Incidence, Predictors, and Outcomes of Prosthesis-Patient Mismatch in 62,125 TAVR Patients

An STS/ACC TVT Registry Report

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NCDR
National Cardiovascular Data Registry
Prosthesis-Patient Mismatch (PPM) was first defined by Rahimtoola in 1978 to describe the mismatch between the hemodynamics of a valve prosthesis and a patient’s requirements for cardiac output. It is defined based on the effective valve orifice area indexed to body surface area (EOAI). Studies of surgical aortic valve replacement (SAVR) have demonstrated associations between PPM and mortality and hospital readmission, as well as adverse effects on functional improvement, exercise tolerance, left ventricular mass regression, and late structural valve deterioration. Transcatheter AVR (TAVR) has been shown to result in larger EOA compared with SAVR, but the associations of PPM with outcomes following TAVR have only been studied in small series or with limited follow up.
Objective

Examine the incidence, predictors, and associations with 1-year outcomes of PPM after TAVR in the large TVT registry of commercial US procedures
Methods

STS/ACC Transcatheter Valve Registry

– Goals of facilitating device and procedure surveillance, promoting quality assurance and improvement, and conducting studies that help with access to new therapies and expand device labelling through evidence development

– Participating centers use standardized definitions to collect patient-specific data on demographics, morbidities, functional status, quality of life, hemodynamics, procedural details and outcomes (in-hospital, 30-day, and 1-year)

• All registry patients treated commercially from Jan 2014 through March 2017 were included in the present investigation

• TVT enrollees > 65 years of age at the time of their procedure and with Fee-for-Service Medicare were linked to claims data by CMS using unique patient identifiers (name and social security number) to assess 1-year survival, stroke, and rehospitalization for heart failure.
Data Analysis

• Baseline factors (demographics, comorbidities, past cardiac history, cardiac anatomy and function, and procedural) were analyzed to identify predictors of PPM using multivariate logistic regression.

• The primary outcomes of interest for this study were 1 year after TAVR:
  – Death
  – Heart failure hospitalization (death or HF)
  – Stroke
  – QOL
    • Overall KCCQ score
    • Favorable outcome at 1 year (alive, KCCQ score >60, <10 point decrease from baseline)

• Prosthesis-Patient Mismatch was classified based on the discharge measured echocardiographic effective valve orifice area (calculated with the continuity equation) indexed to body surface area (EOAI) as severe (<0.65 cm²/m²), moderate (0.65-0.85 cm²/m²), or none (>0.85 cm²/m²)

• Analyses were performed at the TVT Registry Analysis Center at the Duke Clinical Research Institute.
### Study Population

**63,393 Commercial TAVR Procedures (2014-2017)**

- **62,125 Patients**
  - **Severe PPM** (<0.65 cm²/m²), N=7514 (12.1%)
  - **Moderate PPM** (0.65-0.85 cm²/m²), N=15,271 (24.6%)
  - **No PPM** (>0.85 cm²/m²), N=39,340 (63.3%)

**Exclusion 1st and 99th percentile EOAI**

**37,470 Patients Linked to CMS**

- **Severe PPM**, N=4257 (11.4%)
- **Moderate PPM**, N=9131 (24.4%)
- **No PPM**, N=24,082 (64.3%)

**Exclusion 24,665 not linked to CMS**

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**Histogram of EOAI (cm²/m²)**

1.0 ± 0.3 cm²/m² [0.4 - 2.1]
<table>
<thead>
<tr>
<th>Baseline Variable</th>
<th>All (N=62125)</th>
<th>Severe PPM (N=7514)</th>
<th>Moderate PPM (N=15271)</th>
<th>None (N=39340)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>80.8 ± 8.6</td>
<td>77.9 ± 9.4</td>
<td>79.9 ± 8.9</td>
<td>81.8 ± 8.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender (%male)</td>
<td>53.7</td>
<td>53.7</td>
<td>55.0</td>
<td>53.2</td>
<td>0.0007</td>
</tr>
<tr>
<td>Race (%African-American)</td>
<td>3.8</td>
<td>5.2</td>
<td>4.3</td>
<td>3.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior CABG (%)</td>
<td>25.5</td>
<td>29.4</td>
<td>26.3</td>
<td>24.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior Stroke (%)</td>
<td>11.9</td>
<td>11.2</td>
<td>11.7</td>
<td>12.1</td>
<td>NS</td>
</tr>
<tr>
<td>DM (%)</td>
<td>38.3</td>
<td>46.5</td>
<td>41.8</td>
<td>35.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CLD (mod/severe)</td>
<td>26.1</td>
<td>30.4</td>
<td>27.6</td>
<td>24.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CKD (Stage 3, GFR &lt;60) (%)</td>
<td>48.3</td>
<td>50.3</td>
<td>49.7</td>
<td>47.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV EF (mean±SD)</td>
<td>54.1±13.7</td>
<td>51.9±14.2</td>
<td>53.3±13.7</td>
<td>54.8±13.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NYHA III/IV (%)</td>
<td>79.6</td>
<td>82.4</td>
<td>80.2</td>
<td>78.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AF/Fl (%)</td>
<td>40.0</td>
<td>42.6</td>
<td>41.2</td>
<td>39.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BSA (M2, mean±SD)</td>
<td>1.88±0.26</td>
<td>1.99±0.27</td>
<td>1.93±0.25</td>
<td>1.83±0.24</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean aortic gradient (mmHg)</td>
<td>43.1±14.6</td>
<td>42.8±14.9</td>
<td>43.2±14.2</td>
<td>43.2±14.6</td>
<td>NS</td>
</tr>
<tr>
<td>VIV procedure (%)</td>
<td>5.6</td>
<td>14.7</td>
<td>6.1</td>
<td>3.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prosthesis ≤23mm diam (%)</td>
<td>27.9</td>
<td>40.0</td>
<td>32.1</td>
<td>24.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Post AVA (cm2, mean±SD)</td>
<td>1.83±0.57</td>
<td>1.11±0.20</td>
<td>1.46±0.21</td>
<td>2.12±0.50</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LOS (days, mean±SD)</td>
<td>5.9±9.4</td>
<td>6.6±17.0</td>
<td>5.8±8.2</td>
<td>5.7±7.6</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Odds Ratios (95% CI) for Multivariate Model Predictors of Severe PPM

Female: 1.463 (1.353, 1.583) <.001

Age:
- ≤75 yr (per 5 yr decrease): 1.038 (1.003, 1.075) 0.035
- >75 yr (per 5 yr decrease): 1.078 (1.046, 1.112) <.001

Non-White/Hispanic: 1.233 (1.127, 1.348) <.001

Valve-in-Valve Procedure: 2.775 (2.530, 3.043) <.001

Valve size ≤23 mm: 2.773 (2.588, 2.971) <.001

BSA (per 0.2 unit increase): 1.710 (1.656, 1.765) <.001

Lower EF (per 5% decrease): 1.097 (1.084, 1.111) <.001

Afib/Flutter: 1.119 (1.056, 1.186) <.001

Severe MR: 1.077 (1.009, 1.149) 0.026

Severe TR: 1.092 (1.019, 1.170) 0.012
Mortality (%)

Adjusted HR (95% CI)

1.19 (1.09-1.31) p<0.001

17.2% Severe
15.8% Moderate/None

Number at Risk Adjusting for baseline covariates:

<table>
<thead>
<tr>
<th>PPM</th>
<th>Day 0</th>
<th>Month 4</th>
<th>Month 8</th>
<th>Month 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PPM</td>
<td>23635</td>
<td>21080</td>
<td>16734</td>
<td>13136</td>
</tr>
<tr>
<td>Mod PPM</td>
<td>8983</td>
<td>7995</td>
<td>6277</td>
<td>4831</td>
</tr>
<tr>
<td>Sev PPM</td>
<td>4152</td>
<td>3626</td>
<td>2976</td>
<td>2130</td>
</tr>
</tbody>
</table>

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Event Rates (severe vs not severe PPM):

**14.7% vs 12.2%**

**26.8% vs 24.2%**

**3.8% vs 4.2%**

HR 95% CI (severe vs not severe PPM):

1.12 (1.02-1.24) p=0.017

1.13 (1.06 – 1.22) p<0.001

0.98 (0.82-1.16) p=0.798
## Subgroup (Interaction) Analyses (Severe vs Not Severe PPM)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Mortality Effect estimate (95% CI)</th>
<th>Interaction P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;83 years</td>
<td>1.123 (0.999, 1.261)</td>
<td>0.113</td>
</tr>
<tr>
<td>Age &gt;83 years</td>
<td>1.285 (1.129, 1.463)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.153 (1.020, 1.303)</td>
<td>0.352</td>
</tr>
<tr>
<td>Female</td>
<td>1.252 (1.104, 1.420)</td>
<td></td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF &lt;40%</td>
<td>1.082 (0.904, 1.294)</td>
<td>0.171</td>
</tr>
<tr>
<td>LVEF &gt;40%</td>
<td>1.250 (1.127, 1.385)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &lt;30 kg/m2</td>
<td>1.149 (1.031, 1.281)</td>
<td>0.204</td>
</tr>
<tr>
<td>BMI &gt;30 kg/m2</td>
<td>1.277 (1.115, 1.464)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean AV Gradient</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV Gradient &lt;40 mmHg</td>
<td>1.227 (1.084, 1.387)</td>
<td>0.409</td>
</tr>
<tr>
<td>AV Gradient &gt;40 mmHg</td>
<td>1.147 (1.022, 1.288)</td>
<td></td>
</tr>
<tr>
<td><strong>Afib/Flutter</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With A Fib/Flutter</td>
<td>1.193 (1.065, 1.337)</td>
<td>0.995</td>
</tr>
<tr>
<td>No Fib/Flutter</td>
<td>1.193 (1.048, 1.358)</td>
<td></td>
</tr>
</tbody>
</table>
**Multivariable Analysis of Severe vs Not Severe (1-year)**

**Overall score**

OR 0.72 (0.06-8.12)  
*p*=0.8

**Favorable outcome**

(Alive with KCCQ score >60 and <10 point decrease from baseline)

OR 0.99 (0.81-1.20)  
*p*=0.9

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1To avoid the bias of missing non-random KCCQ measurements due to worse baseline health status, sites reporting less than 50% completeness of measurements were excluded. To ensure that the cohort of patients represented the overall TAVR population, we used inverse probability weighting to increase the weight of patients who were most like those with missing KCCQ measurements.
Limitations

• This is an observational registry study and has the inherent limitations associated with retrospective analyses, including residual measured and unmeasured confounding.

• Data is site-reported, but the ACC NCDR warehouse and DCRI data analysis center both implement data quality checks, including feedback reports, and examine data ranges and consistency to optimize completeness and accuracy. Sites receive data dictionaries and use standard definitions. Third party audits are randomly conducted at 10% sites annually.

• EOAI was calculated from individual patient-measured hemodynamics at hospital discharge.
  – It is possible that these measurements could be influenced by peri-procedural issues and might be more accurate if obtained at a later time point. However, a separate analysis of 30-day survivors did not suggest an effect on our conclusions.
  – Furthermore, our measured values for EOAI are consistent with prior studies and more accurate than those obtained by projection or geometric measurement.
Summary and Conclusions

• This is the largest study to date of prosthesis-patient mismatch (PPM) after TAVR and demonstrates that severe and moderate PPM are common, occurring in 12% and 24% of patients, respectively.

• Severe PPM is related to prosthesis and patient factors, including small diameter valve prosthesis, valve-in-valve procedure, larger BSA, female sex, and younger age.

• Severe PPM is associated with increased 1-year mortality and heart failure re-hospitalization when compared with patients with moderate or no PPM. We did not find an association between PPM and stroke or QOL (KCCQ score) at 1 year.

• Our findings suggest that efforts should be made to identify and limit the risk for PPM after TAVR
Prosthesis–Patient Mismatch in 62,125 Patients Following Transcatheter Aortic Valve Replacement
From the STS/ACC TVT Registry

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ABSTRACT

BACKGROUND Prosthesis-patient mismatch (PPM) after surgical aortic valve replacement (AVR) for aortic stenosis is generally associated with worse outcomes. Transcatheter AVR (TAVR) can achieve a larger valve orifice and the effects of PPM after TAVR are less well studied.

OBJECTIVES The authors utilized the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) registry to examine the frequency, predictors, and outcomes of PPM after TAVR in 62,125 patients enrolled between 2014 and 2017.

METHODS On the basis of the echocardiographic effective valve area indexed to body surface area, PPM was classified as severe (≤0.65 cm²/m²), moderate (0.65 to 0.85 cm²/m²), or none (≥0.85 cm²/m²). Multivariable regression models were utilized to examine predictors of severe PPM as well as adjusted outcomes, including mortality, heart failure (HF) rehospitalization, stroke, and quality of life, at 1 year in 37,470 Medicare patients with claims linkage.

RESULTS Severe and moderate PPM were present following TAVR in 12% and 25% of patients, respectively. Predictors of severe PPM included small (≤23-mm diameter) valve prosthesis, valve-in-valve procedure, larger body surface area, female sex, younger age, non-white/Hispanic race, lower ejection fraction, atrial fibrillation, and severe mitral or tricuspid regurgitation. At 1 year, mortality was 17.2%, 15.6%, and 15.9% in severe, moderate, and no PPM patients, respectively (p = 0.03). HF rehospitalization had occurred in 14.7%, 12.8%, and 11.9% of patients with severe, moderate, and no PPM, respectively (p < 0.0001). There was no association of severe PPM with stroke or quality of life score at 1 year.

CONCLUSIONS Severe PPM after TAVR was present in 12% of patients and was associated with higher mortality and HF rehospitalization at 1 year. Further investigation is warranted into the prevention of severe PPM in patients undergoing TAVR. (J Am Coll Cardiol 2018;11-12) © 2018 by the American College of Cardiology Foundation.