial

CoreValve, N=489, STS 10.3%

PARTNER 1B

SAPIEN, N=179, STS 11.2%

PARTNER showed that by 3 years, TAVR had reduced mortality by approximately 30% compared to standard medical management.

Similar survival results were achieved with CoreValve in the US Pivotal Trial
Randomized trial data comparing TAVR to SAVR in lower-risk patients recently became available. Patients at Intermediate Surgical Risk

**SAPIEN XT and SAPIEN 3**
Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

**CoreValve**

Outcomes in the Randomized CoreValve US Pivotal High-risk Trial in Patients With a Society of Thoracic Surgeons Risk Score of 7% or Less

**Structural Heart Disease**

Two-Year Outcomes in Patients With Severe Aortic Valve Stenosis Randomized to Transcatheter Versus Surgical Aortic Valve Replacement

The PARTNER 2A Trial showed that TAVR with SAPIEN XT was non-inferior to surgery for the primary endpoint of all-cause mortality or disabling stroke at 2 years.

Intermediate Risk
PARTNER 2A | SAPIEN XT

The PARTNER 2A Trial showed that TAVR with SAPIEN XT was non-inferior to surgery for the primary endpoint of all-cause mortality or disabling stroke at 2 years.
**Partner 3 and Evolut -- Low Risk Trials:**

<table>
<thead>
<tr>
<th></th>
<th>Partner 3 (%/1 year)</th>
<th>Evolute (%/1 year/2 year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVR</td>
<td>TAVR</td>
<td>TAVR</td>
</tr>
<tr>
<td>Primary End Point**</td>
<td>8.5</td>
<td>15.1</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2</td>
<td>3.1</td>
</tr>
<tr>
<td>PVL</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>PPM</td>
<td>6.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>5.0</td>
<td>39.5</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>7.3</td>
<td>11.0</td>
</tr>
</tbody>
</table>

*Composite Primary Endpoint Partner: All-cause death, all stroke, and rehospitalization at 12 months.
Composite Primary Endpoint Evolute: All-cause mortality or disabling stroke at 24 months.
### Partner 3 and Evolut --
**Low Risk Trials:**

<table>
<thead>
<tr>
<th></th>
<th>Partner 3 (%/1 year)</th>
<th>Evolute (%/1 year/2 year)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR            SAVR</td>
<td>TAVR SAVR</td>
</tr>
<tr>
<td>Primary End Point**</td>
<td>8.5 15.1</td>
<td>2.9/5.3 4.6/6.7</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.0 2.5</td>
<td>4.5 4.5 p&gt;0.05</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2 3.1</td>
<td>1.1 3.5 p&lt;0.05</td>
</tr>
<tr>
<td>PVL</td>
<td>0.6 0.5</td>
<td>3.5 0.5 p&lt;0.05</td>
</tr>
<tr>
<td>PPM</td>
<td>6.5 4.0</td>
<td>17.4 6.1 p&lt;0.05</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>5.0 39.5</td>
<td>7.7 35.4 p&lt;0.05</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>7.3 11.0</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

*Composite Primary Endpoint Partner: All-cause death, all stroke, and rehospitalization at 12 months.
*Composite Primary Endpoint Evolut: All-cause mortality or disabling stroke at 24 months.
TAVR vs. SAVR

- Efficacy
- Mortality
- Stroke
- Para-valvular leak
- Permanent Pacemaker
- Durability
Stroke

PARTNER 1B -- High risk
TAVR vs Medical Therapy:

- Medically treated AS patients
  - Major Stroke: 1.1%
- TAVR treated AS patients:
  - Major Stroke 5.0%

TAVI, as compared with standard therapy, was associated with a higher incidence of major strokes (5.0% vs. 1.1%, P=0.06) and major vascular complications (16.2% vs. 10.8%).
Stroke Rates in Randomized Trials


Stroke rates with contemporary devices

Partner 3 and Evolut -- Low Risk Trials:

<table>
<thead>
<tr>
<th></th>
<th>Partner 3 (%)/1 year</th>
<th>Evolute (%)/1 year/2 year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR</td>
<td>SAVR</td>
</tr>
<tr>
<td>Primary End Point**</td>
<td>8.5</td>
<td>15.1</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2</td>
<td>3.1</td>
</tr>
<tr>
<td>PVL</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>PPM</td>
<td>6.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>5.0</td>
<td>39.5</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>7.3</td>
<td>11.0</td>
</tr>
</tbody>
</table>

*Composite Primary Endpoint Partner: All-cause death, all stroke, and rehospitalization at 12 months.

**Composite Primary Endpoint Evolut: All-cause mortality or disabling stroke at 24 months.

Silent Brain Embolization
Diffusion-weighted MRI of the brain examining silent injury with transcatheter aortic valve implantation (TAVI).

New Ischemic Lesions are Present in a Substantial Number of Patients Undergoing Cardiovascular Interventions with Diffusion weighted (DWI) MRI Estimates: 600,000 pts/year
Cerebral Protection Device Meta-Analysis

Safety and Efficacy of Cerebral Protection Devices in Transcatheter Aortic Valve Replacement: A Clinical End–Points Meta-Analysis

Abstract

Background: While after transcatheter aortic valve replacement (TAVR) occurs with an incidence of 0.1%-1%, a particularly devastating phenomenon associated with the procedure. Several cerebral protection devices (CPDs) have been developed to prevent cerebrovascular events during TAVR. While small studies have shown CPDs to be associated with reduced number and volume of lesions on diffusion-weighted magnetic resonance imaging, the clinical benefit of these devices remains uncertain.

Methods: We aimed to use meta-analytic techniques to study the clinical safety and efficacy of these CPDs in prospective randomized and non-randomized studies. Studies were selected as randomized, non-randomized trials and 95% confidence intervals (CI) were used for Hedges’ g statistic to evaluate heterogeneity.

Results: We found no evidence of difference between patients with and without CPD (RR 0.88 [95% CI 0.55-1.41] CI) for the primary composite or stroke and mortality, at 30 days. The two groups were also comparable in per-procedural stroke (RR 1.02 [95% CI 0.71-1.45]), stroke or death (RR 0.78 [95% CI 0.42-1.45]), and major vascular complications (RR 0.80 [95% CI 0.51-1.29]). There was no difference within the first week of death was significantly lower in the CPD group (RR 0.50 [95% CI 0.26-0.95]).

Conclusion: CPDs are associated with a decreased incidence of death within 1 week of follow-up when using any cerebral protection device during percutaneous transcatheter aortic valve replacement.

Keywords: Cerebral embolism, Safety, Efficacy, Stroke, TAVR.
Cerebral Protection Device Meta-Analysis

Safety and Efficacy of Cerebral Protection Devices in Transcatheter Aortic Valve Replacement: A Clinical End-Points Meta-Analysis


Abstract

Background: Stroke after transcatheter aortic valve replacement (TAVR) occurs with an incidence of 4% and is a particularly devastating adverse event associated with the procedure. Several embolic protection devices (EPDs) have been developed to prevent neurovascular events during TAVR. While small studies have shown EPDs to be associated with decreased number and volume of lesions on diffusion-weighted magnetic resonance imaging, the clinical benefit of these devices remains uncertain.

Methods: We reviewed 15 meta-analyses techniques to study the clinical safety and efficacy of these EPDs in prospective randomized and non-randomized studies. Outcome measures were neurological (National Institute of Health Stroke Scale [NIHSS] score) and 95% confidence intervals (CI). We used the Higgins I² statistic to evaluate heterogeneity.

Results: We found significant differences in NIHSS between patients with and without EPDs, with all EPD groups showing lower NIHSS compared to controls. The pooled weighted mean difference in NIHSS was 1.87 (95% CI: 0.85-2.89, p=0.0004). The difference in major adverse events was also significant, with EPD groups showing lower rates of stroke (p=0.0006) and death (p=0.004). The risk ratio of stroke in the control group was 2.69 (95% CI: 1.46-5.02, p=0.0008).

Conclusions: EPDs are associated with a decreased incidence of strokes after TAVR, without any evidence of increased risk of other per-procedural adverse events.

Keywords: Endovascular protection, Safety and efficacy. Stroke, TAVR.

Cerebral Embolic Protection During TAVR: A Clinical Event Meta-Analysis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Embolic Protection Events</th>
<th>No Embolic Protection Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLEAN-TAVI</td>
<td>4</td>
<td>50</td>
<td>54</td>
<td></td>
<td>1.77%</td>
<td></td>
</tr>
<tr>
<td>DEFLECT-III</td>
<td>2</td>
<td>46</td>
<td>48</td>
<td></td>
<td>1.54%</td>
<td></td>
</tr>
<tr>
<td>EMBOL-X</td>
<td>0</td>
<td>14</td>
<td>14</td>
<td></td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>MISTRAL-C</td>
<td>1</td>
<td>32</td>
<td>33</td>
<td></td>
<td>14.0%</td>
<td></td>
</tr>
<tr>
<td>SENTINEL</td>
<td>16</td>
<td>234</td>
<td>250</td>
<td></td>
<td>12.9%</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 376

Total events: 24

Heterogeneity: CH² = 11.2, df = 3 (P = 0.01), I² = 0%

Test overall effect: Z = 1.73 (P = 0.09)

"for every ~28 patients assigned to an EP device, 1 death or stroke event may be averted"
### Cerebral Protection Devices – Meta-analysis

#### Peri-procedural Stroke

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
<th>p Value</th>
<th>Test for Heterogeneity: df(dfQ)=2 p=0.35</th>
<th>Test for Overall effect: Z=1.78 p=0.075</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poolin-Calvert et al (2016)</td>
<td>0.86</td>
<td>0.44</td>
<td>1.72</td>
<td>0.144</td>
<td>0.144</td>
<td>0.144</td>
</tr>
<tr>
<td>Huang et al (2016)</td>
<td>1.00</td>
<td>0.91</td>
<td>1.08</td>
<td>0.55</td>
<td>0.55</td>
<td>0.55</td>
</tr>
<tr>
<td>Wise et al (2017)</td>
<td>0.83</td>
<td>0.51</td>
<td>1.39</td>
<td>0.59</td>
<td>0.59</td>
<td>0.59</td>
</tr>
<tr>
<td>Test for overall effect: Z=1.78 p=0.075</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Stroke at 7 days

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poolin-Calvert et al (2016)</td>
<td>0.86</td>
<td>0.44</td>
<td>1.72</td>
<td>0.144</td>
</tr>
<tr>
<td>Huang et al (2016)</td>
<td>1.00</td>
<td>0.91</td>
<td>1.08</td>
<td>0.55</td>
</tr>
<tr>
<td>Wise et al (2017)</td>
<td>0.83</td>
<td>0.51</td>
<td>1.39</td>
<td>0.59</td>
</tr>
<tr>
<td>Test for heterogeneity: df(dfQ)=4 p=0.68</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Stroke at 30 days

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poolin-Calvert et al (2016)</td>
<td>1.49</td>
<td>0.67</td>
<td>3.37</td>
<td>2.36</td>
</tr>
<tr>
<td>Lamarche et al (2015)</td>
<td>0.96</td>
<td>0.73</td>
<td>1.29</td>
<td>2.46</td>
</tr>
<tr>
<td>Venugopalan et al (2016)</td>
<td>0.29</td>
<td>0.10</td>
<td>0.83</td>
<td>2.05</td>
</tr>
<tr>
<td>Hsiao et al (2017)</td>
<td>1.00</td>
<td>0.90</td>
<td>1.14</td>
<td>5.13</td>
</tr>
<tr>
<td>Test for heterogeneity: df(dfQ)=4 p=0.74</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**Boston Scientific to Acquire TAVR Embolic Protection Company Claret Medical**

Addition of FDA-cleared Sentinel Cerebral Embolic Protection System will expand Boston’s structural heart offerings.

Claret’s FDA-cleared Sentinel Cerebral Embolic Protection System for TAVR will expand Boston Scientific’s structural heart portfolio. It collects emboli blocked from entering the brain and potentially cause a stroke.

July 20, 2018 — Boston Scientific Corp. today has signed an agreement to acquire Claret Medical Inc.
Boston Scientific to Acquire TAVR Embolic Protection Company Claret Medical

Addition of FDA-cleared Sentinel Cerebral Embolic Protection System will expand Boston’s structural heart offerings.

Claret’s FDA-cleared Sentinel Cerebral Embolic Protection System for TAVR will expand Boston Scientific’s structural heart portfolio. It collects emboli knocked loose that would otherwise lodge in the brain and potentially cause a stroke.

July 20, 2018 — Boston Scientific Corp. today has signed an agreement to acquire Claret Medical Inc.
“All patients” should receive cerebral protection when undergoing TAVI procedures

Data indicate that patients who undergo TAVI with the Sentinel Cerebral Protection System (Clastet Medical) have a significantly higher rate of stroke-free survival than do patients who undergo TAVI without the device. Furthermore, data also suggest Sentinel captures debris in 99% of patients; for this reason, Sanj Kapadia (Cleveland Clinic, Cleveland, USA) believes that the device should be used in all patients.

The risk of stroke after TAVI is an ongoing concern. While newer generation TAVI devices are associated with a lower risk of stroke than are first-generation devices, the risk of stroke after TAVI is still higher than it is after surgery (in non-transient high-risk patients). Kapadia observed that this risk is now a “still significant” 3.7% (major stroke 2.6%).

Kapadia and colleagues’ report in the Journal of the American College of Cardiology that stroke “remains a concerning complication”. They add that weighted MBI (DWI-MBI) two days after TAVI is of potential interest. The investigators, writing this arm didn’t undergo MBI to allow the investigators to “miss safety without increasing the cost of the trial.”

There were no significant differences in the primary safety endpoint—the rate of major adverse cardiac and cerebrovascular events (MACCE) at 30 days between the device groups and the control imaging group. The primary endpoint was reduction in new lesions volume in protected brain territories (via MBI) two to seven days after TAVI and there were no significant differences between the device-imaging arm and the control-imaging arm in randomized controlled trials, reviewing the Sentinel device (SINTENEL, CLEAN TAVI, and MISTRAL-C) provides a total of 638 patients undergoing TAVI with (165) or without the device (473) and central MRA-MBI before and after the procedure.

Associated with a significantly lower risk of stroke or death, corresponding to an approximate 46% absolute reduction of stroke (with a number needed to treat of 22). The authors conclude: “The totality of the data suggests that use of emboli protection during...”
Para-valvular leak (PVL)

- SAVR PVL rates as high as 11% have been reported (1,2).
- TAVR PVL rates as high as 85% (3).
- TAVR pooled estimate of residual moderate or severe PVL is 7.4% (3).

Moderate-to-severe PVL and increased mortality.
Decreased PVL

<table>
<thead>
<tr>
<th>Post Procedure</th>
<th>None</th>
<th>Trace</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>12</td>
<td>13</td>
<td>11</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Trace</td>
<td>34</td>
<td>17</td>
<td>11</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>3</td>
<td>10</td>
<td>14</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Rate (%) of >mild paravalvular leakage at 30 days
### Partner 3 and Evolut -- Low Risk Trials:

<table>
<thead>
<tr>
<th></th>
<th>Partner 3 (%/1 year)</th>
<th>Evolute (%/1 year/2 year)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR</td>
<td>SAVR</td>
</tr>
<tr>
<td>Primary End Point**</td>
<td>8.5</td>
<td>15.1</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2</td>
<td>3.1</td>
</tr>
<tr>
<td>PVL (&gt;moderate)</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>PPM</td>
<td>6.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>5.0</td>
<td>39.5</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>7.3</td>
<td>11.0</td>
</tr>
</tbody>
</table>

*Composite Primary Endpoint Partner: All-cause death, all stroke, and rehospitalization at 12 months.

*Composite Primary Endpoint Evolut: All-cause mortality or disabling stroke at 24 months.

Higher in both groups; significantly higher in the Evolut group.
Philippe Généreux et al. JACC 2013;61:1125-1136

American College of Cardiology Foundation

TAVR vs. SAVR

- Efficacy
- Mortality
- Stroke
- Para-valvular leak
- Permanent Pacemaker
- Durability
Predictors of Conduction Disturbances

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Anatomic</th>
<th>Procedure and Operator-Related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Gender</td>
<td>Variations in location of left bundle exit point</td>
<td>Radial force of the prosthesis</td>
</tr>
<tr>
<td>Age&gt;75 years</td>
<td>Septum thickness</td>
<td>Implant depth</td>
</tr>
<tr>
<td>Right bundle branch block (RBBB)</td>
<td>Thickness of the non-coronary cusp</td>
<td>Balloon aortic valvuloplasty</td>
</tr>
<tr>
<td>Other pre-existing conduction disturbance</td>
<td>Elevated left coronary cusp calcium</td>
<td>Learning curve</td>
</tr>
</tbody>
</table>

Predictors of Permanent Pacemaker Implantation in Patients With Severe Aortic Stenosis Undergoing TAVR: A Meta-Analysis

<table>
<thead>
<tr>
<th>Predictor</th>
<th>No. of studies</th>
<th>No. of patients</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AgeBD</td>
<td>1</td>
<td>1367</td>
<td>1.37 (0.90-2.08)</td>
<td>0.18</td>
</tr>
<tr>
<td>Sex female</td>
<td>11</td>
<td>887</td>
<td>1.09 (0.63-2.11)</td>
<td>0.75</td>
</tr>
<tr>
<td>Severe BD</td>
<td>11</td>
<td>1083</td>
<td>1.07 (0.63-2.02)</td>
<td>0.83</td>
</tr>
<tr>
<td>AES</td>
<td>10</td>
<td>1256</td>
<td>1.54 (1.00-2.36)</td>
<td>0.05</td>
</tr>
<tr>
<td>Left atrial strain</td>
<td>11</td>
<td>1083</td>
<td>2.29 (1.29-4.04)</td>
<td>0.001</td>
</tr>
<tr>
<td>Bilateral ASD</td>
<td>6</td>
<td>699</td>
<td>2.42 (1.41-4.11)</td>
<td>0.001</td>
</tr>
<tr>
<td>PAD</td>
<td>2</td>
<td>203</td>
<td>3.46 (1.24-9.66)</td>
<td>0.014</td>
</tr>
<tr>
<td>BMI</td>
<td>16</td>
<td>1289</td>
<td>1.09 (0.63-2.11)</td>
<td>0.75</td>
</tr>
<tr>
<td>MRS</td>
<td>17</td>
<td>1289</td>
<td>1.10 (0.63-2.27)</td>
<td>0.75</td>
</tr>
<tr>
<td>MFS</td>
<td>4</td>
<td>887</td>
<td>1.09 (0.63-2.11)</td>
<td>0.75</td>
</tr>
<tr>
<td>PPS</td>
<td>4</td>
<td>887</td>
<td>1.09 (0.63-2.11)</td>
<td>0.75</td>
</tr>
</tbody>
</table>
TAVR – Pacemaker Risk

Predictors of Permanent Pacemaker Implantation in Patients With Severe Aortic Stenosis Undergoing TAVR & PPM Analysis

Rate of PPM Implantation Post-TAVR

“True” PPM Rate of 4.9% in FYTD 18
## Partner 3 and Evolut -- Low Risk Trials:

<table>
<thead>
<tr>
<th></th>
<th>Partner 3 (%/1 year)</th>
<th>Evolute (%/1 year/2 year)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR</td>
<td>SAVR</td>
</tr>
<tr>
<td>Primary End Point**</td>
<td>8.5</td>
<td>15.1</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.0</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.05</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2</td>
<td>3.1</td>
</tr>
<tr>
<td></td>
<td>p=0.04</td>
<td></td>
</tr>
<tr>
<td>PVL</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>p=NS</td>
<td></td>
</tr>
<tr>
<td>TAVR related permanent pacemaker</td>
<td>6.5</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td>p=NS</td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>5.0</td>
<td>39.5</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>7.3</td>
<td>11.0</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

*Composite Primary Endpoint Partner: All-cause death, all stroke, and rehospitalization at 12 months.

*Composite Primary Endpoint Evolut: All-cause mortality or disabling stroke at 24 months.

---

### TAVR vs. SAVR

- Efficacy
- Mortality
- Stroke
- Para-valvular leak
- Permanent Pacemaker
- Durability
The Long Quest for the Holy Grail in Transcatheter Aortic Bioprosthesis
Durability and Long-Term Performance

Transcatheter aortic valve replacement (TAVR) is an established treatment option for patients with symptomatic severe aortic stenosis who are at intermediate to high/prohibitive surgical risk. TAVR is noninferior to surgical aortic valve replacement (SAVR) in terms of early and mid-term mortality and is likely to be superior if the transfemoral approach is used. In the real world, the outcome has already started for extending the use of TAVR to patients who are at low surgical risk. Several large randomized trials to examine the value of TAVR versus SAVR in younger patients without major comorbidities are ongoing. To date, the only published randomized trial in low-risk patients is Freedom from SVD:

JACC Journal of the American College of Cardiology

Central Illustration: Freedom From Structural Valve Deterioration Over Time. Kaplan-Meier Curve

Freedom from SVD:
The rate of SVD was higher for SAVR than TAVR (24.0% vs. 4.8%; p < 0.001)
Hemodynamic Performance

Long-Term Valve Performance of TAVR and SAVR
A Report From the PARTNER I Trial

METHODS The aim of this study was to evaluate the long-term performance of transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR) through longitudinal echocardiographic analysis.

RESULTS The long-term performance of the SAPIEN 3 valve is well described. Therefore, we examined the hemodynamic and clinical profile of the SAPIEN 3 valve over 5 years.

RESULTS For post-dilating TAVR, single, dual, and triple balloon dilatation (BD) were uniformly used. The majority of patients underwent single BD (93.6%) with mean gain in annulus/valve area of 0.48 cm²/10 years. In contrast, surgical valve and transvalvular mean pressure gradient (MPG) were higher in the BD group (p < 0.05). The TAVR group had higher aortic valve area and transvalvular mean pressure gradient (p < 0.05), respectively. No significant difference was seen in mean pressure gradient (p = 0.08). Interestingly, the BD group had higher aortic valve area and transvalvular mean pressure gradient (p < 0.05), respectively. No significant difference was seen in mean pressure gradient (p = 0.08). Interestingly, the BD group had higher aortic valve area and transvalvular mean pressure gradient (p < 0.05), respectively. No significant difference was seen in mean pressure gradient (p = 0.08). Interestingly, the BD group had higher aortic valve area and transvalvular mean pressure gradient (p < 0.05), respectively.

Durability

- SAVR
- Rigid ring
- Struts
- PPM
- TAVR
- Stent-like design
- Compliance
- No struts
- No PPM
Durability: TAVR vs. SAVR

TAVR vs. SAVR -- for Isolated Calcific AS

- Efficacy
- Mortality
- Stroke
- Para-valvular leak
- Permanent Pacemaker
- Durability
TAVR vs. SAVR

DEBATE: **ALL PATIENTS WITH SEVERE AORTIC STENOSIS SHOULD NOW UNDERGO TAVR**

**Partner 3: Inclusion/Exclusion Criteria**

- **Inclusion criteria:**
  - Symptomatic high-gradient aortic stenosis
  - Suitable for transfemoral access
  - Society of Thoracic Surgeons (STS) risk of 30-day mortality: <4.0%

- **Exclusion criteria:**
  - Frailty
  - Bicuspid aortic valve
  - Anatomical features that increased the risk of complications
  - Left ventricular ejection fraction <30%
  - Myocardial infarction within the last month
  - Stroke or transient ischemic attack within the last 90 days
  - Severe aortic or mitral regurgitation
  - Moderate mitral stenosis
  - Pre-existing mechanical or bioprosthetic valve in any position
  - Complex coronary artery disease including unprotected left main disease
  - Symptomatic carotid or vertebral artery disease
  - Anemia/thrombocytopenia or high risk for bleeding
  - Severe lung disease or severe pulmonary artery hypertension
  - Body mass index >50 kg/m²

**What are the indications for SAVR?**

- Moderate mitral stenosis
- Pre-existing mechanical or bioprosthetic valve in any position
- Complex coronary artery disease including unprotected left main disease
- Symptomatic carotid or vertebral artery disease
- Anemia/thrombocytopenia or high risk for bleeding
- Severe lung disease or severe pulmonary artery hypertension
- Body mass index >50 kg/m²
Who should be referred for TAVR?"
..."all comers"

- Isolated Severe Calcific AS
- Anatomically Straight Forward TAVR Access
- Life Expectancy > 1 year
- Contraindication for SAVR
- Patient Preference

Expansion of TAVR Indications:
Elimination of TAVR Risk Stratification

Who should be referred for SAVR?

- Contraindication for TAVR
- Failed TAVR
- Vascular Access
  - Guideline directed therapy: patients at low surgical risk (STS or EuroSCORE II <4% and no other risk factors not included in these scores, such as frailty, porcelain aorta, sequelae of chest radiation). **SAVR is recommended** (class I, LOE B).
  - Multi-valve disease
  - Aortic aneurysm
  - Severe CAD
  - Neurological Compromise

74
75