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Incidence and predictors of pacemaker-induced cardiomyopathy with comparison between apical and non-apical right ventricular pacing sites

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Abstract

Background Asynchronous activation of left ventricle (LV) due to chronic right ventricular (RV) pacing has been known to predispose to LV dysfunction. The predictors of LV dysfunction remain to be prospectively studied. This study was designed to follow up patients with RV pacing to look for development of pacing-induced cardiomyopathy (PiCMP), identify its predictors and draw comparison between apical vs non-apical RV pacing sites.

Methods Three hundred sixty-three patients undergoing dual-chamber and single-chamber ventricular implants were enrolled and followed up. Baseline clinical parameters; paced QRS duration and axis; RV lead position by fluoroscopy; LV ejection fraction (LVEF) by Simpson's method on transthoracic echocardiography (TTE); intraventricular dyssynchrony (septal-posterior wall contraction delay) and interventricular dyssynchrony (aortopulmonary ejection delay) on TTE were recorded. The patients were followed up at 6–12 monthly interval with estimation of LVEF and pacemaker interrogation at each visit. Pacemaker-induced cardiomyopathy (PiCMP) was defined as a fall in ejection fraction of 10% as compared to the baseline LVEF. Patients developing PiCMP were compared to other patients to identify predictors.

Results The mean age of study population was 59.8 years, 68.3% being males. Fifty-one percent and 49% patients underwent VVIR and DDDR pacemaker implantation, respectively. After attrition, 254 patients were analysed. PiCMP developed in 35 patients (13.8%) over a mean follow-up of 14.5 months. After multivariate analysis, burden of ventricular pacing > 60% [HR 4.26, $p = 0.004$] and interventricular dyssynchrony (aortopulmonary ejection delay > 40 msec) [HR 3.15, $p = 0.002$] were identified as predictors for PiCMP in patients undergoing chronic RV pacing. There was no effect of RV pacing site (apical vs non-apical) on incidence of PiCMP [HR 1.44, $p = 0.353$).

Conclusions Incidence of PiCMP with RV pacing was found to be 13.8% over a mean follow-up of 14.5 months. Burden of right ventricular pacing and interventricular dyssynchrony were identified as the most important predictors for the development of PiCMP. Non-apical RV pacing site did not offer any benefit in terms of incidence of PiCMP over apical lead position.

Keywords Right ventricular pacing · Left ventricular dysfunction · Pacemaker-induced cardiomyopathy · Apical lead position · Non-apical lead position

1 Introduction

Implantation of an artificial cardiac pacemaker for bradycardia is a routine procedure associated with extended longevity [1] and improved quality of life [2]. Among possible ventricular pacing sites, right ventricular (RV) apex has been selected as the conventional site. RV apex is easy accessible, and allows safe and stable long-term pacing [3]. Abnormal asynchronous activation due to RV pacing causes abnormal contraction patterns, inefficient and depressed pump function, and ventricular remodelling. Studies have shown that morbidity and mortality are higher in patients with long-term RV apex pacing than with atrial pacing [4]. Right ventricular (RV) pacing can lead to progressive left ventricular (LV) systolic dysfunction and heart failure, presumably by causing electrical and mechanical dyssynchrony [5, 6].

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In order to keep a normal cardiac function in patients with permanent ventricular pacing, an alternative pacing site might be superior to RV apex [7]. Mid-septal or outflow RV pacing might be an alternative site, because it is associated with shorter QRS duration and thus lesser dyssynchrony than anywhere else in the RV [8]. Paced QRS duration reflects homogenization of contraction and is a surrogate marker of dyssynchrony of LV contraction which might be useful as a predictor of LV dysfunction. It has been proposed that paced QRS duration, but not pacing site, may be predictors of LV volumes and systolic function after long-term RV pacing [9]. While only a subset of patients exposed to frequent RV pacing develop LV dysfunction, predictors of risk for its occurrence remain to be defined [10]. If accurate predictors could be identified, patients at high risk for developing pacing-induced cardiomyopathy (PiCMP) could be considered for risk factor modification and early institution of therapy, thereby potentially avoiding the development of LV systolic dysfunction and the need for reoperation for upgradation to a biventricular pacemaker. This study is designed to follow up patients with RV pacing to look for development of LV dysfunction and identify predictors of LV dysfunction.

2 Materials and methods

The study was a single-centre prospective longitudinal observational cohort study. Written informed consent was taken prior to inclusion of study. All patients aged more than 12 years undergoing ventricular pacemaker implantation for standard indications from July, 2015 to January, 2017 were included. Patients undergoing re-implantation or pulse generator replacement were excluded. Patients undergoing AAI or AAIR pacemaker implantation were also excluded. Detailed history and examination of all patients were recorded at baseline. All patients were implanted with dual-chamber or single-chamber pacemakers in a sterile manner with a conscious state under local anaesthesia by an experienced operator. All leads were inserted transvenously from the left or right axillary/subclavian vein. The atrial leads were placed at the right atrial appendage. The position of ventricular lead in right ventricle [apical, mid-septal, right ventricular outflow tract (RVOT) or other] was as per operators' discretion (Fig. 1). Baseline electrocardiogram (ECG), fluoroscopic examination (in AP, RAO 30°, LAO 40° and lateral views, Fig. 2) for lead position and transthoracic 2D echocardiogram were done for all patients. QRS axis and paced QRS duration were specifically noted on the ECG. Left ventricular ejection fraction was estimated by applying modified Simpson's method. Ventricular dyssynchrony was also estimated using septal to posterior wall motion delay on M-mode examination and interventricular mechanical delay on pulse Doppler examination of pulmonary and aortic valves. The patients were followed up on outpatient basis for a minimum of 6 months and up to 3 years at a 6–12 monthly interval. ECG, repeat echocardiogram as done on baseline and pacemaker interrogation (to look for various pacemaker parameters including percentage pacing requirement) were done on each visit. Pacemaker-induced cardiomyopathy was defined as a fall in ejection fraction of 10% as compared to the baseline LVEF.

Statistical analysis Quantitative variables like age, LV function and QRS duration were summarized as mean ± SD. Qualitative variables such as sex and site of pacemaker insertion were summarized as proportions. Student t and Pearson χ^2 tests were used to compare continuous and categorical variables, respectively. Univariable analysis was performed on collected clinical data stratified by patients with and without pacemaker-induced LV dysfunction. All analysis was implemented on STATA software 13.0. p value less than 0.05 was taken as statistically significant.

3 Results

At baseline, data was available for 363 patients (Table 1). The mean age of the cohort was 59.8 years with age range of 12 to 92 years. The median age was 63 years with only 3 patients under 18 years of age. Around two third of the cohort comprised of males (68.3%) and rest females. There was high prevalence of hypertension (31.1%) and diabetes mellitus (30.3%), each affecting almost one third of the study population. Known coronary artery disease at baseline was present in 64 patients (17.6%). The mean LVEF by Simpson's method at baseline was 56.7% (range 22 to 75%, standard deviation 10%). At baseline, 58 patients (16%) had LV dysfunction defined as LV ejection fraction less than 50%.

Complete heart block (intermittent or persistent) was the most common indication for pacing affecting 279 patients of the study cohort (76.8%). Nine patients had congenital complete heart block and 16 patients were post-surgery with coronary artery bypass grafting and atrial septal defect closure being the most common surgeries. Two patients had complete heart block associated with sarcoidosis. One patient had limb girdle muscular dystrophy associated with complete heart block. Rest all patients had sclerodegenerative complete heart block. Other indications were 2nd degree AV block (9.4%), conduction disturbances with syncope (8.5%) and sick sinus syndrome (5.3%). One patient with sick sinus syndrome also had long QT syndrome associated with recurrent VT requiring pacing. Fifty-one percent patients received single-chamber pacemaker with the rest receiving a dual-chamber pacemaker.

The most common site of ventricular lead placement was RV apex constituting 210 patients (57.8%). Lead was placed at mid-septum in 74 patients (20.4%) and in RV outflow tract septum in 70 patients (19.3%). Ventricular lead implantation

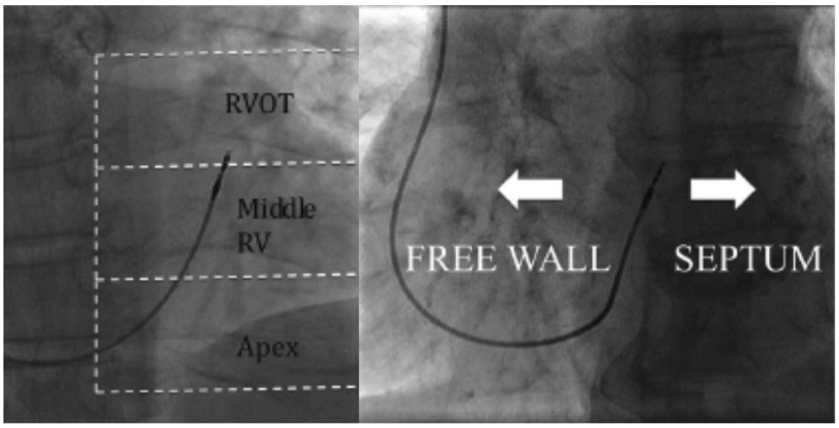

Fig. 1 Fluoroscopic schema of right ventricular (RV) pacing lead location. (Left) Pacing lead position in the posterior-anterior fluoroscopic view was divided into the RV outflow tract, middle RV and RV apex. (Right) In the 40° left anterior oblique (LAO) view, if the RV pacing lead is directed to the left, the lead is on the free wall, and if it is directed to the right, it is on the RV septum

was accidentally done at other uncommon sites away from the septum (including RV free wall, RVOT free wall and RV inferior wall) in nine patients (2.5%). The lead implantation sites were confirmed with fluoroscopy and echocardiography only after completion of the implantation procedure. Seven (1.9%) patients developed pericardial effusion including two with tamponade requiring pigtail drainage. Three (0.8%) patients developed pneumothorax requiring intercostal tube drainage.

At baseline after pacemaker implantation, the mean paced QRS duration decreased from the apical pacing group to the mid-septal pacing group to the RVOT pacing group. The axis also changed from left axis to normal axis to inferior axis, respectively. The data for mean QRS axis and duration along with measures of interventricular and intraventricular dyssynchrony according to pacing site has been presented in Table 2. On comparison of the apical pacing group with non-apical pacing group (including mid-septum and RVOT), mean QRS duration and aortopulmonary ejection delay were found to be significantly more in the apical pacing group (p value of < 0.001 and 0.0011, respectively). However, the two groups were similar in terms of intraventricular dyssynchrony (septal-posterior wall activation delay) (Table 3).

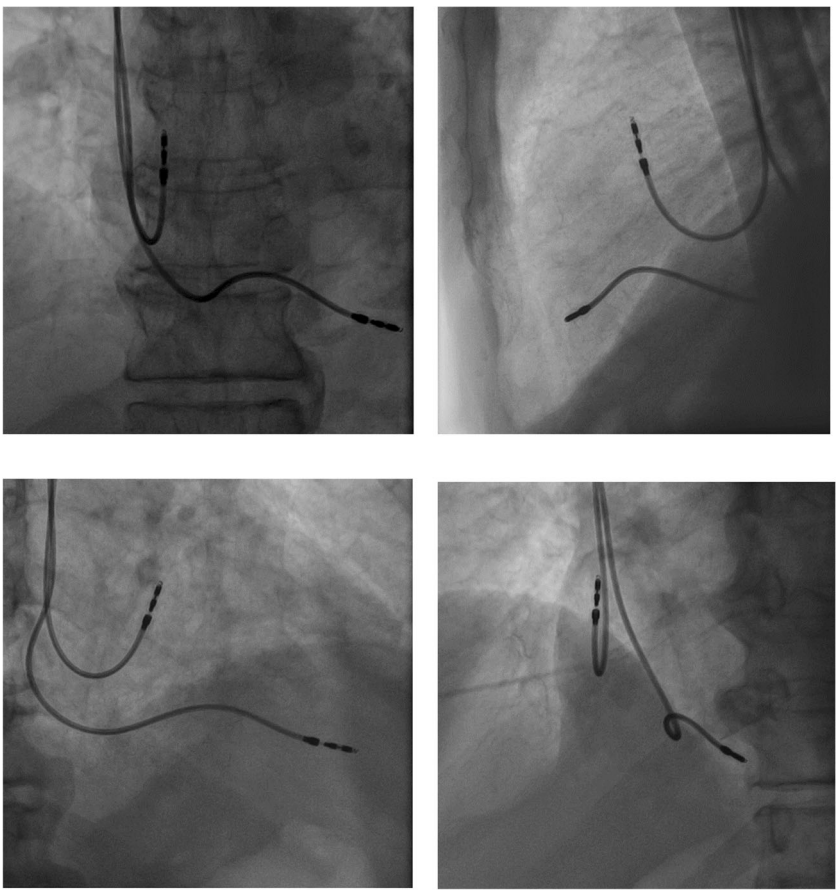

Fig. 2 AP, 40° LAO, 30° RAO and left lateral fluoroscopic images showing lead tip at apical septum in a patient with dual-chamber pacemaker

Table 1 Baseline data of patients at recruitment

Characteristic	Number (%)
Total (*n*)	363
Age in years (mean ± SD)	59.8 ± 15.4
Males	248 (68.3%)
CAD	64 (17.6%)
DM	110 (30.3%)
HTN	113 (31.1%)
LV function (%)	56.7 ± 9.9%
Indication for pacing	
1. Complete heart block	279 (76.8%)
2. 2nd degree AV block	34 (9.4%)
3. Sick sinus syndrome	19 (5.3%)
4. Bundle branch block with syncope	31 (8.5%)
Single chamber (VVIR)	185 (51.0%)
Dual chamber (DDDR)	178 (49.0%)
Paced QRS duration (msec)	145.3 ± 18.5
Pacemaker site	
1. RV apex	210 (57.8%)
2. Mid-septum	74 (20.4%)
3. RV outflow tract	70 (19.3%)
4. Others	9 (2.5%)

Of the 363 patients enrolled, follow-up data was available for 276 patients (76.0%). Twenty-two patients were found to have died on telephonic follow-up without having a follow-up echocardiogram, thus excluded from the analysis. The cause of death in these cases could not be ascertained due to telephonic nature of follow-up for these cases. A total of 254 patients were included for statistical analysis. Figure 3 shows the patient flow diagram for the study. Mean duration of follow-up was 14.5 months (6 to 33 months). Out of these, 35 patients (13.8%) developed PiCMP, defined as a fall in LVEF of more than 10%. The studied parameters for the overall follow-up cohort and cohorts with presence and absence of PiCMP are presented in Table 4. *p* values given in the table are for comparison of the cohorts with presence and absence of PiCMP on follow-up. The mean age and sex were similar in both the cohorts. Same was true with the distribution of hypertension, diabetes and coronary artery disease. There was no significant differences between the pacing site (apex vs non-apex), paced QRS duration (< 150 msec vs ≥ 150 msec) or baseline LV ejection fraction. There was significant difference in terms of burden of pacing being more in the PiCMP group. Aortopulmonary ejection delay (a marker of interventricular dyssynchrony) was significantly different between the two groups. However, both the groups had similar intraventricular dyssynchrony (measured as septal-posterior wall activation delay). Thus to sum up, on univariate analysis, longer duration of follow-up, greater proportion of pacing and greater interventricular dyssynchrony were identified as predictors of PiCMP.

Multivariate analysis was also done to identify predictors after accounting for confounding factors. Proportion of ventricular pacing and presence of interventricular dyssynchrony (aortopulmonary ejection delay > 40 msec) were identified as predictors of pacemaker-induced LV dysfunction (Table 5). Proportion of ventricular pacing was identified as the most important factor with a hazard ratio of 4.26 and a *p* value of 0.004. Interventricular dyssynchrony was also found to be a significant predictor with a hazard ratio of 3.15 and a *p* value of 0.002.

4 Discussion

In the study cohort of 276 patients who had completed the follow-up, death from any cause occurred in 22 patients (8%). This suggests that the prognosis of patients with pacemaker implantation is not benign. Out of the 254 patients who entered analysis, 35 (13.8%) patients developed LV dysfunction (defined by drop in LVEF of > 10%) over a follow-up period of 14.5 ± 7.2 months. This is similar to incidence from other studies ranging between 9 and 19% [10–13]. It is important to note that in the current study population, single-chamber pacemaker was implanted in majority of the patients as compared to other studies where dual-chamber pacemaker remained the most common implant. The current evidence recommends biventricular pacing in patients with LV dysfunction having indication for pacing. There are multiple small trials demonstrating benefit of *de novo* biventricular pacemaker therapy in patients with LV dysfunction with indication for pacing including BLOCK-HF [14], HOBIPACE [15] and COMBAT [16] trials. The largest of these trials, BLOCK-HF trial, showed a significant 28% reduction in combined primary end point of mortality, heart failure and

Table 2 Comparison of QRS axis, QRS duration and dyssynchrony indices with pacing site. Values given in terms of mean ± standard deviation

	RV apex	Mid-septum	RVOT	Others
pQRSd (msec)	149.3 ± 18.1	140.7 ± 21.1	137.9 ± 13.8	145.9 ± 10.0
QRS axis (degrees)	− 66.3 ± 48.2	25.5 ± 8.0	80.7 ± 31.8	− 5.9 ± 83.0
Aortopulmonary ejection delay (msec)	32.4 ± 23.3	24.8 ± 16.2	24.3 ± 31.2	17 ± 10.9
Septal-posterior wall activation delay (msec)	54.9 ± 41.7	52.3 ± 33.5	48.4 ± 38.8	45.3 ± 21.9

Table 3 Comparison of apical vs non-apical sites of pacing in terms of QRS axis, QRS duration and dyssynchrony indices. Values given in terms of mean ± standard deviation

	Apical pacing site	Non-apical pacing site	*p* value
pQRSd (msec)	149.3 ± 18.1	139.7 ± 17.7	< 0.001
QRS axis (degrees)	− 66.3 ± 48.2	48.5 ± 68.8	< 0.001
Aortopulmonary ejection delay (msec)	32.4 ± 23.3	24.1 ± 24.1	0.0011
Septal-posterior wall activation delay (msec)	54.9 ± 41.7	50.1 ± 35.6	0.253

increased end systolic volume. Despite these findings, 22 patients with baseline LV dysfunction (defined as LVEF < 50%) underwent single ventricular pacemaker implantation due to cost constraints, and were included in the analysis. Since the baseline LVEF was variable, a cut-off value of ejection fraction for diagnosing PiCMP could not be used. A value of fall more than 10% was used keeping in mind the variability in measurement of LVEF by Simpson's method. However, this value is likely to underestimate the incidence of PiCMP especially in patients with baseline LV dysfunction. Still, in the present study, the incidence of PiCMP is not uncommon. Thus, a strategy of routine echocardiographic screening at follow-up visits might be useful for patients with pacemaker implants [17].

Univariate and multivariate analysis identified proportion of RV pacing and interventricular dyssynchrony as significant predictors of PiCMP. Out of these, burden of RV pacing is a known predictor from previous studies. Interventricular dyssynchrony was identified as a new risk predictor. The pacing site inside the RV did not predict occurrence of PiCMP.

Total burden of RV pacing, which is affected by both duration of follow-up and proportion of RV pacing, has been shown to be an important player in the causality of PiCMP across all the studies currently available [10–13]. However, in the present study, PiCMP was evident at a shorter mean follow-up of 14.5 months. This is in contrast to the study by Kiehl et al., where they proposed that PiCMP starts occurring after 2–3 years of follow-up and then progressively increases further on longer follow-up [13]. However, in the present study population, most of the patients had higher burden of pacing as compared to other studies. A cut-off value of 60% gave the best ROC curve value of predictability to differentiate between those who develop and do not develop PiCMP on follow-up. It remains evident that higher the pacing, higher the incidence of PiCMP.

This study was novel in terms of including newer dyssynchrony indices (interventricular and intraventricular dyssynchrony) into analysis. Electromechanical dyssynchrony caused by non-physiological activation of myocardium with right ventricular pacing has been proposed to be a mechanism of left ventricular dysfunction. Interventricular dyssynchrony measured as aortopulmonary ejection delay was identified as a significant predictor on both univariate and multivariate analysis. However, intraventricular dyssynchrony measured as septal to posterior wall activation delay failed to show any value for risk prediction. This may be related to the inability to identify the exact systolic activation in the septum consistently during M-mode scan, especially in patients with regional wall motion abnormality and in patient with broad LBBB QRS after pacing. Thus, post implantation echocardiography to look for interventricular dyssynchrony may help to identify patients who are likely to benefit with routine screening on follow-up for development of PiCMP.

Paced QRS duration as a marker of dyssynchrony has been studied in previous studies; however, no significant correlation was ascertained in those studies [10–13]. In line with the previous studies, this study also failed to show any significant association of PiCMP with paced QRS duration (even for pQRSd > 150 msec, $p = 0.13$). In various CRT-D studies, QRSd remains an important predictor for the response to CRT-D therapy; however, narrowing of the paced QRSd may not be a robust predictor of response to therapy. Similarly, paced QRSd in this study (and the also in a population with majority of patients with normal LV function) is not a determinant of PiCMP. It is likely that prognostic significance of paced QRSd is not as robust as that of *de novo* QRSd as they have different electrical activation pattern.

With the advent of active fixation leads which made possible to safely pace non-apical sites, there has been a lot of discussion over the effect of pacing site on long-term outcomes after pacemaker implantation with many studies having mixed results [17–20]. In a systematic review and meta-analysis, Shimony et al. included 14 trials and 754 patients and demonstrated benefit of non-apical RV pacing over apical RV pacing in patients with baseline LVEF < 45% [21]. However, this benefit was absent when baseline LVEF was normal. The benefit of non-apical pacing remains to be definitively demonstrated in a large randomized control trial. Of note, no study has ever shown any harmful effects of non-apical RV pacing. Thus at present, it can be considered as a safe alternative. In the study cohort from the current study, more than 50% of the patients received pacemaker lead implantation at the RV apex at the operator's discretion. So the current generation of electrophysiologists continues to prefer RV apical site in view of lead stability and ease of the procedure. Outflow tract septum

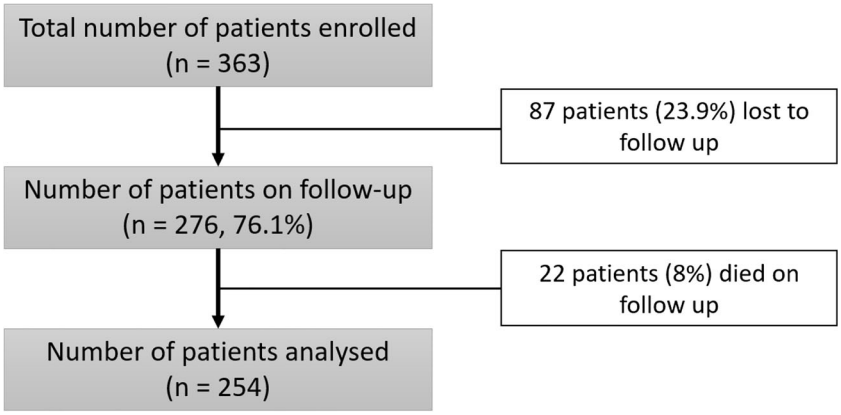

Fig. 3 Patient flow diagram for the study

and mid-septum were chosen as pacing sites in almost 20% of the patients for each site. At baseline, paced QRS duration and aortopulmonary ejection delay were significantly more in the apical pacing group as compared to the non-apical pacing group. Thus, there is evidence that there is significantly more ventricular (especially interventricular) dyssynchrony with apical pacing sites as compared to non-apical pacing sites. However, the benefit of reduction of ventricular dyssynchrony failed to translate into clinical benefit. There was no association of lead position (apical vs non-apical) with the development of PiCMP in the present study. This is similar to studies by Khurshid et al. [12] and Kiehl et al. [13]. The insignificance of apical vs non-apical pacing is consistent with the findings of the recently published randomized controlled PROTECT-PACE study [22]. It should be noted however that a larger sample size and a longer duration of follow-up may unmask a significant beneficial effect of non-apical vs apical pacing.

Table 4 Baseline patient characteristics expressed for the entire cohort and cohort stratified by the presence or absence of pacemaker-induced cardiomyopathy (PiCMP)

Characteristic	Entire cohort ($n = 254$)	Cohort with PiCMP ($n = 35$)	Cohort without PiCMP ($n = 219$)	p value
Age (years)				0.432
< 60 years	95 (37.4%)	11 (31.4%)	84 (38.3%)	
≥ 60 years	159 (62.6%)	24 (68.6%)	135 (61.6%)	
Sex (% males)	68.9%	65.7%	69.4%	0.661
Diabetes	33.5%	25.7%	34.7%	0.295
Hypertension	30.7%	40%	29.2%	0.199
CAD	15.7%	14.3%	15.9%	0.798
Type of pacing				0.585
1 VVIR	127 (50.0%)	19 (54.3%)	108 (49.3%)	
2 DDDR	127 (50.0%)	16 (45.7%)	111 (50.7%)	
Site (other excluded)				0.353
1 Apical	144 (56.7%)	21 (60%)	123 (56.2%)	
2 Non-apical	104 (40.9%)	11 (31.4%)	93 (42.4%)	
Mid-septum	54 (21.2%)	6 (17.1%)	48 (21.9%)	
RVOT	50 (19.7%)	5 (14.3%)	45 (20.5%)	
pQRSd				0.127
< 150 msec	160 (63.0%)	18 (51.4%)	142 (64.8%)	
> 150 msec	94 (37.0%)	17 (48.6%)	77 (35.2%)	
Baseline LVEF	58% ± 7.3%	60% ± 8.0%	58% ± 7.1%	0.400
% pacing				0.002
< 60%	96	12	67	
≥ 60%	158	23	152	
Aortopulmonary ejection delay (msec)	30.2 ± 20.6	42.3 ± 19.1	28.3 ± 20.2	0.001
Septal-posterior wall activation delay (msec)	51.5 ± 35.6	60.3 ± 33.1	50.0 ± 35.8	0.665
FU LVEF	55% ± 8.0%	45% ± 10%	56% ± 6.3%	–

Table 5 Multivariate analysis for identification of predictors of PiCMP

Characteristic	Hazard ratio	*p* value	Confidence intervals
Age (years)	1.35	0.433	0.63–2.91
Sex (% males)	0.84	0.662	0.39–1.79
Diabetes	0.65	0.298	0.29–1.46
Hypertension	1.61	0.202	0.77–3.37
CAD	0.87	0.798	0.32–2.41
Dual vs single chamber	0.819	0.585	0.40–1.67
Site (apical vs non-apical)	1.44	0.355	0.66–3.14
pQRSd (≥ 150 msec vs < 150 msec)	1.74	0.130	0.85–3.57
Baseline LVEF	1.63	0.405	0.51–5.21
% pacing (< 60% vs > 60%)	4.26	0.004	1.59–11.41
Aortopulmonary ejection delay (msec)	3.15	0.002	1.52–6.55
Septal-posterior wall activation delay (msec)	1.41	0.666	0.29–6.83

With respect to the baseline LVEF, Khurshid et al. [12] observed a trend that lower pre-implant LVEF predispodes to PiCMP. However, statistical significance was not met probably due to the inadequate sample size ($p = 0.09$). Kiehl et al. [13] also confirmed this finding by finding a statistically significant association of PiCMP with baseline LVEF. However, the hazard ratio was low and it was found only as a weak predictor. In the present study, baseline LVEF did not have a significant impact on PiCMP as demonstrated in previous studies. This can be attributed to the use of a criteria of 10% fall in ejection fraction for diagnosing PiCMP rather than using a cut-off value. A fall of 5% in ejection fraction may carry much more significance at a baseline EF of 25% vs 55%. Although not significant, a trend towards greater PiCMP incidence was noted in patients with baseline LV dysfunction. In the current study, 22 patients in the analysis cohort of 254 patients had baseline LV dysfunction (defined as LVEF < 50%). Out of these 22 patients, four developed PiCMP on follow-up defined as fall in LVEF by more than 10%. Thus, there was a higher incidence of PiCMP of 18.2% in patients with baseline LV dysfunction. However, this higher incidence can partly be attributed to the natural progression of the baseline LV dysfunction. Khurshid et al. identified male sex and native QRS duration to be predictors of PiCMP. However, no such associations could be drawn in the current study.

The major strength was the prospective nature of the study. All the previous studies for identification of PiCMP and its risk factors have been retrospective [10, 12, 13]. Retrospective studies are known to get flawed by selection bias. Another major strength was that it was an all comers study including all the patients requiring permanent ventricular pacing irrespective of the baseline LV function or indication of pacing. Therefore, the study offered an opportunity to analyse patients with baseline LV dysfunction with permanent pacing. The study also included novel echocardiographic parameters of dyssynchrony in the form of interventricular and intraventricular dyssynchrony, which have not been included in the previous studies. The major limitation of the present study was loss to patient follow-up. Follow-up data was available for 76.1% with 23.9% patients being lost to follow-up. However, due to a large initial sample size, even after loss to follow-up, we were able to include 254 patients for analysis. The other major limitation was the limited duration of follow-up available for the patients with a mean follow-up of only 14.5 months. Still a PiCMP incidence of 13.8% was detected which is in line with other studies. This was probably due to a higher burden of RV pacing in the study population mitigating the effect of shorter follow-up.

5 Conclusion

The incidence of right ventricular pacing-induced left ventricular dysfunction is not uncommon, with an observed incidence of 13.8% in the current study cohort. Burden of right ventricular pacing and interventricular dyssynchrony are the most important predictors for the development of pacing-induced cardiomyopathy. There is no association of paced QRS duration or pacing site with the risk of development of left ventricular dysfunction. Thus, the only modifiable factor at present to minimize pacing-induced cardiomyopathy remains burden of RV pacing, and efforts should be directed towards minimizing it. There remains a need for large randomized controlled trials to demonstrate if protocols to reduce right ventricular pacing can have beneficial effects on occurrence of pacing-induced left ventricular dysfunction.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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