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Chronology of cardiac dysfunction after permanent pacemaker implantation: an observational 2 year prospective study in North India

Harshit Gupta¹, Hakim Irfan Showkat^{2*} , Naved Aslam¹, Rohit Tandon¹, G. S. Wander¹, Shweta Gupta¹, Sadaf Anwar³ and Mohd Maqbool Sohil⁴

Abstract

Background: The purpose of this study is to evaluate cardiac functions using transthoracic echocardiography, change in lead parameters and electrocardiogram (ECG) morphology in patients undergoing permanent pacemaker implantation over a follow-up period of 6 months.

Methods: This is a prospective study in patients undergoing permanent pacemaker implantation in a tertiary care hospital. Patients undergoing permanent pacemaker implantation were enrolled for up to one year and Echocardiographic parameters (by 2 blind operators) and ECG parameters were recorded at admission (within 24 h), before discharge (within 7 days of pacemaker implantation), after 1 month (± 7 days) and after 6 months (± 7 days) of follow-up.

Results: A total of 96 patients (60.4% males and 39.6% female, mean age 66.65 years) were implanted with permanent pacemaker. The mean QRS duration was 133.18 ms and increased significantly to 146.03 ms by 6 months despite septal lead placement in majority (92%) of patients. The mean baseline ejection fraction of 51.47 decreased significantly to 47.83 by 6 months. Diastolic parameters like left atrial volume index, early to late diastolic transmitral flow velocity (E/A) and early diastolic mitral annular tissue velocity (E/e') showed a significant increase ($> 5\%$) from baseline by the end of first week. By the end of first month, systolic dysfunction of RV sets in with significant ($> 5\%$) change from baseline in parameters like Right ventricle myocardial performance index, transannular plane systolic excursion and right ventricle systolic excursion velocity (RVSV).

Conclusion: We have observed that pacemaker recipients with baseline reduced left ventricle (LV) systolic functions perform significantly worse compared to those with baseline normal cardiac functions and had a higher rate of deterioration of LV function. RV dysfunction is the first abnormality that occurs, by 1 week followed by LV dysfunction which starts by 1 month and the diastolic dysfunctions precede the systolic dysfunction. QRS duration also showed a gradual increase despite septal lead placement in majority (92%) and lead parameters showed no significant change over 6 months.

Keywords: Pacemaker, Echocardiography, RV dysfunction, LV dysfunction

*Correspondence: Docirfanshahi512@gmail.com

² Grecian Superspeciality Hospital, Mohali 110065, India

Full list of author information is available at the end of the article



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Background

Permanent cardiac pacing is the most efficient treatment for patients with chronic high-degree atrio-ventricular (AV) block and symptomatic sick sinus syndrome (SSS). The right ventricular (RV) apex has been the preferred site for ventricular lead placement because of good pacing and sensing function, the ease of implantation and long-term stability of passive pacing leads [1]. Emerging clinical evidence has confirmed that RV pacing leads to abnormal ventricular activation and contraction that are associated with adverse long-term clinical outcomes [2, 3]. More studies are needed to fully understand the beneficial and deleterious effects of RV pacing and better identify the patients who are at risk for its detrimental effects. However, the early prediction of myocardial dyssynchrony might provide opportunities to prevent further deterioration into advanced heart failure. With this background we planned this prospective study to identify the patients at high risk for deteriorating heart functions.

Methods

Aims and objectives

To assess the ventricular functions, QRS duration and pacemaker lead parameters over a period of 6 months in patients after permanent Pacemaker implantation.

Study population

This is a prospective study in patients undergoing permanent pacemaker implantation in a tertiary care hospital in North India. Patients undergoing permanent pacemaker implantation were enrolled for up to one year and Echocardiographic parameters and ECG parameters were recorded at admission (within 24 h), before discharge (within 7 days of pacemaker implantation), after 1 month (± 7 days) and after 6 months (± 7 days) of follow-up. All patients eligible for permanent pacemaker implantation according to current guidelines were included.

We included patients over 18 years of age who needed permanent pacemaker according to indications of the ACC/AHA guidelines for implantation of a permanent pacemaker. We excluded patients participating in other studies or patients who cannot perform follow-up in the centre.

Particulars of all the study participants along with presenting complaints, detailed present, past, personal and family history were noted at admission. The indication of pacing, type of pacemaker (Single Chamber/Dual Chamber), lead position (Apical/Septal), pacing mode (DDD or VVI) and the lead parameters were noted after pacemaker implantation. All the study participants underwent routine echocardiography (2 blind operators) and ECG at admission (within 24 h), before discharge (within 7 days of procedure), after 1 month (± 7 days)

and 6 months (± 7 days) of follow-up using a standardized protocol and required parameters were noted and recorded. Pacemaker Interrogation was done on follow-up of 1 month and 6 month and the lead parameters like resistance, voltage, sensitivity and pacing percentages were recorded. Cumulative per cent ventricular paced (Cum%VP) was calculated by (1) finding, for each visit, the mean per cent ventricular paced over all visits up to and including that visit, weighted by the number of days between visits, and (2) using linear interpolation to determine the values for days between visits. Mean value of all these parameters was calculated at 0, 1 week, 1 month and 6 month and a change of more than 5% from the mean value of these parameters was regarded as practically significant change. The study was approved by the institutional review board, and all included subjects gave informed consent to participate in the registry.

Statistical analysis

Data were described in terms of range; mean \pm standard deviation (\pm SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using paired *t* test for independent samples for parametric data. For comparing categorical data, Chi square (Z^2) test was performed and exact test was used when the expected frequency is less than 5. A probability value (*p* value) less than 0.05 was considered statistically significant.

Results

A total of 128 patients received a conventional single- or dual-chamber pacemaker during this period and were assessed for eligibility. Among all pacemaker recipients, 28 did not meet the entry criteria and 4 patients had pacing percentage less than 85% and were excluded from analysis. Hence, the study population consisted of 96 patients (58 male, 60.4%) with a mean age of 66 ± 11 years. Over the 6 month follow-up, 2 (out of the 96) patients died. One patient had a haemorrhagic stroke and died within 3 month period and the other having documented coronary artery disease died suddenly within 1 month. Four patients were lost to follow-up. One patient did not report at 1 month and the other three at 6 month. Data could therefore be obtained for all 96 patients at baseline and before discharge, in 94 patients at 1 month and 90 patients at 6 months. History of diabetes was present in 43 (44.8%) patients, history of hypertension was present in 62 (64.6%) patients, while history of coronary heart disease was present in 28 (29.2%) patients. Only 19.8% (19) of the patients had a history of alcohol intake and 6% (6) patients had positive history of smoking while only 2 (2.1%) patients had history

of any substance abuse. Presyncope was the most common presenting complaint in 47 (49%) patients while syncope was present in 25 (26%) patients. Important clinical characteristics of the study population, including detailed information on the pacing indications, implanted cardiac pacing devices and site of pacing, are presented in Table 1. Patients were followed for a mean of 6 months. Around 34% patients needed single chamber pacemaker (Mainly including Complete heart block with advanced age or financial constraints in whom single chamber-VVI pacemaker was put with all patients having septal lead placement and just few patients of high grade AV block with advanced age or financial constraints had single chamber VVI pacemaker).

Pacemaker lead parameters (Table 2)

In majority of patients (66%) dual chamber pacemaker was implanted with DDD. Single chamber pacemaker was implanted in 34% patients with VVI mode

Table 1 Baseline characteristics

	No. of patients	Percentage
Gender		
F	38	39.6
M	58	60.4
Total	96	100.0
Past history		
Diabetes	43	44.8
Hypertension	62	64.6
CAD	28	29.2
Personal history		
Alcohol	19	19.8
Smoking	6	6.3
Others	2	2.1
Presenting complaints		
Non-specific symptoms	11	11.5
Dyspnea	8	8.3
Palpitation	5	5.2
Presyncope	47	49.0
Syncope	25	26.0
Indication of pacing		
CHB (complete heart block)	62	64.6
High degree AV block	15	15.6
SSS (sick sinus syndrome)	19	19.8
Total	96	100.0
Type of pacemaker		
Single chamber	33	34.4
Dual chamber	63	65.6
Lead position		
Apical	8	8.3
Septal	88	91.7

and in majority around 92% patients septal lead was placed. The mean value of resistance of the atrial lead was 535.49 Ohms at the time of pacemaker implantation, 511.34 ohms after 1 month and was 575.13 ohms at the end of 6 months. While the mean value of resistance of the ventricular lead was 595.20 ohms at the time of pacemaker implantation, 565.33 ohms after 1 month and was 628.16 ohms after 6 months. The mean value of threshold of the atrial lead was 1.0 V at the time of pacemaker implantation, 0.85 V after 1 month and was 0.77 V at the end of 6 months. While the mean value of threshold of the ventricular lead was 0.96 V at the time of pacemaker implantation, 0.85 V after 1 month and was 0.87 V after 6 months. The mean value of sensitivity of the atrial lead was 2.71 mV at the time of pacemaker implantation, 2.57 mV after 1 month and was 2.45 mV at the end of 6 months. While the mean value of sensitivity of the ventricular lead was 5.82 mV at the time of pacemaker implantation, 6.24 mV after 1 month and was 6.4 mV after 6 months. Pacing percentage was above 90% in maximum patients and patient with pacing percentage below 85% were excluded from study. So this bias was tried to be minimized by excluding low pacing percentage cases which may have altered the results.

QRS duration (Table 2)

Majority of our patients (92%) had septal lead placement. The mean QRS duration at the time of admission was 133.18 ms which had increased significantly to 150.29 ms before discharge (p value < 0.0001). At the end of 1 month the mean QRS duration was 140.87 ms (p value = 0.001) and increased to 146.03 ms by the end of 6 months (p value < 0.0001). Out of the total of 96 patients, an increase of more than 10% in QRS duration was present in 16 patients at 1 week (out of which 69% were diabetics, 81% were hypertensives and had a mean age of 66 years) while in 27 patients at 1 month (out of which 52% were diabetics, 66% were hypertensives) and only 39 patients at 6 month (out of which 49% were diabetics, 64% were hypertensives).

Echocardiographic parameters (Table 3)

The mean EF of the patients at the time of admission was 51.47 and showed an insignificant rise to 51.73 (p value = 0.084) before discharge. By the end of 1 month, the mean EF was 50.10 (p value < 0.0001) and decreased significantly to 47.83 by 6 months (p value < 0.0001). Out of the total of 96 patients, 52 patients (54%) had EF of more than 50% at baseline (average age of 65 years). These patients had an average decrease of 0.2% by 1 week, 2.4% by 1 month and 6.0% by 6 months in EF as compared to baseline. No patient out of these 52 patients had an EF of less than 50% during the 6 month follow-up.

Table 2 Pacemaker parameters and QRS duration

	N	Min	Max	Mean	SD	p value
Resistance-A (Ohm)						
Before Discharge	63	430.0	695.0	535.49	61.32	
1 month	62	62.0	671.0	511.34	90.66	0.566
6 month	60	425.0	722.0	575.13	61.43	0.108
Resistance-V (Ohm)						
Before Discharge	96	345.0	1380.0	595.20	112.47	
1 month	94	318.0	1335.0	565.33	111.19	
6 month	90	355.0	1445.0	628.16	119.59	0.7
Voltage-A (Volt)						
Before Discharge	63	0.5	4.0	1.00	0.44	
1 month	62	0.3	1.5	0.85	0.26	0.053
6 month	60	0.3	1.5	0.77	0.24	0.066
Voltage-V (Volt)						
Before Discharge	96	0.3	4.0	0.96	0.39	
1 month	94	0.3	2.0	0.85	0.27	0.1
6 month	90	0.3	6.2	0.87	0.63	0.1
Sensitivity-A						
Before Discharge	63	0.5	6.2	2.71	1.37	
1 month	62	0.5	6.0	2.57	1.23	0.099
6 month	60	0.5	6.5	2.45	1.24	0.085
Sensitivity-V						
Before Discharge	96	0.0	15.6	5.82	5.45	
1 month	94	0.0	15.0	6.24	5.63	0.100
6 month	90	0.0	15.6	6.40	5.61	0.126
Pacing percentage (%)						
Before Discharge	96	91	96	93.5	2.12	0.723
1 month	92	89	94	91.5	1.32	0.542
6 month	95	92	97	94.5	3.21	0.891
QRS duration (msec)						
At admission	96	82.0	202.0	133.18	29.45	
Before Discharge	96	92.0	204.0	150.29	24.74	0.000
1 month	94	84.0	188.0	140.87	20.38	0.001
6 month	90	98.0	184.0	146.03	19.82	0.000

Forty-four patients (46%) had EF of less than or equal to 50% at baseline (average age of 68 years). These patients had an average decrease of 1.7% by 1 week, 2.2% by 1 month and 9.0% by 6 months in EF from baseline. At 1 month >5% decrease in EF as compared to baseline EF was seen in 11 patients (25%). At 6 month >5% decrease in EF as compared to baseline EF was seen in 29 patients (66%).

The mean RV stroke volume at the time of admission was 42.34 ml which had increased to 43.86 ml before discharge. At the end of 1 month the mean RV stroke volume was 41.05 ml (decrease of 3%) and decreased to 38.32 ml (decrease of 9.4%) by the end of 6 months which shows statistically significant change.

The mean LV stroke volume at the time of admission was 44.58 ml which had increased to 46.29 ml before discharge (p value < 0.0001). At the end of 1 month the mean LV stroke volume was 43.37 ml (decrease of 2.6%) and decreased to 41.10 ml (change of 7.6%) by the end of 6 months which shows significant change (p value < 0.0001). Cardiac output showed an statistically insignificant change over a period of 6 months.

Left ventricle end systolic diameter and diastolic diameter (LVESD and LVEDD) also show significant changes after period of 1 month and 6 month. Right ventricle end systolic diameter and diastolic diameter (RVESD and RVEDD) showed significant increase at 1 month and continued to increase progressively till 6 months. Practically

Table 3 Echocardiographic parameters

	N	Minimum	Maximum	Mean	SD	p value
LVEF						
At admission	96	28.0	60.0	51.47	9.83	
Before discharge	96	28.0	60.0	51.73	9.54	0.084
1 month	94	26.0	60.0	50.10	9.88	0.000
6 month	90	24.0	60.0	47.83	10.41	0.000
RV SV						
At admission	96	28.0	62.0	42.34	7.67	
Before discharge	96	23.0	66.0	43.86	8.38	0.000
1 month	94	22.0	62.0	41.05	8.22	0.002
6 month	90	23.0	58.0	38.32	8.08	0.000
LV SV						
At admission	96	22.0	70.0	44.58	9.21	
Before discharge	96	25.0	75.0	46.29	8.71	0.000
1 month	94	24.0	68.0	43.37	8.45	0.010
6 month	90	22.0	64.0	41.10	8.73	0.000
CO						
At admission	96	1.1	30.4	3.32	3.08	
Before discharge	96	2.2	34.0	3.96	3.19	0.665
1 month	94	1.8	25.6	3.56	2.39	0.569
6 month	90	1.7	4.8	3.09	0.69	0.461
LV ESD						
At admission	96	12.0	49.0	31.31	7.72	
Before discharge	96	12.0	48.0	29.80	7.48	0.000
1 month	94	12.0	50.0	32.73	7.61	0.000
6 month	90	14.0	51.0	35.39	7.69	0.000
LV EDD						
At admission	96	26.0	60.0	45.60	7.19	
Before discharge	96	26.0	61.0	46.05	7.13	0.051
1 month	94	26.0	66.0	48.96	7.49	0.000
6 month	90	30.0	68.0	52.21	7.31	0.000
RV ESD						
At admission	96	8.0	24.0	10.30	2.68	
Before discharge	96	5.0	23.0	10.59	3.10	0.109
1 month	94	9.0	24.0	13.13	3.29	0.000
6 month	90	9.0	28.0	16.63	4.07	0.000
RV EDD						
At admission	96	20.0	38.0	23.08	3.53	
Before discharge	96	20.0	38.0	24.38	3.59	0.000
1 month	94	20.0	42.0	27.83	4.21	0.000
6 month	90	22.0	48.0	32.66	5.53	0.000
LAVI						
At admission	96	17.0	55.0	23.86	4.83	
Before discharge	96	13.5	57.0	24.83	5.29	0.000
1 month	94	15.1	56.6	27.08	5.46	0.000
6 month	90	14.7	57.5	29.50	6.18	0.000

significant change (>5%) occurs as early as first month in diastolic dimensions of both LV and RV.

Right ventricle myocardial performance index (RVMPI) at the time of admission was 0.60 which showed a gradual increase to 0.61 before discharge. At the end of 1 month the mean RV MPI was 0.66 (an increase of 10%) and increased to 0.72 by the end of 6 months (p value < 0.0001 for 1 month and 6 month). Mean left ventricle myocardial performance index (LVMPI) also increased similarly, becoming statistically significant by 1 month and 6 months (p value < 0.0001). Practically significant increase (>5%) in the value of both LVMPI and RVMPI occurs by first month of pacemaker implantation.

The left atrial volume index (LAVI) showed a gradual and progressive increase over a period of 6 months with a change of 4%, 13% and 23% at first week, first month and 6 months of pacemaker implantation.

The mean TAPSE at the time of admission was 19.0 mm and 19.42 mm before discharge (p value = 0.02). At the end of 1 month the mean TAPSE was 16.84 (fall of 11%) and decreased further to 14.58 (fall of 23% from baseline) by the end of 6 months (p value < 0.0001 for 1 month and 6 month).

Our study shows an insignificant decrease in PASP within first week of pacemaker implantation followed by progressive increase over the period of 6 month.

E/A ratio and E/e' ratio showed a progressive increase over a period of 6 month suggesting deteriorating LV diastolic function. Practically significant change (>5%) in both E/A ratio and E/e' ratio occurs as early as first week of pacemaker implantation.

RVS' and LVS' showed an increase within the first week of pacemaker implantation followed by a gradual and progressive decrease over the follow-up period of 6 months suggesting the worsening of ventricular systolic functions.

Discussion

RV pacing has been rigorously evaluated in numerous trials which have shown that it may be associated with a worse clinical outcome like deterioration of LV systolic function, development of heart failure and atrial fibrillation [4–8].

Similar to the results by Zhang et al. [9], our study showed that the deterioration of LV functions was higher in elderly patients and patients having more number of risk factors like both diabetes and hypertension than patients having only hypertension or only diabetes.

The DANPACE study randomized 1415 patients with sinus node dysfunction to AAIR or DDDR pacing and concluded that predictors of development of HF included older age, reduced baseline LVEF, and previous myocardial infarction [10]. Our study also showed that the

decrease in EF was more in patients who had prior LV dysfunction, were older in age and had higher number of risk factors like diabetes, hypertension, coronary artery diseases. Studies by Fang et al. [11] and Kiehl et al. [12] have confirmed that pre implant EF is an important predictor for the development of pacemaker induced cardiomyopathy. Tse et al. did not notice any improvement of LV function during follow-up period for 6 month in their comparative studies of alternate site of pacing but noticed significant improvement in global LV systolic and diastolic function after 18 months [13]. A study conducted by Yu et al. (2009) [14] showed that in patients with normal systolic function, conventional right ventricular apical pacing resulted in adverse left ventricular remodelling and in a reduction in the left ventricular ejection fraction.

Similar to the results by Ebert et al. [15], our study showed that the deterioration in LVEF was gradual and progressive and more in patients who had baseline LV dysfunction. Our findings were in accordance with the study conducted by Sarkar et al. [16] which have shown worsening LV diastolic and systolic functions after pacemaker implantation. Our findings were in accordance with the study by Dwivedi et al. [17] which showed that diastolic dysfunction develops as early as first week after pacemaker implantation. They also suggested that diastolic abnormalities are first to appear which are followed by appearance of systolic abnormalities. Tantengco et al. also studied the left ventricular dysfunction after long-term right ventricular apical pacing and concluded that in young patients requiring long-term RV pacing, alternative sites of ventricular pacing that simulate normal biventricular electrical activation should be explored [18].

Both Ahmad et al. [19] and Schmidt et al. [20] have concluded that RV pacing prolongs QRS duration independent of EF. Majority of our patients (92%) had septal lead placement. In our study, the worsening of cardiac functions after pacemaker implantation was also evident on ECG as indicated by significant increase in QRS duration over a 6 month follow-up despite septal lead placement. A study conducted by Lee et al. 2014 [21] revealed the best cut-off value of QRS width to be 150 ms for the prediction of myocardial dyssynchrony. Out of 96 patients, 12 patients had QRS duration of more than 150 ms at baseline but none of them had symptoms of heart failure. These patients presented with the symptoms of either syncope or presyncope.

There were no incidence of any complications like pocket hematoma, acute perforation, infection, lead dislodgement, erosion, lead fracture or insulation break.

Our study requires further evaluation using modalities like cardiac MRI which have been regarded as gold standard for assessing cardiac functions [22]. In literature,

various therapeutic options have been suggested in patients with a conventional pacemaker indication. The upgrade to CRT may partially reverse the deleterious effects of RV apical pacing [23, 24]. New pacing strategies and alternative RV pacing sites [25] may prevent the induction of ventricular dyssynchrony and the deterioration of LV function.

Limitations

The major limitation of our study was small sample size and short follow-up period. Our study requires further evaluation using modalities like cardiac MRI and cardiac strain imaging which have been regarded as gold standard for assessing cardiac functions. Our study also required us to assume a deterioration of >5% in the echocardiographic parameters from baseline as a significant change in practical assessment.

Conclusion

- The mean QRS duration increased significantly by 6 months despite septal lead placement.
- Diastolic parameters like LAVI, E/A and E/e' showed a significant increase from baseline by the end of first week.
- By the end of first month, systolic dysfunction of RV sets in with significant change from baseline in parameters like RVMPI, TAPSE and RVS'.
- Significant change in both systolic and diastolic function was present by the end of 6 months without any change in the resting cardiac output.

Abbreviations

ECG: Electrocardiogram; LV/RV: Left/right ventricle; LVESD and LVEDD: Left ventricle end systolic diameter/ diastolic diameter; EF: Ejection fraction; LAVI: Left atrial volume index; TAPSE: Tricuspid annular plane systolic excursion; LV/RV MPI: Left/right ventricle myocardial performance index (Tei Index); MRI: Magnetic resonance imaging; PASP: Pulmonary artery systolic pressure; CRT: Cardiac resynchronisation therapy.

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Authors' contributions

HG helped in design of the work, echocardiography and electrophysiology assessment. HIS did acquisition, analysis of data and prepared the study content. NA helped in compiling data, pacemaker implantation, pacemaker parameters assessment and discussion. RT helped in interpretation of data; GSW have drafted the work or substantively revised it. SG helped in statistical data compilation. SA: Helped in calculating data and in noninvasive work. MMS: Helped in revision of study. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request on email docirfanshahi512@gmail.com or the corresponding address as given.

Declarations

Ethics approval and consent to participate

Yes all formal written consents taken (Approved by DMC ethical committee—DMC Ludhiana Punjab with no reference number).

Consent for publication

The participants and all authors certify that all appropriate written consent forms were given and formally written consents were taken. In the form the patient(s) has/have given his/her/their written consent for his/her/their images and other clinical information to be reported in the journal. The patient(s) understand that his/her/their name(s) and initials will not be published and due efforts will be made to conceal his/her/their identity, but anonymity cannot be guaranteed. DMC Ethical committee cleared after cross checking the consent forms and format.

Competing interests

The authors declare that they have no competing interests.

Author details

¹DMC, Ludhiana, Punjab, India. ²Grecian Superspeciality Hospital, Mohali 110065, India. ³Fortis Escorts Heart Institute, Delhi, India. ⁴Narayana Hrudayalaya Hospital, Ahmedabad, India.

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