BRIEF REPORT

Incidence and predictors of cardiomyopathy after implantation of leadless pacemakers: A comparative analysis with patients with transvenous systems

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Introduction

Pacing-induced cardiomyopathy (PICM) is a known complication in patients with permanent pacemakers (PPMs), typically occurring in patients with high right ventricular pacing burden. The introduction of the leadless pacemaker (LP) has eliminated pocket- and lead-related complications, but limited data are available on the incidence of PICM in the population with LPs and how this incidence compares to that of patients with transvenous pacemakers (TVPs).[1,2] With this retrospective analysis, we sought to report the differences in PICM from a cohort where all implantation procedures were performed within the same health care system in the modern era.

Methods

Population

Patients implanted with either LPs or TVPs in 1 of 8 hospitals of Northwell Health between January 2015 and December 2021 were identified. Patients with a baseline left ventricular ejection fraction (LVEF) of $<50\%$ and a history of myocardial infarction or coronary artery bypass graft were excluded.

Data gathering

Medical history, using international classification of diseases, 10th revision codes, and baseline demographic data were obtained from our electronic medical record system. The medical records of patients identified were then manually reviewed for baseline echocardiogram within 6 months before implantation, follow-up echocardiogram at least 1 year postimplantation, pacing indications, and clinical outcomes during the perioperative period and during follow-up. In addition, we manually reviewed the 12-lead electrocardiograms (ECGs) and calculated native and pacing QRS widths, as well as the postoperative chest radiograph to determine the location of the pacing bipole. The baseline QRS width was taken from an ECG within 6 months before implantation. The width was taken from an escape beat only if there were no other ECGs from this period showing a beat conducted through the atrioventricular node. Pacing percentages for LPs were pulled from the Medtronic datamart, and those for TVPs were pulled through the common health system device monitoring platform. Patients from the LP or TVP group missing the above data were excluded from the study.

KEY FINDINGS

- Pacing-induced cardiomyopathy (PICM), associated with high pacing burden, is a known complication in patients with permanent pacemakers.
- We conducted a retrospective study examining baseline and follow-up echocardiograms, and we found that there was no significant difference in the incidence of PICM between the 2 groups, with 13% and 12% of patients developing cardiomyopathy in the leadless pacemaker (LP) and transvenous pacemaker (TVP) groups, respectively.
- Predictors for the development of PICM were chronic kidney disease, wide baseline QRS width, and medical history of congestive heart failure.
- Although there were similar overall complications in both groups, there were fewer reinterventions in the LP group.
- Our study further reveals the safety of LPs, which may be a better option than TVPs in patients without sinus node dysfunction and who are at high risk for periprocedural complications.

KEYWORDS Pacemaker-induced cardiomyopathy; Leadless pacemaker; Permanent pacemaker; Cardiomyopathy; Pacemaker implantation (Heart Rhythm O^2 2024;5:597–600)

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Comparator study groups and outcome measures

After identifying patients with LPs meeting the inclusion and exclusion criteria, we randomly selected patients with TVPs implanted during the same period in a 3:1 ratio.

Our primary end point was the development of PICM defined as a decline in LVEF by ≥10% and with an absolute LVEF of <50%. Patients who met the primary end point were manually adjudicated to rule out alternative etiologies for cardiomyopathy. The secondary end points were device-related complications and mortality.

Statistical analysis

Baseline clinical and demographic variables were compared using the Wilcoxon *T* test (continuous) or Fisher exact test (categoric). Patients were grouped on the basis of the type of device into 2 groups: LP and TVP. We constructed a logistic regression model for the development of cardiomyopathy as a function of age, sex, diabetes, history of congestive heart failure (CHF), hypertension, QRS width at baseline, QRS width postimplantation, lead location, and pacing location. Finally, we constructed a Cox regression model for all-cause mortality, and a 2-sided *P* value of <.05 was used as a measure of statistical significance. R version 4.0.0 (2023) and STATA (Stata/IC 16.1, StataCorp LP, College Station, TX) were used to perform statistical analysis.

Results

Study population

The final study population consisted of 223 patients, 61 in the LP group and 162 in the TVP group. Of the 61 patients with LPs, 41 had Micra VR devices and 20 had Micra AV devices. In the TVP group, 143 had dual-chamber PPMs and 19 had single-lead PPMs. The only statistically significant difference in baseline characteristics between the 2 groups was sex (37% vs 51% female in the LP vs TVP group, respectively; $P = .04$). The percentage of patients with QRSd > 120 ms was 32.35% ($P = .72$). Of the patients with QRSd > 120 ms, 60% had right bundle branch block, 27.1% had left bundle branch block, and 12.9% had intraventricular conduction delay. Regarding lead location, apical bipole implantation occurred earlier in the study period. Demographic and clinical characteristics stratified by study group are displayed in Table 1.

Table 1 Baseline demographic characteristics, characteristics, and medical history

Clinical characteristic	TVP (n = 162)	LP (n = 61)
Age at implantation (y)	79 (73–85)	79 (72–85)
Sex: female	86 (51.5%)	23 (37.7%)
Race		
White	125 (77%)	52 (85%)
African American	14 (8.6%)	2 (3.2%)
Asian	5 (3%)	1 (1.6%)
Native American	1 (0.6%)	0 (0.0%)
Other	15 (9%)	4 (6%)
BMI (kg/m^2)	27.4 (24.1–31.2)	28.0 (24–33)
CAD	73 (45%)	31 (51%)
CHF	49 (30%)	24 (39%)
HTN	125 (77%)	56 (91%)
DM	52 (32%)	16 (26%)
CKD	23 (14%)	6 (10%)
Stroke or TIA	21 (13%)	5 (9%)
LVEF at baseline (%)	63 (57–67)	63 (57–75)
Implant indication		
SND	77 (47.5%)	16 (26.2%)
AV node dysfunction	77 (47.5%)	34 (55.7%)
Unspecified AV conduction disease	8 (5.0%)	11 (18.0%)
nQRS (ms)	102 (90–126)	103 (96–133)
pQRS (ms)	157.5 (143–173)	162 (146–173)
Implant location		
Apical	110 (67.9%)	14 (23.0%)
Septal	52 (32.1%)	47 (77.0%)

Values are presented as median (interquartile range) or percentage.

AV = atrioventricular; BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; CKD = chronic kidney disease; DM = diabetes mellitus; HTN = hypertension; LP = leadless pacemaker; LVEF = left ventricular ejection fraction; nQRS = native QRS duration; pQRS = paced QRS duration; SND = sinus node dysfunction; TIA = transient ischemic attack; TVP = transvenous pacemaker.

Complications

Overall, the rate of acute procedural complications was 3.28% in the LP group compared with 1.23% in the TVP group ($P = .50$), which included 2 hematomas in both groups. There were no chronic complications recorded in the LP group as compared with 1 microperforation with pericardial effusion and 2 revisions due to malfunction or infection in the TVP group.

Clinical outcomes

In total, 12.1% of our patients developed cardiomyopathy in the span of 3 years. The percentage of cardiomyopathy in the LP group was 13% (8 of 61) vs 12% in the TVP (19 of 162) ($P = .77$). On average, LVEF decreased to 26% in those with LPs who developed PICM compared with 22% in those with TVPs. The change in LVEF 1 year postimplantation for both the TVP and LP groups is presented in Figure 1. Those in the LP group were pacing, on average, 50% compared with 37% in the TVP group ($P = .03$). In the TVP group, 64 (38%) paced, on average, over 40% compared with 34 (55%) in the LP group ($P = .03$).

In a multivariate approach, the 2 factors that were independently associated with the development of cardiomyopathy were prolonged baseline QRS width (odds ratio [OR] 5.36; 95% confidence interval [CI] 1.39–20.70; $P = .015$) and a history of CHF (OR 3.53; 95% CI 1.00–12.40; $P = .049$) (Table 2). Cox regression analysis showed no difference in PICM between the leadless and control groups (Figure 2). There were 4 deaths from any cause (6%) in the TVP group compared with 21 (12%) in the LP group ($P = .177$).

Discussion

In a highly selective cohort consisting of patients within a large health care system with all implantation procedures performed in the current era, we report that the incidence of unexplained cardiomyopathy after pacemaker implantation was

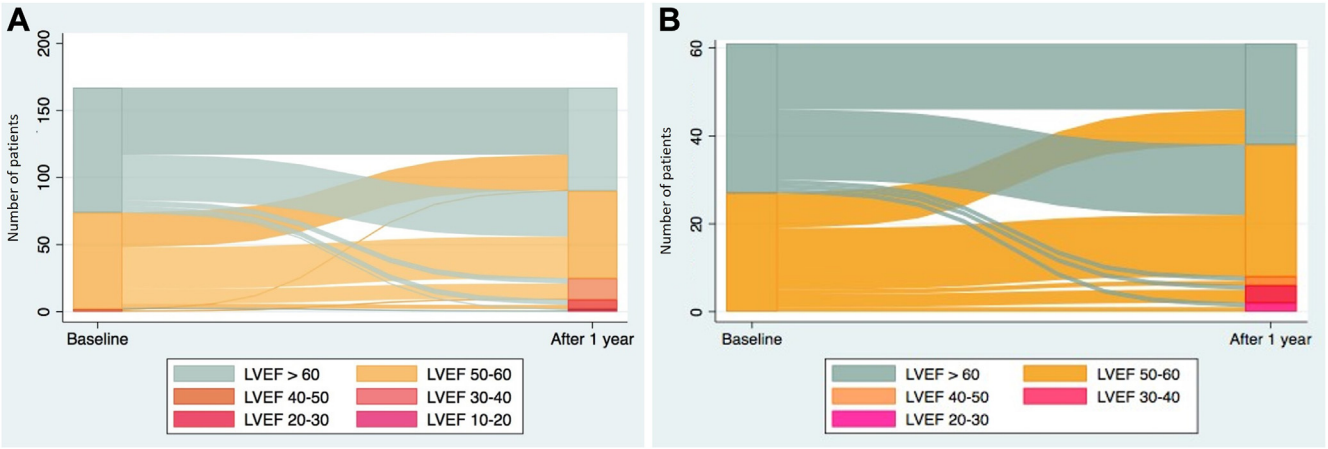

Figure 1 Development of pacing-induced cardiomyopathy from baseline to 1 year postimplantation in the (**A**) transvenous pacemaker group and (**B**) leadless pacemaker group. LVEF = left ventricular ejection fraction.

not significantly different between patients with TVPs and those with LPs after adjusting for known predictors of PICM, including lead location and percent pacing. The cardiomyopathy incidence observed in our study is likely an overestimation because of the inherent selection bias of a retrospective study. As routine echocardiographic evaluation a year after pacemaker implantation is not a standard practice in our institution, patients included in the analyses had a clinical indication to undergo echocardiography. Therefore, we cannot ascertain the true incidence of PICM in this population. However, this selection bias affects both groups equally. Although comparable incidence rates of PICM have been reported in patients with transvenous systems, 12.3%–16.1%, the most recent data from the Micra post-approval registry revealed a lower PICM incidence of 0.3% in patients with leadless systems.[3–6] This is lower than what we found in our study and what is reported by a similar study by Sanchez et al,[4] our results offer an estimate of the real-world incidence of PICM in a diverse health system.

Table 2 Multivariate analysis assessing independent predictors of PICM in LP and TVP groups combined

Variable	OR	95% CI	*P*
TVP vs LP	2.80	0.43–18.4	.282
Age	1.03	0.96–1.10	.468
Sex: male	0.40	0.11–1.43	.160
Race	0.87	0.64–1.18	.366
BMI	0.94	0.85–1.05	.267
Baseline LVEF	1.00	0.91–1.09	.94
CAD	0.77	0.022–2.65	.672
HTN	0.69	0.12–3.82	.671
DM	1.22	0.33–4.5	.766
CKD	4.10	0.83–20.4	.084
CHF	3.53	1.00–12.4	.049
nQRS > 120 ms	5.36	1.39–20.7	.015
pQRS	0.99	0.97–1.0	.981
Pacing > 40%	0.24	0.03–1.74	.159

BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; CI = confidence interval; CKD = chronic kidney disease; DM = diabetes mellitus; HTN = hypertension; LP = leadless pacemaker; LVEF = left ventricular ejection fraction; nQRS = native QRS duration; OR = odds ratio; PICM = pacing-induced cardiomyopathy; pQRS = paced QRS duration; TVP = transvenous pacemaker.

The only predictors in the development of cardiomyopathy were a history of CHF and a QRSd > 120 ms, which has been reported as a predictor of PICM by Khurshid et al.[7] A meta-analysis by Somma et al[8] found for every 1% increase in baseline LVEF, there was a reduced risk of PICM (OR 0.95; 95% CI 0.93–0.97; $P < .001$).[8] Similarly, our analysis found that a history of CHF as a predictor of PICM. Patients with a history of heart failure likely had a preserved LVEF, though they may have had a reduced LVEF at some point that recovered before implantation. These patients may have had more frequent echocardiographic evaluation and opportunities for diagnosing PICM because of their medical history, which is a limitation of our study as mentioned above. Another limitation of our study is that we did not factor in the use of algorithms to reduce right ventricular pacing, which would be important in future analyses, given the relationship between increased pacing burden and cardiomyopathy.[3,7,9]

A prevalent clinical practice is the preferential selection of LPs in patients with relatively short life expectancy and high infectious risk because of the proven low infectious long-term risk and decreased incidence of acute procedural complications associated with LPs.[10–12] This is reflected by our cohort and others, where LPs are chosen over TVPs, even for primary sinus node dysfunction. Such practice leads to unnecessary ventricular pacing with various degrees of fusion between conducted and paced beats that worsens ventricular dyssynchrony and increases the risk of cardiomyopathy.[13–15] Management options for patients with LPs and PICM are limited, as the concerns of device-related risks of implantation of a resynchronization device are the same or even greater than during the initial implantation. This difference is evident in the high all-cause mortality observed in the LP group.

Conclusion

Our comparative analysis suggests that the development of cardiomyopathy in patients with LPs is not negligible, and

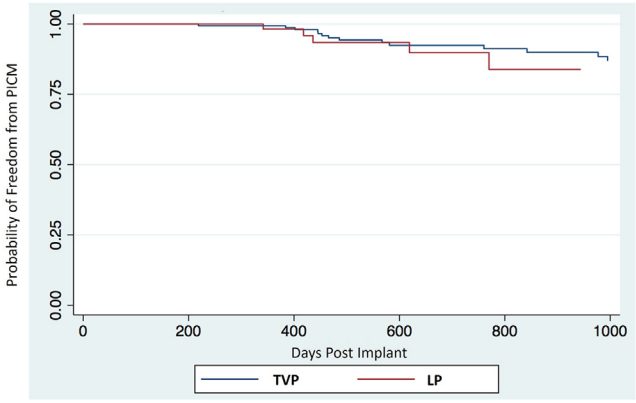

Figure 2 Kaplan-Meier curve depicting freedom from development of pacing-induced cardiomyopathy (PICM) over time (days postimplantation) in the transvenous pacemaker (TVP) and leadless pacemaker (LP) groups ($P = .72$).

therefore this risk should be weighed against the lower periprocedural and infectious risks associated with an LP, especially for patients requiring atrial pacing.

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Patient Consent: The Northwell Health Human Research Protection Program approved the study through expedited approval and a waiver of consent was obtained.

Ethics Statement: This study was approved by the Northwell Health Human Research Protection Program (21-1290).

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