Structural Heart Disease and Transcatheter Aortic Valve Replacement—Update for 2020

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Disclosures

- Institutional Grant/Research Support—Philips Medical Systems
Outline

• Background
• Data Supporting Current Valve Technologies
• Current FDA Approved Indications
• Who should get surgical AVR?
• Challenges Going Forward with TAVR
Background

- Surgical Valve Replacement has been the gold standard for treatment of severe valve stenosis since the 1960’s
- In 2011, the STS database reported over 48,000 patients underwent surgical mitral and aortic valve replacement in the US
- Median mortality rates for isolated surgical valve replacement in the TAVR era in the STS database in 2016:
  - 2.2% for AVR
  - 4.4% for MVR
- Unfortunately, as our population ages, with more co-morbid conditions, the surgical risk is increasing!

US Population Projection by Age Group: US Census Bureau

Figures for projections from 2020 through 2060 are from Table 1: Jonathan Vespa, Lauren Medina, and David M. Armstrong P25-1144
Issued March 2018 Revised February 2020 Population Division, U.S. Census Bureau; Revised February 2020

From 2016-2060:
92% ↑ in >65 y/o
198% ↑ in >85 y/o
Valvular Heart Disease Increases with Age—Pooled Echo Data from ARIC/CARDIA/CHS

Nkomo VT et al. Lancet 2006, 368;1005-11
Aortic Stenosis

Degenerative Calciﬁed

Bicuspid

Rheumatic

Normal
Natural History of Aortic Stenosis

- **Latent Period**
- **Increasing obstruction, myocardial overload**
- **Symptoms**

- **Average Age Death**

Adapted from Ross and Braunwald, Circulation 1968;38:V-61
Echo Findings of Aortic Stenosis
Diagnostic Criteria for Severe Aortic Stenosis in the TAVR Era

• Echo based (transthoracic)
• Mean aortic gradient > 40 mmHg or
• Peak velocity > 4.0 m/sec
• and Valve area of <0.8 cm² (Indexed EOA of <0.5 cm²/m²)
• In setting of low-flow, low-gradient AS
  – dobutamine up to 40 mcg/kg/min can be given
Factors Associated with Increased Risk for Surgical Aortic Valve Replacement

**Clinical**
- Prior Sternotomy
- Female gender
- Renal dysfunction
- Diabetes
- Moderate to severe COPD
- Low EF
- NYHA Class IV
- Cerebrovascular disease
- Immunosuppression

**Anatomic**
- Porcelain aorta
- Prior radiation
- Bypass graft course under sternum
- Prior sternectomy

**Non-Traditional**
- Frailty
- High operative risk
  - Cirrhosis
  - Pulmonary Hypertension
Individualized Risk Calculation

Key Variables:

- Age
- Gender
- Renal Function
- Ejection Fraction
- CAD
- # of Prior Sternotomies
- Insulin use

http://riskcalc.sts.org/stswebriskcalc/#/calculate
Disruptive Technologies: The Tale of Transcatheter Valve Therapy

• “Disruptive Technology” was first described by Clayton M. Christensen in his 1997 Best-Seller, The Innovators Dilemma.

• An innovation that creates a new market (percutaneous valve therapies) and value network that will eventually disrupt an already existing market (open heart surgery) and replace an existing product (traditional surgical heart valves) and existing suppliers (CT surgeons)
TAVR: A Disruptive Technology
Percutaneous Implanted Heart Valve

1st animal implant 1989--The Andersen Valve

First In Human TAVR for AS:
The Cribier-Edwards Valve

Alain Cribier, MD, Rouen, France 2002

Antegrade transseptal approach
TAVR Valve Implant and Anatomical Considerations
TAVR Valve FDA Approval Dates

https://www.accessdata.fda.gov
Edwards – SAPIEN THV

Balloon Expandable Percutaneous Valve

Edwards-SAPIEN THV

- Two Valve Sizes:
  - 23 mm
  - 26 mm

Cribier-Edwards THV

- Two Sheath Sizes:
  - 22F (inner diameter)
  - 24F

Bovine Tissue ThermaFix Treatment Pericardial Mapping Leaflet Deflection Proprietary Processing

Untreated Equine Tissue

New Skirt Height

Current Skirt Height
PARTNER Study Design—

Symptomatic Severe Aortic Stenosis

ASSESSMENT: High-Risk AVR Candidate
3,105 Total Patients Screened

N = 699

High Risk

ASSESSMENT: Transfemoral Access

Yes

Transfemoral (TF)

N = 244

TF TAVR

1:1 Randomization

N = 244

VS

AVR

Primary Endpoint: All-Cause Mortality at 1 yr (Non-inferiority)

No

Transapical (TA)

N = 103

TA TAVR

1:1 Randomization

N = 104

VS

AVR

Cohort A

Total = 1,057 patients

2 Parallel Trials: Individually Powered

Inoperable

N = 358

ASSESSMENT: Transfemoral Access

Yes

Transfemoral (TF)

N = 179

TF TAVR

1:1 Randomization

N = 179

VS

AVR

Primary Endpoint: All-Cause Mortality Over Length of Trial (Superiority)
Co-Primary Endpoint: Composite of All-Cause Mortality and Repeat Hospitalization (Superiority)

No

Not In Study

Cohort B
### Baseline Characteristics—Inoperable Patients

<table>
<thead>
<tr>
<th></th>
<th>TAVR (N=179)</th>
<th>Control (N=179)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>83 ± 9</td>
<td>83 ± 8</td>
</tr>
<tr>
<td><strong>Female gender</strong></td>
<td>54.2%</td>
<td>54.1%</td>
</tr>
<tr>
<td><strong>STS Risk Score</strong></td>
<td>11.2 ± 5.8</td>
<td>12.2 ± 6.1</td>
</tr>
<tr>
<td><strong>STS &gt; 15%</strong></td>
<td>21.2%</td>
<td>24.7%</td>
</tr>
<tr>
<td><strong>Prior MI</strong></td>
<td>18.6%</td>
<td>26.4%</td>
</tr>
<tr>
<td><strong>Prior CABG</strong></td>
<td>37.4%</td>
<td>45.6%</td>
</tr>
<tr>
<td><strong>Cerebrovascular Dz</strong></td>
<td>27.4%</td>
<td>27.5%</td>
</tr>
<tr>
<td><strong>COPD (O2 dependent)</strong></td>
<td>21.2%</td>
<td>25.7%</td>
</tr>
<tr>
<td><strong>Creatinine &gt; 2.0 mg/dl</strong></td>
<td>5.6%</td>
<td>9.6%</td>
</tr>
<tr>
<td><strong>Frailty</strong></td>
<td>18.1%</td>
<td>28.0%</td>
</tr>
</tbody>
</table>

P=NS for all comparisons
PARTNER Cohort B-Inoperable
Primary Endpoint: All-Cause Mortality

The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela C. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators

<table>
<thead>
<tr>
<th></th>
<th>TAVI</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers at Risk</td>
<td>179</td>
<td>138</td>
<td>122</td>
<td>67</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Standard Rx</td>
<td>179</td>
<td>121</td>
<td>83</td>
<td>41</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

Δ at 1 yr = 20.0%
NNT = 5.0 pts
50.7%
HR [95% CI] = 0.54 [0.38, 0.78]
P (log rank) < 0.0001

Leon et al, NEJM 2010; 363:1597-1607
## Repeat Hospitalizations

### Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>Standard Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>179</td>
<td>179</td>
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<tr>
<td></td>
<td>115</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>89</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>64</td>
<td>17</td>
</tr>
</tbody>
</table>

### Repeat Hospitalization (%)

- **Standard Rx**
  - ∆ at 1 yr = 26.9%
  - NNT = 3.7 pts
  - ∆ at 2 yr = 37.5%
  - NNT = 2.7 pts

- **TAVR**
  - ∆ at 1 yr = 53.9%
  - ∆ at 2 yr = 72.5%

### HR [95% CI]

- 0.41 [0.30, 0.58]

**p (log rank) < 0.0001**
Quality of Life Assessment for TAVR:
Kansas City Cardiomyopathy Questionnaire

- Spertus J et al
  - Am Heart J 2005; 150:707-15

546 outpts with HF
KCCQ assessed at baseline and 5 weeks
Extent of deterioration or improvement assessed by physician based on sx and exam and correlated with KCCQ-Overall Summary

Clinically Important Change
- Small = 5 points
- Moderate = 10 points
- Large = 20 points
Primary Endpoint:
KCCQ Overall Summary

**MCID** = minimum clinically important difference

- **TAVR**
  - Δ = 13.9
  - P < 0.001

- **Control**
  - Δ = 20.7
  - P < 0.001

- Δ = 24.5
  - P < 0.001

**MCID** = 5 points
Prohibitive Risk—Approved 2011
Five Year Mortality:
Inoperable Arm of PARTNER

PARTNER Study Design—

Symptomatic Severe Aortic Stenosis

ASSESSMENT: High-Risk AVR Candidate
3,105 Total Patients Screened

Total = 1,057 patients
2 Parallel Trials: Individually Powered

N = 699
High Risk

ASSESSMENT: Transfemoral Access

Yes

Transfemoral (TF)
1:1 Randomization
N = 244
TF TAVR VS
No

Transapical (TA)
1:1 Randomization
N = 248
AVR

Primary Endpoint: All-Cause Mortality at 1 yr
(Non-inferiority)

Cohort A

N = 358
Inoperable

ASSESSMENT: Transfemoral Access

Yes

Transfemoral Access
1:1 Randomization
N = 179
TF TAVR VS

No
Not In Study

N = 179

Primary Endpoint: All-Cause Mortality Over Length of Trial (Superiority)
Co-Primary Endpoint: Composite of All-Cause Mortality and Repeat Hospitalization (Superiority)

Cohort B
High-Risk Operable PARTNER Cohort A
Primary Endpoint: All-Cause Mortality

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>AVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>348</td>
<td>351</td>
</tr>
<tr>
<td>6</td>
<td>298</td>
<td>252</td>
</tr>
<tr>
<td>12</td>
<td>260</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>147</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>67</td>
<td>65</td>
</tr>
</tbody>
</table>
New Technology: Medtronic CoreValve

Self-Expanding, Nitinol Scaffold, Porcine Pericardium
CoreValve US Pivitol Trial: Surgical AVR versus TAVR in High Risk Patients with Aortic Stenosis

As-Treated Population
N=750

Underwent Attempted TAVR
N=391

1-Year TAVR
N=323/328
(98.5%)

Died-28
Exited-3
Pending follow-up-2

2-Year TAVR
N=278/295
(94.2%)

Underwent Attempted SAVR
N=359

1-Year SAVR
N=265/281
(94.3%)

Died-31
Exited-13

2-Year SAVR
N=221/237
(93.2%)
CoreValve High Risk US Trial: Surgical AVR vs TAVR

TAVR in High Risk Patients—Approved 2012
Five Year Mortality:
PARTNER Study High Risk Cohort

Mack MJ et al *Lancet* 2015; 385: 2477–84
PARTNER 2 and SURTAVI

TF Primary Endpoint
All-cause Mortality or Disabling Stroke

HR: 0.79 [95% CI: 0.62, 1.00]
p (log rank) = 0.05

SURTAVI Trial

All-Cause Mortality or Disabling Stroke

<table>
<thead>
<tr>
<th>Months Post-Procedure</th>
<th>SAVR</th>
<th>TAVR</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>796</td>
<td>864</td>
</tr>
<tr>
<td>6</td>
<td>674</td>
<td>755</td>
</tr>
<tr>
<td>12</td>
<td>555</td>
<td>612</td>
</tr>
<tr>
<td>18</td>
<td>407</td>
<td>456</td>
</tr>
<tr>
<td>24</td>
<td>241</td>
<td>272</td>
</tr>
</tbody>
</table>

24 Months

- **SAVR**: 12.6%
- **TAVR**: 14.0%
PARTNER 2 and SURTAVI

Key Findings

Surgery better

Vascular complications
Paravalvular Leak

TAVR better

Mortality
Strokes
AKI
Severe bleeding
New onset AF
Valve area
30-day QOL
30-day 6MWT
ICU/hospital LOS
Days alive OOH
TAVR in Intermediate Risk Patients—Approved 2016
Five Year Outcomes of SAVR vs TAVR—PARTNER 2 Trial of Intermediate Risk

Hazard ratio, 1.09 (95% CI, 0.95–1.25)
P=0.21

Five Year Quality of Life—PARTNER 2
Trial of Intermediate Risk

Low Risk/TI ASSESSMENT by Heart Team (STS < 4%)

1:1 Randomization
1000 Patients

TAVR (SAPIEN 3 THV)

Surgery (Surgical Bioprosthetic Valve)

Follow-up: 30 day, 6 mos, and annually through 10 years

PRIMARY ENDPOINT:
Composite of all-cause mortality, stroke, or CV re-hospitalization at 1 year post-procedure
Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Demographics &amp; Vascular Disease</th>
<th>TAVR (N=496)</th>
<th>Surgery (N=454)</th>
<th>TAVR (N=496)</th>
<th>Surgery (N=454)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73.3 ± 5.8</td>
<td>73.6 ± 6.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>67.5%</td>
<td>71.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI – kg/m²</td>
<td>30.7 ± 5.5</td>
<td>30.3 ± 5.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STS Score</td>
<td>1.9 ± 0.7</td>
<td>1.9 ± 0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA Class III or IV*</td>
<td>31.3%</td>
<td>23.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary Disease</td>
<td>27.7%</td>
<td>28.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior CABG</td>
<td>3.0%</td>
<td>1.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior CVA</td>
<td>3.4%</td>
<td>5.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>6.9%</td>
<td>7.3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>31.3%</td>
<td>30.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD (any)</td>
<td>5.1%</td>
<td>6.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>4.6%</td>
<td>5.3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine &gt; 2mg/dL</td>
<td>0.2%</td>
<td>0.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frailty (overall; &gt; 2/4+)</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation (h/o)</td>
<td>15.7%</td>
<td>18.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Permanent Pacemaker</td>
<td>2.4%</td>
<td>2.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Bundle Branch Block</td>
<td>3.0%</td>
<td>3.3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Bundle Branch Block</td>
<td>10.3%</td>
<td>13.7%</td>
<td></td>
<td></td>
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</table>

*p = 0.01
# Procedural & Hospital Findings

% or mean ± SD

<table>
<thead>
<tr>
<th>Variable</th>
<th>TAVR (N=496)</th>
<th>Surgery (N=454)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Conscious Sedation</td>
<td>65.1%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Procedure Time (min)</td>
<td>58.6 ± 36.5</td>
<td>208.3 ± 62.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fluoroscopy Time (min)</td>
<td>13.9 ± 7.1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Aortic Cross-Clamp Time (min)</td>
<td>NA</td>
<td>74.3 ± 27.8</td>
<td>NA</td>
</tr>
<tr>
<td>Total CPB Time (min)</td>
<td>NA</td>
<td>97.7 ± 33.8</td>
<td>NA</td>
</tr>
<tr>
<td>Median ICU Stay (days)</td>
<td>2.0</td>
<td>3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median Total LOS (days)</td>
<td>3.0</td>
<td>7.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Discharge to Home/Self-care</td>
<td>96.0%</td>
<td>73.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Concomitant Procedures</td>
<td>7.9%</td>
<td>26.4%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Primary Endpoint
Death, Stroke or Rehospitalization

Number at risk:

<table>
<thead>
<tr>
<th>Months after Procedure</th>
<th>Surgery</th>
<th>TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>454</td>
<td>496</td>
</tr>
<tr>
<td>3</td>
<td>408</td>
<td>475</td>
</tr>
<tr>
<td>6</td>
<td>390</td>
<td>467</td>
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<td>9</td>
<td>381</td>
<td>462</td>
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<td>12</td>
<td>377</td>
<td>456</td>
</tr>
<tr>
<td></td>
<td>374</td>
<td>451</td>
</tr>
</tbody>
</table>

Death, Stroke, or Rehosp (%)
P_{non-inferiority} < 0.001

Upper 95% CI of risk diff = -2.5%

HR [95% CI] = 0.54 [0.37, 0.79]
P_{superiority} = 0.001

Death or Disabling Stroke

Number at risk:

- Surgery: 454, 444, 436, 432, 430, 426
- TAVR: 496, 494, 494, 493, 491, 488

HR [95% CI] = 0.34 [0.12, 0.97]

P = 0.03

In a population of severe symptomatic aortic stenosis patients who were at low surgical risk, TAVR (using the SAPIEN 3 valve) compared to surgery:

- Significantly reduced the primary endpoint of death, stroke, or rehospitalization by 46% at 1-year
- Reduced new-onset AF, hospitalization, bleeding and poor treatment outcome (death or low KCCQ score at 30 d)
- TAVR had more rapid improvement in iNYHA class, 6-minute walking distance, and KCCQ scores
- No differences in the need for new permanent pacemakers, major vascular complications, coronary obstruction, and moderate-severe paravalvular regurgitation
*Additional patients were randomized to permit completion of the LTI substudy and to enroll a Japanese cohort.

- **1468* Randomized Patients**
  - **TAVR ITT N=734**
    - 12 Not attempted
  - **TAVR AT* N=725**
  - **TAVR implanted N=722**
  - **SAVR ITT N=734**
    - 53 Not attempted
  - **SAVR AT* N=678**
    - 1 Not implanted
  - **SAVR implanted N=680**
    - 4 TAVR patients underwent SAVR and 1 SAVR patient underwent TAVR
K-M All-Cause Mortality or Disabling Stroke at 1 Year

Death or Disabling Stroke (%)

- **TAVR**
  - 30 Days: 2.5%
  - 1 Year: 4.6%

- **SAVR**
  - 30 Days: 0.7%
  - 1 Year: 2.7%

No. at risk:

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>725</td>
<td>678</td>
</tr>
<tr>
<td>1 Year</td>
<td>648</td>
<td>576</td>
</tr>
</tbody>
</table>

Log-rank P = 0.065


**Figure:** Life table showing the cumulative risk of death or disabling stroke in patients who underwent TAVR or SAVR. The graph displays the percentage of patients at risk over 12 months, with a clear distinction between the two treatment groups. The log-rank test indicates a statistically significant difference in mortality or disabling stroke between TAVR and SAVR at 1 year.
Clinical Implications

Death, Disabling Stroke and Heart Failure Hospitalizations to 1 Year

Estimated KM rates, %

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>SAVR</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>5.6%</td>
<td>10.2%</td>
<td>-4.5%</td>
</tr>
<tr>
<td>Disabling Stroke</td>
<td>0.7%</td>
<td>2.3%</td>
<td></td>
</tr>
<tr>
<td>HF Hospitalization</td>
<td>3.1%</td>
<td>6.4%</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

P = 0.002
Medtronic Low Risk Trial

**Take-Home**

- TAVR with a self-expanding valve was noninferior to surgery for the primary endpoint of death or disabling stroke at 1 year in patients with severe aortic stenosis at low surgical risk
- At 30 days, TAVR was better than SAVR:
  - shorter length of stay
  - better QOL
- At 30 days, SAVR was better than TAVR:
  - fewer pacemakers implanted
  - less residual AR
- At 1 year, both groups had excellent survival
  - TAVR showed fewer disabling strokes, heart failure rehospitalizations with superior hemodynamics manifest by lower gradients
PARTNER 3 and Medtronic
Low Risk Trials

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

ABSTRACT

BACKGROUND

TAVR in Low Risk Patients—Approved in 2019!
Pipeline of TAVR Trials across the spectrum of aortic stenosis

Investigational devices
- Edwards Sapien/Sapien XT/S3
- Medtronic CoreValve/Evolut R
- Boston Lotus
- Direct Flow Medical Direct Flow
- Abbott Vascular Portico
- Symetis Acurate Neo
- Any available TAVR system

24 TAVR RCTs

Capodanno D, Leon MB. EuroIntervention 2016
Surgical AVR Risk Categories

(risk is a continuum)

Operable AS patients

Low-Intermediate Risk

STS PROM <3%  3-8%  >8%

90%  10%

High Risk

Too Sick

Inoperable

Current FDA Approval
Current FDA Approval in 2020

TAVR is approved for patients with severe symptomatic aortic stenosis in the following cohorts:

• Evaluated by Heart Team (IC and at least one CT surgeon)
  – Inoperable or High risk (STS>8% or other high risk clinical features) for surgical AVR
  – Intermediate risk (STS of 4-8%)
  – Low Risk (STS of <4%)
  – Valve in Valve, including TAVR in TAVR in high risk patients
  – No FDA restriction on bicuspid aortic valve treatment
Current Screening Approach—An Imaging Intensive Technology

- **TTE**
  - Gradients, annulus
  - DSE for low gradient AS
- **TEE**
  - Less of a role in screening
- **Cardiac catheterization**
  - Coronaries, RHC, Ascending and Abdominal aortography and wire straightening
- **ETT for severe AS w/o sxs**
- **Cardiac CT**
  - Critical role in screening and procedural planning
  - Identify aortopathy
- **Peripheral CTA**
  - Evaluate route
Key Measurements of Aortic Root

Method #1: Annulus

LVOT
- Length: 2.846 cm
- Area: 6.592 cm²
  - Mean: 580.000
  - SD: 55.522
  - Sum: 243014.86
  - Min: 116.000
  - Max: 728.000
  - Length: 9.112 cm

STJ
- Ca- (Magenta)
  - Length: 2.721 cm
- Length: 2.850 cm

Method #2: Annulus

SOV
- Length: 3.528 cm

LCA Leaflet Length/Height
- Length: 1.367 cm
- Length: 1.580 cm

RCC Leaflet Length/Height
- Length: 1.823 cm
- Length: 1.434 cm

LCC Height
- Length: 2.274 cm

RCC Height
- Length: 2.291 cm

NCC Height
- Length: 2.382 cm

RCA Leaflet Length/Height
- Length: 1.882 cm

LCC Height

Area: 6593.29 cm²
  - Mean: 549.157
  - SD: 72.166
  - Sum: 21937160
  - Min: 167.000
  - Max: 728.000
  - Length: 9.127 cm

Method #1: Annulus

Method #2: Annulus

Area: 665.44 mm²
  - Min: 28.6 mm
  - Max: 30.0 mm
  - Perimeter: 91.8 mm
CT – Lower Extremity Angiography

RCIA 8.1 mm

REIA 7.3 mm

RCFA 7.4 mm

LCIA 7.3 mm

LEIA 7.1 mm

LCFA 7.4 mm

Aorta 16 mm
Optimal View based on Aortic Root

LAO 30 CAUD 5

Click to Play the Video for Visualization of Calcium Distributions
Aortic Stenosis
The “New” AHA/ACC Focused Update

2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease
A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Severe AS
Symptomatic

Low Surgical Risk Strata
Intermediate
High Prohibitive

TAVR
IA
SAVR or TAVR
IA
SAVR or TAVR
IIa
B
SAVR
IB
TAVR
IA
TAVR
IA
TAVR Procedural Approach
TAVR Procedural Approach
Outcome Monitoring—
Mandatory STS/ACC TVT National Registry

- Comprehensive prospective observational database (>400 data elements)—**Mandated by CMS/FDA!**
- FU includes 30-days, 1-year (incl. QOL measures)
- TVT compliance linked to reimbursement
Outcome Report Metrics – Risk Adjusted

- In hospital
  - Mortality & Adverse events
  - Procedure success
  - Acute kidney injury
- 30-Day and 1-Year outcomes
  - All cause mortality
  - Stroke
  - MI
  - Bleeding events
  - Valve performance
- Quality of Life (KCCQ)
Surgical and Transcatheter AVR Trends

Data from the TVT and STS Registries
The State of TAVR
Trends in U.S. from 2011 to 2019

TAVR Volume

Sites Performing TAVR

Indication Expansion

Outcomes

Access Site
Outcomes in Patients with Bicuspid Aortic Valve

Table 3. Procedural Outcomes and Postprocedure Valve Performance

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Bicuspid n=5412</th>
<th>Tricuspid n=165547</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device success, n (%)</td>
<td>5146 (96.0)</td>
<td>158959 (96.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Missing</td>
<td>51 (0.9)</td>
<td>1178 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Conversion to open heart surgery, n (%)</td>
<td>39 (0.7)</td>
<td>938 (0.6)</td>
<td>0.139</td>
</tr>
<tr>
<td>Missing</td>
<td>7 (0.1)</td>
<td>229 (0.1)</td>
<td></td>
</tr>
<tr>
<td>Need for second valve, n (%)</td>
<td>90 (1.7)</td>
<td>1967 (1.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Missing</td>
<td>10 (0.2)</td>
<td>212 (0.1)</td>
<td></td>
</tr>
</tbody>
</table>
Long Term Durability of TAVR Valves

TAVR Data from 2007 to 2011 were obtained from the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) registry.

Reoperation in Patients with Bioprosthetic and Mechanical Aortic Valve Aged 50-69 y/o

Retrospective analysis of 4253 patients undergoing AVR with mechanical or bioprosthetic surgical in New York State between 1997-2004

Propensity matched cohort of 2002 patients, followed through 2013

Chiang YP et al. *JAMA*. 2014;312(13):1323-1329
Paravalvular Leak—Achille’s Heel of TAVR
TAVR and Valve Leaflet Thrombosis using MDCT

Reduced leaflet motion was observed in all valve types including surgical bioprostheses

Makkar R et al. NEJM 2015
Observational Data: Subclinical Leaflet Thrombosis—SOLVE Registries

Frequency of Reduced Leaflet Motion

<table>
<thead>
<tr>
<th>TAVR Valves 101/752 pts (13%)</th>
<th>Surgical BPVs 5/138 (4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards XT/S3 63/453 (14%)</td>
<td>Magna 4/37 (11%)</td>
</tr>
<tr>
<td>Medtronic CoreValve/Evolut 9/145 (6%)</td>
<td>Perimount 1/39 (3%)</td>
</tr>
<tr>
<td>Boston Sci Lotus 12/83 (14%)</td>
<td>Trifecta 0/33</td>
</tr>
</tbody>
</table>

Follow Up Data Quality Submission Status

2014-2018 Q2
Proposed Decision Memo for Transcatheter Aortic Valve Replacement (TAVR) (CAG-00430R)

Revised National Coverage Decision and TAVR

Qualifications to begin a TAVR program for hospitals without TAVR experience:

The hospital program must have the following:

- a. ≥ 50 open heart surgeries in the previous year prior to TAVR program initiation, and;
- b. ≥ 20 aortic valve related procedures in the 2 years prior to TAVR program initiation, and;
- c. ≥ 2 physicians with cardiac surgery privileges, and;
- d. ≥ 1 physician with interventional cardiology privileges, and;
- e. ≥ 300 percutaneous coronary interventions (PCIs) per year.

Qualifications to begin a TAVR program for heart teams without TAVR experience:

The heart team must include:

- a. Cardiovascular surgeon with:
  - i. ≥ 100 career open heart surgeries of which ≥ 25 are aortic valve related; and,
- b. An interventional cardiologist with:
  - i. Professional experience of ≥ 100 career structural heart disease procedures; or, ≥ 30 left-sided structural procedures per year; and,
  - ii. Device-specific training as required by the manufacturer.

There are two sets of qualifications; the first set outlined below is for hospital programs and heart teams without previous TAVR experience and the second set is for those with TAVR experience.

Qualifications to begin a TAVR program for hospitals without TAVR experience:

The hospital program must have the following:

- a. ≥ 50 open heart surgeries in the previous year prior to TAVR program initiation, and;
- b. ≥ 20 aortic valve related procedures in the 2 years prior to TAVR program initiation, and;
- c. ≥ 2 physicians with cardiac surgery privileges, and;
- d. ≥ 1 physician with interventional cardiology privileges, and;
Volume-Outcome Relationship in TAVR

TAVR Quality Review for New NCD Guidelines and Shared Decision-Making Standards

• An external accreditation process is being formed by the ACC to help TAVR centers meet new NCD standards and undergo remediation if they under-perform on quality measures¹
  – Includes “alive-and-well” assessment using the results of the change in the KCCQ (Kansas City Cardiomyopathy Questionnaire) score, which includes physical function, symptom (frequency and severity), social function and quality of life measurements
  – Monitoring of low-volume centers for root-cause analysis of any complications or deaths
  – Remediation process for programs that are outliers in quality, giving centers a way to evaluate and address quality gaps

• Shared decision making tools for TAVR/SAVR have been developed, including:
  1. A Patient-Centered Outcomes Research Institute (PCORI) sponsored project directed out of the Duke Clinical Research Institute (DCRI) that features a web-based resource for patient education regarding TAVR and SAVR, plus a patient-specific assessment of the risks of TAVR and SAVR using quality measures from the STS/ACC TVT Registry²
  2. An ACC CardioSmart-sponsored initiative directed out of the University of Colorado that features two paper decision aids and web-based videos that address patients at moderate SAVR risk who are making a choice between TAVR and SAVR³, and patients considered inoperable making a choice between TAVR and medical management⁴
Challenges and Unanswered Questions

- What is the valve durability of current TAVR valves in younger, low risk patients?
- What is the optimal antiplatelet/anticoagulation regimen post TAVR?
- What patient populations should undergo surgery?
- How do we train the proceduralists of the future?
Who May Get Surgical AVR in 2020?

• Patients with bicuspid aortic valve and root/arch aneurysm
• Patients with concomitant complex CAD and AS
• Anatomic features best treated with SAVR
  – mitral valve disease
  – Low coronary heights/risk of coronary artery obstruction
• Patients concerned about valve durability
Bicuspid aortic valve (BAV) disease is the most common congenital cardiac disorder, being present in 1% to 2% of the general population.

Associated aortopathy is a common finding in patients with BAV disease, with thoracic aortic dilation noted in approximately 40% of patients in referral centers.

AATS consensus guidelines on bicuspid aortic valve–related aortopathy
### Recommendations for aortic repair in patients with bicuspid aortic valve aortopathy

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Class/LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repair of the ascending aorta/root is recommended when the aortic diameter is ≥55 mm in patients without risk factors.</td>
<td>I/B&lt;sup&gt;13,20,39-41&lt;/sup&gt;</td>
</tr>
<tr>
<td>Repair of the ascending aorta/root should be performed when the aortic diameter is ≥50 mm in patients with risk factors (i.e., root phenotype or predominant aortic insufficiency, uncontrolled hypertension, family history of aortic dissection/sudden death, or aortic growth &gt;3 mm/y).</td>
<td>IIa/B&lt;sup&gt;13,20,39-41&lt;/sup&gt;</td>
</tr>
<tr>
<td>Repair of the ascending aorta/root may be performed in patients with an aortic diameter of ≥50 mm when the patients are at low surgical risk and operated on by an experienced aortic team in a center with established surgical results.</td>
<td>IIb/C&lt;sup&gt;32,33&lt;/sup&gt;</td>
</tr>
<tr>
<td>Concomitant repair of the ascending aorta/root should be performed when the aortic diameter is ≥45 mm in patients undergoing cardiac surgery.</td>
<td>IIa/B&lt;sup&gt;13,19,39,42&lt;/sup&gt;</td>
</tr>
</tbody>
</table>


AATS consensus guidelines on bicuspid aortic valve–related aortopathy
Conclusions

• TAVR is currently FDA approved for treatment of inoperable, high risk and intermediate risk patients with symptomatic aortic stenosis
  – Including valve in valve and patients with bicuspid aortic valves
• TAVR has been demonstrated to be equivalent or superior to SAVR now in low surgical risk patients
  – Expect FDA approval soon
  – Disruptive technology with need for Heart Team approach for success
• Mitral valve repair/replacement timeline will be much longer than TAVR due to the complexity of the mitral valve
  – Transcatheter Mitral Valve Repair with MitraClip is only FDA approved for high surgical risk patients (STS>8%) with degenerative MR
Discussion/Questions

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