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ORIGINAL RESEARCH

Temporal Trends in the Incidence and Outcomes of Pacemaker Implantation After Transcatheter Aortic Valve Replacement in the United States (2012–2017)

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BACKGROUND: Nationwide studies documenting temporal trends in permanent pacemaker implantation (PPMI) following transcatheter aortic valve replacement (TAVR) are limited.

METHODS AND RESULTS: We selected patients who underwent TAVR between 2012 and 2017 in the National Readmission Database. The primary end point was the 6-year trend in post-TAVR PPMI at index hospitalization and at 30, 90, and 180 days after discharge. The secondary end point was the association between PPMI and in-hospital mortality, stroke, cost, length of stay, and disposition. Among the 89 202 patients who underwent TAVR, 77 405 (86.8%) with no prior pacemaker or defibrillator were included. Patients who required PPMI had a higher prevalence of atrial fibrillation (43.6% versus 38.7%, $P<0.001$) and conduction abnormalities (28.4% versus 15.3%, $P<0.001$). The incidence of PPMI during index admission increased from 8.7% in 2012 to 13.2% in 2015, and then decreased to 9.6% in 2017. The incidence of inpatient PPMI within 30 days after discharge increased from 0.5% in 2012 to 1.25% in 2017 ($P_{trend}<0.001$). Inpatient PPMI beyond 30 days remained rare (<0.5%) during the study period. After risk adjustment, PPMI was not associated with in-hospital mortality or stroke but was associated with increased nonhome discharge, longer hospitalization, and higher cost. The incremental expenditure associated with post-TAVR PPMI during index admission increased from $9.6 million to $72.2 million between 2012 and 2017.

CONCLUSIONS: After an upward trend, rates of PPMI after TAVR in the United States stabilized at ~10% in 2016 to 2017, but there was a notable increase in PPMI within 30 days after the index admission. PPMI was not associated with increased in-hospital morbidity or mortality but led to longer hospitalization, higher cost, and more nonhome discharges.

Key Words: aortic stenosis ■ cardiac resynchronization therapy ■ heart block ■ permanent pacemaker implantation ■ transcatheter aortic valve replacement

Conduction disturbances requiring permanent pacemaker implantation (PPMI) are known complications of aortic valve interventions.[1–3] With surgical aortic valve replacement, the incidence of postoperative PPMI in the United States has been stable around 5% to 6% in the past 2 decades.[1,2,4] In contrast, the incidence of PPMI after transcatheter aortic valve replacement (TAVR) has been both variable and dynamic over time. In the earliest randomized trial of TAVR, PPMI was only required postoperatively in 3.4% of patients.[5] Subsequent trials have shown higher rates of PPMI after TAVR, especially with self-expanding valves.[6] A survey of the early commercial TAVR experience in the United States between 2011 and 2014 documented a 30-day incidence of PPMI following TAVR of 6.7%.[7] However, TAVR practice in the United States

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CLINICAL PERSPECTIVE

What Is New?

- About 1 in 10 patients undergoing transcatheter aortic valve replacement in the United States receive a permanent pacemaker before discharge and that number has not decreased over time.
- There is a temporal increase in the incidence of permanent pacemaker implantation after discharge among patients undergoing transcatheter aortic valve replacement.

What Are the Clinical Implications?

- The rising incidence of postdischarge conduction abnormalities requiring pacemaker after transcatheter aortic valve replacement suggests the need for careful monitoring, especially with the increasing practice of early postprocedural dismissal.
- More research is needed to understand the long-term clinical and economic impact of permanent pacemaker after transcatheter aortic valve replacement in light of the expanding indications for this therapy.

Abbreviations

CRT	cardiac resynchronization therapy
LOS	length of stay
NRD	National Readmission Database
PPMI	permanent pacemaker implantation
TAVR	transcatheter aortic valve replacement
THV	transcatheter heart valve

has evolved markedly since 2014 with the emergence of second- and third-generation transcatheter heart valves (THV), and the recognition of anatomical and procedural factors that increase the risk of PPMI.[2,8–11] Although there is a plethora of literature on post-TAVR PPMI, nationwide data on the temporal incidence and outcomes of PPMI after TAVR are limited.[12] To address this knowledge gap, we used a national representative database to assess the temporal change in the incidence, timing, and outcomes of PPMI following TAVR between 2012 and 2017.

METHODS

Data obtained from the National Readmission Database (NRD) could not be shared directly by the authors, but requests to access the NRD data set from qualified researchers trained in human subject confidentiality protocols may be sent to the Healthcare Cost and Utilization Project (HCUP; https://www.hcup-us.ahrq.gov/team/NationwideDUA.jsp).

Study Data

The NRD was used to derive patient-relevant information. The NRD is a publicly available, all-payer data set of inpatient stays in hospitals from 27 geographically dispersed states. These hospitalizations account for 60% of all hospitalizations in the United States annually. The NRD also contains verified patient linkage numbers that can be used to track readmissions across hospitals for individual patients within the same calendar year. The institutional review board exempted the study because it utilizes public deidentified data. NRD is a convenience sample that is drawn from HCUP State Inpatient Databases and is poststratified to reflect the target universe of inpatient discharges treated at community hospitals in the United States that are not rehabilitation or long-term acute care facilities. The NRD database includes variables for sampling weights (DISCWT), hospital clusters (HOSP_NRD), and stratification (NRD_STRATUM).

Study Population

Adult patients (aged >18 years) who underwent TAVR between January 1, 2012, and December 31, 2017, were identified in the NRD using *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) and tenth revision (*ICD-10-CM*) codes (Table S1). To calculate the rate of new PPMI after TAVR during the index admission, patients with prior permanent pacemaker or internal cardioverter-defibrillator were excluded (Figure 1). In addition, to calculate the rate of PPMI after discharge, the following subgroups of patients were excluded: TAVRs performed in December were excluded from calculating 30-day postdischarge rate of PPMI; TAVRs performed in October through December were excluded from calculating 90-day postdischarge rate of PPMI; TAVRs performed in July through December were excluded from calculating 180-day postdischarge rate of PPMI. This approach was necessary because the NRD does not track patients across consecutive years.

Study End Point

The primary end point of this study was the temporal trend in the incidence of post-TAVR PPMI during the index hospitalization and at 30, 90, and 180 days beyond discharge. The secondary end points were the temporal trends in the association between PPMI and in-hospital mortality, stroke, cost, length of stay (LOS), and discharge disposition. This association was assessed across 3 equally divided time periods

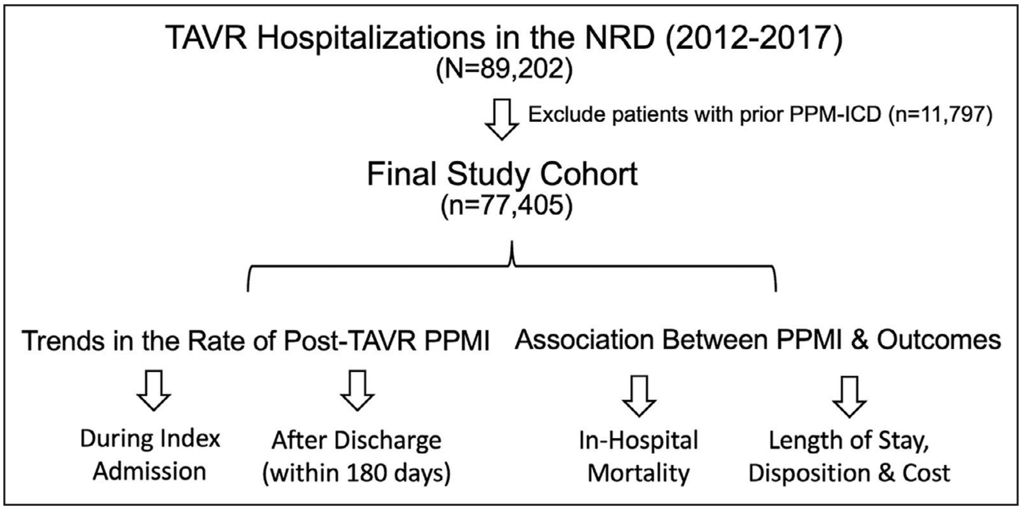

Figure 1. Study flow chart.
ICD indicates internal cardioverter-defibrillator; NRD, National Readmission Database; PPM, permanent pacemaker; PPMI, permanent pacemaker implantation; and TAVR, transcatheter aortic valve replacement.

(2012–2013, 2014–2015, 2016–2017). These periods roughly corresponded with the timeline of various generations of THVs introduced into the commercial market in the United States. We also described the baseline characteristics of patients who required PPMI after TAVR versus those who did not, trends of cardiac resynchronization therapy (CRT) utilization, and trends of annual expenditure related to post-TAVR PPMI in the United States.

Statistical Analysis

Descriptive statistics were presented as frequencies with percentages for categorical variables. Means, standard deviations, medians, and interquartile ranges were reported for continuous variables. Patient demographics, comorbidities, hospital characteristics, and in-hospital outcomes were compared between patients who needed PPMI after TAVR and those who did not, using the Pearson χ^2 test for categorical variables and independent-samples *t* test for continuous variables. We used the Cochrane-Armitage test for trend analyses of categorical variables (eg, incidence of post-TAVR PPMI over years) and as a sensitivity analysis for trends, and a logistic regression model was used as well; PPMI status was the outcome, and the calendar year was included in the model as a continuous variable. To assess the association between PPMI and in-hospital outcomes, we excluded patients who died within 24 hours of the TAVR procedure and those in whom the procedure was converted to open surgery. Excluding deaths that happened during the TAVR procedure or shortly after was necessary to avoid selection bias because the majority of the patients who died did not get a chance to receive a permanent pacemaker. To account for the differences in baseline characteristics between patients who received a PPMI and those who did not, risk adjustment for clinical risk factors and hospital characteristics was performed using mixed-effects logistic regression survey models. The Stata survey command was used in these models. This command considered the NRD sampling design (strata, hospital clusters, and post-stratification weights). Year was added to NRD strata and clusters. Dependent (outcome) variables included death, ischemic stroke, nonhome discharge, LOS, and costs. Mixed-effects models were used because of the clustering of the observations within hospitals. Logistic regression was used for binary outcomes (death, ischemic stroke, and nonhome discharge), and linear regression was used for continuous outcomes (LOS and costs). The independent variable of interest was the PPMI status. The models were adjusted for the following confounders, which are listed in Table S2: age, sex, diabetes mellitus, hypertension, peripheral vascular disease, carotid artery disease, chronic pulmonary disease, home oxygen use, prior sternotomy, anemia, prior history of stroke, atrial fibrillation, chronic kidney disease, smoking, dementia, Parkinson disease, calorie protein malnutrition, malignancy, obesity, liver cirrhosis, coronary artery disease, teaching status of the hospital, Medicare or Medicaid insurance, hospital bed size, household income quartile, elective admission, and TAVR access. NRD discharge weights were used to calculate national estimates. Covariates included in the risk adjustment models are listed in Table S2. Unadjusted and adjusted *P* values are reported. Hospital charges were obtained from the hospital accounting reports collected by the Centers for Medicare and Medicaid Services. The HCUP Cost-to-Charge ratio file was then used to calculate costs by multiplying the charges by the cost-to-charge ratio. Cost data were additionally adjusted for inflation using the Consumer Price Index (www.bls.gov); costs are reported in 2017 US dollars. Costs and LOS have a skewed distribution, so median and interquartile range are reported. LOS and total costs were transformed to the normal log scale and included in the multivariate linear model. However, given the large sample size, parametric tests (mean and linear regression) were also used as a sensitivity analysis based on the suggestion of Thompson and Barber[13] that these tests are also robust. A multivariable mixed-effects linear regression model was used to estimate the adjusted coefficient of cost, which can be interpreted as the adjusted difference in the average cost between both groups (OR indicates odds ratio): $\text{Percentage}_{case} = (\text{OR} \times \text{Percentage}_{control})/(1 + \text{OR} \times \text{Percentage}_{control} - \text{Percentage}_{control})$. Adjusted percentages were also calculated using the rate ratios obtained from a multivariable Poisson regression with robust error variance.[14–17] To evaluate the associations of PPMI–LOS and PPMI–cost across the 3 periods, we reran 4 models and included the interaction term between period and PPMI as an independent variable in each of them: (1) linear regression of LOS over PPMI status, period, and the interaction term between both; (2) linear regression of LOS over PPMI status, period, the interaction term, and all other confounders that are listed in Table S2; (3) linear regression of costs over PPMI status, period, and the interaction term between both; and (4) linear regression of the costs over PPMI status, period, the interaction term, and all other confounders that are listed in Table S2.

To calculate the total expenditure associated with PPMI during hospital admissions, we used the national weighted estimates of TAVR procedures and multiplied them by the mean difference in the cost of hospitalization between the PPMI and no PPMI groups per year. Some data were missing, particularly for hospital size. The remaining variables were largely complete with <5% missing. Because hospital size was not the focus of this study, it was not imputed using complex statistical methods. A type I error of <0.05 was considered statistically significant. All analyses were performed using SPSS v24 (IBM Corp), Microsoft Excel (2010), and STATA v15.1 (StataCorp).

RESULTS

A total of 89 202 unique hospitalizations for TAVR were identified in the NRD between January 1, 2012, and December 31, 2017. After excluding 11 797 patients with prior pacemaker or internal cardioverter-defibrillator, 77 405 were included in the assessment of the primary end point (Figure 1). Compared with patients who did not receive a PPMI, those who required post-TAVR PPMI were older (81.7±7.4 versus 80.1±8.6, *P*<0.001), were more likely to be male (54.8% versus 51.9%, *P*<0.001), and had higher prevalence of atrial fibrillation (43.6% versus 38.7%, *P*<0.001) and baseline conduction abnormalities (18.6% versus 7.6%, *P*<0.001). They also had higher rates of hypertension, diabetes mellitus, anemia, and chronic kidney disease (Table 1). The temporal change in baseline characteristics in both groups is shown in Table S3.

Incidence of Post-TAVR PPMI

The incidence of post-TAVR PPMI during the index admission increased from 8.7% in 2012 to a peak of 13.2% in 2015 before decreasing to 9.6% in 2017

Table 1. Baseline Characteristics of Patients With and Without Post-TAVR PPMI

Patient Characteristic	TAVR Without PPMI (n=69 527)	TAVR With PPMI (n=7878)	*P* Value
Age, y, mean±SD	80.1±8.6	81.7±7.4	<0.001
Male sex	51.9	54.8	<0.001
Diabetes mellitus	37.7	39.9	<0.001
Hypertension	62.1	64.9	<0.001
Peripheral vascular disease	23.1	22.5	0.20
Carotid artery disease	2.1	1.7	0.06
Chronic pulmonary disease	27.0	26.8	0.65
Home oxygen	5.6	5.4	0.57
Prior sternotomy	19.9	19.5	0.43
Anemia	24.2	26.3	<0.001
Prior history of stroke	9.9	9.1	0.02
Atrial fibrillation	38.7	43.6	<0.001
Conduction disorders	18.6	57.6	<0.001
Chronic kidney disease	34.5	38.6	<0.001
Dialysis dependence	2.5	3.2	<0.001
Smoking	11.7	12.0	0.54
Dementia	4.8	6.1	<0.001
Parkinson disease	1.3	1.2	0.40
Calorie protein malnutrition	2.2	2.4	0.37
Malignancy	5.7	5.8	0.82
Obesity	17.2	17.8	0.20
Liver cirrhosis	0.5	0.4	0.01
Coronary artery disease	67.5	68.6	0.04
Teaching hospital	54.0	60.1	<0.001
Medicare/Medicaid insurance	91.7	93.1	<0.001
Large hospital bed size	78.1	80.5	0.001
Lowest quartile household income	19.7	16.8	<0.001
Elective admission	78.6	75.6	<0.001
Transfemoral TAVR access	94.3	95.6	<0.001

Data are percentages except as noted. PPMI indicates permanent pacemaker implantation; and TAVR, transcatheter aortic valve replacement.

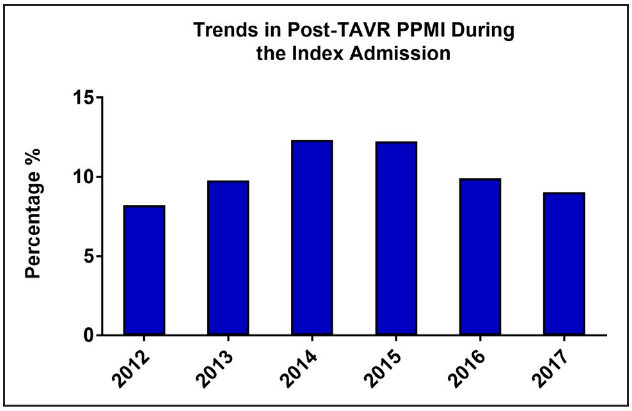

Figure 2. Temporal trend in the incidence of post-TAVR PPMI during the index admission between 2012 and 2017. PPMI indicates permanent pacemaker implantation; and TAVR, transcatheter aortic valve replacement.

(P_{trend}<0.001, logistic regression model P=0.045) (Figure 2). A minority of patients undergoing PPMI received CRT, and this did not change significantly over time (6.0% in 2012 to 6.4% in 2017, P_{trend}=0.66) (Figure 3). Notably, the incidence of inpatient post-TAVR PPMI within 30 days of hospital discharge increased significantly from 0.5% in 2012 to 1.25% in 2017 (P_{trend}<0.001) (Figure 4). This finding correlated with a temporal increase in the proportion of 30-day readmissions for conduction disturbances (among all 30-day readmissions post-TAVR) from 4.1% in 2012 to 12.0% in 2017 (Figure 5). PPMI beyond 30 days was uncommon overall (0.29% between 31 and 90 days, and 0.31% between 91 and 180 days), with no statistically significant temporal change (P_{trend}=0.07 and P_{trend}=0.89, respectively) (Figure 2).

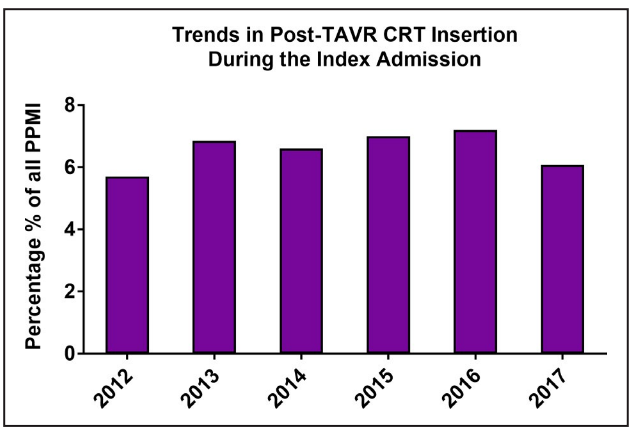

Figure 3. Utilization of CRT among patients undergoing post-TAVR PPMI in the United States between 2012 and 2017. CRT indicates cardiac resynchronization therapy; PPMI, permanent pacemaker implantation; and TAVR, transcatheter aortic valve replacement.

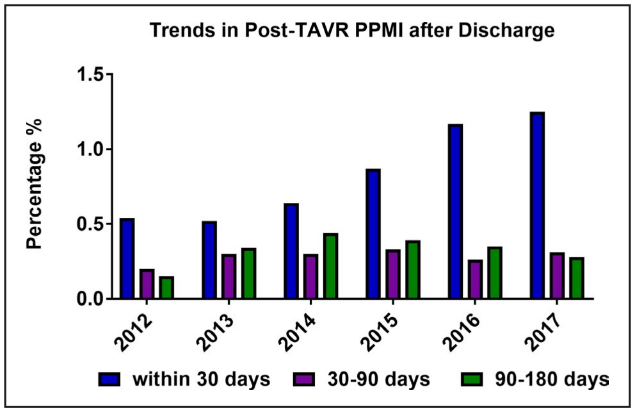

Figure 4. Temporal trend in the incidence of inpatient post-TAVR PPMI after discharge between 2012 and 2017. PPMI indicates permanent pacemaker implantation; and TAVR, transcatheter aortic valve replacement.

Association Between PPMI During the Index Admission and Outcomes

Patients who underwent PPMI had lower unadjusted in-hospital mortality compared with those who did not (1.8% versus 2.6%, P<0.001). However, they had higher unadjusted incidence of acute kidney injury, new dialysis, blood transfusion, tamponade, and mechanical ventilation (Table 2). PPMI was also associated with higher cost, longer hospitalizations, and higher rates of nonhome discharge (Table 2), and these associations were consistent over time (Table S4). Differences in baseline conduction disorder between patients with and without post-TAVR PPMI are listed in Table S5. After adjustment for risk factors and hospital characteristics, and exclusion of patients who had emergent surgery or who died within 24 hours of the procedure, PPMI was not associated with higher in-hospital mortality; the OR ranged between 0.61 (95% CI, 0.39–0.97) in 2016 to 2017 and 0.88 (95% CI, 0.67–1.16) in 2014–2015.

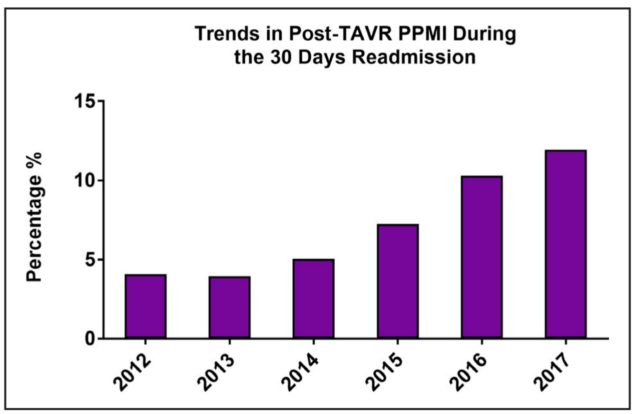

Figure 5. Proportion of 30-day readmissions for PPMI among all 30-day readmissions after TAVR. PPMI indicates permanent pacemaker implantation; and TAVR, transcatheter aortic valve replacement.

Table 2. Outcomes of Patients With and Without Post-TAVR PPMI

In-Hospital Outcome	TAVR Without PPMI (n=69 527)	TAVR With PPMI (n=7878)	*P* Value
Death	2.6	1.8	<0.001
Acute ischemia stroke	1.2	1.2	0.55
Acute kidney injury	13.1	19.0	<0.001
AKI requiring dialysis	1.0	1.2	0.048
Blood transfusion	12.0	15.1	<0.001
Vascular complication	3.7	3.8	0.45
Tamponade	0.9	1.6	<0.001
Gastrointestinal bleed	1.3	1.4	0.41
Mechanical ventilation	3.0	4.0	<0.001
Length of stay, median (IQR)	3 (2–7)	6 (4–9)	<0.001
Hospital cost, USD, median (IQR)	47 661 (37 304–62 244)	63 471 (50 925–80 709)	<0.001
Length of stay >5 d	31.9	51.8	<0.001
Discharged to a facility	16.6	27.3	<0.001

Data are percentages except as noted. AKI indicates acute kidney injury; IQR, interquartile range; PPMI, permanent pacemaker implantation; TAVR, transcatheter aortic valve replacement; USD, US dollars.

Moreover, there was no association between PPMI and the incidence of acute ischemic stroke (Table 3). Nevertheless, PPMI was associated with significantly higher odds of nonhome discharges. The adjusted OR for the association between PPMI and nonhome discharge increased from 1.48 (95% CI, 1.16–1.89) in 2012 through 2013 to 1.83 (95% CI, 1.62–2.07) in 2016 through 2017. In addition, the associations between PPMI and LOS and cost remained consistent over time (Table 4). The total estimated incremental expenditure associated with post-TAVR PPMI increased from $9.6 million in 2012 to $72.2 million in 2017 ($P_{trend}$<0.001) (Figure 6). The *P* values for the interaction terms were nonsignificant in all models. These findings suggest that the PPMI–LOS and PPMI–cost associations were consistent across periods.

DISCUSSION

The current investigation has 2 main findings. First, the incidence of post-TAVR PPMI during the index admission increased between 2012 and 2015 but decreased to a stable rate of ≈10% afterward. In contrast, the need for PPMI within 30 days after discharge, although it remained uncommon, increased by >2-fold between 2012 and 2017. Second, after risk adjustment, the need for PPMI after TAVR did not increase in-hospital morbidity or mortality. However, it did substantially increase the LOS, cost, and the need for an intermediate care facility. The total national expenditure on post-TAVR PPMI increased >7-fold between 2012 and 2017.

The demonstrable benefit of TAVR across all patient risk categories expanded its role to the majority of patients with aortic stenosis.[2,6] However, concerns remain about unresolved issues with TAVR such as the attendant risk of needing PPMI.[18] Consequently, a growing number of publications concerning post-TAVR PPMI are surfacing in the literature.[19] Although such studies have established the incidence, predictors, and outcomes of post-TAVR PPMI, they included heterogenous or selected cohorts of patients and often reached contradictory conclusions.[20–24] Nationwide surveys of post-TAVR PPMI remain scarce. The largest nationwide assessment of post-TAVR PPMI, from the Transcatheter Valve Therapeutics (TVT) registry, provided key insights into the issue of post-TAVR PPMI in the United States.[7] However, this study was limited to 9785 patients who received TAVR before September 2014, which does not represent contemporary practice. In addition, to our knowledge, no prior studies have assessed the timing of PPMI or the resource utilization and cost associated with it. Therefore, our study

Table 3. Association Between Post-TAVR PPMI and In Hospital Outcomes

Outcome	2012–2013		2014–2015		2016–2017	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Death						
Unadjusted	0.82 (0.55–1.24)	0.35	0.87 (0.67–1.14)	0.31	0.74 (0.54–1.02)	0.062
Adjusted	0.79 (0.46–1.37)	0.41	0.88 (0.67–1.16)	0.36	0.61 (0.39–0.97)	0.036
Ischemic stroke						
Unadjusted	0.74 (0.41–1.3)	0.32	0.81 (0.6–1.09)	0.16	1.1 (0.78–1.6)	0.53
Adjusted	0.76 (0.37–1.58)	0.46	0.82 (0.61–1.11)	0.21	1.39 (0.88–2.22)	0.16
Nonhome discharge						
Unadjusted	1.56 (1.29–1.88)	<0.001	1.55 (1.39–1.73)	<0.001	1.98 (1.83–2.14)	<0.001
Adjusted	1.48 (1.16–1.89)	0.001	1.51 (1.35–1.69)	<0.001	1.86 (1.64–2.09)	<0.001

OR indicates odds ratio; PPMI, permanent pacemaker implantation; and TAVR, transcatheter aortic valve replacement.

Table 4. Association Between Post-TAVR PPMI and Cost and Length of Stay

Outcome	2012–2013					2014–2015					2016–2017				
	PPMI	No PPMI	*P* Value	Adjusted Coefficient	*P* Value	PPMI	No PPMI	*P* value	Adjusted Coefficient	*P* Value	PPMI	No PPMI	*P* Value	Adjusted Coefficient	*P* Value
LOS,* median (IQR)	8 (6, 14)	6 (4, 11)	<0.001	NA	NA	6 (4, 10)	4 (3, 8)	<0.001	NA	NA	5 (3, 8)	3 (2, 5)	<0.001	NA	NA
LOS, mean (95% CI)	11.6 (10.8–12.5)	9.4 (9–9.9)	<0.001	1.9 (1.2–2.5)	<0.001	9.1 (8.5–9.7)	7.3 (6.9–7.6)	<0.001	1.7 (1.3–2.1)	<0.001	7 (6.6–7.4)	4.8 (4.7–5)	<0.001	1.8 (1.3–2.2)	<0.001
LOS (normal log scale)	2.08 (1.79–2.64)	1.79 (1.38–2.39)	<0.001	0.26 (0.21–0.3)	<0.001	1.79 (1.39–2.3)	1.39 (1.1–2.08)	<0.001	0.28 (0.25–0.32)	<0.001	1.61 (1.1–2.08)	1.1 (0.69–1.61)	<0.001	0.4 (0.35–0.45)	<0.001
Cost,** median (IQR)	67 744 (54 252, 88 916)	52 117 (40 445, 69 401)	<0.001	NA	NA	64 445 (51 458, 82 614)	49 864 (39 580, 65 625)	<0.001	NA	NA	62 169 (50 367, 78 344)	45 912 (36 120, 59 372)	<0.001	NA	NA
Cost, mean (95% CI)	74 399 (70 570–78 228)	58 905 (57 102–60 707)	<0.001	13 094 (9548–16 639)	<0.001	68 460 (65 687–71 233)	56 171 (54 410–57 933)	<0.001	12 396 (10 613–14 178)	<0.001	67 068 (64 782–69 354)	50 600 (49 140–52 059)	<0.001	15 368 (13 428–17 308)	<0.001
Cost (normal log scale)	11.19 (10.96–11.45)	10.92 (10.67–11.2)	<0.001	0.23 (0.18–0.28)	<0.001	11.11 (10.88–11.36)	10.85 (10.62–11.13)	<0.001	0.22 (0.2–0.25)	<0.001	11.08 (10.87–11.31)	10.78 (10.54–11.04)	<0.001	0.27 (0.25–0.3)	<0.001

Clinical covariates used for adjustment are listed in Table S2. In addition, cost data were adjusted for inflation. IQR indicates interquartile range; LOS, length of stay; NA, nonapplicable; PPMI, permanent pacemaker implantation; and TAVR, transcatheter aortic valve replacement.

* Days.

** US dollars.

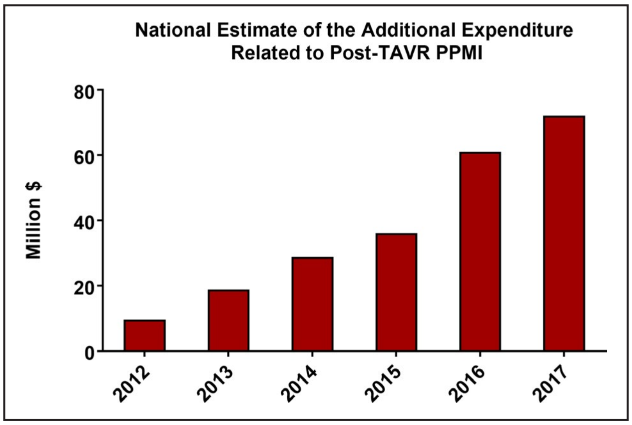

Figure 6. Annual expenditure associated with PPMI during the index admission after TAVR.
PPMI indicates permanent pacemaker implantation; and TAVR, transcatheter aortic valve replacement.

sought to reduce the knowledge gap on this increasingly important issue.

We found a temporal increase in the rate of post-PPMI after TAVR between 2012 and 2015 followed by a decline to a stable rate of ≈10% in 2016 to 2017. This initial observed increase was likely related to the introduction of the CoreValve (Medtronic) and Sapien-XT (Edwards Lifesciences) devices into the US market in January 2014 and June 2014, respectively. Both valves were associated with higher PPMI rates compared with Sapien, which was the only THV available in the United States before 2014.[7,25] Although speculative, the later decrease may have been related to the stabilization of the US market with a larger share of balloon versus self-expandable THVs and the adoption of procedural strategies that have been shown to reduce the risk of PPMI (eg, higher THV implantation).[9,26] The rates of PPMI after TAVR may have surged again in 2018 to 2019, given the dynamic change in the types and market share of THVs and the variable risk of PPMI associated with those valves.[27–30] For example, the approval of the Lotus THV (Boston Scientific) in April 2019 might affect the national post-TAVR PPMI, given that Lotus was associated with a 2-year PPMI rate of 41.7% in the pivotal trial (Repositionable Percutaneous Replacement of Stenotic Aortic Valve Through Implantation of Lotus™ Valve System - Randomized Clinical Evaluation).[31] These findings emphasize the need for continuous assessment of PPMI after TAVR, especially with the rising number of younger and low-risk patients receiving TAVR.

The timing of PPMI after TAVR has been an area of interest and ongoing debate, but little relevant data exist. The median time to PPMI after TAVR is ≈3 days in most studies.[22,32] In the TVT registry, >95% of PPMIs were performed within 14 days after TAVR, but the percentage of PPMIs during subsequent hospitalizations was not reported.[7] The distinction between PPMI during the index admission versus after discharge is critical in light of the growing literature on delayed post-TAVR heart block that is detected after discharge.[22,33,34] Our study showed a significant temporal increase in the incidence of PPMI within 30 days after discharge (0.5% in 2012 to 1.25% in 2017). Although small overall, this increase represented a tripling of the percentage of 30-day readmissions for PPMI (out of all 30-day readmissions) from 4% to 12%. Whether this is related to the shorter LOS in contemporary TAVR practice (ie, missed opportunity to detect late conduction disturbances in the hospital) or represents a device-specific effect, with some THVs tending to cause late conduction abnormalities, remains to be studied.[32] Nonetheless, these observations should raise awareness of delayed heart block after TAVR and prompt further investigations of its mechanisms and mitigation strategies such as remote monitoring with implantable or wearable devices.

The association between PPMI after TAVR and clinical outcomes has been studied previously.[7,21,35–39] Our population-based analysis confirms the findings of those prior smaller studies that showed no association between post-TAVR PPMI and short-term mortality or stroke. This observation was consistent across the study period. Unfortunately, Our study is unable to assess long-term impact of PPMI after TAVR because of the lack of long-term follow-up in the NRD. Nonetheless, the associations between PPMI and long-term mortality and heart failure hospitalizations after TAVR are well established.[7,36–39] A potentially relevant observation that may be pertinent to long-term outcomes in our study is the utilization of CRT. Cardiac resynchronization has been suggested as a potential strategy to reduce the negative long-term impact of PPMI among patients as PPMI dependability has increased.[21,40] We found that a very small percentage (≈6%) of patients undergoing PPMI following TAVR receive CRT, and this percentage was consistent over time. Whether this is due to the patient's specific characteristics, the lack of data supporting the role of CRT among patients who receive TAVR, or the potential incremental financial loss with CRT, given that PPMI after TAVR are not separately reimbursable, remains unknown. With the continuous expansion of TAVR to lower risk and younger patients, the role of various pacing modalities (single-chamber, wireless, and CRT pacemakers) needs to be further investigated.

The impact of PPMI on resource utilization and cost after TAVR is increasingly relevant in light of anticipated Medicare payment cuts and the growing number of TAVR procedures at the site level and nationally.[41] However, few data exist regarding the economic impact of post-TAVR PPMI. Our study documented a substantial impact of post-TAVR PPMI on

LOS, cost, and discharge disposition, and this impact was consistent over time. Specifically, post-TAVR PPMI was associated with a 48% to 86% increase in nonhome discharge, ≈2-day increase in LOS, and a $12 000 to $15 000 incremental cost after adjustments for clinical covariates, hospital characteristics, and inflation. This cost increase translated into a cost of ≈$72 million in 2017 for index TAVR hospitalizations alone. The true overall cost associated with PPMI is likely higher because these cost figures do not include PPMIs at subsequent visits, the cost related to the increase in intermediate care facility utilization, and the increased number of heart failure hospitalizations that has been shown for patients with post-TAVR PPMI in prior studies.[7,37–39] These data highlight the need for long-term cost analyses, especially with the increasing number of TAVR procedures and the availability of various THVs with varied associated PPMI risks.[42]

Limitations

First, the NRD is a claim-based database. Data provided by the NRD are collected mainly for billing purposes and thus are prone to the pitfalls of under- or overcoding. However, coding of procedures, vital status, and major complications is essential for adequate reimbursement by hospitals and are less prone to major errors. Second, the NRD does not track patients across different years. Consequently, we are unable to identify patients who underwent subsequent PPMI during prolonged follow-up. However, our findings suggest that the vast majority of PPMIs after TAVR occur either during the index admission or within 30 days after discharge; therefore, this limitation is unlikely to have a large impact on our results. Third, the NRD includes only inpatient visits, and PPMI that occurs during encounters that are coded as observational and/or outpatient are not captured. Fourth, the NRD does not contain essential granular data related to the electrophysiologic findings or the indication for the PPMI. As a result, description of post-TAVR conduction abnormalities that might have led to the PPMI (eg, high degree of atrioventricular blockage, bifascicular or trifascicular block) could not be performed. In addition, some selection bias may exist because the threshold to proceed with PPMI may vary among different operators. However, this limitation also applies to all registry-based studies addressing post-TAVR PPMI. Fifth, data on valve type are not available in the NRD; therefore, we could not study the association between self- or balloon-expandable valves and PPMI. Nonetheless, this association is well established in the literature.[43] Because our study did not aim to specifically assess predictors of PPMI after TAVR, we believe that this limitation has little impact on the overall findings. Further studies assessing the temporal impact of THV selection on PPMI incidence and outcomes are needed to address this issue.

CONCLUSIONS

The incidence of PPMI following TAVR in the United States increased significantly between 2012 and 2015 but stabilized at ≈10% afterward. However, a small but significant temporal increase in PPMI beyond the index TAVR admission was observed. PPMI was not associated with increased risk-adjusted morbidity or mortality but led to longer hospitalizations, higher cost, and more nonhome discharges.

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Supplementary Materials

Tables S1–S5

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Supplemental Material

Table S1. List of the Key International Classification of Diseases, 9th & 10th Revisions, Clinical Modification Codes Used in the Study.

Transcatheter Aortic Valve Replacement

ICD-9-CM 35.05, 35.06

ICD-10-CM 02RF3JZ, 02RF3KZ, 02RF38Z, 02RF37Z, 02RF3JZ, 02RF37H, 02RF38H, 02RF3JH, 02RF3KH

History of Prior Pacemaker/ICD:

Prior Pacemaker

ICD-9-CM V45.01, ICD-10-CM Z950

Prior Defibrillator

ICD-90CM V45.02, ICD-10-CM Z95810

History of Conduction Disorder:

ICD-9-CM 42613, 4264, 4263, 42653, 4260, 4269

ICD-10-CM I444, I445, I4460, I4469, I447, I450, I4510, I4519, I452, I453, I454, I4589, I459

New Permanent Pacemaker Implantation:

ICD-9-CM 37.80, 37.81, 37.82, 37.83

ICD-10-CM 0JH604Z, 0JH634Z, 0JH804Z, 0JH834Z, 0JH605Z, 0JH635Z, 0JH805Z, 0JH835Z, 0JH606Z, 0JH636Z, 0JH806Z, 0JH836Z

New Cardiac Resynchronization Therapy:

ICD-9-CM 00.50, 00.51

ICD-10-CM 0JH607Z, 0JH637Z, 0JH807Z, 0JH837Z, 0JH609Z, 0JH639Z, 0JH809Z, 0JH839Z

Table S2. Covariates used for Risk Adjustment for Outcomes in Patients with or without Post-TAVR PPMI.

Age	Dementia
Sex	Parkinson disease
Diabetes mellitus	Calorie protein malnutrition
Hypertension	Malignancy
Peripheral vascular disease	Obesity
Carotid artery disease	Liver cirrhosis
Chronic pulmonary disease	Coronary artery disease
Home oxygen	Teaching hospital
Prior sternotomy	Medicare/Medicaid insurance
Anemia	Large hospital bed size
Prior history of stroke	Lowest quartile household income
Atrial fibrillation	Elective admission
Chronic kidney disease	TAVR access
Smoking	

TAVR; transcatheter aortic valve replacement, PPMI; permanent pacemaker implantation

Table S3. Trends in Baseline characteristics of patients with and without post-TAVR PPMI.

Patient Characteristics	2012-2013			2014-2015			2016-2017		
	TAVR without PPMI (n=7,684)	TAVR with PPMI (n=779)	P-value	TAVR without PPMI (n=18,882)	TAVR with PPMI (n=2,642)	P-value	TAVR without PPMI (n=42,961)	TAVR with PPMI (n=4,457)	P-value
Age years, mean ± SD	80.8±9.3	83.0±7.4	<0.001	80.5±8.7	82.1±7.3	<0.001	79.7±8.4	81.2±7.4	<0.001
Male (%)	49.7%	52.2%	0.176	51.2%	53.7%	0.014	52.6%	55.9%	<0.001
Diabetes mellitus	33.2%	32.9%	0.861	36.6%	37.4%	0.403	39.1%	42.7%	<0.001
Hypertension	78.0%	77.0%	0.517	72.3%	73.5%	0.193	54.8%	57.7%	<0.001
Vascular disease	31.0%	28.4%	0.126	27.9%	25.3%	0.006	19.6%	19.8%	0.816
Carotid artery disease	2.0%	1.2%	0.089	2.0%	1.5%	0.049	2.1%	2.0%	0.793
Chronic lung disease	34.9%	30.2%	0.008	31.8%	31.2%	0.517	23.5%	23.6%	0.914
Home oxygen	6.7%	5.3%	0.113	6.0%	6.2%	0.668	5.2%	5.0%	0.589
Prior sternotomy	21.7%	22.8%	0.441	21.2%	18.5%	0.001	19.0%	19.5%	0.375
Anemia	25.9%	27.0%	0.515	24.3%	25.5%	0.178	23.8%	26.6%	<0.001
Prior history of stroke	6.7%	5.3%	0.113	7.1%	7.1%	0.925	11.7%	11.0%	0.169
Atrial fibrillation	42.3%	47.1%	0.009	40.3%	45.3%	<0.001	37.3%	42.0%	<0.001
Conduction disorders	11.4%	75.9%	<0.001	17.6%	78.5%	<0.001	20.4%	42.0%	<0.001
Chronic kidney disease	34.2%	38.1%	0.028	34.6%	38.1%	<0.001	34.5%	39.0%	<0.001
Dialysis dependence	2.8%	2.6%	0.739	2.9%	3.7%	0.038	2.3%	3.0%	0.003
Smoking	22.7%	21.8%	0.590	23.5%	23.2%	0.741	4.6%	3.6%	0.002
Dementia	4.6%	5.0%	0.638	4.9%	5.9%	0.021	4.7%	6.4%	<0.001
Parkinson disease	1.5%	2.2%	0.132	1.4%	1.4%	0.977	1.3%	0.9%	0.058
malnutrition	5.2%	6.7%	0.071	3.6%	3.0%	0.110	1.0%	1.2%	0.302
Malignancy	4.3%	3.6%	0.380	4.6%	4.2%	0.382	6.4%	7.0%	0.117
Obesity	13.7%	13.4%	0.808	16.6%	16.9%	0.643	18.1%	19.1%	0.118
Liver cirrhosis	0.6%	0.5%	0.869	0.6%	0.5%	0.316	0.5%	0.3%	0.136
Coronary artery disease	65.1%	64.7%	0.819	67.2%	66.7%	0.575	68.0%	70.5%	0.001
Teaching hospital	56.2%	60.8%	0.014	90.9%	93.5%	<0.001	37.3%	40.2%	<0.001
Medicare/Medicaid	91.6%	91.8%	0.418	91.7%	92.8%	0.056	91.8%	93.5%	<0.001
Large hospital bed size	81.5%	82.9%	0.152	77.8%	80.0%	0.022	77.6%	80.4%	0.011
Lowest quartile income	20.1%	16.8%	0.006	19.6%	16.2%	<0.001	19.7%	17.1%	<0.001
Elective admission	74.8%	72.5%	0.159	78.1%	76.0%	0.016	79.5%	75.9%	<0.001
Transfemoral TAVR	73.5%	77.7%	0.012	89.9%	92.8%	<0.001	97.4%	97.7%	0.159

TAVR; transcatheter aortic valve replacement; PPMI; permanent pacemaker implantation, SD; standard deviation.

Table S4. Trends in the Outcomes of Patients with and without Post TAVR PPMI.

In-Hospital Outcomes	2012-2013			2014-2015			2016-2017		
	TAVR without PPMI (n=7,684)	TAVR with PPMI (n=779)	P-value	TAVR without PPMI (n=18,882)	TAVR with PPMI (n=2,642)	P-value	TAVR without PPMI (n=42,961)	TAVR with PPMI (n=4,457)	P-value
Died	5.3%	3.9%	0.090	3.3%	2.4%	0.016	1.8%	1.1%	0.002
Acute ischemia stroke	2.6%	1.9%	0.277	2.0%	1.6%	0.217	0.7%	0.8%	0.572
Acute kidney injury	19.6%	26.2%	<0.001	15.7%	20.1%	<0.001	10.8%	17.0%	<0.001
AKI requiring dialysis	1.8%	2.1%	0.608	1.3%	1.6%	0.249	0.7%	0.8%	0.239
Blood transfusion	27.7%	31.7%	0.018	15.3%	17.9%	0.001	7.7%	10.4%	<0.001
Vascular complication	5.4%	4.5%	0.263	3.8%	3.9%	0.798	3.3%	3.7%	0.169
Tamponade	1.0%	1.2%	0.657	1.1%	1.4%	0.091	0.8%	1.7%	<0.001
Gastrointestinal bleed	1.3%	1.3%	0.960	1.5%	1.4%	0.616	1.2%	1.5%	0.172
Mechanical ventilation	3.4%	4.7%	0.048	2.5%	3.0%	0.167	3.1%	4.6%	<0.001
Length of stay (day) *median, 25th-75th per.*	3 2-5	5 3-8	<0.001	4 3-8	6 4-10	<0.001	3 2-5	5 3-8	<0.001
Hospital cost (US $) *median, 25th-75th per.*	45,970 36,149-59,482	62,211 50,372-78,580	<0.001	49,903 39,590-65,640	64,457 51,483-82,622	<0.001	45,970 36,149-59,482	62,211 50,372-78,580	<0.001
Length of stay >5 days	59.0%	80.2%	<0.001	40.2%	58.7%	<0.001	23.4%	42.8%	<0.001
Discharged to a facility	29.2%	40.4%	<0.001	21.3%	30.1%	<0.001	12.3%	23.3%	<0.001

TAVR; transcatheter aortic valve replacement, PPMI; permanent pacemaker implantation, AKI; acute kidney injury, US; United States.

Table S5. Conduction abnormalities of Patients with and without Post-TAVR PPMI.

Patient Characteristics	TAVR without PPMI (n=69,527)	TAVR with PPMI (n=7,878)	P-value
Left bundle branch block	9.4%	11.3%	<0.001
Right bundle branch block	2.4%	8.6%	<0.001
1st Degree AV block	3.5%	4.6%	<0.001
2nd Degree AV block	0.6%	4.5%	<0.001
Left anterior fascicular block	0.2%	0.5%	<0.001
Left posterior fascicular block*	NA		
Right fascicular block*	NA		
Bifascicular block	0.9%	4.9%	<0.001
Trifascicular block	0.1%	1.0%	<0.001
Non-specific AV node block	0.5%	1.4%	<0.001
Any type at or below AV node	15.3%	28.4%	<0.001

TAVR; transcatheter aortic valve replacement, PPMI; permanent pacemaker implantation, AV; atrioventricular

* numbers less than 10 are not reportable to comply with the HCUP guidelines