Transcatheter Valve Therapies in 2020: A Surgeon’s Perspective

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I Michael J. Reardon, M.D

Consultant:

Medtronic

Boston Scientific
Agenda

Understand the data
What are the knowledge gaps
Who should be considered for TAVR in 2020
Extreme Risk

FDA Approved
HIGH RISK

FDA Approved
Intermediate risk

FDA Approved

DONE
High and Intermediate risk

TAVR vs. AVR must show equivalent or better

- TAVR ties/wins
- TAVR wins
- TAVR wins
- Unknown
- TAVR wins

TAVR ties/wins
- Stroke
- Hemodynamics
- Atrial fibrillation
- Transfusions

Surgery wins
- PVL
- Pacers for SEV

High risk age 84
Intermediate risk
age 80/81

Patient acceptance
Low risk

PARTNER 3 Study Design

Symptomatic Severe Aortic Stenosis

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

1:1 Randomization 1000 Patients

TAVR (SAPIEN 3 TVR)

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

Study Design

Low Surgical Risk

Heart Team Evaluation

Screening Committee

Confirmed eligibility

1:1 Randomization

Stratified by site and need for revascularization

TAVR

SAVR

SAVR + CABG

LTI Sub-Study

TAVR only

TAVR + PCI

SAVR only

SAVR + CABG

LTI Sub-Study

Original Article

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


New York Transcatheter Valves

2019

PATIENT-FOCUSED EVIDENCE-BASED APPROACH
Primary Endpoints

- Non-hierarchical composite of all-cause mortality, all strokes, or CV re-hospitalization at 1 year
- Primary analysis was non-inferiority, followed by superiority
- Analysis cohort was the ‘as-treated’ (AT) population, defined as all randomized patients in whom the procedure was initiated.
- Multiple sensitivity analyses performed

Valves Used

- SAPIEN Valve Evolution
  - SAPIEN
  - SAPIEN XT
  - SAPIEN 3
- Valve Technology
- Sheet Compatibility
- Available Valve Sizes

Study Timeline and Valves Studied

- First Patient Randomized: Mar 28, 2016
- Last Patient Randomized: Nov 27, 2018
- CoreValve 23 mm
- CoreValve 26, 30 mm
- CoreValve 29 mm
- CoreValve 31 mm
- CoreValve 34 mm
- CoreValve 36 mm
- CoreValve 38 mm
- CoreValve 40 mm
- CoreValve 42 mm

Vascular access:
- 6F/8F transfemoral
- 0.9% subclavian
- 0% direct aortic

New York Transcatheter Valves
2019
PATIENT FOCUSED EVIDENCE-BASED APPROACH
### Baseline Patient Characteristics

#### Demographics & Vascular Disease

<table>
<thead>
<tr>
<th></th>
<th>TAVR (N=496)</th>
<th>Surgery (N=454)</th>
<th>Other Co-Morbidities</th>
<th>TAVR (N=496)</th>
<th>Surgery (N=454)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age</strong></td>
<td>73.3 ± 5.8</td>
<td>73.0 ± 5.1</td>
<td>Diabetes</td>
<td>31.3%</td>
<td>32.2%</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>87.5%</td>
<td>71.1%</td>
<td>COPD (any)</td>
<td>5.1%</td>
<td>6.2%</td>
</tr>
<tr>
<td><strong>BMI, Kg/m²</strong></td>
<td>30.7 ± 6.6</td>
<td>30.3 ± 5.1</td>
<td>Pulmonary Hypertension</td>
<td>4.6%</td>
<td>5.3%</td>
</tr>
<tr>
<td><strong>STS Score</strong></td>
<td>1.8 ± 0.7</td>
<td>1.8 ± 0.6</td>
<td>Creatinine &gt; 2mg/dL</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>NYHA Class III or IV</td>
<td>31.3%</td>
<td>23.8%</td>
<td>Atrial Fibrillation (hs)</td>
<td>15.7%</td>
<td>18.8%</td>
</tr>
<tr>
<td>Chronic Lung Disease</td>
<td>77.7%</td>
<td>28.0%</td>
<td>Permanent Pacer</td>
<td>2.4%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Prior Cavo</td>
<td>3.4%</td>
<td>5.1%</td>
<td>Left Bundle Branch Block</td>
<td>3.0%</td>
<td>3.3%</td>
</tr>
<tr>
<td>PTFE</td>
<td>6.9%</td>
<td>7.3%</td>
<td>Right Bundle Branch Block</td>
<td>10.3%</td>
<td>13.7%</td>
</tr>
</tbody>
</table>

* p = 0.01

### Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>TAVR (N=725)</th>
<th>SAVR (N=678)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>74.1 ± 5.8</td>
<td>73.6 ± 5.9</td>
</tr>
<tr>
<td><strong>Female sex</strong></td>
<td>36.0%</td>
<td>33.8%</td>
</tr>
<tr>
<td><strong>Body surface area, m²</strong></td>
<td>2.0 ± 0.2</td>
<td>2.0 ± 0.2</td>
</tr>
<tr>
<td><strong>STS PROM, %</strong></td>
<td>3.9 ± 0.7</td>
<td>3.4 ± 0.7</td>
</tr>
<tr>
<td>NYHA Class III or IV</td>
<td>25.1%</td>
<td>28.5%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>84.8%</td>
<td>82.6%</td>
</tr>
<tr>
<td>Chronic lung disease (COPD)</td>
<td>15.0%</td>
<td>18.0%</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>10.2%</td>
<td>11.8%</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>7.5%</td>
<td>8.3%</td>
</tr>
</tbody>
</table>

There are no significant differences between groups.
Primary Endpoint

Outcomes
**KM Curves**

1 Year All-cause Mortality

**All-Cause Mortality**

- Surgery: 1.1%
- TAVR: 2.5%

HR [95% CI] = 0.41 [0.14, 1.17]

P = 0.09

**K-M Rates of All-Cause Mortality at 1 Year**

- TAVR: 3.0%
- SAVR: 2.3%

Log-rank P = 0.412

Number at risk:
- Surgery: 454, 445, 438, 433, 431, 427
- TAVR: 496, 494, 493, 492, 488

No. at risk:
- TAVR: 725, 720, 651, 435
- SAVR: 678, 665, 583, 373
Embolic Protection Devices Were Not Allowed
KM Curves

Rehospitalization

Rehospitalization

K-M Heart Failure Hospitalization at 1 Year

Surgery
TAVR

HR [95% CI] = 0.65 [0.42, 1.00]
P = 0.046

6.5%
3.4%
11.0%
7.3%

Number at risk:
Surgery 454 416 399 389 385 382
TAVR 496 477 469 465 459 453

Months from Procedure

Heart Failure Hospitalization (%)

No. at risk
TAVR 725 712
SAVR 678 649

Log-rank P = 0.006
1 Year
6.4
3.1

Months

New York Transcatheter Valves 2019
Patient Focused Evidence-Based Approach
Death, Stroke, Hospitalization

**Primary Endpoint**

- Surgery
- TAVR

Upper 95% CI of risk diff = -2.5%

\[ \text{P}_{\text{non-inferiority}} < 0.001 \]

HR [95% CI] = 0.54 [0.37, 0.79]

\[ \text{P}_{\text{superiority}} = 0.001 \]

**Clinical Implications**

Death, Disabling Stroke and Heart Failure Hospitalizations to 1 Year

- **Composite Rates**
  - TAVR: 5.6%
  - SAVR: 10.2%
  - Difference = -4.5%
  - \( P = 0.002 \)

- **Estimated MA rates, %**
  - TAVR: 3.1%
  - SAVR: 6.4%

- **HF Hospitalization**: 2.3%
- **Disabling Stroke**: 0.7%
- **Death**: 3.0%
Conclusions

The PARTNER 3 Trial

Clinical Implications

- Based upon these findings, TAVR, through 1-year, should be considered the preferred therapy in low surgical risk aortic stenosis patients!
- PARTNER randomized trials over the past 12 years, clearly indicate that the relative value of TAVR compared with surgery is independent of surgical risk profiles.
- The choice of TAVR vs. surgery in aortic stenosis patients should be a shared-decision making process, respecting patient preferences, understanding knowledge gaps (esp. in younger patients), and considering clinical and anatomic factors.

TAVR may be a preferred strategy to surgery in patients with severe aortic stenosis at low risk of surgical mortality.

This applies to the population tested!
Know the trial data!
Low Risk

Primary Endpoint

- FDA Approved

 DONE
2017 Up Date

Rick A. Nishimura, MD, MACC, FAHA, Co-Chair, Catherine M. Otto, MD, FACC, FAHA, Co-Chair, Robert O. Bonow, MD, MACC, FAHA, Blase A. Carabello, MD, FACC, John P. Erwin III, MD, FACC, FAHA, Lee A. Fleisher, MD, FACC, FAHA, Hani Jneid, MD, FACC, FAHA, FSCA, Michael J. Mack, MD, FACC, Christopher J. McLeod, MBChB, PhD, FACC, FAHA, Patrick T. O’Gara, MD, MACC, FAHA, Vera H. Rigolin, MD, FACC, Thoralf M. Sundt III, MD, FACC, Annemarie Thompson, MD, 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease, Circulation. 2017;135:e1159–e1195.
The Aortic Valve “Universe” in the USA

Linked TVT and STS Data. From the STS/ACC TVT Steering Committee
Represents approx. 93% and 97% of SAVR and TAVR respectively

Presented By Joe Bavaria MD at EACTS 2019
### Other Secondary Endpoints

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAVR</strong> (N=496)</td>
<td><strong>Surgery</strong> (N=454)</td>
<td><strong>P-value</strong></td>
</tr>
<tr>
<td><strong>Bleeding - Life-threat/Major</strong></td>
<td>3.6% (18)</td>
<td>24.5% (111)</td>
</tr>
<tr>
<td><strong>Major Vascular Complications</strong></td>
<td>2.2% (11)</td>
<td>1.5% (7)</td>
</tr>
<tr>
<td><strong>AKI - stage 2 or 3</strong></td>
<td>0.4% (2)</td>
<td>1.8% (8)</td>
</tr>
<tr>
<td><strong>New PPM (incl baseline)</strong></td>
<td>6.5% (32)</td>
<td>4.0% (18)</td>
</tr>
<tr>
<td><strong>New LBBB</strong></td>
<td>22.0% (106)</td>
<td>8.0% (35)</td>
</tr>
<tr>
<td><strong>Coronary Obstruction</strong></td>
<td>0.2% (1)</td>
<td>0.7% (3)</td>
</tr>
<tr>
<td><strong>AV Re-intervention</strong></td>
<td>0% (0)</td>
<td>0% (0)</td>
</tr>
<tr>
<td><strong>Endocarditis</strong></td>
<td>0% (0)</td>
<td>0.2% (1)</td>
</tr>
<tr>
<td><strong>Asymp Valve Thrombosis</strong></td>
<td>0.2% (1)</td>
<td>0% (0)</td>
</tr>
</tbody>
</table>

Event rates are KM estimates (%) and p-values are based on Log-Rank test.
*Event rates are incidence rates and p-value is Fisher’s Exact test.

### Clinical Outcomes at 30 Days

<table>
<thead>
<tr>
<th>Outcome</th>
<th>TAVR (N=725)</th>
<th>SAVR (N=678)</th>
<th>(95% BCI for Difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>30-Day composite safety endpoint</strong></td>
<td>5.3</td>
<td>10.7</td>
<td>(-8.3, -2.6)</td>
</tr>
<tr>
<td><strong>All-cause mortality</strong></td>
<td>0.5</td>
<td>1.3</td>
<td>(-1.9, 0.2)</td>
</tr>
<tr>
<td><strong>Disabling stroke</strong></td>
<td>0.5</td>
<td>1.7</td>
<td>(-2.4, -0.2)</td>
</tr>
<tr>
<td><strong>Life-threatening or disabling bleeding</strong></td>
<td>2.4</td>
<td>7.5</td>
<td>(-7.5, -2.9)</td>
</tr>
<tr>
<td><strong>Acute kidney injury, stage 2-3</strong></td>
<td>0.9</td>
<td>2.8</td>
<td>(-3.4, -0.5)</td>
</tr>
<tr>
<td><strong>Major vascular complication</strong></td>
<td>3.8</td>
<td>3.2</td>
<td>(-1.4, 2.5)</td>
</tr>
<tr>
<td><strong>Atrial Fibrillation</strong></td>
<td>7.7</td>
<td>35.4</td>
<td>(-31.8, -23.6)</td>
</tr>
<tr>
<td><strong>Permanent pacemaker implant</strong></td>
<td><strong>17.4</strong></td>
<td><strong>6.1</strong></td>
<td><strong>(8.0, 14.7)</strong></td>
</tr>
<tr>
<td><strong>All-cause mortality or disabling stroke</strong></td>
<td>0.8</td>
<td>2.6</td>
<td>(-3.2, -0.5)</td>
</tr>
<tr>
<td><strong>All stroke</strong></td>
<td>3.4</td>
<td>3.4</td>
<td>(-1.9, 1.9)</td>
</tr>
<tr>
<td><strong>Aortic valve reintervention</strong></td>
<td>0.4</td>
<td>0.4</td>
<td>(-0.8, 0.7)</td>
</tr>
</tbody>
</table>

*Significantly favors TAVR, *Significantly favors SAVR

BCI = Bayesian credible interval
Site-level Variation and Predictors of PPI
Variability in 30-Day PPI Rate by Center

Remember the S curve and find a RAO projection

Presented by Dr. Gada at TCT 2019
Trial Differences

Hemodynamics
That is the data
What are the knowledge gaps?
Who was excluded?

Bicuspid Valves
Partner 3 Syntax > 32
Evolut Syntax > 22
### Baseline Cardiac Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>TAVR (N=725)</th>
<th>SAVR (N=678)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYNTAX Score</td>
<td>1.9 ± 3.7</td>
<td>2.1 ± 3.9</td>
</tr>
<tr>
<td>Permanent pacemaker, CRT or ICD</td>
<td>3.2</td>
<td>3.8</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>2.5</td>
<td>2.1</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>14.2</td>
<td>12.8</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>6.6</td>
<td>4.9</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>15.4</td>
<td>14.5</td>
</tr>
<tr>
<td>Aortic valve gradient, mm Hg</td>
<td>47.0 ± 12.1</td>
<td>46.6 ± 12.2</td>
</tr>
<tr>
<td>Aortic Valve area, cm²</td>
<td>0.8 ± 0.2</td>
<td>0.8 ± 0.2</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>61.7 ± 7.9</td>
<td>61.9 ± 7.7</td>
</tr>
</tbody>
</table>

No significant differences between groups.
Who was excluded after local heart team approval?
520/1,520 (34%) screen failed

255/1,723 (14.8%) screen failed
Age?
Mean age
Sex
STS PROM

7% were < 65 years
6% were < 65 years
1.3% were < 60 years
Safety is the key difference in outcomes in both trials with most of the benefit in the first month.
Causes of Death
Risk of death lower in low-risk patients

Presented by Dr. Ramlawi at AATS 2019
Causes of Death
Hierarchical Causes of Death – Low Risk

Presented by Dr. Ramlawi at AATS 2019
Bicuspid Valves

Prevalence of Bicuspid Valve Disease in US SAVR Patients by Age (n = 1,725) ²

- 21 - 50: Unicuspid 44, 39%, Bicuspid 638, 51%, Tricuspid 55, 4%
- 51 - 79: Unicuspid 546, 44%, Bicuspid 269, 78%, Tricuspid 14, 82%
- ≥ 80: Unicuspid 9, 8%, Bicuspid 38, 18%, Tricuspid 20, 11%

Prevalence of Bicuspid Valve Disease in TAVR Patients by Country³

- Poland (n = 417): 6.7%
- France (n = 417): 6.6%
- Italy (n = 468): 4.5%
- Germany (n = 1,395): 2.7%
- USA (n = 7,710): 1.6%

1 Ward. Heart, 2000;
2 Roberts. AJC, 2012;
4 Wang, J of Heart Valve Disease, 2017;
Data from STS/ACC TVT Registry. 92,236 patients treated with the third-generation balloon-expandable Sapien 3 from 2015-2018
## Procedural Outcomes

<table>
<thead>
<tr>
<th>KM estimate %</th>
<th>Bicuspid</th>
<th>Tricuspid AS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>2.6</td>
<td>2.5</td>
<td>0.82</td>
</tr>
<tr>
<td><strong>All stroke</strong></td>
<td>2.4</td>
<td>1.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Life-threatening bleeding</td>
<td>0.1</td>
<td>0.1</td>
<td>0.99</td>
</tr>
<tr>
<td>Major vascular complication</td>
<td>0.9</td>
<td>1.0</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>New pacemaker</strong></td>
<td><strong>9.1</strong></td>
<td><strong>7.5</strong></td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td>Aortic valve reintervention</td>
<td>0.2</td>
<td>0.3</td>
<td>0.79</td>
</tr>
</tbody>
</table>
### 30-day Outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bicuspid AS (n=2691)</th>
<th>Tricuspid AS (n=2691)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device success</td>
<td>96.5</td>
<td>96.6</td>
<td>0.87</td>
</tr>
<tr>
<td>Procedure Time, min</td>
<td>100.7 ± 51.80</td>
<td>96.2 ± 52.09</td>
<td>0.08</td>
</tr>
<tr>
<td>Fluoroscopy Time, min</td>
<td>18.5 ± 10.96</td>
<td>17.1 ± 10.17</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Conversion to open surgery</td>
<td>0.9</td>
<td>0.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Annulus Rupture</td>
<td>0.3</td>
<td>0.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Cardiopulmonary bypass</td>
<td>1.4</td>
<td>1.0</td>
<td>0.13</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>0.3</td>
<td>0.1</td>
<td>0.34</td>
</tr>
<tr>
<td>Coronary Obstruction</td>
<td>0.4</td>
<td>0.3</td>
<td>0.34</td>
</tr>
<tr>
<td>Need for a second valve</td>
<td>0.4</td>
<td>0.2</td>
<td>0.16</td>
</tr>
</tbody>
</table>

1-Year mortality

1-Year stroke

Paravalvular Leak

Hemodynamics
Patient Prosthesis Mismatch

**SEVERITY OF PPM**
DEFINITION IN THE AORTIC VALVE POSITION

<table>
<thead>
<tr>
<th>Severe</th>
<th>Moderate</th>
<th>Green</th>
</tr>
</thead>
</table>

Indexed EOA (cm\(^2\)/m\(^2\))

<table>
<thead>
<tr>
<th>Severe</th>
<th>Moderate</th>
<th>Green</th>
</tr>
</thead>
</table>

EOA\(_i\) in obese (cm\(^2\)/m\(^2\))

<table>
<thead>
<tr>
<th>Severe</th>
<th>Moderate</th>
<th>Green</th>
</tr>
</thead>
</table>

CoreValve High Risk Trial

Prosthesis-Patient Mismatch

Severe PPM at 1 year

- Severe PPM occurs significantly more after SAVR than TAVR
  - At 1 month rates are 7.0% for TAVR and 20.7% for SAVR (P<0.001)
- Moderate PPM occurred in 20.8% of TAVR and 30.6% of SAVR patients at 1 year

N=53

P<0.0001

N=17

TAVR

SAVR
Prosthesis–patient mismatch in high-risk patients with severe aortic stenosis: A randomized trial of a self-expanding prosthesis

George L. Zorn III, MD,1 Stephen H. Little, MD,2 Peter Tadros, MD,3 G. Michael Deeb, MD,1 Thomas G. Gleason, MD,1 John Heiser, MD,1 Neil S. Kleiman, MD,1 Jae K. Oh, MD,1 Jeffrey J. Popma, MD,2 David Adams, MD,2 Jian Huang, MD, and Michael J. Reardon, MD

ABSTRACT

Objectives: We compared the incidence of prosthesis–patient mismatch (PPM) between transcatheter aortic valve replacement (TAVR) using a self-expanding bioprosthesis and surgical aortic valve replacement (SAVR) in the CoreValve US High Risk Pivotal Trial. We sought to determine the influence of PPM on clinical outcomes.

Methods: Patients with severe aortic stenosis and at increased risk for surgery were randomized 1:1 to TAVR or SAVR. Postoperative PPM was defined by the effective orifice area index (EOA) as severe PPM (EOA ≤ 0.65 cm²/m²) and no severe PPM (EOA > 0.65 cm²/m²); clinical outcomes were analyzed in the TAVR arm (n = 380) and SAVR arm (n = 353). Left ventricular mass index and regression were analyzed at baseline and 1 year.

Results: The incidence of severe PPM in the SAVR group at 1 year was 25.7% versus 6.2% in the TAVR group (P < .0001). Left ventricular mass index regression at 1 year was 6.8% for TAVR and 15.1% for SAVR in patients with severe PPM. At 1 year the rate of all-cause mortality and acute kidney injury were significantly greater in all patients (TAVR + SAVR) with severe PPM compared with no severe PPM (23.6% vs 12.0% [P = .0145] for death and 19.2% vs 8.5% [P = .0008] for acute kidney injury).

Central Message

Patients with severe PPM are at greater risk for death and acute kidney injury than patients without severe PPM.

Perspective

Prosthesis–patient mismatch (PPM) is significantly more common after surgical aortic valve replacement than after transcatheter aortic valve replacement in patients at high risk with symptomatic severe aortic stenosis. Patients with severe PPM are at a greater risk for death and acute kidney injury than patients without severe PPM.

CoreValve High Risk

30-Day PPM by Annular Size for TAVR and SAVR

Percent of Patients

Any PPM, P=0.39
Severe PPM, P=0.62

Any PPM, P=0.01
Severe PPM, P=0.08

TAVR

Large (n=102)
22.5
2.9
14.5
Large (n=77)
24.7
14.3

Medium (n=152)
7.9
22.2
32.4

Small (n=90)
7.8

SAVR

Large (n=139)
30.0

Medium (n=60)
36.7

Severe
Moderate

Moderate + Severe = Any PPM

Any PPM defined as EOA ≤ 0.85cm²
Severe PPM defined as EOA ≤ 0.65cm²

New York Transcatheter Valves 2019
Patient Focused Evidence-Based Approach
Low Risk

Hemodynamics
30-day PPM by Annular Size

Presented by Dr. Mumtaz at TVT 2019

<table>
<thead>
<tr>
<th>Annular Size</th>
<th>Moderate PPM</th>
<th>Severe PPM</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large</td>
<td>7.4</td>
<td>1</td>
<td>0.070</td>
</tr>
<tr>
<td>Medium</td>
<td>13.3</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>6.8</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Large</td>
<td>12.8</td>
<td>2.5</td>
<td>0.031</td>
</tr>
<tr>
<td>Medium SAVR</td>
<td>16</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>20.4</td>
<td>10.2</td>
<td></td>
</tr>
</tbody>
</table>

P=0.031

TAVR
SAVR
Herrmann HC, Daneshvar SA, Fonarow GC, Stebbins A, ID, Malenka DJ, Thourani VH, Rymer sis-
patients Undergoing Valve Replacement: From the J Am Coll Cardiol. 2018 Dec
Pibarot P, Clavel MA., Prosthesis-Patient Mismatch After Transcatheter Aortic Valve Replacement: It Is Neither Rare Nor Benign., J Am Coll Cardiol. 2018 Dec 4;72(22):2712-2716.
Evolut Low Risk PPM

**Prosthesis-Patient Mismatch**

<table>
<thead>
<tr>
<th></th>
<th>1 Month</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAVR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N = 609</td>
<td>1.1</td>
<td>1.8</td>
</tr>
<tr>
<td><strong>SAVR</strong></td>
<td>9.9</td>
<td>5.0</td>
</tr>
<tr>
<td>N = 541</td>
<td>15.5</td>
<td>15.7</td>
</tr>
<tr>
<td><strong>TAVR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N = 341</td>
<td>4.4</td>
<td></td>
</tr>
<tr>
<td><strong>SAVR</strong></td>
<td>15.5</td>
<td></td>
</tr>
<tr>
<td>N = 293</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P < 0.001

Implant population. Core lab assessments.
Background. The goal of this study was to determine the relationship of prosthesis-patient mismatch (PPM) with long-term survival and to assess whether growing concern about PPM has resulted in a decreased incidence over time.

Methods. Using The Society of Thoracic Surgeons Adult Cardiac Surgery Database, we identified 59,779 patients ≥65 years old who underwent isolated surgical aortic valve replacement (AVR) between 2004 and 2014. The degree of PPM was calculated using literature-derived effective orifice areas for commonly used valves. Outcomes to 10 years were stratified by degree of PPM.

Results. The distribution of PPM was as follows: 35%, none (n = 21,053); 54%, moderate (n = 32,243); and 11%, severe (n = 6,483). Compared with patients with no PPM, patients with moderate or severe PPM had a significantly increased risk of readmission for heart failure (hazard ratio [HR], 1.15; 95% confidence interval [CI], 1.09 to 1.21; HR, 1.37; 95% CI, 1.26 to 1.48) and redo AVR (HR, 1.41; 95% CI, 1.13 to 1.77; HR, 2.68; 95% CI, 2.01 to 3.56) for moderate or severe PPM, respectively. Survival was significantly worse for any degree of PPM (moderate to none: HR, 1.08; 95% CI, 1.05 to 1.12; severe to none: HR, 1.32; 95% CI, 1.25 to 1.39), with 10-year adjusted survival rates of 46%, 43%, and 35% for none, moderate, and severe, respectively (p < 0.001). The incidence of severe PPM decreased by 55% over the study period, from 13.8% in 2004 to 6.2% in 2014.

Conclusions. Any degree of PPM significantly decreased long-term survival and increased readmission rates for both heart failure and reoperation for AVR. Temporal trends show a significant decrease in the incidence of PPM over the past decade.


Sapien 3 mean EOA 1.66
Evolut mean EOA 2.01

all CoreValve valve sizes, the mean EOA = 1.88 ± 0.56 cm² with mean gradient of 8.85 ± 4.14 mm Hg. For all Evolut R valve sizes, the mean EOA = 2.01 ± 0.65 cm² with mean gradient of 7.52 ± 3.19 mm Hg. The SAPIEN 3 post-implant EOA was progressively larger for each quintile of baseline annular area by computed tomography (p < 0.001). Similarly, for the Evolut R valve, post-implantation EOA was significantly larger for each quintile of baseline annular perimeter (p < 0.001).

### TABLE 2 Mean Gradient and EOA for Balloon-Expandable SAPIEN Valves

<table>
<thead>
<tr>
<th>Valve Iteration</th>
<th>20</th>
<th>23</th>
<th>26</th>
<th>29</th>
<th>All Sizes</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic Valve Size, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAPIEN 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EOA, cm(^2)</td>
<td>1.22 ± 0.22 (47)</td>
<td>1.45 ± 0.26 (471)</td>
<td>1.74 ± 0.35 (626)</td>
<td>1.89 ± 0.37 (326)</td>
<td>1.66 ± 0.38 (1,470)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean gradient, mm Hg</td>
<td>16.23 ± 5.01 (47)</td>
<td>12.79 ± 4.65 (471)</td>
<td>10.59 ± 3.88 (626)</td>
<td>9.28 ± 3.16 (326)</td>
<td>11.18 ± 4.35 (1,470)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DVI</td>
<td>0.42 ± 0.07 (47)</td>
<td>0.43 ± 0.08 (471)</td>
<td>0.43 ± 0.09 (626)</td>
<td>0.40 ± 0.09 (326)</td>
<td>0.43 ± 0.09 (1,470)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n). This table shows the mean gradients and EOA for each balloon-expandable valve iteration by valve size implanted. All mean valve areas and EOAs were significantly different for each valve size for a given valve type (range p < 0.03 to p < 0.0001). DVI = Doppler velocity index; EOA = effective orifice area; NA = not available.
Table 5: Normal Reference Values for the CoreValve and Evolut R Valves by Native Annular Diameter Quintiles at 30 Days

<table>
<thead>
<tr>
<th>Quintiles</th>
<th>≤22.3 mm</th>
<th>&gt;22.3 to ≤23.2 mm</th>
<th>&gt;23.2 to ≤24.7 mm</th>
<th>&gt;24.7 to ≤26.2 mm</th>
<th>&gt;26.2 to ≤30.2 mm</th>
<th>p Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evolut R</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EOA, cm²</td>
<td>1.66 ± 0.42 (53)</td>
<td>1.82 ± 0.43 (38)</td>
<td>1.98 ± 0.56 (62)</td>
<td>1.98 ± 0.59 (49)</td>
<td>2.56 ± 0.77 (53)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>EOA/m²</td>
<td>0.99 ± 0.27 (53)</td>
<td>1.09 ± 0.26 (38)</td>
<td>1.10 ± 0.32 (62)</td>
<td>1.06 ± 0.34 (49)</td>
<td>1.29 ± 0.37 (53)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mean gradient, mm Hg</td>
<td>7.94 ± 3.10 (58)</td>
<td>6.91 ± 2.58 (43)</td>
<td>7.66 ± 2.94 (63)</td>
<td>8.53 ± 3.49 (56)</td>
<td>6.40 ± 3.34 (57)</td>
<td>0.21</td>
</tr>
<tr>
<td>DVI</td>
<td>0.61 ± 0.11 (57)</td>
<td>0.61 ± 0.14 (41)</td>
<td>0.61 ± 0.15 (63)</td>
<td>0.56 ± 0.14 (51)</td>
<td>0.58 ± 0.15 (55)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n). Trend test p value from generalized linear modeling with quintiles as independent ordinal variable. Abbreviations as in Tables 1 and 3.
30 Day PPM

30 Day PPM

Evolut TAVR
- Severe: 9.9%
- Moderate: 53.8%
- Total: 63.7%

Partner TAVR
- Severe: 8.3%
- Moderate: 53.8%
- Total: 62.1%
Clinical Studies

Dynamics of the Circulation in Aortic Valvular Disease

Hemodynamics


Grossman Text, Hemodynamics Chapter

Normal Flow

High Flow

Rahimtoola
Mismatches
6-Minute Walk Test
Change from Baseline

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>35.4</td>
<td>-14.4</td>
</tr>
<tr>
<td>1 Year</td>
<td>37.1</td>
<td>17.8</td>
</tr>
<tr>
<td>2 Years</td>
<td>26.5</td>
<td>11.7</td>
</tr>
</tbody>
</table>

Change is mean increase or decrease in meters walked in 6 minutes

p<0.01
p<0.01
p=0.04
Durability
Mechanical vs. Biologic
Randomized trials

Survival after AVR

Randomized Clinical Trials on
Mechanical vs. Bioprosthetic Valves

AVR: Mechanical vs. Bioprosthetic Valve

Mortality at 15 yr

AVR
79% Bioprosthetic
66% Mechanical

Mean age at surgery: 55 years

Hammermeister KE et al. JACC 2000;36:1152
Edinburgh Randomized Trial
Patients’ Survival

Survival at 20 years:
Mechanical $= 28\pm 4\%$
Bioprostheses $= 31\pm 5\%$

All patients

Oxenham H et al. – Heart 2003;89:715-21
AVR: Mechanical vs. Bioprosthetic

Stassano P et al. - JACC 2009;54:1862-8

RCT – 310 patients 55 to 70 years (~64 years): 1995-2003

Patients with CAD included
NYHA and CAD = independent predictors of death
Survival, %

Follow-up time, y

No. at Risk
Mechanical 410
Bioprosthetic 410

P = .03

Survival data for mechanical and bioprosthetic valves over follow-up time.

New York Transcatheter Valves 2019
Patient Focused Evidence-Based Approach
Survival

HR 1.34 (95% CI 1.09-1.66), \( P = 0.006 \)

Cumulative survival (%)

Time (years)

Number at risk
Mechanical 1099
Biological 1099

664 257 35
675 212 25
AVR: Mechanical vs Bioprosthetic
Patients’ Survival

Tissue versus mechanical aortic valve replacement in younger patients: A multicenter analysis.

Iribarne A¹, Leavitt BJ², Robich MP³, Sardella GL⁴, Geib DJ⁵, Banibeau YR⁶, McCullough JN⁵, Weldner PW⁷, Clough RA⁸, Ross CS³, Malenka DJ⁷, DiSculpo AW⁹; Northern New England Cardiovascular Disease Study Group

Abstract

OBJECTIVE: The goal of this study was to examine the long-term survival of patients between the ages of 50 and 65 years who underwent tissue versus mechanical aortic valve replacement (AVR) in a multicenter cohort.

METHODS: A multicenter, retrospective analysis of all AVR patients (n = 9388) from 1991 to 2015 among 7 medical centers reporting to a prospectively maintained clinical registry was conducted. Inclusion criteria were: patients aged 50 to 65 years who underwent isolated AVR. Baseline comorbidities were balanced using inverse probability weighting for a study cohort of 1449 AVRs: 840 tissue and 609 mechanical. The primary end point of the analysis was all-cause mortality. Secondary end points included in-hospital morbidity, 30-day mortality, length of stay, and risk of reoperation.

RESULTS: During the study period, there was a significant shift from mechanical to tissue valves (P < .001). There was no significant difference in major in-hospital morbidity, mortality, or length of hospitalization. Also, there was no significant difference in adjusted 15-year survival between mechanical versus tissue valves (hazard ratio, 0.87; 95% confidence interval [CI], 0.67-1.13; P = .29), although tissue valves were associated with a higher risk of reoperation with a cumulative incidence of 19.1% (95% CI, 14.4%-24.3%) versus 3.0% (95% CI, 1.7%-4.9%) for mechanical valves. The reoperative 30-day mortality rate was 2.4% (n = 2) for the series.

CONCLUSIONS: Among patients 50 to 65 years old who underwent AVR, there was no difference in adjusted long-term survival according to prosthesis type, but tissue valves were associated with a higher risk of reoperation.

50 – 65 years old – no survival difference
### Tissue vs. mechanical

<table>
<thead>
<tr>
<th>I</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>B-NR</td>
</tr>
<tr>
<td>See Online Data Supplement 20 (Updated From 2014 VHD Guideline)</td>
<td></td>
</tr>
</tbody>
</table>

Age-Dependent SVD in CE pericardial Perimount Bioprosthesis

- 2,659 patients with AVR using CE pericardial Perimount bioprosthesis followed for 20 years
- Competing risk regression evaluating the cumulative risk of reoperation due to SVD with age at surgery

Early Failures of Surgical Valves

Early stenosis of Medtronic Mosaic positioning

Jennifer S. Lewton, MD, Nader Mouzumi, MD, Michael K. Pasque, MD, St Louis, Mo

The third-generation Medtronic Mosaic porcine bioprosthesis (Medtronic Inc, Minneapolis, Minn) was introduced in 1994. The valve leaflets are fixed in glutaraldehyde at zero pressure (applying equal pressure to the inflow and outflow ends of the valve), the root is dilated to a pressure of 40 mm Hg ("physiologic fixation"), the fixed tissue is treated with aminolevulinic acid (a long-chain fatty acid that binds to the aldehyde fractions of the glutaraldehyde-preserved porcine tissue) to reduce calcification, and the tissue is mounted on a Hancock II (Medtronic Inc) flexible stent made of acetyl copolymer covered with Dacron fabric.

Circulation

Early Trifecta valve failure: Report of a cluster of cases from a tertiary care referral center

Souren Arakelian, MD, Hussain Banerji, MD, Mahesh Ramachandran, MD, Colin M. Barker, MD, Gerald M. Layne, MD, Ross M. Reid, MD, Michael J. Readon, MD, and Neil S. Kleiman, MD

ABSTRACT

The Trifecta valve (Medtronic Inc, St Paul, Minn) was approved for commercial use by the US Food and Drug Administration in 2007. Several isolated cases have been reported since then, describing early structural valve destruction. We report a case series of 8 Trifecta valve failures, describing patients' clinical situations and management, and the pathologic characteristics of the explanted valves.

Methods: Trifecta valve failure occurred in 7 patients (8 valves) involving 30-mm (n = 2), 23-mm (n = 3), 25-mm (n = 1), and 29-mm (n = 2) valves. The mean duration of valve durability was 12.4 ± 2.2 months, and the most common lesion was prosthetic regurgitation. The mean Society of Thoracic Surgeons risk score for patients undergoing surgery at the time of valves failure was 0.73% ± 0.17%. Heart failure exacerbation was the most common presenting symptom.

Results: Five patients underwent surgical repair valve replacement, 2 patients received valve-in-valve transcatheter aortic valve replacement, and 1 patient died of cardiogenic shock before intervention. The most common pathologic finding in the explanted valves was a yellow-brown circumscribed prominent adherent to the inflow portion of the Trifecta valve.

Conclusions: Our findings provide further insights into the pathologic mechanisms leading to early Trifecta valve failure. In addition to tear of the nonnative root of the Trifecta prosthetic described as the most common mechanism in the literature for its failures, circumferential perivalve formation composed of fibrous tissue in the inflow portion and leaflet calcification concentrated around the posts in the outflow portion are important mechanisms contributing toward early Trifecta valve failure. (J Thorac Cardiovasc Surg 2017;154:1223-401)

Received for publication April 7, 2013; revisions received July 14, 2013; accepted for publication July 19, 2013. Available ahead of print Sept 6, 2013.

Address for reprints: Kevin L. Grossman, MD, Division of Cardiovascular Surgery, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (E-mail: grossman.kavin@mayo.edu)

J Thorac Cardiovasc Surg 2014;147:e10-11

0025-5832/10/

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e10 The Journal of Thoracic and Cardiovascular Surgery, Vol 147, No 3 (September 2014): e10-11

New York Transcatheter Valves 2019

PATIENT FOCUSED EVIDENCE-BASED APPROACH
TAVR Durability

Valve Performance

New York Transcatheter Valves 2019
PATIENT-FOCUSED EVIDENCE-BASED APPROACH
THV degeneration = ≥ 20 mmHG after 30 days and/or at least moderate AR, without endocarditis
Freedom from either reoperation, or if asymp, echo mean valve gradient >40 mmHg or severe AR (effective ROA > 0.3cm²)

Among survivors, none with MG >40 and only 1 pt with severe AR resulting in ViV procedure
The NOTION Trial
structural valve deterioration

<table>
<thead>
<tr>
<th></th>
<th>TAVI (n=139)</th>
<th>SAVR (n=135)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate haemodynamic SVD</td>
<td>2.9% (4/139)</td>
<td>20.7% (28/135)</td>
</tr>
<tr>
<td>Severe haemodynamic SVD</td>
<td>0.7% (1/139)</td>
<td>3.0% (4/135)</td>
</tr>
</tbody>
</table>

P < 0.0001

Number at risk:
- TAVI: 139, 134, 130, 124, 112, 94, 50
- SAVR: 135, 118, 112, 101, 92, 74, 41

Months Post-Procedure
- TAVI: 0, 12, 24, 36, 48, 60
- SAVR: 0, 12, 24, 36, 48, 60
High Risk 5-year

Cumulative Incidence of Moderate Hemodynamic SVD

Cumulative Incidence* (%)

- TAVR
- SAVR

P < 0.001

Month Post Procedure

0% 5% 10% 15% 20% 25% 30% 35% 40%

0 12 24 36 48 60
High Risk 5-year

Cumulative Incidence of Severe Hemodynamic SVD

- TAVR
- SAVR

Cumulative Incidence (%)

0% 5% 10% 15% 20% 25% 30% 35% 40%

Months Post Procedure
0 12 24 36 48 60

P = 0.23

1.8
0.8
Annual number of candidates for transcatheter aortic valve implantation per country: current estimates and future projections

Andras P. Durko¹*, Ruben L. Osnabrugge¹, Nicolas M. Van Mieghem², Milan Milojevic¹, Darren Mylotte³, Vuyisile T. Nkomo⁴, and A. Pieter Kappetein¹

¹Department of Cardio-Thoracic Surgery, Erasmus University Medical Center, s’Gravendijkwal 230 3015CE Rotterdam, The Netherlands; ²Department of Interventional Cardiology, Erasmus University Medical Center, s’Gravendijkwal 230, 3015 CE Rotterdam, The Netherlands; ³Galway University Hospital, Newcastle Rd, Galway H91 YR71, Ireland; and ⁴Division of Cardiovascular Diseases, Mayo Clinic, 1216 2nd St SW Rochester, 55902 MN, USA

Received 12 September 2017; revised 28 November 2017; editorial decision 16 February 2018; accepted 19 February 2018
Under Diagnosis

Enrolled 2500 individuals aged ≥65 years from a primary care population and screened for undiagnosed VHD using transthoracic echocardiography. Newly identified (predominantly mild) VHD was detected in 51% of participants.

The most common abnormalities were aortic sclerosis (34%), mitral regurgitation (22%), and aortic regurgitation (15%). Aortic stenosis was present in 1.3%. The likelihood of undiagnosed VHD was two-fold higher in the two most deprived socioeconomic quintiles than in the most affluent quintile, and three-fold higher in individuals with atrial fibrillation.
Clinically significant valve disease will double by 2050 in the UK
THE HEART TEAM DISCUSSION

• 90 and above = High Risk
  – TAVR

• 80 = Intermediate to High Risk
  – 10 year valve is all they will ever need

• 70 = Low to Intermediate Risk
  – Likely will require a VIV, start with the largest platform

• 60 = Shared decision making
  – “Kicking the can”

ppm vs ppm
• Coronary Access
• Durability
How do we choose?

TAVR vs. AVR must show equivalent or better

Age
Life span
Anatomy
Choice

mortality
hemodynamics
morbidity
quality of life
durability
patient acceptance
Conclusions – From the surgeon’s perspective

Demand for TAVR will increase

Love your surgeon

complex and a good surgeon will become even more valuable to the best programs
Thank You