TAVR vs SAVR:
Is There Really Any Debate?

Jeffrey A Southard, MD, FACC
Aortic Stenosis

– Etiology

- Calcific degenerative
  - Degenerative process with proliferative & inflammatory changes, lipid accumulation, upregulation ACE, infiltration with macrophages & T lymphocytes. Bone formation (vascular calcification)

- Congenital - Bicuspid
  - Turbulent flow - traumatizes leaflet fibrosis, rigidity, calcification & narrowed orifice

- Rheumatic
  - Adhesion & fusion of commissures & cusps retraction & stiffening cusps borders.
  - Calcific nodules both surfaces - small round or triangular opening
According to the 2008 ACC/AHA guidelines, severe aortic stenosis is defined as:

- Aortic valve area (AVA) less than 1.0 cm²
- Mean gradient greater than 40 mmHg or jet velocity greater than 4.0 m/s
Natural History-Severe Aortic Stenosis

Sobering Perspective

5-Year Survival

<table>
<thead>
<tr>
<th>Survival, %</th>
<th>Breast Cancer</th>
<th>Lung Cancer</th>
<th>Colorectal Cancer</th>
<th>Prostate Cancer</th>
<th>Ovarian Cancer</th>
<th>Severe Inoperable AS*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>23</td>
<td>4</td>
<td>12</td>
<td>30</td>
<td>28</td>
<td>3</td>
</tr>
</tbody>
</table>

5 year survival of breast cancer, lung cancer, prostate cancer, ovarian cancer and severe inoperable aortic stenosis
Aortic Stenosis

• Symptomatic Aortic Stenosis - Surgical Aortic Valve Replacement is the standard of care

• Surgical Aortic Valve Replacement - Mortality Risk
  - Isolated AVR - 3.3 to 5.7%
  - AVR with CABG - 6.8 to 7.3%

• Percutaneous Aortic Valve Implantation in high risk aortic stenosis patients - feasible and safe
Operative Risk

- **Highest Risk Factors**
  - Shock
  - Emergency surgery
  - Age - especially > 80 years
  - Renal dysfunction - worse with dialysis
  - Left Ventricular dysfunction - LVEF < 30-35%
  - Previous Cardiac Surgery
  - CHF
  - Diabetes

Adapted from - Ambler G. et al. Circulation 2005;112(2):224-231
Many Patients Do Not Receive Surgery Due to Co-Morbidities

Reasons for Absence of Intervention in Symptomatic Patients (NYHA Class III / IV) Extra Cardiac Causes

<table>
<thead>
<tr>
<th>(%)</th>
<th>AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 Cause (%)</td>
<td>68</td>
</tr>
<tr>
<td>Age</td>
<td>35</td>
</tr>
<tr>
<td>Renal failure</td>
<td>10</td>
</tr>
<tr>
<td>COPD</td>
<td>21</td>
</tr>
<tr>
<td>Other EC</td>
<td>26</td>
</tr>
<tr>
<td>Short life expectancy</td>
<td>26</td>
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</tbody>
</table>

-This is why we need another option for patients

SEVERE AORTIC STENOSIS

AORTIC VALVE REPLACEMENT SURGERY

NON-SURGICAL REFUSALS
MEDICAL THERAPY
ASYMPTOMATIC
BALLOON AORTIC VALVULOPLASTY
Addressing a Serious Unmet Need

- Studies show at least 40% of SAS patients are not treated with an AVR\textsuperscript{9-15}
Definitive Results Through Rigorous Design

THE PARTNER TRIAL PROTOCOL

Severe Symptomatic Native Aortic Valve Stenosis

ASSESSMENT: OPERABILITY (N = 3,105)

Yes

ASSESSMENT: TRANSFEMORAL ACCESS

Cohort A High-Risk (n = 699)

2 Cohorts Individually Powered

Cohort B Inoperable (n = 358)

No

TF (n = 492)

1:1 Randomization

TF TAVR (n = 244)

VS

AVR (Control) (n = 248)

TA (n = 207)

1:1 Randomization

TA TAVR (n = 104)

VS

AVR (Control) (n = 103)

TF TAVR (n = 179)

1:1 Randomization

Standard Therapy (Control) (n = 179)

Not in Study

THE PARTNER TRIAL COHORT B
Absolute Reduction in Mortality Continues to Diverge at 2 Years

**ALL-CAUSE MORTALITY AT 1 YEAR AND 2 YEARS**

- **HR [95% CI]** = 0.56 [0.43, 0.73]
- **P (log rank)** < .0001

<table>
<thead>
<tr>
<th>Months</th>
<th>Edwards SAPIEN THV</th>
<th>Standard Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>6</td>
<td>68.0%</td>
<td>43.3%</td>
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<tr>
<td>12</td>
<td>50.7%</td>
<td>30.7%</td>
</tr>
<tr>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NNT** = 5.0 pts for Edwards SAPIEN THV
**NNT** = 4.0 pts for Standard Therapy

Numbers at Risk:
- Edwards SAPIEN THV: 179
- Standard Therapy: 179

**Δ at 1 yr = 20.0%**
**Δ at 2 yrs = 24.7%**
> 30% Absolute Reduction in Cardiovascular Mortality

**Cardiovascular Mortality at 1 Year and 2 Years**

HR [95% CI] = 0.44 [0.32, 0.60]

*P* (log rank) < .0001

- **At 1 Year**
  - Edwards SAPIEN THV: 44.6%
  - Standard Therapy: 20.5%
  - Δ at 1 yr = 24.1%
  - NNT = 4.1 pts

- **At 2 Years**
  - Edwards SAPIEN THV: 62.4%
  - Standard Therapy: 31.0%
  - Δ at 2 yrs = 31.4%
  - NNT = 3.2 pts

**Numbers at Risk**

<table>
<thead>
<tr>
<th></th>
<th>Edwards SAPIEN THV</th>
<th>Standard Therapy</th>
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</thead>
<tbody>
<tr>
<td>Months</td>
<td>0</td>
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<tr>
<td></td>
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<tr>
<td></td>
<td>110</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>83</td>
<td>42</td>
</tr>
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</table>
Reduced Mean Gradient

**Mean Gradient Over Time**

- **Baseline:**
  - Edwards: 44.2
  - Standard Therapy: 43.0

- **30 Days:**
  - Edwards: 33.0
  - Standard Therapy: 10.2

- **1 Year:**
  - Edwards: 44.4
  - Standard Therapy: 10.9

- **2 Years:**
  - Edwards: 41.9
  - Standard Therapy: 10.6

**Numbers Observed**

<table>
<thead>
<tr>
<th>Time</th>
<th>Edwards SAPIEN THV</th>
<th>Standard Therapy</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>162</td>
<td>172</td>
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<tr>
<td>30 Days</td>
<td>143</td>
<td>124</td>
</tr>
<tr>
<td>1 Year</td>
<td>89</td>
<td>54</td>
</tr>
<tr>
<td>2 Years</td>
<td>65</td>
<td>22</td>
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Error bars = ± 1 Std Dev
Increased Valve Area

AORTIC VALVE AREA OVER TIME

Error bars = ± 1 Std Dev

Numbers Observed

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<thead>
<tr>
<th></th>
<th>Edwards SAPIEN THV</th>
<th>Standard Therapy</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>158</td>
<td>166</td>
</tr>
<tr>
<td>30 Days</td>
<td>137</td>
<td>122</td>
</tr>
<tr>
<td>1 Year</td>
<td>84</td>
<td>53</td>
</tr>
<tr>
<td>2 Years</td>
<td>65</td>
<td>22</td>
</tr>
</tbody>
</table>
All-Cause Mortality
High Risk Patients

HR [95% CI] = 0.93 [0.71, 1.22]
P (log rank) = 0.62

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>Surgical AVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>348</td>
<td>351</td>
</tr>
<tr>
<td>18</td>
<td>298</td>
<td>252</td>
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<td>12</td>
<td>260</td>
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<tr>
<td>6</td>
<td>147</td>
<td>139</td>
</tr>
<tr>
<td>0</td>
<td>67</td>
<td>65</td>
</tr>
</tbody>
</table>
Next Generation Transfemoral TAVR Devices

- Direct Flow Medical - Percutaneous Aortic Valve
- Boston Scientific - Sadra Lotus™ Valve
- Symetis Acurate TF
- St. Jude Medical - Portico TAVI System
- Edwards - Sapien 3
- Edwards - Centera
Final Thoughts

• The greatest new technology since stents- without question

• We have as good of results with TAVR as surgery has with over 100 years of experience

• It will only get better- that I assure you!
Thanks