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

An STS/ACC TVT Registry Report

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Background

- 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
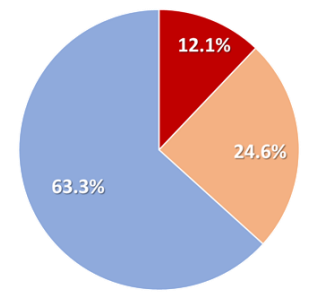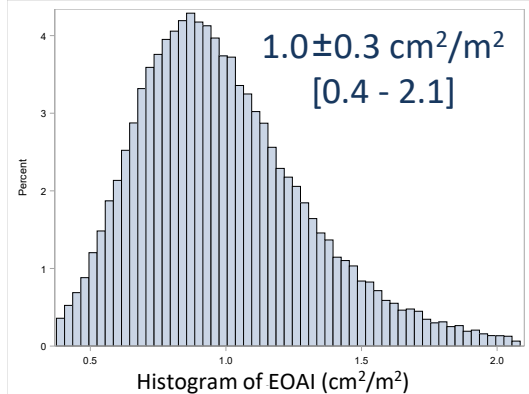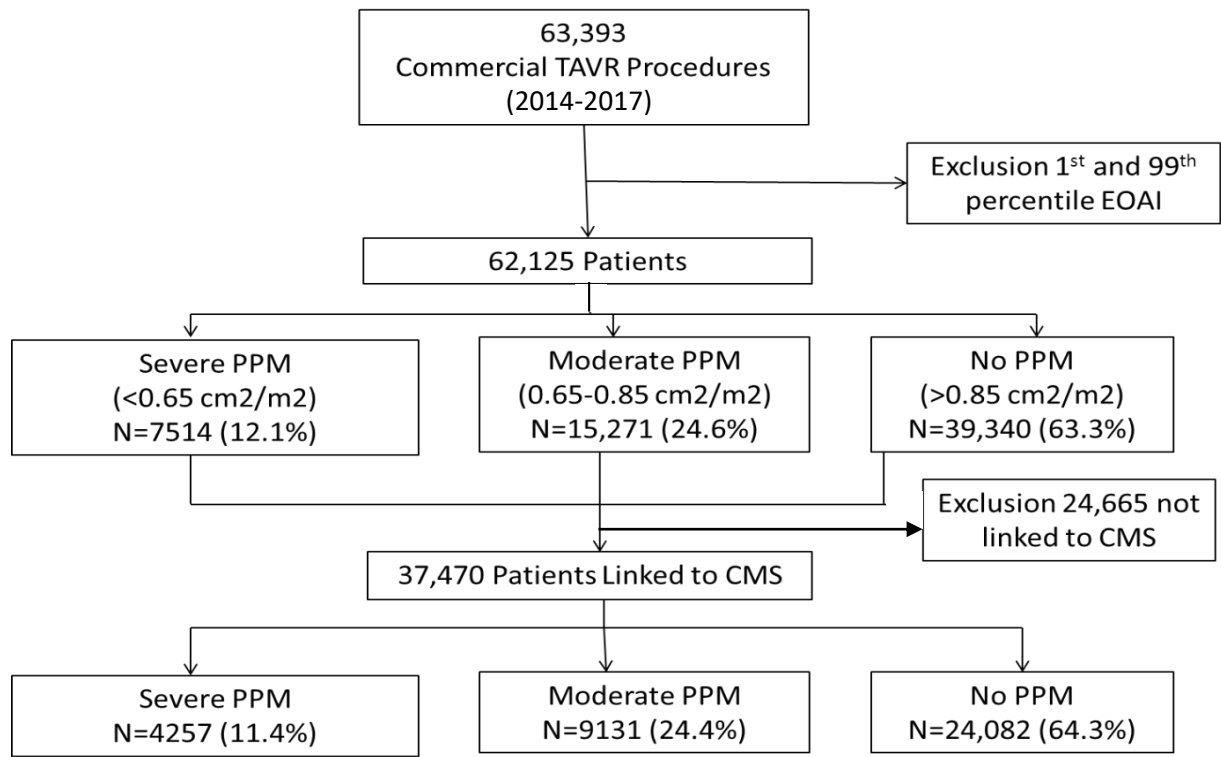
Methods

STS/ACC Transcatheter Valve Registry

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

– Participating centers use <u>standardized definitions</u> 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 $\geq$ 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.
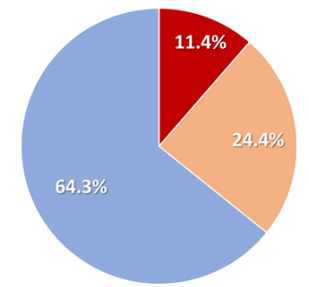
Data Analysis

- 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 cm^2/m^2), moderate (0.65-0.85 cm^2/m^2), or none (>0.85 cm^2/m^2)

- Analyses were performed at the TVT Registry Analysis Center at the Duke Clinical Research Institute.

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Study Population

63,393
Commercial TAVR Procedures
(2014-2017)

Exclusion 1st and 99th percentile EOAI

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 24,665 not linked to CMS

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%)

1.0 ± 0.3 cm^2/m^2
[0.4 - 2.1]

Histogram of EOAI (cm^2/m^2)

12.1%

24.6%

63.3%

■ Severe ■ Moderate ■ None

11.4%

24.4%

64.3%

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

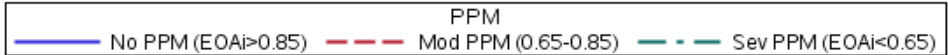# Odds Ratios (95% CI) for Multivariate Model Predictors of Severe PPM

Predictor	Odds Ratio (95% CI)	p-value
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 (%)

17.2% Severe

15.8% Moderate/None

Adjusted HR (95% CI)

1.19   (1.09-1.31)   p<0.001

Months from Procedure

PPM
—— No PPM (EOAi>0.85)   - - - Mod PPM (0.65-0.85)   -·-· Sev PPM (EOAi<0.65)

Number at Risk Adjusting for baseline covariates:				
	Day 0	Month 4	Month 8	Month 12
No PPM	23635	21080	16734	13136
Mod PPM	8983	7995	6277	4831
Sev PPM	4152	3626	2976	2130

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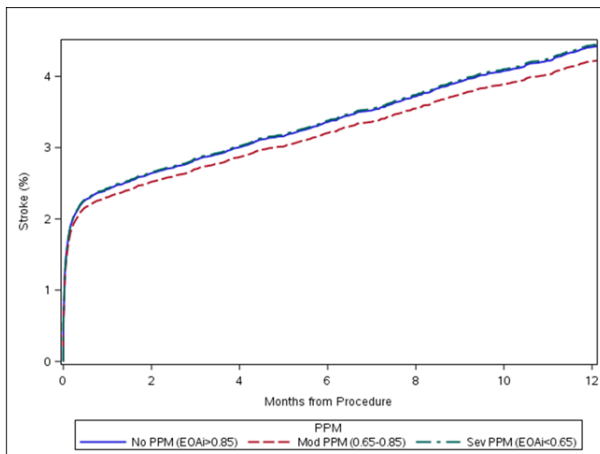NATIONAL CARDIOVASCULAR DATA REGISTRY

HF Rehospitalization (%)
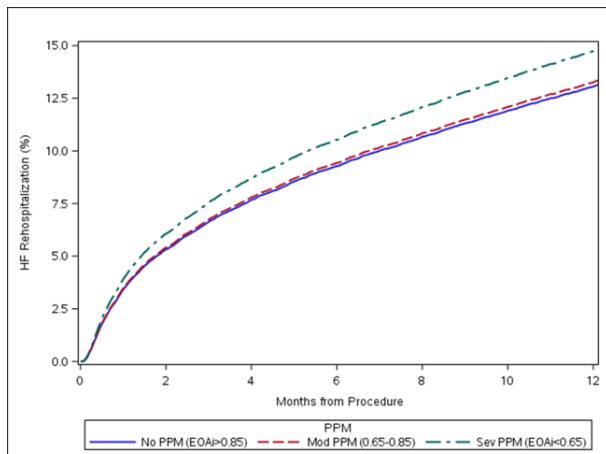
Death or HF Rehosp. (%)
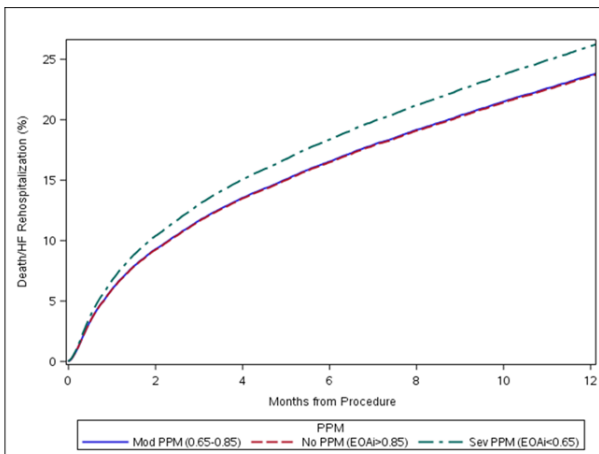
Stroke (%)

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

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Subgroup (Interaction) Analyses (Severe vs Not Severe PPM)

	Mortality Effect estimate (95% CI)	Interaction P-value
Age		0.113
Age ≤83 years	1.123 (0.999, 1.261)	
Age >83 years	1.285 (1.129, 1.463)	
Gender		0.352
Male	1.153 (1.020, 1.303)	
Female	1.252 (1.104, 1.420)	
LVEF		0.171
LVEF <40%	1.082 (0.904, 1.294)	
LVEF ≥40%	1.250 (1.127, 1.385)	
BMI		0.204
BMI <30 kg/m2	1.149 (1.031, 1.281)	
BMI ≥30 kg/m2	1.277 (1.115, 1.464)	
Mean AV Gradient		0.409
AV Gradient <40 mmHg	1.227 (1.084, 1.387)	
AV Gradient ≥40 mmHg	1.147 (1.022, 1.288)	
Afib/Flutter		0.995
With A Fib/Flutter	1.193 (1.065, 1.337)	
No Fib/Flutter	1.193 (1.048, 1.358)	

KCCQ Overall Score
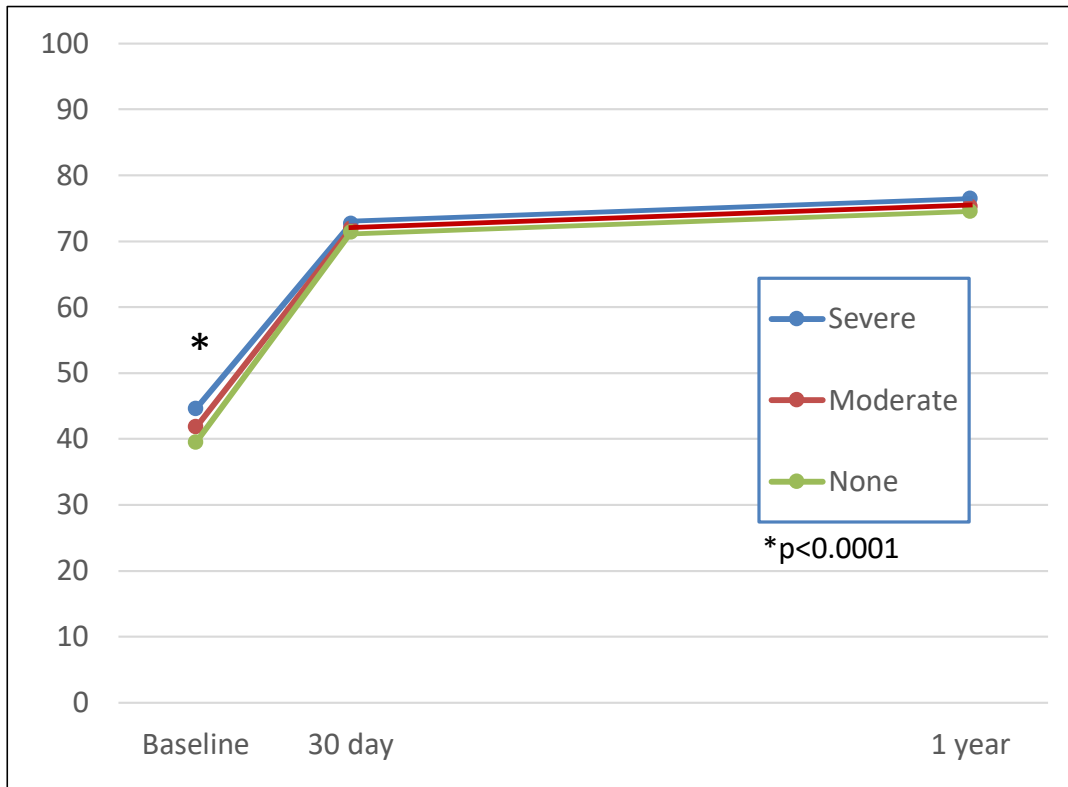
Multivariable Analysis of Severe vs Not Severe (1-year)[1]:

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

[1]To 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*

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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 association with outcomes of PPM after TAVR in 62,125 patients enrolled between 2014 and 2017.

METHODS On the basis of the discharge echocardiographic effective valve area indexed to body surface area, PPM was classified as severe (<0.65 cm^2/m^2), moderate (0.65 to 0.85 cm^2/m^2), or none (>0.85 cm^2/m^2). 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 ($\leq$23-mm diameter) valve prosthesis, valve-in-valve procedure, larger body surface area, female sex, younger age, non-white/Hispanic race, lower ejection fraction, atrial fibrillation, and severe mitral or tricuspid regurgitation. At 1 year, mortality was 17.2%, 15.6%, and 15.9% in severe, moderate, and no PPM patients, respectively ($p = 0.02$). HF rehospitalization had occurred in 14.7%, 12.8%, and 11.9% of patients with severe, moderate, and no PPM, respectively ($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;1:1–12) © 2018 by the American College of Cardiology Foundation.