ESC HEART FAILURE
ESC Heart Failure 2019; **6**: 686–693
Published online 20 May 2019 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.12445

ORIGINAL RESEARCH ARTICLE

Post-pacemaker implant QRS duration and heart failure admission in patients with sick sinus syndrome and complete atrioventricular block

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Abstract

Aims High demand right ventricular pacing may elicit left ventricular systolic dysfunction known as pacing-induced cardiomyopathy, increasing the risks of heart failure (HF) hospitalization. Percentage of demand ventricular pacing is different between patients with sick sinus syndrome (SSS) and those with complete atrioventricular block (CAVB). This study aims to compare the incidence of HF admission and pacing-induced cardiomyopathy between patients with SSS and CAVB.

Methods and results A total of 824 patients who received single ventricular or dual-chamber pacemaker implantation at our hospital between January 2003 and December 2012 were recruited for the study. Patients with HF, those without complete cardiac echocardiography, and those with significant coronary artery disease were excluded. Finally, 315 patients with SSS and 289 patients with CAVB were enrolled in this study. The CAVB group had a higher pacing percentage (39.37 ± 9.17% vs. 83.82 ± 33.06%; $P < 0.001$), longer pacing QRS duration (142.56 ± 33.02 ms vs. 156.63 ± 25.18 ms; $P < 0.001$), and higher prevalence of follow-up left ventricular ejection fraction ≤40% (1.3% vs. 4.2%; $P = 0.040$). However, the incidence of HF admission was similar between the two groups (log-rank $P = 0.647$). Age [hazard ratio (HR), 95% confidence interval (CI): 1.121, 1.054–1.193], diabetes mellitus (HR, 95% CI: 2.667, 1.159–6.136), pacing QRS duration ≥163 ms (HR, 95% CI: 3.506, 1.491–8.247), and left atrial size (HR, 95% CI: 1.070, 1.012–1.131) were independent predictors of HF admission. The Kaplan–Meier curve showed a significant difference in HF admission over a 3.5 year follow-up period (3.5 years: P value = 0.004; 5 years: P value = 0.002) between patients with pacing QRS duration ≥163 and <163 ms.

Conclusions There was no difference in HF admission between patients with SSS and CAVB, although the CAVB group had a higher pacing percentage. Post-pacemaker implant pacing QRS duration ≥163 ms was the most important predictor of HF admission.

Keywords Pacing-induced cardiomyopathy; Heart failure admission; Longer pacing QRS duration; Sick sinus syndrome; Complete atrioventricular block

Received: 19 November 2018; Accepted: 9 April 2019
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Introduction

An ageing population with increasing prevalence of symptomatic bradycardia will result in an increase in the number of cardiac device implantations worldwide.[1] The development of artificial permanent pacemakers (PPMs) for electrical control of cardiac rhythm has greatly enhanced a physician's ability to treat cardiac dysrhythmias including sick sinus syndrome (SSS) and complete atrioventricular block (CAVB) and reduced cardiac morbidity and mortality related to symptomatic bradycardia.[2] However, chronic right ventricular (RV) pacing-related pacing-induced cardiomyopathy (PICM) has a

potentially deleterious effect on left ventricular (LV) performance.[3,4] According to previous reports, pacing anatomical site, pacing percentage, and pre-implantation LV performance affect the occurrence of PICM and its subsequent clinical outcomes.[5–7] However, the mechanisms of PICM remain controversial because only a small subset of patients exposed to frequent RV pacing develop PICM.[4]

In one recent report, Kiehl *et al*. reported that PICM is common among patients receiving PPM for CAVB with preserved LV ejection fraction (LVEF) and is strongly associated with an RV pacing burden >20%.[8] Others reported that patients with a pacing QRS duration ≥150 ms should be screened using echocardiography to assess for PICM if the RV pacing percentage is >20%.[9] However, many studies have focused on patients with CAVB because of the high pacing percentage in these patients and have reported mainly on the risk factors for PICM. Until now, only a few studies have investigated the incidence of PICM and heart failure (HF) admission among patients with SSS and in the whole population with PPM. Accordingly, this study aimed to explore the difference in HF admission and PICM between patients with SSS and CAVB. In addition, this study also examined the impact of different pacing percentages and pacing QRS durations on HF admission and PICM between patients with SSS and CAVB.

Methods

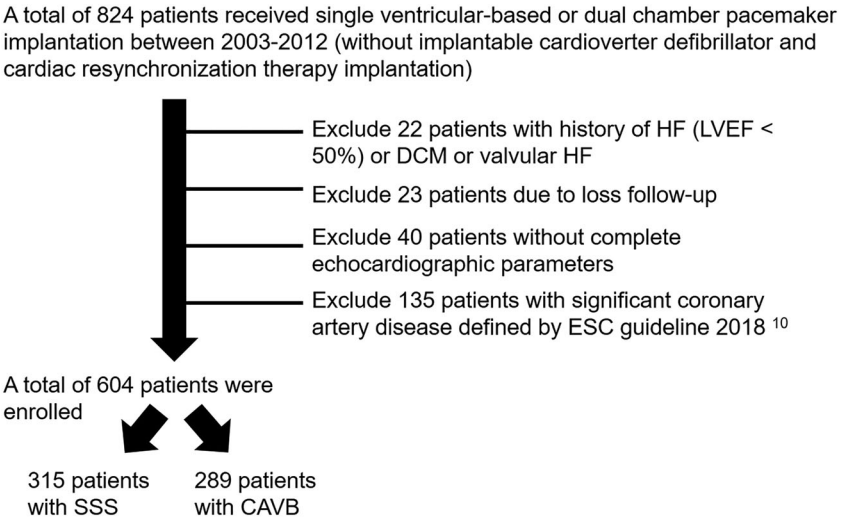
Patient population

A total of 824 patients who underwent single ventricular or dual-chamber PPM implantation at our hospital between January 2003 and December 2012 were recruited for this study after excluding patients with an implantable cardioverter defibrillator and those undergoing cardiac resynchronization therapy (CRT). Furthermore, 22 patients with a history of HF and LVEF <50%, dilated cardiomyopathy, or valvular heart disease; 23 patients without follow-up records for PPM; 40 patients without complete cardiac echocardiography; and 135 patients with significant coronary artery disease were excluded (*Figure 1*). Finally, a total of 315 patients with SSS and another 289 patients with CAVB were enrolled in this study. All patients with dual-chamber PPM implantation received pacing in the DDDR mode. All patients with single ventricular PPM implantation received pacing in the VVIR pacing mode. General demographics, comorbidities, lead positions, pacing QRS durations, pacing percentages, LV performance, HF admission, and cardiovascular and all-cause mortality were compared between the SSS and CAVB groups.

Follow-up

Baseline electrocardiography (ECG) parameters were acquired from the ECGs that were performed closest to the implant period. Pacing leads locations were reviewed using the anterior–posterior and right oblique and left oblique views after implantation. Pacemaker data were also acquired at regular intervals (at least 6 months), and the pacing burden (atrial and ventricular pacing percentage) was recorded at the time of follow-up. The pacing QRS duration was also measured within 3 days after PPM implantation from the surface 12-lead ECG.

Figure 1 Flowchart of the study enrolment. CAVB, complete atrioventricular block; ESC, European Society of Cardiology; HF, heart failure; LVEF, left ventricular ejection fraction; SSS, sick sinus syndrome.



DOI: 10.1002/ehf2.12445

Ethics statement

This study conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved for human research by the institutional review committee of Kaohsiung Chang Gung Memorial Hospital.

Study endpoints

The primary study endpoint was HF admission or PICM. The secondary study endpoints were sudden death or ventricular tachyarrhythmias, cardiovascular mortality, and all-cause mortality.

Echocardiography

Echocardiographic parameters, including LVEF and LV end-diastolic volume (LVEDV), were measured using GE Vivid 9 or Philips IE33. LVEF and LVEDV were quantified by the M mode and corrected by the two-dimensional guided biplane Simpson's method of disc measurements by echocardiography. Echocardiography was performed before implantation and at 2 year intervals thereafter in the absence of clinical events and the onset of HF.

Definition

Pacing-induced cardiomyopathy was defined as a ≥10% decrease in the LVEF, with a resultant LVEF <50%. Medical records were thoroughly searched for alternative causes of cardiomyopathy, including myocardial infarction, myocardial ischaemia on stress testing, severe valvular heart disease, atrial arrhythmias with rapid ventricular response, frequent (>20%) premature ventricular depolarizations, and uncontrolled hypertension. When a potentially alternative explanation for a decrease in LVEF was identified, the patients were excluded from further analysis of HF admission and PICM. HF admission was defined as symptoms of occurrence of HF events of a New York Heart Association functional class of III or IV in the absence of other alternative diagnoses. Symptoms of HF were defined as the need for medical treatment with symptoms of a New York Heart Association functional class of II–IV. Cardiovascular mortality was defined as sudden death related to arrhythmias, HF, and myocardial infarction. All-cause mortality was defined as death related to any cause, including sudden death with undefined reasons, natural course, sepsis, malignancy, and cardiovascular death.

Statistical analysis

Data are presented as mean ± standard deviation or numbers (percentages). The clinical characteristics of the study groups were compared using the *t*-test or Mann–Whitney *U*-test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. Statistical analysis was carried out using statistical software (SPSS for Windows, Version 22). A two-sided *P* value <0.05 indicated statistical significance.

Results

In the SSS group, 74 (23.5%) patients received single ventricular PPM implantation, and 241 (76.5%) patients received dual-chamber PPM implantation. In the CAVB group, all patients received dual-chamber PPM implantation.

Receiver operating characteristic curves

Receiver operating characteristic curves for pacing QRS duration were plotted and revealed that the cut-off point of HF admission was 163 ms. QRS duration ≥163 ms had the best sensitivity and specificity of HF admission, and the area under the curve was 0.652 ($P = 0.009$). However, receiver operating characteristic curves for pacing percentage did not reveal statistically significant values for HF admission.

Baseline characteristics of the study patients

The baseline characteristics of the study participants are listed in *Table 1*. The SSS group included a total of 315 patients (mean age 74.1 ± 9 years; 65.4% female). The CAVB group included a total of 289 patients (mean age 70.7 ± 14 years; 50.5% female). The SSS group was older and had a higher prevalence of female individuals. Furthermore, the SSS group also had a higher prevalence of prior stroke, atrial fibrillation (paroxysmal or non-paroxysmal), and end-stage renal disease. Compared with the SSS group, the CAVB group had longer pacing QRS durations (142.56 ± 33.02 ms vs. 156.63 ± 25.18 ms; $P < 0.001$), a higher prevalence of pacing QRS durations ≥163 ms (25.1% vs. 34.6%; $P = 0.009$), and a higher pacing percentage (39.37 ± 9.17% vs. 83.82 ± 33.06%; $P < 0.001$). The pre-implant and post-implant LVEF and LVEDV were similar between the two groups. Compared with the SSS group, the CAVB group had a higher prevalence of post-implant LVEF <40% (1.3% vs. 4.2%; $P = 0.040$). The incidence of HF admission, PICM, sudden death or ventricular tachyarrhythmias, cardiovascular death, and all-cause death showed no difference between the two groups.

Table 1 Baseline characteristics and clinical outcomes of study patients

	Sick sinus syndrome (N = 315)	Complete AV block (N = 289)	P value
General demographics			
Age (years)	74.1 ± 9	70.7 ± 14	<0.001
Female sex (%)	206 (65.4)	146 (50.5)	0.004
BMI (kg/m^2)	24.77 ± 3.93	24.71 ± 3.73	0.863
Risk factors			
Hypertension (%)	220 (69.8)	197 (68.2)	0.661
Diabetes mellitus (%)	84 (26.7)	88 (30.4)	0.322
Hyperlipidaemia (%)	36 (11.4)	34 (11.8)	0.900
Prior stroke (%)	66 (21.0)	33 (11.4)	0.002
Atrial fibrillation (%)	155 (49.2)	23 (8.0)	<0.001
Paroxysmal (%)	59 (18.7)	23 (8.0)	<0.001
Non-paroxysmal (%)	96 (30.5)	0 (0)	<0.001
ESRD (%)	19 (6.0)	4 (1.4)	0.003
PAOD (%)	5 (1.6)	6 (2.1)	0.765
Lead position			0.580
Lower septum or apex (%)	86 (27.3)	73 (25.3)	
High septum or near RVOT region (%)	229 (72.7)	217 (75.1)	
Pacing QRS duration (ms)	142.56 ± 33.02	156.63 ± 25.18	<0.001
≥163 ms (%)	79 (25.1)	100 (34.6)	0.009
Pacing percentage	39.37 ± 9.17	83.82 ± 33.06	<0.001
Laboratory examination			
Creatinine (exclude ESRD) (mg/dL)	1.16 ± 0.73	1.22 ± 0.76	0.355
Parameters of cardiac echo			
Pre-implant			
LVEDV (mL)	105.29 ± 31.30	106.07 ± 29.35	0.771
LVEF (%)	69.89 ± 8.79	70.26 ± 8.35	0.626
Post-implant			
LVEDV (mL)	109.15 ± 33.42	111.99 ± 44.84	0.474
LVEF (%)	65.89 ± 11.35	63.88 ± 12.62	0.099
LVEF <40% (%)	4 (1.3)	12 (4.2)	0.040
Medication			
ACEI/ARB use (%)	149 (47.3)	148 (51.2)	0.410
β-Blocker use (%)	72 (22.9)	61 (21.1)	0.556
The incidence of HF admission (%)	15 (4.8)	16 (5.5)	0.711
The incidence of PICM (%)	15 (4.8)	22 (7.6)	0.174
The incidence of sudden death or ventricular tachyarrhythmias (%)	7 (2.2)	7 (2.4)	1.000
The incidence of cardiovascular mortality (%)	6 (2.3)	7 (2.9)	0.780
The incidence of all-cause mortality (%)	56 (17.8)	58 (20.1)	0.532
F/U duration (years)	6.6 ± 3.7	6.5 ± 3.6	0.443

Data are expressed as mean ± standard deviation or as number (percentage). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; AV, atrioventricular; BMI, body mass index; ESRD, end-stage renal disease; F/U, follow-up; HF, heart failure; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; PAOD, peripheral arterial occlusive disease; PICM, pacing-induced cardiomyopathy; RVOT, right ventricular outflow tract.

Univariate and multivariate Cox regression analyses of heart failure admission during a 5 year follow-up period

On univariate Cox regression analyses, age, body mass index, diabetes mellitus (DM), pacing QRS duration, pacing QRS duration ≥163 ms, renal insufficiency (estimated glomerular filtration rate <30 mL/min/1.73 m^2), pre-implant LVEF, and left atrial size were found to be statistically significant predictors of HF admission among patients with PPM (*Table 2*). On multivariate Cox regression analyses of the significant predictors from univariate Cox regression analyses, age, DM, pacing QRS duration ≥163 ms, and left atrial size were found to be independent predictors of HF admission among patients with PPM (*Table 2*).

Difference between patients with pacing QRS length <163 and ≥163 ms

Patients who died because of a non-cardiac problem within 2 years were excluded. A total of 560 patients were categorized into two groups according to pacing QRS duration ≥163 or <163 ms. A total of 381 patients were included in the QRS duration <163 ms group, and 179 patients were included in the QRS duration ≥163 ms group (*Table 3*). The percentage of ventricular lead in the low septum and apex was similar in the two groups. Patients with a pacing QRS duration ≥163 ms had a lower post-implant LVEF, a higher prevalence of LVEF <40%, a higher prevalence of post-implant LVEDV increase ≥25%, a higher incidence of PICM, and a higher incidence of HF admission compared with

DOI: 10.1002/ehf2.12445

Table 2 Univariate and multivariate Cox regression analyses of heart failure admission during 5 year follow-up period

	Univariate analyses			Multivariate analyses		
Variables	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
Male	1.022	0.501–2.086	0.952			
Age	1.070	1.024–1.119	0.003	1.121	1.054–1.193	<0.001
BMI	1.113	1.016–1.221	0.022			
Hypertension	1.012	0.507–2.393	0.807			
Diabetes mellitus	2.721	1.345–5.505	0.005	2.667	1.159–6.136	0.021
Atrial fibrillation (all type)	1.252	0.600–2.613	0.549			
Lead position (apex or lower septum)	1.580	0.303–1.321	0.223			
Pacing QRS duration	1.014	1.000–1.029	0.047			
Pacing QRS duration ≥163 ms	3.373	1.531–7.432	0.003	3.506	1.491–8.247	0.004
Pacing percentage	1.014	0.987–1.041	0.304			
Renal insufficiency (eGFR <30 mL/min/1.73 m^2)	1.445	1.126–1.855	0.004			
Pre-implant LVEF	0.961	0.924–1.000	0.049			
LA size	1.057	1.010–1.106	0.017	1.070	1.012–1.131	0.018
LVEDV	1.010	0.999–1.021	0.086			
ACEI/ARB use	0.720	0.350–1.482	0.372			
β-Blocker use	0.725	0.296–1.774	0.482			

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; LA, left atrial; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction.

Table 3 The differences between the patients with pacing QRS duration <163 or ≥163 ms

	Pacing QRS duration <163 ms (*N* = 381)	Pacing QRS duration ≥163 ms (*N* = 179)	*P* value
Ventricular lead at lower septum or apex (%)	80 (21.0)	51 (28.5)	0.269
Post-implant LVEF (%)	67.31 ± 10.50	60.88 ± 13.18	<0.001
Post-implant LVEF <40% (%)	4 (1.0)	11 (6.1)	0.001
Increase in LVEDV >25% (%)	46 (12.1)	38 (21.2)	0.007
The incidence of PICM (%)	10 (2.6)	24 (13.4)	<0.001
The incidence of HF readmission over a 5 year follow-up period (%)	10 (2.6)	16 (8.9)	0.002
The incidence of cardiovascular death at 5 year follow-up period (%)	6 (1.8)	4 (2.6)	0.733
The incidence of sudden death or ventricular tachyarrhythmias (%)	7 (1.8)	6 (3.4)	0.366

Data are expressed as number (percentage). HF, heart failure; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; PICM, pacing-induced cardiomyopathy.

patients with a pacing QRS duration <163 ms. The incidence of cardiovascular death and sudden death or ventricular tachyarrhythmias was similar in the two groups, although the pacing QRS duration differed.

Kaplan–Meier curve for heart failure admission

The Kaplan–Meier curve analysis for HF admission showed no statistically significant difference between the SSS and CAVB groups (log-rank *P* = 0.647) (*Figure 2A*). The Kaplan–Meier curve analysis for HF admission showed a statistically significant difference between the group with pacing QRS durations ≥163 ms and the group with pacing QRS durations <163 ms over a 3.5 year follow-up period (log-rank *P* = 0.004) as well as a 5 year follow-up period (log-rank *P* = 0.002) (*Figure 2B*).

Comparison of patients in the sick sinus syndrome and complete atrioventricular block groups with heart failure admission or pacing-induced cardiomyopathy

Twenty-two patients (7.0%) developed HF admission and/or PICM (HF admission: 15 patients; PICM: 15 patients) in the SSS group, and 29 patients (10.0%) developed HF admission and/or PICM (HF admission: 16 patients; PICM: 22 patients) in the CAVB group. Among patients with HF admission or PICM (*Table 4*), patients in the SSS group were older and had a higher prevalence of atrial fibrillation compared with those in the CAVB group. Compared with the SSS group, the CAVB group had a higher pacing percentage, longer pacing QRS duration, lower post-implant LVEF, higher prevalence of post-implant LVEF <40%, and larger post-implant LVEDV, although the difference did not reach statistical significance.

DOI: 10.1002/ehf2.12445

Figure 2 Kaplan–Meier curve for heart failure (HF) admission. (A) Kaplan–Meier curve for HF admission between the sick sinus syndrome and complete atrioventricular (AV) block groups. The Kaplan–Meier curve showed no statistically significant difference, with log-rank $P = 0.647$. (B) Kaplan–Meier curve for HF admission between patients with pacing QRS duration ≥163 and <163 ms. The Kaplan–Meier curve showed a statistically significant difference in HF admission between patients with pacing QRS duration ≥163 and <163 ms, with log-rank $P = 0.004$ over a 3.5 year follow-up period and log-rank $P = 0.002$ over a 5 year follow-up period.

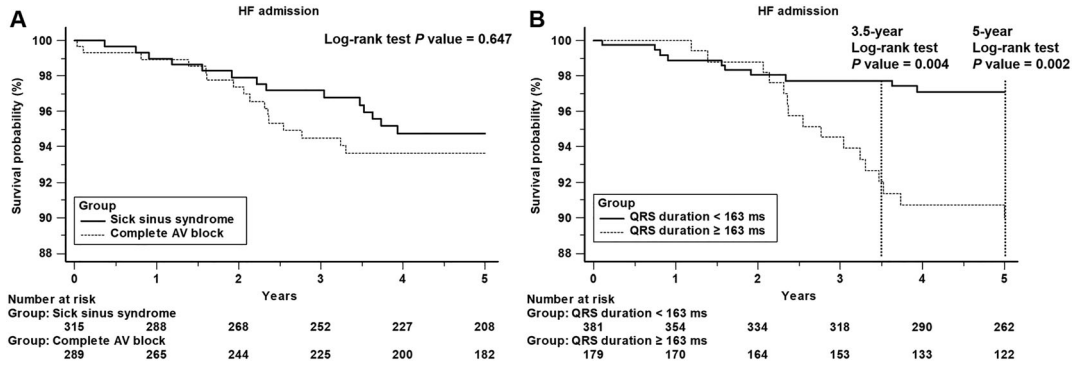


Table 4 Baseline characteristics and clinical outcomes of patients with heart failure admission and/or pacing-induced cardiomyopathy

	Sick sinus syndrome ($N = 22$)	Complete AV block ($N = 29$)	P value
General demographics			
Age (years)	78.5 ± 8	70.9 ± 12	0.016
Female sex (%)	11 (50.0)	16 (55.2)	0.782
Risk factors			
Diabetes mellitus (%)	13 (59.1)	12 (41.4)	0.264
Atrial fibrillation (%)	14 (63.6)	5 (17.2)	0.001
Lead position			
Lower septum or apex (%)	8 (36.4)	8 (27.6)	0.554
Pacing QRS duration (ms)	158.20 ± 38.38	172.64 ± 35.25	0.196
≥163 ms (%)	12 (54.5)	18 (62.1)	0.527
Pacing percentage	47.75 ± 9.90	87.77 ± 32.91	0.110
Parameters of cardiac echo			
Pre-implant			
LVEDV (mL)	123.27 ± 39.33	110.96 ± 27.05	0.207
LVEF (%)	64.50 ± 9.00	66.31 ± 8.87	0.448
Post-implant			
LVEDV (mL)	131.10 ± 41.19	166.19 ± 42.99	0.055
LVEDV increase ≥25%	5 (22.7)	12 (41.4)	0.233
LVEF (%)	50.62 ± 14.30	44.89 ± 12.73	0.149
LVEF <40% (%)	4 (18.2)	11(37.9)	0.214
The average duration for the first onset of HF admission or diagnosis of PICM (years)	2.5 ± 1.4	1.9 ± 1.0	0.169

Data are expressed as mean ± standard deviation or as number (percentage). AV, atrioventricular; HF, heart failure; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; PICM, pacing-induced cardiomyopathy.

The average duration for the first onset of HF admission or diagnosis of PICM was 2.5 ± 1.4 years in the SSS group and 1.9 ± 1.0 years in the CAVB group.

Discussion

In our study, the incidence of HF admission and/or PICM was less than 10% in the SSS and CAVB groups if the patient had a preserved LVEF without coronary artery disease before pacemaker implant. The pacing percentage did not play an important role in terms of HF admission in the SSS and CAVB groups. However, the pacing QRS duration plays an important role in HF admission, and post-implant QRS duration ≥163 ms was the most important predictor of HF admission. Moreover, it took a short duration after implant for patients who developed HF admission or PICM, and the average duration for the first onset of HF admission or diagnosis of PICM after implant was 2.5 ± 1.4 years in the SSS groups and 1.9 ± 1.0 years in the CAVB groups.

DOI: 10.1002/ehf2.12445

In a previous study, the incidence of PICM was found to be 22.8% among CAVB patients with frequent ventricular pacing,[9] and the incidence of HF was found to be 26% among SSS patients.[10] Among SSS patients, the incidence of HF is not associated with the pacing percentage, lead position, and pacing mode and is related to clinical characteristics (age, hypertension, coronary artery disease, LV volume, and/or previous systolic dysfunction).[10] According to previous studies, a high pacing percentage and the pacing QRS duration play an important role in the development of PICM among patients with CAVB.[8,9,11] A higher prevalence of DM was noted among CAVB patients with PICM.[9] In our study, DM was also found to be significantly associated with HF admission among patients with PPM. In a previous study of PICM in the Asian population, patients with ischaemic heart disease were not excluded, and this factor should have certain impact on the development of PICM.[11] In our study, we completely excluded patients with ischaemic heart disease and valvular heart disease, and the incidence of HF admission after implant was found to be 4.8% among patients with SSS and 5.5% among patients with CAVB.

In one meta-analysis study, the association between pacing site and PICM remained inconclusive although LVEF was higher among patients with RV non-apical pacing than among those with RV apical pacing.[12] In another study, RV non-apical pacing was not found to have a protective effect on LV performance when compared with RV apical pacing over a 2 year period.[6] Nakamura *et al*. reported that 32% of the patients presented similar pacing QRS durations while pacing in either the septum or apex.[13] In our study, only 28.5% of the patients with pacing QRS length $\geq$163 ms had a ventricular pacing site at the apical or low septum. Electrical pacing alters the morphology and QRS duration depending on the degree of activation of the specific conduction tissue, the presence of previous heart diseases and underlying cardiomyopathy, and the topography of the electrode in the RV.

In animal and cohort studies, a longer pacing QRS duration was found to be prognostic indicator of HF and the occurrence of PICM.[9,11,14] Maximum cardiac efficiency depends on mechanically synchronous contraction of the ventricular walls and enables coordinated action of different segments through propagation of electrical stimuli in all components of the conduction system, represented graphically by a QRS length $<$120 ms on an ECG.[15,16] Electrical pacing from the right heart compromises the mechanical ventricular efficiency and causes dyssynchrony. Myocardial contraction by pacing from the right heart would be haemodynamically efficient, but it was mechanically anti-physiological, and the patient will be forced to live with a certain degree of ventricular dysfunction and dyssynchronopathy, consequently increasing in LVEDV. This is an important reason for the development of PICM after PPM implantation, although the QRS duration derived by electrical pacing does not necessarily reflect the degree of mechanical dyssynchrony.[11] In our study, 10.4% of the patients with a pacing QRS duration $\geq$163 ms were admitted for HF, and 13.4% of the patients with pacing QRS duration $\geq$163 ms had post-implantation LVEF $<$50% over a 5 year follow-up period. Moreover, our study showed that a higher prevalence of dilated LV volume was noted in patients with pacing QRS duration $\geq$163 ms over a 5 year follow-up period. Reasonably, CRT is considered to reverse this electrical dyssynchronopathy-related LV dysfunction. In one recent study, CRT was proved to be highly efficacious in reversing PICM, with 72% of the severe PICM patients achieving LVEF $>$35% and most of the improvement occurring within 1 year.[17] In addition, another study reported that the use of CRT was found to be associated with a better LVEF and a smaller LV volume over a 1 year and long-term follow-up period.[16] CRT could solve the problem of dyssynchronopathy-related PICM with a good response, but it is still an expensive device in many countries and is only reimbursed for selective patients in many countries.

In our study, 22 SSS patients who developed HF admission and/or PICM had an average pacing percentage of 47.8%, and 54.5% of these patients had the pacing QRS duration $\geq$163 ms, and it took an average time of 2.5 years for the first onset of HF admission or diagnosis of PICM. Twenty-nine CAVB patients who developed HF admission and/or PICM had an average pacing percentage of 87.8%, and 62.1% of these patients had the pacing QRS duration $\geq$163 ms, and it took an average time of 1.9 years for the first onset of HF admission or diagnosis of PICM. Therefore, more than 50% pacing percentage in conjunction with pacing QRS duration $\geq$163 ms might contribute to early onset of PICM and HF admission, and it was reasonable to have more frequent follow-up echocardiograms in patients with pacing QRS duration $\geq$163 ms and pacing percentage $>$50%.

Study limitations

This is a retrospective study including data from only one medical centre. Because of their older age, the all-cause mortality among the study patients was higher. Other limitations were the absence of baseline and follow-up echocardiographic diastolic parameters and the absence of systolic parameters by speckle tracking echocardiography. Therefore, we may underestimate the incidence of patients without decreased LVEF but with impaired systolic function unlike the classic PICM definition. However, we still provided important information on the relationship between pacing QRS duration and the incidence of HF admission and/or PICM in the patients with PPM for SSS and CAVB.

Conclusions

There was no difference in HF admission between the SSS and CAVB groups, although the CAVB group had a higher pacing percentage. Post-pacemaker implant pacing QRS duration ≥163 ms was the most important predictor of HF admission.

Conflict of interest

None declared.

Funding

None.

Human rights statements and informed consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later revisions.

References

1. de Vries LM, Dijk WA, Hooijschuur CAM, Leening MJG, Stricker BHC, van Hemel NM. Utilisation of cardiac pacemakers over a 20-year period: results from a nationwide pacemaker registry. *Neth Heart J* 2017; **25**: 47–55.
2. Akerström F, Pachón M, Puchol A, Jiménez-López J, Segovia D, Rodríguez-Padial L, Arias MA. Chronic right ventricular apical pacing: adverse effects and current therapeutic strategies to minimize them. *Int J Cardiol* 2014; **173**: 351–360.
3. Ghani A, Delnoy PP, Ottervanger JP, Ramdat Misier AR, Smit JJ, Elvan A. Assessment of left ventricular dyssychrony in pacing-induced left bundle branch block compared with intrinsic left bundle branch block. *Europace* 2011; **13**: 1504–1507.
4. Dreger H, Maethner K, Bondke H, Baumann G, Melzer C. Pacing-induced cardiomyopathy in patients with right ventricular stimulation for >15 years. *Europace* 2012; **14**: 238–242.
5. Khurshid S, Epstein AE, Verdino RJ, Lin D, Goldberg LR, Marchlinski FE, Frankel DS. Incidence and predictors of right ventricular pacing-induced cardiomyopathy. *Heart Rhythm* 2014; **11**: 1619–1625.
6. Kaye GC, Linker NJ, Marwick TH, Pollock L, Graham L, Pouliot E, Poloniecki J, Gammage M, on behalf of the Protect-Pace trial investigators, Kaye G, Martin P, Pepper C, Tang K, Crozier I, Goode G, Young G, Petkar S, Langford E, Linker NJ, Rozkovec A, Rinaldi A, Yousef Z, Lever N, Denman R, Young G, Williams I, McGavigan A. Effect of right ventricular pacing lead site on left ventricular function in patients with high-grade atrioventricular block: results of the Protect-Pace study. *Eur Heart J* 2015; **36**: 856–862.
7. Udo EO, van Hemel NM, Zuithoff NP, Doevendans PA, Moons KG. Risk of heart failure- and cardiac death gradually increases with more right ventricular pacing. *Int J Cardiol* 2015; **185**: 95–100.
8. Kiehl EL, Makki T, Kumar R, Gumber D, Kwon DH, Rickard JW, Kanj M, Wazni OM, Saliba WI, Varma N, Wilkoff BL, Cantillon DJ. Incidence and predictors of right ventricular pacing-induced cardiomyopathy in patients with complete atrioventricular block and preserved left ventricular systolic function. *Heart Rhythm* 2016; **13**: 2272–2278.
9. Khurshid S, Liang JJ, Owens A, Lin D, Schaller R, Epstein AE, Marchlinski FE, Frankel DS. Longer paced QRS duration is associated with increased prevalence of right ventricular pacing-induced cardiomyopathy. *J Cardiovasc Electrophysiol* 2016; **27**: 1174–1179.
10. Riahi S, Nielsen JC, Hjortshøj S, Thomsen PE, Højberg S, Møller M, Dalsgaard D, Nielsen T, Asklund M, Friis EV, Christensen PD, Simonsen EH, Eriksen UH, Jensen GV, Svendsen JH, Toff WD, Healey JS, Andersen HR, DANPACE Investigators. Heart failure in patients with sick sinus syndrome treated with single lead atrial or dual-chamber pacing: no association with pacing mode or right ventricular pacing site. *Europace* 2012; **14**: 1475–1482.
11. Kim JH, Kang KW, Chin JY, Kim TS, Park JH, Choi YJ. Major determinant of the occurrence of pacing-induced cardiomyopathy in complete atrioventricular block: a multicentre, retrospective analysis over a 15-year period in South Korea. *BMJ Open* 2018; **8**: e019048.
12. Shimony A, Eisenberg MJ, Filion KB, Amit G. Beneficial effects of right ventricular non-apical vs. apical pacing: a systematic review and meta-analysis of randomized-controlled trials. *Europace* 2012; **14**: 81–91.
13. Nakamura H, Mine T, Kanemori T, Ohyanagi M, Masuyama T. Effect of right ventricular pacing site on QRS width. *Asian Cardiovasc Thorac Ann* 2011; **19**: 339–345.
14. Wang Y, Gong X, Su Y, Cui J, Shu X. Implications of QRS duration in dogs with pacing-induced heart failure. *Physiol Res* 2011; **60**: 861–868.
15. Sweeney MO, Prinzen FW. Ventricular pump function and pacing: physiological and clinical integration. *Circ Arrhythm Electrophysiol* 2008; **1**: 127–139.
16. Fang F, Zhang Q, Chan JY, Razali O, Azlan H, Chan HC, Sanderson JE, Xie JM, Yu CM. Early pacing-induced systolic dyssynchrony is a strong predictor of left ventricular adverse remodeling: analysis from the Pacing to Avoid Cardiac Enlargement (PACE) trial. *Int J Cardiol* 2013; **168**: 723–728.
17. Khurshid S, Obeng-Gyimah E, Supple GE, Schaller R, Lin D, Owens AT, Epstein AE, Dixit S, Marchlinski FE, Frankel DS. Reversal of pacing-induced cardiomyopathy following cardiac resynchronization therapy. *JACC Clin Electrophysiol* 2018; **4**: 168–177.