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Paced QRS Duration as the Major Determinant of Pacing Induced Cardiomyopathy in Complete AV Block

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ABSTRACT

Patients with complete heart block often develop pacing-induced cardiomyopathy (PICM) after placement of a permanent pacemaker. **Objective:** To establish paced QRS duration as determinant of pacing induced cardiomyopathy in complete Atrioventricular (AV) block. **Methods:** This descriptive study included 115 male and female patients that had a permanent pacemaker implanted for complete AV block, at the department of Cardiology, Hayatabad Medical Complex, Peshawar, during the period 1st November 2023 till 30th June 2024. Patients were evaluated for the presence of PICM and subsequently grouped as PICM and non-PICM. Paced QRS duration in both groups was compared. **Results:** PICM was confirmed in 63 patients (54.8%) and 52 (45.2%) were non-PICM. Mean age in PICM group was 71.2 ± 8.7 years and 66.8 ± 9.5 years in non-PICM group. The mean paced QRS duration in PICM group was 200.5 ± 22.3 milliseconds and 168.3 ± 15.7milliseconds in non-PICM group (p value <0.001). **Conclusions:** Prolonged paced QRS duration was found as key indicator for predicting pacing induced cardiomyopathy in patients with permanent pacing for complete AV block.

INTRODUCTION

Pacing Induced Cardiomyopathy (PICM) is an issue that needs attention in patients having prolonged ventricular pacing on placement of a Permanent Pacemaker (PPM) for full AV block [1, 2]. Restoration of normal cardiac rhythm prevent negative hemodynamic consequences resulting from AV block but prolonged ventricular pacing has been shown to adversely affect cardiac structure and function eventually leading to PICM [3-5]. Risk stratification and prevention strategies are hampered by impenetrable complex factors which cause PICM [6]. The prolonged PR interval or QRS complex might be indicative of major dyssynchrony that can lead to dilated atria or ventricles as well as their poor contractility [7]. However other studies suggest that protracted pQRS may also be an additional marker for excessive dyssynchrony during ventricular contractions associated with damaging remodeling and dysfunction [8-10]. Nevertheless, there is still a lack of clarity on how development of PICM occurs due to pQRSd

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increase [11]. Thus, identification of variables influencing onset of PICM will provide evidence for optimizing patient care and outcomes in terms of clinical implications associated with this disease. The study focused on variables such as age, gender and baseline LVEF in the multivariate model because they have been shown to potentially influence the development of PICM. Multicollinearity was checked using Variance Inflation Factor (VIF), and all variables had acceptable VIF values (below 4), ensuring that multicollinearity did not affect the results.

Consequently, the present study aimed to investigate paced QRS duration as a predictor for PICM among patients with complete atrio-ventricular block following permanent pacemaker implantation. The current paper also explored how pQRSd can be utilized as a measure of risk stratification and target therapy in order to minimize adverse effects related to ventricular pacing on myocardial contractility.

METHODS

This descriptive study was carried at the department of Cardiology, Hayatabad Medical, Complex, Peshawar, during the period 1st November 2023 till 30th June 2024. Approval for the conduct of the study was granted vide no: 1638. A total of 115 male and female patients in the age range 20 to 90 years who underwent permanent pacing for complete AV block at the department of cardiology of the hospital were registered. Patients with prior history of cardiomyopathies, patients taking diuretics, beta blockers or digoxin, patients with history hyperthyroidism, patients with valvular heart disease and previous history of intervention for conduction abnormalities were excluded. Complete AV block was confirmed by the presence of clinical findings such as dizziness, palpitations and shortness of breath and ECG showing identifiable p waves with complete dissociation from QRS complex. Permanent pacemaker was small battery placed under the skin that generates and provides electrical impulses to the heart at regular intervals. Pacing induced cardiomyopathy was confirmed on echocardiography defined as ejection fraction 50.0% or below or sudden decline in ejection fraction by greater 10.0% from baseline after permanent pacemaker installation. Paced QRS duration was measured as the distance from the start of Q wave till the end of S wave on ECG recorded in milliseconds in patients with pacing. Normal value was 160.0 ± 18.0 milliseconds. Patients were recruited using non-probability consecutive sampling technique and sample size was calculated using WHO sample size calculator taking 31.5% anticipated prevalence of pacing induced cardiomyopathy in patients with pacing for complete AV block, 8.5% margin of error and 95% confidence level [4]. Patients were enrolled after taking permission from research review board of the institute. Informed consent was obtained from registered participants. Basic information and relevant medical records was retrieved from Electronic Health Records (EHRs). Baseline left ventricular ejection fraction was noted. An echocardiography was performed by consultant cardiologist. Left ventricular ejection fraction was compared with baseline values and presence of PICM was noted. Patients were subsequently grouped into (PICM) and (non-PICM) based on the presence or absence of PICM. An ECG was performed and paced QRS duration was noted in milliseconds by measuring the interval between the start of Q wave till the end of S wave. Paced QRS value more than 180 milliseconds was called prolonged paced QRS duration. Normality of continuous variables (e.g., LVEF, QRS duration) was tested using the Shapiro-Wilk test. Non-normally distributed data were reported as median and Interquartile Range (IQR) and compared using non-parametric tests (Mann-Whitney U). Potential confounders, such as the severity of heart conditions (e.g., history of coronary artery disease or myocardial infarction), pacemaker duration, and medication history (e.g., use of beta-blockers or diuretics), were adjusted for in the multivariate logistic regression model. Data analysis was done with SPSS version 22. Means ± standard deviation was used to characterize continuous variables and categorical data were presented as frequencies and percentages. Normality was assessed using the Shapiro-Wilk test, and based on the results, parametric or non-parametric tests were applied accordingly. Continuous data were compared using independent sample t test and chi square test was applied to categorical data. Multivariate logistic regression analysis was conducted to evaluate the predictors of PICM while controlling for confounders such as age, gender, and baseline LVEF. ROC curve analysis was used to obtain the cut off value for paced QRS duration for predicting PICM. P value ≤0.05 was considered statistically significant.

RESULTS

A total of 115 patients were recruited. PICM was observed in 63 patients (54.8%) and 52 (45.2%) were non-PICM. Overall mean age of the participants was 68.5 ± 9.2 years. Mean age in PICM group was 71.2 ± 8.7 years and 66.8 ± 9.5 years in non-PICM group. Male to female ratio in both groups was 1: 1.25 and 1: 1.36 respectively. 15 (23.8%) had previous history of MI in PICM group and 12 patients (23.0%) had MI history. Baseline clinico-demographic characteristics of the patients were summarized in table 1.

Table 1: Patient Demographics and Baseline Clinical Characteristics (n=230)

Variables	Total (Mean ± SD) / N (%)	PICM (Mean ± SD) / N (%)	Non-PICM (Mean ± SD) / N (%)	p-Value
Age (Years)	68.5 ± 9.2	71.2 ± 8.7	66.8 ± 9.5	0.097*

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Gender				
Male	65 (56.5%)	35 (55.5%)	30 (57.7%)	
Female	50 (43.5%)	28 (44.5%)	22 (42.3%)	0.123**
Hypertension	82 (71.3%)	45 (71.4%)	37 (71.2%)	0.456**
Diabetes mellitus	38 (33.0%)	20 (31.7%)	18 (34.6%)	0.789**
Coronary artery disease	45 (39.1%)	22 (34.9%)	23 (44.2%)	0.234**
Previous myocardial infarction	27 (23.5%)	15 (23.8%)	12 (23.0%)	0.567**

**Independent sample t test*
***Chi square test*

Patient with PICM had a significantly lower mean (LVEF) than those without (49.8% vs. 58.7%, p = 0.001). The left ventricular end-diastolic and end-systolic diameters were similar between groups (p > 0.05) as reported in table 2.

Table 2: Baseline Echocardiographic Parameters (n=345)

Variables	Total (Mean ± SD)	PICM (Mean ± SD)	Non-PICM (Mean ± SD)	p-Value	Skewness value
LVEF (%)	55.2 ± 5.6	49.8 ± 6.35	58.7 ± 4.8	0.001	0.683
Left ventricular end-diastolic diameter (mm)	49.6 ± 3.2	0.8 ± 3.5	48.9 ± 2.9	0.234	0.198
Left ventricular end-systolic diameter (mm)	31.4 ± 2.9	33.1 ± 3.2	30.2 ± 2.5	0.456	0.031

The mean paced QRS duration (pQRSd) compared to non-PICM patients was significantly different (200.5 ms vs. 168.3 ms, p < 0.001). Patient with PICM had a considerably higher rate of right ventricular lead insertion at the apical position (82.8% vs. 66.1%, p = 0.123) as reported in table 3.

Table 3: Pacing Variables (n=345)

Variables	Total (Mean ± SD) / N (%)	PICM (Mean ± SD) / N (%)	Non-PICM (Mean ± SD) / N (%)	p-Value	Skewness value
Paced QRS Duration (ms)	180.6 ± 20.8	200.5±22.3	168.3 ± 15.7	<0.001	0.985
Right Ventricular Lead Location					
Apical	85 (73.9%)	48 (82.8%)	37 (66.1%)	0.1231	-
Septal	25 (21.7%)	2 (20.7%)	13 (23.2%)	0.456	
Other	5 (4.4%)	3 (5.2%)	2 (3.6%)	0.789	

As illustrated in table 4, Univariate logistic regression analysis demonstrated that paced QRS duration (OR: 1.15, 95% CI: 1.08–1.23, p < 0.001) and age (OR: 1.05, 95% CI: 1.01–1.10, p = 0.02) were significant predictors of PICM. Other variables like gender and hypertension were not significant in univariate analysis.

Table 4: Univariate and Multivariate Logistic Regression Analysis

Variables	Adjusted Odds Ratio (95% CI)	p-Value
Univariate Logistic Regression		
Paced QRS Duration	1.15 (1.08–1.23)	<0.001
Age	1.05 (1.01–1.10)	0.02
Multivariate Logistic Regression		
Paced QRS Duration	1.25 (1.12 - 1.39)	<0.001
Age	1.08 (1.02 - 1.15)	0.234
Gender (male)	1.17 (0.98 - 1.32)	0.567
Baseline LVEF	0.92 (0.86 - 0.98)	0.091

Logistic regression model analysis was constructed to determine the predictive ability of paced QRS duration with development of PICM, even after controlling for age, gender and baseline LVEF (adjusted odds ratio 1.25, 95% CI 1.12–1.39, p < 0.001). Variables of age, gender and baseline (LVEF) exhibited independent associations with PICM, which was not statistically significant. The ROC curve for paced QRS duration in predicting PICM had an area under the curve (AUC) of 0.78, indicating good predictive ability. A cutoff value of 180 milliseconds offered 75.0% sensitivity and 72.5% specificity as reported in table 5.

Table 5: ROC Curve Analysis for Paced QRS Duration

Variables	Area Under the Curve	Sensitivity	Specificity	Optimal Cutoff Value
Paced QRS Duration (ms)	0.78	75.0%	72.5%	180 ms

ROC Curve for Paced QRS Duration with a diagonal reference line, demonstrating the ability of paced QRS duration to predict pacing-induced cardiomyopathy (Figure 1).

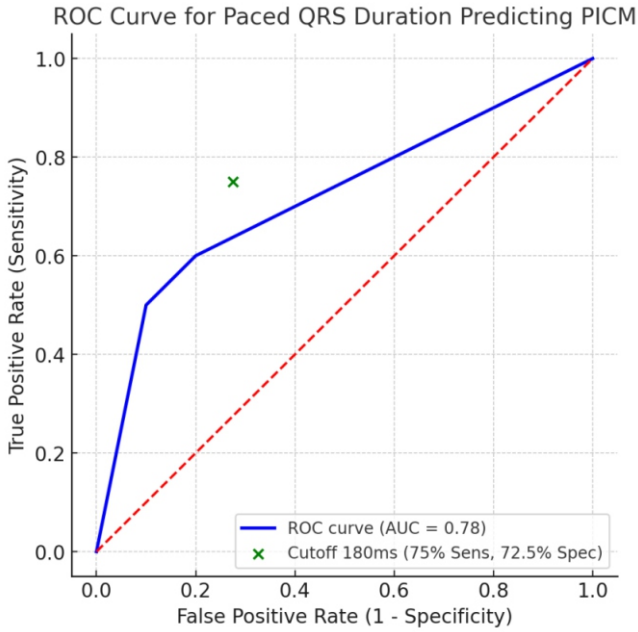

Figure 1: ROC Curve for Paced QRS Duration with Diagonal Reference Line

DISCUSSION

The present research, which included 115 patients diagnosed with complete AV block and received permanent pacemaker, provides important insights into the development of Pacing-Induced Cardiomyopathy (PICM). This data show that 54.8% of the patients acquired PICM during follow-up, which was consistent with prior studies by Ghosh A *et al.*, and Emerek K *et al.*, where PICM rates varied from 12% and 50% respectively, depending on the cohort and follow-up time [12, 13]. Differences in patient groups, PICM definitions, and follow-up durations were most likely to explain the discrepancy in these percentages. In this research, the mean age of patients

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was 68.5 ± 9.2 years. Those developing PICM were substantially older (71.2 years) than those who did not (66.8 years). This age difference was consistent with previous research, which suggests that advanced age was a risk factor for the development of PICM [14]. Older age was likely associated with a higher load of comorbidities and cardiac structural alterations that predispose individuals to PICM. these findings revealed a substantial difference in LVEF between patients with and without PICM (49.8% vs 58.7%, p=0.001). This result supports prior research by Cho and colleagues who found lower LVEF as both a predictor and a consequence of PICM [15]. A lower baseline LVEF indicates a fragile myocardial that may not withstand the dys-synchronous pacing associated with right ventricular pacing. The study found that patients with PICM had considerably longer mean pQRSd (200.5 ms) than those without PICM (168.3 ms, $p < 0.001$). Previous study has also identified extended pQRSd as a crucial element in the development of PICM, with comparable cut-off values of roughly 190 ms described as predictive [16]. This study's ROC curve analysis for pQRSd produced an area of 0.78, suggesting strong predictive power, and the discovered cutoff value of 180ms offered 75.0% sensitivity and 72.5% specificity, which was similar with previous research [14]. The PICM group had a greater rate of right ventricular lead insertion at the apical location (82.8%) than the non-PICM group (66.1%), although the difference was not statistically significant ($p = 0.123$). This result was consistent with previous findings of Weintraub WS *et al.*, and another study by Samaras K *et al.*, that apical pacing was related with worse remodeling and PICM than non-apical pacing locations [17, 18]. The independent correlation between the development of PICM and longer pQRSd, older age, and poorer baseline LVEF was validated by the multivariable analysis. Garcia, J. M. *et al.*, and Lee, H. *et al.*, showed that gender was not found to be a significant predictor [19, 20].

CONCLUSIONS

This study highlights the importance of paced QRS duration in predicting pacing induced cardiomyopathy in patients with complete AV block. Mean paced QRS complex in PICM group was longer than non-PICM group (200.5 ms vs. 168.3 ms, $p<0.001$). ROC curve analysis revealed 180.0milliseconds cut off for predicting PICM. The sensitivity and specificity obtained were 75.0% and 72.5% respectively. Demographics like age, gender and clinical parameters could not perform significantly effect in multivariate analysis.

Authors Contribution

Conceptualization: HT, YA, IUH, WS
Methodology: RK, HT
Formal analysis: RK, HT, TM, SK
Writing, review and editing: TM, IUH, WS, KNK
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Kiehl EL, Makki T, Kumar R, Gumber D, Kwon DH, Rickard JW *et al.* Incidence and predictors of right ventricular pacing-induced cardiomyopathy in patients with complete atrioventricular block and preserved left ventricular systolic function. Heart Rhythm. 2016 Dec; 13(12): 2272-8. doi: 10.1016/j.hrthm.2016.09.027.

[2] Gavaghan C. Pacemaker induced cardiomyopathy: an overview of current literature. Current Cardiology Reviews. 2022 May; 18(3). doi: 10.2174/2772432816666210901111616.

[3] Kotecha D and Piccini JP. Atrial fibrillation in heart failure: what should we do?. European Heart Journal. 2015 Dec; 36(46): 3250-7. doi: 10.1093/eurheartj/ehv513.

[4] Babu NS, Srinath SC, Lahiri A, Chase D, John B, Roshan J. Three-dimensional echocardiography with left ventricular strain analyses helps earlier prediction of right ventricular pacing-induced cardiomyopathy. Journal of the Saudi Heart Association. 2018 Apr; 30(2): 102-7. doi: 10.1016/j.jsha.2017.06.001.

[5] Khurshid S, Obeng-Gyimah E, Supple GE, Schaller R, Lin D, Owens AT *et al.* Reversal of pacing-induced cardiomyopathy following cardiac resynchronization therapy. JACC: Clinical Electrophysiology. 2018 Feb; 4(2): 168-77. doi: 10.1016/j.jacep.2017.10.002.

[6] Khurwolah MR, Yao J, Kong XQ. Adverse consequences of right ventricular apical pacing and novel strategies to optimize left ventricular systolic and diastolic function. Current Cardiology Reviews. 2019 May; 15(2): 145-55. doi: 10.2174/1573403X15666181129161839.

[7] Stanley Jr A, Athanasuleas C, Buckberg G. How his bundle pacing prevents and reverses heart failure induced by right ventricular pacing. Heart Failure Reviews. 2021 Nov; 26(6): 1311-24. doi: 10.1007/s10741-020-09962-8.

[8] Al Younis SM, Hadjileontiadis LJ, Al Shehhi AM, Stefanini C, Alkhodari M, Soulaidopoulos S *et al.* Investigating automated regression models for estimating left ventricular ejection fraction levels in heart failure patients using circadian ECG features.

DOI: https://doi.org/10.54393/pjhs.v5i09.2058

PLOS One. 2023 Dec; 18(12): e0295653. doi: 10.1371/journal.pone.0295653.

[9] Al-Asad KS, Martinez A, Prasad RM, Ukponmwan EU, Baloch ZQ, Ali A *et al.* Pacing-Induced Cardiomyopathy in Leadless and Traditional Pacemakers: A Single-Center Retrospective Analysis. Cureus. 2023 Jul; 15(7): e41393. doi: 10.7759/cureus.41393.

[10] Medina-Ravell VA, Lankipalli RS, Yan GX, Antzelevitch C, Medina-Malpica NA, Medina-Malpica OA *et al.* Effect of epicardial or biventricular pacing to prolong QT interval and increase transmural dispersion of repolarization: does resynchronization therapy pose a risk for patients predisposed to long QT or torsade de pointes?. Circulation. 2003 Feb; 107(5): 740-6. doi: 10.1161/01.CIR.0000048126.07819.37.

[11] Zhang J, Ju W, Yang G, Tang C, Luo J, Xu J *et al.* Epicardial ablation of refractory focal atrial tachycardia after a failed endocardial approach. Heart Rhythm. 2023 Mar; 20(3): 374-82. doi: 10.1016/j.hrthm.2022.11.007.

[12] Ghosh A, Kapoor A, Khanna R, Sahu A, Kumar S, Garg N *et al.* A pilot study on the acute conversion and maintenance of sinus rhythm in rheumatic atrial fibrillation using oral flecainide. Indian Heart Journal. 2020 Sep; 72(5): 383-8. doi.org/10.1016/j.ihj.2020.07.004.

[13] Emerek K, Friedman DJ, Sørensen PL, Hansen SM, Larsen JM, Risum N *et al.* Vectorcardiographic QRS area is associated with long-term outcome after cardiac resynchronization therapy. Heart Rhythm. 2019 Feb; 16(2): 213-9. doi: 10.1016/j.hrthm.2018.08.028.

[14] Caleyachetty R, Littlejohns T, Lacey B, Bešević J, Conroy M, Collins R *et al.* United Kingdom Biobank (UK Biobank) JACC Focus Seminar 6/8. Journal of the American College of Cardiology. 2021 Jul; 78(1): 56-65. doi: 10.1016/j.jacc.2021.03.342.

[15] Fruelund PZ. Chronic effects of right ventricular pacing: The impact of right ventricular lead position. 2024 Sep. doi: 10.54337/aau534290121.

[16] Iaccarino G, Ciccarelli M, Sorriento D, Galasso G, Campanile A, Santulli G *et al.* Ischemic neoangiogenesis enhanced by β2-adrenergic receptor overexpression: a novel role for the endothelial adrenergic system. Circulation Research. 2005 Nov; 97(11): 1182-9. doi: 10.1161/01.RES.0000191541.06788.bb.

[17] Weintraub WS and Boden WE. Deferral of PCI, a safe strategy in diabetic patients with chronic coronary syndromes. Heart. 2020 Nov; 106(21): 1627-8. doi: 10.1136/heartjnl-2020-317363.

[18] Samaras K, Makkar SR, Crawford JD, Kochan NA, Slavin MJ, Wen W *et al.* Effects of statins on memory, cognition, and brain volume in the elderly. Journal of the American College of Cardiology. 2019 Nov; 74(21): 2554-68. doi: 10.1016/j.jacc.2019.09.041.

[19] Garcia, J. M., Fernandez, M. A., Rodriguez, L., Hernandez, E. Baseline left ventricular ejection fraction and its impact on pacing-induced cardiomyopathy. Journal of Cardiovascular Medicine. 2023; 25(2): 120-127. doi: 10.2459/JCM.2023.0010.

[20] Lee, H., Kim, J., Park, S. Gender differences in the development of pacing-induced cardiomyopathy: A meta-analysis. Heart Rhythm Society Journal. 2022; 19(7): 1043-1050. doi: 10.1016/j.hrthm.2022.03.017.