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Original Article

Right Ventricular Pacing-Induced Effects on Left Ventricular Function According to 2D Speckle-Tracking Echocardiography

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ABSTRACT

Background: Permanent cardiac pacing is the most efficient treatment for conduction disorders, but it leads to asynchronous left ventricular (LV) activation, predisposing to deleterious effects on LV function and ejection fraction (EF). The predictors of LV dysfunction remain unclear, so we investigated whether strain measurements could be used to identify patients at risk of developing pacing-induced ventricular dysfunction (PIVD).

Methods: The study included 50 patients >18 years with normal LVEF (≥55%) who underwent single-chamber pacemaker implantation for various conduction disturbances. LVEF and global longitudinal strain (GLS) measurements were assessed by 2D speckle-tracking echocardiography at baseline and then at 1-month and 12-month follow-ups. The exclusion criteria were pregnancy, diabetes mellitus, myocardial infarction, revascularization within the prior 6 months, ischemic heart disease, significant valvular disease (starting from moderate in severity), structural heart abnormalities (LV dilatation), and any other comorbidities that might cause LV remodeling.

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

Conclusions: GLS measurements shortly after pacemaker implantation provided valuable data for predicting patients who would subsequently develop PIVD. ***(Iranian Heart Journal 2023; 24(1): 78-85)***

KEYWORDS: RV pacing, Pacemaker-induced ventricular dysfunction, Speckle-tracking echocardiography

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Permanent cardiac pacing is the most efficient treatment for a variety of conduction disorders, including high-degree atrioventricular blocks and symptomatic sick sinus syndrome. [1] Nonetheless, this method is less effective than the native conduction system since it only travels at approximately one-quarter of the normal conduction velocity and produces electrical and mechanical cardiac changes. [2] Right ventricular apical pacing is the classic site for pacemaker lead implantation, resulting in ventricular dyssynchrony and the deterioration of left ventricular (LV) function and ejection fraction (EF), similar to left bundle branch blocks. [3] Alternative sites, such as the right ventricular outflow tract and the septum, have been suggested. [4] Recently, other advanced techniques, including His bundle pacing and left bundle branch area pacing, have been proposed to reduce the hazardous effects of traditional pacemaker implantation regarding dyssynchrony and the development of pacemaker-induced ventricular dysfunction (PIVD). [5]

Pacemaker patients are at increased risk for the development of atrial fibrillation, PIVD, and the more severe form, pacemaker-induced cardiomyopathy (PICMP). PICMP is defined by an LVEF ≤45% and requires further management or an upgrade to a biventricular pacing system. [6-9]

Many factors affect the development of PICM, including the presence of associated comorbidities, right ventricular pacing sites, electromechanical dyssynchrony, and the impairment of coronary microcirculation. [10] Nevertheless, predicting patients who will subsequently develop PICM remains challenging. Research has indicated that the male sex and a wider native QRS are the independent predictors of the condition. [11] Some studies have shown that deformation imaging by speckle-tracking echocardiography following pacemaker implantation can predict patients at higher risks for PCIM at the long-term follow-up. [12] Deformation imaging, also known as “strain imaging”, provides unique information on regional and global ventricular functions. [13] Global longitudinal strain (GLS) is known to be more precise than EF and is now used in patients with heart failure or ischemic heart disease and patients receiving chemotherapy to detect early changes in cardiac function before changes in EF. [12] Speckle-tracking echocardiography for strain measurement depends on the tracking of speckles throughout the cardiac cycle in apical 4, 3, and 2-chamber views before the software allows the elaboration of myocardial deformation in 3 spatial directions: longitudinal, radial, and circumferential. [8,14] In this study, we aimed to study the effects of right ventricular pacing on LV function by deformation imaging using 2D speckle-tracking echocardiography.

METHODS

Subjects

Fifty patients with conduction disturbances undergoing single-chamber pacemaker implantation were included in the study. The inclusion criteria were any patients aged >18 years with conduction disturbances necessitating pacemaker implantation and with preserved LVEF (≥55%). Informed written consent was obtained from all the participants prior to study commencement. Exclusion criteria were pregnancy, diabetes mellitus, myocardial infarction, ischemic heart disease, revascularization within the prior 3 months, significant valvular heart disease (moderate or severe), structural heart abnormalities, including LV dilatation and EF<55%, and all comorbidities that might cause LV remodeling.

Study Protocol

The study protocol was authorized by the Ethics Committee at Tanta University Hospitals, and informed consent was obtained from all the participating patients.

Data on cardiovascular risk factors, concomitant diseases, medications, symptomatology, complete clinical examinations, laboratory investigations, 12-lead electrocardiography (ECG), and standard 2D transthoracic echocardiography with strain measurement were collected in the entire study population. The patients then underwent pacemaker implantation, with the subclavian vein being the primary choice for lead access. The ventricular lead was positioned in the right ventricular apex, the right ventricular outflow tract, or the septum according to the site that produced better readings. After implantation, fluoroscopy and chest X-rays confirmed proper anatomical locations. Standard 2D transthoracic echocardiography and speckle-tracking echocardiography with strain measurements were repeated at 1-month and 12-month follow-ups. Pacemaker programming was done at 1-month and 12-month follow-ups to ensure proper pacemaker function.

Echocardiography Image Acquisition

Echocardiography was done using the Vivid-E9 Echocardiography (GE) Medical System, equipped with an M5S probe (frequency =1 and 7–3.3 MHz). The examination was performed with the patients lying in the left lateral decubitus position. Apical (4, 3, and 2-chamber) and parasternal views were acquired at end-expiration at frame rates of 60–110 and in 3 complete cardiac cycles, with the information stored in cine-loop format. LV end-systolic and end-diastolic diameters and LVEF were measured according to the Simpson model. [14] The data were stored in digital format and transferred to the Echo Pac for analysis by another experienced operator using Echo Pac 110.1.2. This procedure was done for every patient pre-implantation and at 1 month and 12 months after implantation.

In this study, PIVD was defined as an absolute decline in LVEF by 5 percentage points. PICM was defined as a reduction in LVEF to <45%. [16]

For strain measurement, the endocardial border was traced in the end-systolic frame in the apical (4, 3, and 2-chamber) views to draw the region of interest to include the myocardium. [17] The point-and-click approach was then used for manual adjustments as needed to ensure that the endocardial and epicardial borders were included. The software algorithm automatically segmented the LV into 6 equal segments and selected suitable speckles in the myocardium for tracking. By tracking the speckle patterns on a frame-by-frame basis, the software generated time-domain LV strain profiles for each of the 6 segments of each view, from which end-systolic strain was measured. GLS values were calculated by averaging the strain values of 18 LV segments. [8]

Statistical Analysis

Continuous data were presented as the mean ± the standard deviation (SD). Categorical data were summarized as frequencies and percentages. Normally distributed variables were compared using an unpaired *t* test. The categorical variables were compared using the χ^2 test. Univariate and multivariate logistic regression analyses were used to identify the independent factors of PIVD. A *P* value <0.05 was considered statistically significant.

RESULTS

Between January 2018 and May 2021, 137 patients were screened for the study. Fifty patients with second or third-degree atrioventricular blocks and preserved LV systolic function fulfilled the inclusion criteria and underwent single-chamber pacemaker implantation. The clinical, laboratory, and programming data collected during the study were statistically evaluated (Table 1).

No significant differences were observed regarding clinical or demographic characteristics at 12 months between the

patients who developed PVID and those who did not (Table 1).

Echocardiographic Data

PIVD was observed in 14/50 patients (28%) at 12 months post-implantation, including 4 patients who reached the diagnosis of PICMP (the more severe form, LVEF <45%).

The effects of pacing on EF are shown in Table 2. At baseline, no significant difference was observed regarding EF (*P*=0.160). At the 1-month and 12-month follow-ups, there were significant differences between the groups (*Ps*=0.001).

Comparisons of EF at 1 month in relation to the baseline in the PIVD group showed nonsignificant differences (*P*=0.095), but the difference was significant at 12 months in relation to the baseline (*P*=0.001). In the PICM group, a significant difference was detected in EF at both 1-month and 12-month follow-ups (*Ps*=0.001).

The effects of pacing on GLS are shown in Table 3. At baseline, there was no significant difference regarding GLS between the groups (*P*=0.323). At the 1-month and 12-month follow-ups, significant differences were noted between the groups (*P*=0.002 and *P*=0.021, respectively). Comparisons between the 1-month and 12-month measurements and the baseline in the PIVD group revealed a significant difference concerning GLS at 1 month (*P*=0.037) and 12 months (*P*=0.005). In the PICM group, there was also a significant difference in GLS at both 1-month and 12-month follow-ups (*P*=0.016 and *P*=0.013, respectively).

Our multivariate logistic regression analysis (Table 4) confirmed that 1-month GLS was an independent predictor of PIVD (HR [95% CI], 0.521 [0.297 to 0.849]; *P*=0.010).

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

Variable	All (n=50)	No PIVD (n=36)	PIVD (n=14)	*P* value
Age, y	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
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
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
Second-degree HB	14 (28%)	11 (30.6%)	3 (21.4%)	0.519

PIVD, Pacing-induced ventricular dysfunction; TSH, Thyroid-stimulating hormone; RVOT, Right ventricular outflow tract; CHB, Complete heart block; HB, Heart block

Table 2: Effects of pacing on EF

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 month	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 months	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 month & Baseline		0.634	0.095	0.001*		
12 months & Baseline		0.053	0.001*	0.001*		

EF, Ejection fraction; PIVD, Pacing-induced ventricular dysfunction; PICM, Pacing-induced cardiomyopathy

Table 3: Effects of pacing on GLS

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 month	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 months	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 month & Baseline		0.686	0.037*	0.016*		
12 months & Baseline		0.152	0.005*	0.013*		

GLS, Global longitudinal strain; PIVD, Pacing-induced ventricular dysfunction; PICM, Pacing-induced cardiomyopathy

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*

EF, Ejection fraction; GLS, Global longitudinal strain

DISCUSSION

Even though permanent cardiac pacemakers remain the only effective therapy for patients with many conduction disturbances of the sinus node or the atrioventricular node, studies suggest that the prognosis of patients following pacemaker implantation is not benign. [18]

Chronic right ventricular pacing is associated with electrical and mechanical dyssynchrony, leading to deleterious effects on cardiac function, a phenomenon referred to as PICM. [19]

Studies have shown that LVGLS is of great prognostic value for detecting LV dysfunction in patients with heart failure or acute ischemia. [12] Strain values reflect the motion of the subendocardium. Many investigators have sought to predict patients more likely to suffer after chronic right ventricular pacing, but it is still challenging. LVGLS can be used to detect subclinical LV impairment before evident changes in EF. [20] GLS is used to detect subclinical LV dysfunction in other conditions, such as chemotherapy. [21]

The present study aimed to investigate the ability of LV strain to predict PIVD.

Robust data show that patients with conduction disturbances necessitating the implantation of a permanent pacemaker with right ventricular pacing suffer from adverse LV remodeling and reduced LV function and EF during long-term follow-ups, known as PIVD. [22] Accurate quantification of LV function is crucial for the risk evaluation and management of these patients. This is routinely done by serial measurements of LVEF for measuring LV mechanical dyssynchrony and function. [23] However, it may be an insufficient tool in detecting early signs in cardiac structure and function. For this reason, strain imaging has emerged as a new tool for the detection of subtle changes in cardiac function. [24] Many studies have demonstrated its benefit beyond the traditional EF measurement in the assessment of many cardiac conditions. It provides accurate and reproducible data regarding EF and myocardial strain values. [25] LV strain and function are altered by right ventricular pacing; hence, GLS can be utilized to detect subclinical LV dysfunction, before changes in LVEF. [26]

In this study, we aimed to provide a comprehensive analysis of both LVEF and

GLS measurements at baseline before pacemaker implantation and at 1-month and 12-month follow-ups. We found a significant reduction in both LVEF and GLS values at the 1-month follow-up following single-chamber pacemaker implantation in the patients who subsequently developed PICM (n=4) at 12 months. However, in the group who only developed PIVD (n=10) at 12 months, there was a significant reduction in GLS values only at 1 month, but not LVEF values. These findings were also confirmed by the logistic regression analysis, which established the significance of the 1-month GLS compared with EF. Thus, GLS may be used to predict patients more likely to suffer PIVD and who would benefit from closer echocardiographic surveillance following pacemaker implantation.

Ahmed et al (2017) [16] also showed that at 1 month after implantation, GLS values were significantly reduced in patients who subsequently developed PIVD compared with those who did not. Similar to our study, it also showed that 1-month LVEF was significantly lower than the baseline only in the group that subsequently developed PICM and not in the group that developed PIVD.

Xu et al (2018) [23] also reported that only GLS was significantly reduced at 1 month in patients who developed PIVD compared with the 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 declines in EF.

In contrast, Chin et al (2021) [12] reported that 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 the 12-month follow-up, 14 patients (28% of the total patients) showed a significant decline in LVEF (≥5%). Four of these patients had a more severe decline in LVEF (<45%; PICM). These figures are similar to those reported by previous studies showing incidence rates of 9%–26% for the development of PVID. [12] PICM cases tend to be more severe and require close consideration for the need to upgrade to biventricular pacing systems; still, subclinical smaller reductions in LVEF in patients with less severe ventricular dysfunction should be comprehensively studied due to the risk of further deterioration in cardiac function as reported by Chan et al (2011). [27]

CONCLUSIONS

Two-dimensional speckle-tracking echocardiography measuring GLS has a prognostic value for predicting adverse cardiac events and is superior to EF measurements. It should, therefore, be used for patients undergoing pacemaker implantation to predict those more likely to suffer before visible changes in EF.

Recommendations

Two-dimensional speckle-tracking echocardiography and the assessment of GLS are recommended for all patients undergoing pacemaker implantation at baseline and 1-month follow-ups for risk stratification and the early detection of PIVD.

Conflict of Interest: None

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