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Pacemaker following transcatheter aortic valve replacement and tricuspid regurgitation: A single-center experience

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Abstract

Background: As transcatheter aortic valve replacement (TAVR) procedures increase, more data is available on the development of conduction abnormalities requiring permanent pacemaker (PPM) implantation post-TAVR. Mechanistically, new pacemaker implantation and incidence of associated tricuspid regurgitation (TR) post-TAVR is not well understood. Studies have evaluated the predictability of patient anatomy towards risk for needing permanent pacemaker (PPM) post-TAVR; however, little has been reported on new PPM and TR in patients post-TAVR.

Methods: This retrospective study identified patients at our health system who underwent PPM following TAVR from January 2014 to June 2018. Data from both TAVR and PPM procedures as well as patient demographics were collected. Echocardiographic data before TAVR, between TAVR and PPM placement, and the most recent echocardiogram at the time of chart review were analyzed.

Results: Of 796 patients who underwent TAVR between January 2014 and June 2018, 89 patients (11%) subsequently required PPM. Out of the 89 patients who required PPM implantation, 82 patients had pre-TAVR and 2-year post-TAVR echocardiographic imaging data. At baseline, 22% (18/82) of patients had at least moderate TR. At 2-year post-TAVR echocardiographic imaging follow-up; 27% (22/82) of patients had at least moderate TR. Subgroup analysis was performed according to the TAVR valve size implanted. In patients who received a TAVR device < 29 mm in diameter in size, 25% (11/44) had worsening TR. In patients who received a TAVR device ≥ 29 mm in diameter, 37% (14/38) had worsening TR.

Conclusion: We have demonstrated a patient population that may be predisposed to developing worsening TR and right heart function after TAVR and Pacemaker implantation.

KEYWORDS

cardiovascular research, pacemaker, TAVR, tricuspid regurgitation, valve repair/replacement

1 | INTRODUCTION

Transcatheter aortic valve replacement (TAVR) for severe symptomatic aortic stenosis has been studied extensively in the high, intermediate, and low surgical risk patient populations. The need for new permanent pacemaker (PPM) implantation post-TAVR is a recognized potential complication, through multiple pathways associated with injury to the intrinsic cardiac conduction system during device deployment.[1–4] New PPM requirements post-TAVR have been reported with rates between 17.8% and 35%.[1,5–7] Additionally, new conduction abnormalities requiring PPM are more common following TAVR than SAVR.[8,9] Studies have evaluated the predictability of patient-anatomy toward risk for PPM post-TAVR; however, little has been reported on the incidence and degree of TR after new PPM placement in patients who underwent TAVR.

2 | METHODS

This retrospective study identified patients at our academic health system who underwent PPM following TAVR from January 2014 to June 2018. The Institutional Review Board reviewed and approved this study. Data from both TAVR and PPM procedures as well as patient demographics were collected. Echocardiographic data before TAVR, between TAVR and PPM placement, and the most recent echocardiogram at the time of chart review were obtained. Data points collected included ejection fraction (EF), degree of tricuspid regurgitation (based on a numerical scale seen in Table 1), tricuspid annular plane systolic excursion (TAPSE), degree of inferior vena cava (IVC) dilation, right ventricular basal diameter (RVD), right ventricle systolic pressure (RVSP), and right atrium (RA) area.

Change in outcome variables was analyzed using the paired *t*-test in the presence of distributional normality and the Wilcoxon signed-rank test in the absence of distributional normality. Continuous variables were described as means and standard deviations. Categorical data were described with frequencies and percentages. $p < .05$ was considered statistically significant.

3 | RESULTS

Out of the 796 patients who underwent TAVR between January 2014 and June 2018, 89 patients (11%) subsequently required PPM implantation (Figure 1). Of these 89 study patients, the majority were Caucasian (87%), Male gender (60%), with a mean age of 79.6 ± 8.7 years (Table 2). Twenty-four patients (27%) received a self-expanding TAVR device (Medtronic, Minneapolis, MN) and 65 patients (73%) received a balloon-expandable valve (Edwards Lifesciences, Irvine, CA).

Out of the 89 patients who received a PPM implantation, 82 patients had pre-TAVR and 2-year post-TAVR echocardiographic imaging data available for review. At baseline, 22% (18/82) of patients had at least moderate tricuspid regurgitation. At 2-year post-TAVR echocardiographic imaging follow-up, 27% (22/82) of patients had at least moderate tricuspid regurgitation.

Subgroup analysis of the rate of tricuspid regurgitation was performed according to TAVR valve size implanted. In the population receiving a TAVR device < 29 mm in diameter in size, follow-up echocardiographic data were available in 44 out of the 47 patients. In the population who received a TAVR device ≥ 29 mm in diameter in size, follow-up echocardiographic information was available in 38 out of the 42 patients. On 2-year follow-up imaging, a comparison was made between TAVR device < 29 mm and TAVR device ≥ 29 mm in regard to change in TR score (Table 1). If the TR score pre-TAVR matched or was followed by a lower TR score 2-year post-TAVR, then this was considered a TR Score Difference of 0. If the TR score pre-TAVR was 1 and the TR score 2-year post-TAVR was 2, then this would be a TR Score Difference of 1 (Table 6). On 2-year follow-up imaging, in patients who received a TAVR device < 29 mm in size, 25% (11/44) were found to have a TR Score Difference of 1 or greater. Of these 11 smaller device sized patients, 3 were implanted with a self-expanding valve, and the remaining 8 patients were implanted with a balloon-expandable valve. On 2-year follow-up imaging, patients who received a TAVR device ≥ 29 mm in diameter, 37% (14/38) were found to have a TR Score Difference of 1 or greater. Of these 14 larger device sized patients, 3 were implanted with a self-expanding valve, and the remaining 11 patients were implanted with a balloon-expandable valve.

Beyond tricuspid regurgitation grading, additional right heart echocardiographic parameters were evaluated for secondary effects of tricuspid regurgitation (Tables 3–5). There was a statistically significant decrease in right ventricular systolic pressure ($p = .010$) in the full set of study patients (Table 3). In patients who received a TAVR device < 29 mm in diameter, there were no statistically significant changes in secondary right heart echocardiographic parameters (Table 4). In patients who received a TAVR device ≥ 29 mm in size, there was a trend toward an increase in RV basal diameter size, Tricuspid Regurgitation Score, and RA area that did not reach statistical significance (Table 3). In this larger device group, there was a statistically significant decrease in measured right ventricular systolic pressure ($p = .024$; Table 5).

TABLE 1 Tricuspid regurgitation scale

Tricuspid Regurgitation Score	Tricuspid Regurgitation Severity Definition
0	No tricuspid regurgitation
1	Trivial tricuspid regurgitation
2	Mild tricuspid regurgitation
3	Mild-moderate tricuspid regurgitation
4	Moderate tricuspid regurgitation
5	Moderate-severe tricuspid regurgitation
6	Severe tricuspid regurgitation

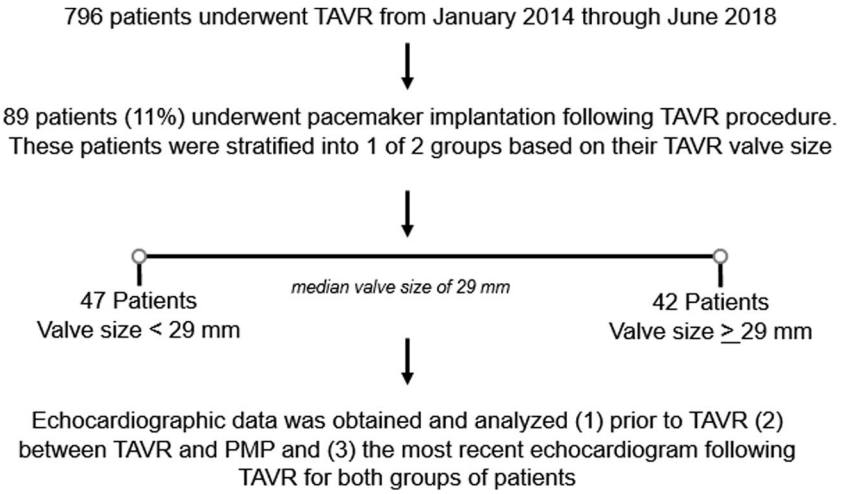

FIGURE 1 Patient stratification. PPM, permanent pacemaker; TAVR, transcatheter aortic valve replacement

4 | DISCUSSION

This study is the first to offer long-term follow-up insight into the hemodynamic context of TR following new PPM implantation immediately post-TAVR. Novel to this study, there was a signal between the size of TAVR device implanted and the risk of progression of severity of baseline TR. On 2-year follow-up imaging studies, patients who received TAVR devices larger than or equal to diameters of 29 mm in size, with a PPM, were noted to have a TR score difference of 1 or greater in 12% more patients than those who received smaller devices (Table 6) with a pacemaker. Of note, this observation was made in the subgroup of patients who had some degree of underlying tricuspid regurgitation present pre-TAVR. In our patient population who received a TAVR device size greater than or equal to 29 mm in size and a post-TAVR PPM, there was an additional trend toward early signs of right-sided structural heart disease as evidenced by an increase in RVD (Δ = 0.4 cm, p = .220) and a statistically significant decrease in RVSP (Δ = 7.2 mmHg, p = .024) at 2-year follow-up.

TABLE 2 Patient demographics

Age at TAVR	79.6 years (±8.7 years)
Sex	
Male	53 (60%)
Female	36 (40%)
Race	
White	78 (87%)
African American	9 (10%)
Other	2 (2%)
Body mass index	31.0 kg/m^2 (±14.0 kg/m^2)
Comorbidities	
Atrial fibrillation	43 (48%)
COPD	20 (22%)
Diabetes	35 (39%)
Hypertension	66 (74%)
Chronic kidney disease	36 (40%)
Type of valve placed during TAVR	
Balloon-expandable	65 (73%)
Self-expandable	24 (27%)

Abbreviations: COPD, chronic obstructive pulmonary disease; TAVR, transcatheter aortic valve replacement.

Anatomically, device size associated rate of PPM implantation and TR severity could be secondary to the proximity of the aortic annulus right and non-coronary cusps to the location of the cardiac conduction system; triangle of Koch.[10] The triangle of Koch is located posterior to the right and noncoronary cusps of the aortic annulus. Native aortic annuli are elliptical in shape, post-TAVR implantation, the native aortic annuli become circular. Deformation of the tricuspid commissure by the smoothing of the aortic annulus causes increased pressure on the triangle of Koch. Larger TAVR valves and over-sizing during valve anchoring can also result in tricuspid annular deformation and increased malcoaptation of tricuspid leaflet coaptation. This changes the septal:anterolateral and septal:posterolateral diameter of the tricuspid commissures resulting in the annulus being more prone to TR due to alteration of the shape of the septal wall of tricuspid annulus and anteroseptal commissure. Additionally, if a pacer wire is implanted, deformation of the tricuspid anteroseptal commissure may anatomically shift pacer leads to migrate from commissure implantation to increased contact with the body of the septal leaflet. Our results suggest an increased incidence of TR with a larger valve size ≥ 29 mm in diameter after PPM post-TAVR.

Other mechanisms for pacemaker induced tricuspid regurgitation have been reported.[11–14] PPM mechanisms of TR may be secondary to pacemaker leads causing tethering of the septal leaflet along the tricuspid annulus thereby impairing leaflet coaptation and closure, lead entanglement, lead adherence, and less commonly leaflet perforation.[12,15] Additionally, asynchronous right ventricle (RV) pacing from abnormal RV activation from the PPM may manifest later in time as biventricular heart failure with RV cavitary dilatation and clinically significant TR.[15] Pre-existing clinically significant TR has additionally been identified as a predictor for the need of PPM post-TAVR.[16]

TABLE 3 Echocardiographic changes from before TAVR to 2 years after Permanent Pacemaker implantation

Variable	Baseline echo pre-TAVR	Echocardiogram after pacemaker placement	Difference in echocardiographic data	*p*
EF (%)	53.8 ± 13.8	52.6 ± 14.3	−1.2 ± 11.7	.393 (W)
Tricuspid Regurgitation Score	2.5 ± 1.5	2.5 ± 1.3	0.0 ± 1.2	.926 (T)
TAPSE (cm)	2.0 ± 0.4	2.0 ± 0.4	0.0 ± 0.4	.983 (T)
IVC dilation (cm)	2.3 ± 0.5	2.3 ± 0.5	0.0 ± 0.6	1.000 (W)
RVD (cm)	3.2 ± 0.9	3.4 ± 0.8	0.1 ± 1.0	.467 (T)
RVSP (mmHg)	38.7 ± 12.4	33.9 ± 14.5	−4.7 ± 14.2	.010 (T)
RA area (cm^2)	16.2 ± 7.8	17.6 ± 7.9	1.3 ± 7.2	.534 (T)

Abbreviations: EF, ejection fraction; IVC, inferior vena cava; RA, right atrium; RVD, right ventricular diameter; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion; TAVR, transcatheter aortic valve replacement; (T), paired t-test; (W), Wilcoxon signed-rank test.

TABLE 4 Echocardiographic changes from before TAVR to 2 years after permanent pacemaker implantation for valve size < 29 mm in diameter

Variables	Baseline echo pre-TAVR	Echocardiogram after pacemaker placement	Difference in echocardiographic data	*p*
EF (%)	58.0 ± 11.5	54.8 ± 15.8	−3.2 ± 12.8	.137 (W)
Tricuspid Regurgitation Score	2.8 ± 1.5	2.7 ± 1.4	−0.2 ± 1.1	.383 (T)
TAPSE (cm)	1.9 ± 0.4	1.9 ± 0.5	0.0 ± 0.4	.896 (T)
IVC dilation (cm)	2.3 ± 0.5	2.3 ± 0.5	0.0 ± 0.7	1.000 (W)
RVD (cm)	3.1 ± 1.0	3.0 ± 0.7	−0.1 ± 0.9	.738 (T)
RVSP (mmHg)	39.8 ± 12.5	36.9 ± 14.0	−2.9 ± 12.8	.189 (T)
RA area (cm^2)	18.8 ± 11.2	18.5 ± 10.8	−0.3 ± 10.5	.625 (W)

Abbreviations: EF, ejection fraction; IVC, inferior vena cava; RA, right atrium RVD, right ventricular diameter; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion; TAVR, transcatheter aortic valve replacement; (T), paired t-test; (W), Wilcoxon signed-rank test.

TABLE 5 Echocardiographic changes from before TAVR to 2 years after permanent pacemaker implantation for valve size ≥ 29 mm in diameter

Variables	Baseline echo pre-TAVR	Echocardiogram after pacemaker placement	Difference in echocardiographic data	*p*
EF (%)	49.3 ± 14.7	50.3 ± 12.4	1.0 ± 10.2	.560 (T)
Tricuspid Regurgitation Score	2.1 ± 1.4	2.3 ± 1.1	0.2 ± 1.4	.400 (T)
TAPSE (cm)	2.0 ± 0.4	2.0 ± 0.4	0.0 ± 0.4	.837 (T)
IVC dilation (cm)	2.3 ± 0.4	2.3 ± 0.5	0.0 ± 0.5	1.000 (W)
RVD (cm)	3.3 ± 0.9	3.7 ± 0.8	0.3 ± 1.1	.220 (T)
RVSP (mmHg)	37.3 ± 12.2	30.1 ± 14.6	−7.1 ± 15.7	.024 (T)
RA area (cm^2)	14.4 ± 4.3	16.9 ± 6.0	2.5 ± 4.3	.176 (T)

Abbreviations: EF, ejection fraction; IVC, inferior vena cava; RA, right atrium RVD, right ventricular diameter; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion; TAVR, transcatheter aortic valve replacement; (T), paired t-test; (W), Wilcoxon signed-rank test.

TABLE 6 Tricuspid Regurgitation Score Difference from before TAVR to 2 years after PPM

	TR Score Difference 0	TR Score Difference 1	TR Score Difference 2	TR Score Difference 3	TR Score Difference 4
Valve size < 29 mm (44)	33 (75%)	9 (20%)	2 (5%)	0 (0%)	0 (0%)
Valve size ≥ 29 mm (38)	24 (63%)	8 (21%)	5 (13%)	0 (0%)	1 (3%)

Note: TR Score Difference calculated using pre-TAVR TR score subtracted from post-TAVR TR score.

Abbreviations: TAVR, transcatheter aortic valve replacement; TR, tricuspid regurgitation.

5 | LIMITATIONS

This is a single-center retrospective study with a small sample size of patients. This study is unable to elucidate if patients with pre-TAVR imaging would have had worsening tricuspid regurgitation as a progression of their natural pathophysiological disease, as a result of larger TAVR device implantation, or if pacemaker implantation accelerated the process. This study is additionally unable to differentiate if the worsening tricuspid regurgitation mechanistically was caused by pacer wire impingement on focal leaflets, versus tricuspid annular dilatation, tricuspid annulus deformation due to TAVR device, or presence of underlying disease states such as atrial fibrillation. Mechanistically, this study has demonstrated that tricuspid regurgitation, TAVR device, and pacemaker implantation is a more complex anatomical interaction than previously appreciated and 2-year follow-up echocardiographic information may not be sufficient to extrapolate long-term right heart function conclusions for this patient population. Prospective studies with larger sample size and longer follow-up are needed to gain more insight.

6 | CONCLUSION

Tricuspid regurgitation is a clinically significant and undertreated disease. Defining the etiology and anatomical pathophysiology of tricuspid regurgitation is a work in progress. In this study, we have demonstrated a patient population that may be predisposed to developing worsening tricuspid regurgitation and right heart function after TAVR and pacemaker implantation. Given the recent advances in transcatheter-based valvular therapies, larger studies with long-term follow-up are necessary to prospectively study the interactions of TAVR devices, pacemaker implantation, and right heart function for clarity on optimal intervention strategies.[17]

DISCLOSURES

Dr. Marvin Eng is a clinical proctor for Edwards Lifesciences, Medtronic, and Boston Scientific. Dr. Tiberio Frisoli is a clinical proctor for Edwards Lifesciences, Abbott, Boston Scientific, and Medtronic. Dr. Brian O'Neill has served as a consultant and received research support from Edwards Lifesciences. Dr. James Lee is a consultant for HeartFlow. Dr. William W. O'Neill has served as a consultant for Abiomed, Edwards Lifesciences, Medtronic, Boston Scientific, Abbott Vascular, and St. Jude Medical; and serves on the Board of Directors of Neovasc Inc. Dr. Dee Dee Wang is a consultant to Edwards Lifesciences, Boston Scientific, receives research grant support from Boston Scientific assigned to employer Henry Ford Health System, is a member of the Edwards CLASP IITR Steering Committee, and Abbott PARADIGM Steering Committee. All other authors report no relevant financial disclosures.

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