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ORIGINAL ARTICLE

Global Longitudinal Strain to Predict Pacing Induced Ventricular Dysfunction

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ABSTRACT

Background: Permanent cardiac pacing is the most efficient treatment for conduction disorders, however, leads to asynchronous left ventricular activation which predisposes to deleterious effects on the left ventricular (LV) function and ejection fraction. The predictors of LV dysfunction remain unclear, so we investigated whether strain measurements can be used to identify patients at risk of developing pacing induced ventricular dysfunction (PIVD). The aim of this work was to study the effects of right ventricular pacing on left ventricular function by deformation imaging using 2D speckle tracking echocardiography.

Methods: The study included 50 patients with normal LVEF (≥55%) who underwent single and dual chamber pacemaker implantation for various conduction disturbances. LVEF and global longitudinal strain measurements assessed by 2D special tracking echocardiography at baseline and at 1 month and 12 months follow up.

Results At 12 months follow up, 14 (28%) patients developed PIVD; 4 of which developed pacemaker induced cardiomyopathy (PICM). At the one month follow up, the GLS was significantly reduced in the 14 patients who subsequently developed PIVD at 12 months, compared to those who did not show significant decline in EF. (n = 38) (GLS -12.46 ± 2.77 vs-16.05- ± 2.57 vs. -16.4 respectively; p = 0.001). The ejection fraction was also significantly reduced in this group at 1 month follow up compared to those without PIVD (EF 53.57 ± 5.05 vs 61.28 ± 4.67 respectively; p value= 0.001) When the 4 patients with PICMP were excluded, only the 1-month GLS was significantly reduced compared to baseline.

Conclusions: Global longitudinal strain measurements shortly after pacemaker implantation provides valuable data in predicting patients who subsequently develop pacemaker induced dysfunction.

Keywords: Right ventricular pacing; Left ventricular; 2D speckle tracking echocardiography

INTRODUCTION

Permanent cardiac pacing is the most efficient treatment for a variety of conduction disorders including high degree atrio-ventricular block and symptomatic sick sinus syndrome [1]. However, this method is less effective than the native conduction system, it only travels approximately one quarter of the normal conduction velocity and produces electrical and mechanical cardiac changes [2]. RV apical pacing being the classic site for pacemaker lead implantation results in ventricular dys-synchrony and deterioration of left ventricular (LV) function and ejection fraction, like left bundle branch block [3]. Recently alternative sites are arising as right ventricular outflow tract (RVOT) and the septum [4].

Pacemaker patients are at increased risk for the development of atrial fibrillation, pacemaker induced ventricular dysfunction and the more severe form pacemaker induced cardiomyopathy (PICMP). PICMP has been defined by an LVEF ≤45%; and requires further managements or an upgrade to a biventricular pacing system [5-8].

Many factors affect the development of pacing induced cardiomyopathy including the presence of associated co-morbidities, RV pacing site, electromechanical dys-synchrony, impairment of coronary microcirculation [9].

Despite this data, predicting the patients who will subsequently develop PICM remains challenging. Studies are reporting that male sex and a wider native QRS are independent predictors of the condition [10], other studies show that deformation imaging by speckle tracking echocardiography following pacemaker implantation can predict the patients at higher risk for PCIM at long term follow up [11]. Deformation imaging also known as strain imaging provides unique information on regional and global ventricular function [12]. Global longitudinal strain is known to be more precise than ejection fraction and is now used in patients with heart failure, ischemic heart disease and patients receiving chemotherapy to detect early changes in cardiac function before changed in ejection fraction [11]. Speckle tracking echocardiography for strain measurement depends on tracking of speckles throughout the cardiac cycle in apical 4,3 and 2 chamber views, then the software allows elaboration of myocardial deformation in 3 spatial directions: longitudinal, radial, and circumferential [7,13]. In this study, we aimed to study the effects of right ventricular pacing on left ventricular function by deformation imaging using 2D speckle tracking echocardiography.

METHODS

Fifty patients with conduction disturbances undergoing single or dual chamber pacemaker implantation were included in the study. The inclusion criteria of the patients were any patients aged more than 18 years with conduction disturbances necessitating pacemaker implantation and had preserved LVEF (≥55%). An informed written consent was obtained from all participants prior to the study. The study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Exclusion criteria were as follows: pregnancy, myocardial infarction or revascularization within the prior 3 month or IHD, significant valvular heart disease (moderate or severe), structural heart abnormality including LV dilatation or ejection fraction <55%, and all co morbidities that may cause LV remodeling.

Study protocol: The study was authorized by the ethical comity at Tanta University Hospitals. After obtaining an informed consent all studied patients were subjected to i) full history taking including assessment of cardiovascular risk factors, history of concomitant diseases, medications, ii) symptomatology, iii) complete clinical examination, iv) laboratory investigations, v) 12 lead electrocardiograms (ECG), and vi) standard 2D transthoracic echocardiography. The patients then underwent pacemaker implantation with the subclavian vein being the primary choice for lead access. The atrial lead in case of dual chamber pacemaker implantation, was placed in the right atrial appendage, and the ventricular lead in the right ventricular apex, right ventricular outflow tract of the septum according to the site with produces the better readings. Post implantation, fluoroscopy and a chest x-ray are used to confirm proper anatomical locations. Standard 2D transthoracic echocardiogram and speckle tracking echocardiography with strain measurements is repeated at 1 and 12 months follow up. Pacemaker programing is done at 1 and 12 months follow up to ensure proper pacemaker function.

Echocardiography Image acquisition: An echocardiogram was done using vivid- E9 echocardiography (GE) medical system equipped with M5S probe (frequency 1,7-3.3) MHz. The examination was performed with the patients lying in the left lateral decubitus position. Apical (4,3, and 2 chamber views) and parasternal views were acquired at end expiration at frame rates 60-110 and three complete cardiac cycles acquired stored in cine loop format. Left ventricular end-systolic and end-diastolic diameters (LVESD and LVEDD) and ejection fraction (LVEF) were measured according to Simpson model [14]. The data was stored in digital format and transferred to

Echo Pac for analysis by another experienced operator using Echo Pac 110.1.2. This procedure was done for every patient pre-implantation and after 1 and 12 months follow up.

In this study, pacemaker induced ventricular dysfunction (PIVD) was defined if there was an absolute decline in LVEF by 5 percentage points. Pacemaker induced cardiomyopathy (PICMP) was defined as a reduction in LVEF to <45% [15].

For the strain measurement, the endocardial border was traced in the end systolic frame in the apical (4 and 2 chamber) and long axis viewsto draw the region of interest drawn to include the myocardium [16]. Point and click approach wad then used for Manual adjustments as needed to ensure that endocardial and epicardial borders were included. The software algorithm then automatically segments the LV into six equal segments and selects suitable speckles in the myocardium for tracking. By tracking the speckle patterns on a frame-by-frame basis, the software would then generate time-domain LV strain profiles for each of the six segments of each view, from which end-systolic strain was measured. Global longitudinal strain values were calculated from averaging the strain values of the 18 LV segments [7].

Statistical analysis: Continuous data were presented as mean ± standard deviation (SD). Categorical data were summarized as frequencies and percentages. Normally distributed variables were compared using an unpaired t-test. Categorical variables were compared by Chi-squared test. Univariate and multivariate logistic regression analyses were used to identify the independent factors of pacing induced ventricular dysfunction. A p-value of <0.05 was considered statistically significant.

RESULTS

Between January 2018 and May 2021, 137 patients were screened for the study; out of which fifty patients with second or third-degree atrioventricular block and preserved LV systolic function fulfilled the inclusion criteria and underwent single or dual chamber pacemaker implantation. The clinical, laboratory and programming data collected during the study were statistically evaluated as shown in table 1.

There was no significant difference regarding clinical or demographic characteristics at 12months between the patients who developed pacing induced dysfunction and those who did not with the exception of diabetes which showed to be clinically significant.

Echocardiographic data: Pacemaker induced ventricular dysfunction was observed in 14/50 (28%) patients after 12 months post implantation, including 4 patients who reached the diagnosis of PICMP (the more severe form, LVEF <45%).

The effects of pacing on ejection fraction are shown in table 2. At baseline there was no significant difference regarding the ejection fraction (p value 0.160). At 1 month and 12 months follow up there was significant differences between the groups (p values 0.001).

When comparing the ejection fraction at 1 month in relation to the baseline, in the PIVD group there was non-significant difference in the ejection fractions (p value= 0.095), but significant at 12 months in relation to the baseline (p value 0.001). In the PICM group there was significant difference in the ejection fraction at both 1 month and 12 months follow up (p values 0.001).

The effects of pacing on global longitudinal strain (GLS) are shown in table 3. At baseline there was no significant difference regarding the GLS between the groups (p value 0.323). At 1 month and 12 months follow up there was significant differences between the groups (p values 0.002 and 0.021 respectively).

And when comparing the 1 month and 12 months measurements to the baseline the results were that in the PIVD group there was significant difference in the GLS at 1 month (p value= 0.037), as well as at 12 months (p value 0.005). In the PICM group there was also significant difference in the GLS at both 1 month and 12 months follow up (p values 0.016 and 0.013 respectively).

Multivariate logistic regression analysis was done to confirm that 1-month GLS was an independent predictor of pacemaker induced ventricular dysfunction (HR (95% CI)

=0.521(0.297-0.849), p value= 0.010) as shown in table 4.

Table 1: Clinical characteristics of patients with and without pacing-induced left ventricular dysfunction

Variables	All (n=50)	No PIVD (n=36)	PIVD (n=14)	P value
Age	61.9±10.7	61.67±11.22	62.57±9.67	0.792
Female	36 (72%)	26 (72.2%)	10 (71.4%)	0.955
Hypertension	23 (46.0%)	14 (38.9%)	9 (64.3%)	0.106
Diabetes	18 (36%)	8 (22.2%)	10(71.4%)	0.005*
Hemoglobin g/dl	10.3± 0.73	10.31± 0.72	10.23 ±0.78	0.724
Urea mg/dl	34.5± 6.8	34.06± 6.44	35.50± 7.88	0.507
TSH mIU/l	1.9±1.0	1.72± 0.95	2.27± 1.09	0.084
Single chamber	35(70%)	27(75%)	8(57.1%)	0.465
Dual chamber	15(30%)	9(25%)	6(42.9%)	0.465
Apical pacing site	34 (68.0%)	24 (66.7%)	10 (71.4%0)	0.746
Septal pacing site	14 (28.0%)	10 (27.8%)	4 (28.6%)	0.955
RVOT pacing site	2 (4.0%)	2 (5.6%)	0 (.0%)	0.368
CHB	36 (72%)	25 (69.4%)	11 (78.6%)	0.519
2^{nd} degree HB	14 (28%)	11 (30.6%)	3 (21.4%)	0.519

Table 2: Effect of pacing on ejection fraction.

EF		Normal	PIVD (n=10)	PICM (n=4)	F test	P value
Baseline	Range	51 – 70	51 – 67	57 – 60	1.903	0.160
	Mean ± SD	61.38 ± 5.17	59.50 ± 5.40	58.25 ± 1.50		
1 m.	Range	51 – 69	48 – 60	45 – 52	22.830	0.001*
	Mean ± SD	61.28 ± 4.67	55.90 ± 3.54	47.75 ± 3.10		
12 m.	Range	49 – 68	42 – 55	42 – 48	30.900	0.001*
	Mean ± SD	59.50 ± 4.90	50.80 ± 3.94	43.50 ±3.00		
1 m. & Baseline		0.634	0.095	0.001*		
12 m. & Baseline		0.053	0.001*	0.001*		

Table 3: Effect of pacing on global longitudinal strain

GLS		Normal	PIVD (n=10)	PICM (n=4)	t. test	p. value
Baseline	Range	-20 – -10.6	-26.4 – -8.8	-19.1 – -9.8	1.141	0.323
	Mean ± SD	-16.30 ± 2.66	-17.73 ± 5.39	-16.38 ± 4.42		
1 m.	Range	-19.3 – -10.3	-15.3 – -12.1	-15.4 – -8	7.672	0.002*
	Mean ± SD	-16.05 ± 2.57	-13.76 ± 1.38	-9.20 ± 2.81		
12 m.	Range	-19 – -9.9	-13.5 – -10	-12.2 – -6.5	6.108	0.021*
	Mean ± SD	-15.39 ± 2.65	-12.12 ± 1.27	-8.85 ± 2.83		
1 m. & Baseline		0.686	0.037*	0.016*		
12 m. & Baseline		0.152	0.005*	0.013*		

Table 4: Logistic regression analysis for EF and GLS

	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
EF	3.625 (1.684 – 8.521)	0.005*	2.084 (0.754 – 6.927)	0.108
GLS	0.394 (0.148 – 0.754)	0.001*	0.521 (0.297 – 0.849)	0.010*

DISCUSSION

Even though permanent cardiac pacemaker remains the only effective therapy for patients with many conduction disturbances with sinus node or atrioventricular node related, studies suggest that the prognosis of patients following pacemaker implantation is not benign [17].

Chronic right ventricular pacing is associated with electrical and mechanical dys-synchrony which leads to deleterious effects on cardiac function, a phenomenon referred to as pacemaker induced cardiomyopathy [18].

Studies are reporting that LV GLS has greater prognostic value for detecting left ventricular dysfunction in patients with heart failure or acute ischemia [11]. Strain values reflect the motion of the subendocardium. Many studies are trying to predict the patients more likely to suffer after chronic RV pacing, but it is still challenging. LV GLS can be used to detect subclinical LV impairment before evident changes in EF [19]. GLS is being used to detect subclinical LV dysfunction in other conditions such as following chemotherapy [20].

The present study aimed to investigate the ability of LV strain to predict pacing induced ventricular dysfunction. There is solid data reported that patients with conduction disturbances necessitating the implantation of a permanent pacemaker with right ventricular pacing suffer from adverse LV remodeling and hence a drop in the LV function and ejection fraction during long term follow up; known as pacemaker induced ventricular dysfunction [21]. Accurate quantification of LV function is crucial for risk evaluation and management of these patients. This is routinely done by serial measurements of LVEF for measuring LV mechanical dys-synchrony and function [22]. However, it may be an insufficient tool in detecting early signs in cardiac structure and function; for this reason, strain imaging is arising as a new tool for detection of subtle changes in cardiac function [23].

Many studies have demonstrated its benefit beyond the traditional EF measurement in assessment of many cardiac conditions. It provides accurate and reproducible data regarding ejection fraction and myocardial strain values [24]. Left ventricular strain and function are altered by RV pacing, hence global longitudinal strain can be utilized to detect subclinical LV dysfunction, before changes in LV ejection fraction [25].

In this study we aimed to provide a comprehensive analysis of both LVEF and GLS measurements at baseline before pacemaker implantation, at 1 month and 12 months follow up.

There was a significant reduction in both LVEF and GLS values at one month follow up post single or dual chamber pacemaker implantation in the patients who subsequently developed pacemaker induced cardiomyopathy (PICM) (n=4) at 12 months. However, in the group who only developed pacemaker induced ventricular dysfunction (PIVD) (n=10) at 12 months, there was a significant reduction in GLS values only at one month, but not the LVEF values. These findings were also confirmed by the logistic regression analysis which established the significance of the 1-month GLS over ejection fraction. Thus, GLS may be used to predict patients more likely to suffer from PIVD and who would benefit from closer echocardiographic surveillance following pacemaker implantation.

Ahmed et al., [15] also showed that at 1 month post implantation, the GLS values were significantly reduced in the patients who subsequently developed PIVD compared to those who did not. Similar to our study, it also showed that 1-month LVEF was significantly lower compared to the baseline only in the group that subsequently developed PICM and not in the group that developed PIVD.

Xu et al., [22] also reported that only GLS was significantly reduced at one month in patients who developed PIVD compared to baseline.

In our study, baseline GLS values were not significantly different between all the studied patients, those who did or did not show subsequent significant decline in ejection fraction.

On the contrary, Chin et al., [11] reported that the initial GLS was significantly lower in patients who subsequently developed PICM than in those who did not even though the baseline LVEF values were nearly the same.

In our study, at 12 months follow up, 14 patients (28% of the total patients) showed a significant decline in LVEF ≥5 percentage points, 4 of whom had a more severe decline in LVEF to <45% (PICM). These numbers are similar to the previous studies which show a percentage of 9-26% incidence rate for the development of pacing induced dysfunction [11]. Pacemaker induced cardiomyopathy cases tend to be more severe and require close consideration for the need to upgrade to biventricular pacing system; however, the subclinical smaller reductions in LVEF in the less severe ventricular dysfunction patients should still be widely studied due to the risk of further deterioration in cardiac function with extended follow as reported by Chan et al. [26].

CONCLUSIONS

2D speckle tracking echocardiography measuring GLS has a prognostic value for predicting adverse cardiac events, and is superior to ejection fraction measurements; hence, should be used for patients undergoing pacemaker implantation to predict those patients more likely to suffer before visible changes in ejection fraction.

RECOMMENDATIONS

2D speckle tracking echocardiography and assessment of GLS is recommended for all patients undergoing pacemaker implantation at baseline and 1 month follow up for risk stratification and early detection of pacing induced ventricular dysfunction.

Conflicts of interest: None.

Financial disclosure: None.

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