Original Article

Association Between Left Ventricular Function and Recurrent Premature Ventricular Contractions in Patients Referred to Baqiyatullah Hospital

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ABSTRACT

Background: Premature ventricular contractions (PVCs) cause left ventricular (LV) dysfunction and may lead to premature ventricular contraction-induced cardiomyopathy (PVC-CM). Evaluation of left ventricular ejection fraction (LVEF) using 2D transthoracic echocardiography allows PVC-CM diagnosis only in the later stages. Therefore, this study aimed to investigate the association between left ventricular global longitudinal strain (LVGLS) and PVCs.

Methods: We assessed 53 patients admitted to Baqiyatullah Hospital with complaints of heart palpitations. These patients, who had normal LVEF and PVCs between 5000 and 10,000 based on ECG underwent LVGLS evaluation by echocardiography. Then, their LV strain values were compared with those of a corresponding control group.

Results: The patient and control groups were well-matched concerning age, sex, and LVEF and had no significant differences. LVGLS was significantly lower in the patient group. ROC curve evaluation showed an acceptable diagnostic value for LVGLS regarding PVCs (AUC, 0.82; *P*=0.0001), with a sensitivity of 71.7% and a specificity of 84.9%.

Conclusions: Recurrent PVCs may cause LV dysfunction and CM independently of any underlying heart disease, despite a normal LVEF. Early detection of subtle ventricular dysfunction can be achieved with speckle-tracking echocardiographic methods other than conventional echocardiographic procedures. The former methods are, therefore, valuable as a critical adjunct in systolic function assessment. ***(Iranian Heart Journal 2024; 25(2): 56-64)***

KEYWORDS: LVGLS, LVEF, PVC, Arrhythmia, 2D-STE

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Premature ventricular contractions (PVCs) are extra heartbeats that begin in one of the heart ventricles and are a very common cause of arrhythmias. [1] In the general population, 1%–4% of PVCs are detected in ECG, and 40%–75% of cases on 24-hour Holter ECG evaluation. [2] In patients with recurrent PVCs, left ventricular

ejection fraction (LVEF) is measured to determine cardiac systolic function and assess the effects of PVCs on the heart. Some patients with recurrent PVCs have reversible low LVEF, called "premature ventricular contraction-induced cardiomyopathy (PVC-CM)". [3-5] The mechanism of PVC-CM is hypothesized to be related to PVC-induced LV desynchrony. Indeed, any known mechanisms of LV desynchronization, including left bundle branch block, right ventricular pacing, and prestimulation, can cause CM. [6, 7]

Early identification and intervention in patients with PVC-CM risks can significantly improve outcomes. [1,8] PVCs greater than 20% in 24 hours are more likely to be associated with LV dysfunction. [9-11] Nonetheless, in some PVCs, LVEF may be regular despite impaired LV function. [12-15] Transthoracic echocardiography (TTE) is recommended in the first-line evaluation of PVCs to detect possible underlying structural heart diseases because of its availability and ability to demonstrate cardiac pathology. [16] Since most PVC patients have a normal LVEF on TTE, early signs of ventricular function deterioration may be missed by standard echocardiographic examinations, whereas comprehensive echocardiographic evaluations can detect early electromechanical dysfunction. [17-19] Rapid detection of ventricular dysfunction is expected to be clinically significant, and echocardiography can be the most suitable noninvasive tool because it is a widespread and inexpensive method of diagnosis. [18] Two-dimensional speckle-tracking echocardiography (STE) is a technique that measures the ability of the heart muscle to change shape (contraction or relaxation) over time and has been shown to detect early LV systolic dysfunction reliably even before obvious changes. [20-22] STE can detect even minimal changes and establish early diagnosis. Left ventricular global longitudinal strain (LVGLS) resulting from these assessments provides information on LV systolic function. In patients with recurrent PVCs, LVEF is impaired in approximately 23%–36% of patients. [23-25] Still, no clear information exists regarding the value of LVGLS evaluation in patients with PVCs. [26] Recent studies have shown that STE may be superior to conventional measurements for the early detection of myocardial dysfunction (eg, in patients with anthracycline-induced CM, diabetes, muscular dystrophy, and pacemaker-induced ventricular dysfunction.) [26-30] The ability to detect dysfunction early can lead to earlier medical treatment or management and potential prevention of PVC-CM.

The present study aimed to evaluate the association between LVGLS and PVCs in patients with normal LVEFs and recurrent PVCs compared with the values obtained from normal individuals.

METHODS

This case-control study used ECG to assess patients with heart palpitations admitted to Baqiyatullah Hospital between October 2021 and October 2022. For patients with recurrent PVCs, a Holter rhythm was set. Patients with PVCs between 5000 and 10,000 underwent echocardiography performed with the modified Simpson formula by skilled staff. Additionally, individuals with a normal LVEF and no risk factors or underlying diseases were included in the study. Ultimately, 53 patients were included and evaluated for LVGLS by echocardiography. In addition, 53 normal individuals who complained of heart palpitations but had regular ECGs and LEVEFs and no PVCs, risk factors, and underlying diseases were examined as the control group. The control subjects were matched with the patient group regarding risk factors affecting LVEF and strain

values, including age, underlying diseases (eg, diabetes and hypertension), and smoking. Individuals with risk factors or underlying diseases, patients with more than 1 PVC morphology in ECG, unstable ventricular tachycardia in ECG, and patients with morphological disorders leading to PVCs were excluded from the study. Signed informed consent was obtained from all the participants, and the study protocol was approved by the Ethics Committee of Baqiyatullah University of Medical Sciences (IR.BMSU.BAQ.REC.1402.063).

The basic characteristics of the patients were recorded by history taking through a questionnaire. The presence and rate of PVCs were recorded by ECG and 24-hour Holter, and LVGLS was evaluated by echocardiography. Thereafter, LV strain values were compared between the 2 matched groups.

Statistical Analysis

Quantitative variables were presented with means and standard deviations, and qualitative variables were reported with numbers and percentages. First, quantitative data were analyzed from the perspective of following the normal distribution with the Kolmogorov-Smirnov test and were then compared using the *t* test. Qualitative variables were compared using the χ^2 test between the 2 groups. Predictive values were checked via the receiver operating characteristic (ROC) curve analysis. The significance level was set at 0.05 and 95% confidence intervals. All the statistical analyses were performed in SPSS, version 22, and graphs related to the statistical analyses were drawn with the same software.

RESULTS

Fifty-three patients with recurrent PVCs and 53 healthy controls were investigated. The study population consisted of 55 men (51.9%) and 51 women (48.1%). Table 1 presents the distribution of the other patient characteristics, including age, LVEF, LVGLS, and PVCs per 24 hours.

Table 1: Distribution of Patients Based on Basic and Clinical Characteristics

Parameter	Min	Max	Mean	SD
Age, y	17	63	37/14	10/37
Left ventricular ejection fraction, %	50	60	55/61	2/82
Left ventricular global longitudinal strain, %	-27/5	-14/1	-19/41	3/07
Premature ventricular contractions (per 24 h)	5004	10006	-6726/13	1164/1

The patient and control groups were compared regarding sex, age, LVEF, and LVGLS. Sex, age, and LVEF were not significantly different between the recurrent PVC and control groups, whereas LVGLS exhibited a statistically significant difference between the groups (*P*=0.0001): LVGLS values were significantly lower in the PVC group than in the control group (Table 2 and Fig. 1).

Table 2: Comparison of the Patients and Control Subjects Concerning Demographic and Clinical Characteristics

Parameter	Group	Mean (SD)	*P* value
Age, y	Cases	37.73 (10.83)	0.55
	Controls	36.54 (9.96)	
Left ventricular ejection fraction, %	Cases	55.56 (3.48)	0.86
	Controls	55.66 (1.97)	
Left ventricular global longitudinal strain, %	Cases	-17.77 (2.74)	0.0001
	Controls	-21.04 (2.46)	
Sex (male)	Cases	27 (50.9) *	0.99
	Controls	28 (52.8)	

* Sex is given as a number (%).

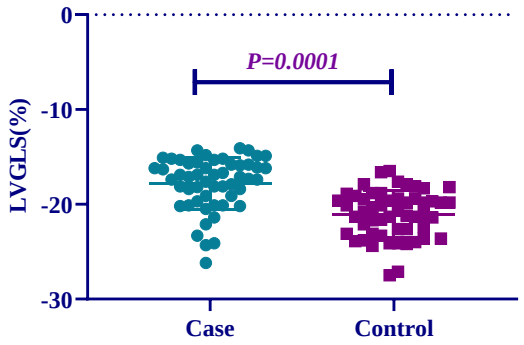

Figure 1: The image presents a comparison of LVGLS between patients with PVCs and healthy controls.
LVGLS: left ventricular global longitudinal strain; PVCs: premature ventricular contractions

To evaluate the diagnostic value of LVGLS in identifying patients with PVCs, ROC curve analysis was performed. The diagnostic and predictive value of LVGLS in detecting patients with recurrent PVCs was acceptable (AUC, 82; *P*=0.0001). The threshold LVGLS value was determined based on a Youden index of 0.56, a sensitivity of 71.7%, and a specificity of 84.9%. Figure 2 depicts the corresponding ROC curve.

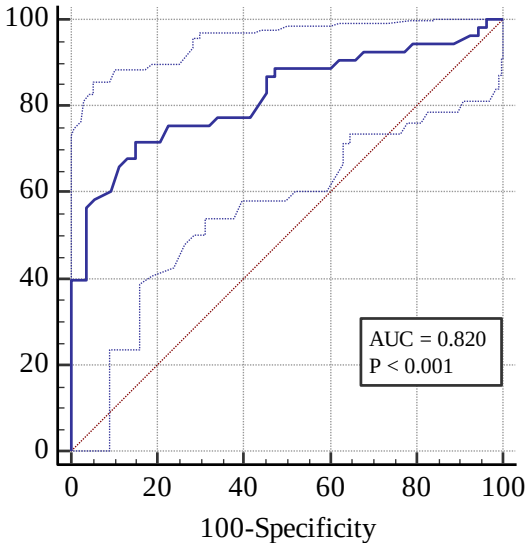

Figure 2: The image presents the ROC curve analysis regarding the diagnostic value of LVGLS in the detection of patients with PVCs.
ROC: receiver operating characteristics; LVGLS; left ventricular global longitudinal strain; PVCs: premature ventricular contractions

Afterward, the correlation between the PVC occurrence rate in 24 hours and LVEF and LVGLS values was investigated. LVEF had an inverse and significant correlation with the PVC rate, but LVGLS showed no significant correlation with the number of PVCs. The details of this review are given in Table 3 and Figure 3.

Table 3: Examination of the Correlation Coefficient Between PVCs in 24 Hours With LVEF and LVGLS

	r coefficient	*P* value
PVC vs LVEF	-0.46	0.24
PVC vs LVGLS	0.0001	0.08

PVCs: premature ventricular contractions; LVGLS: left ventricular global longitudinal strain; LVEF: left ventricular ejection fraction

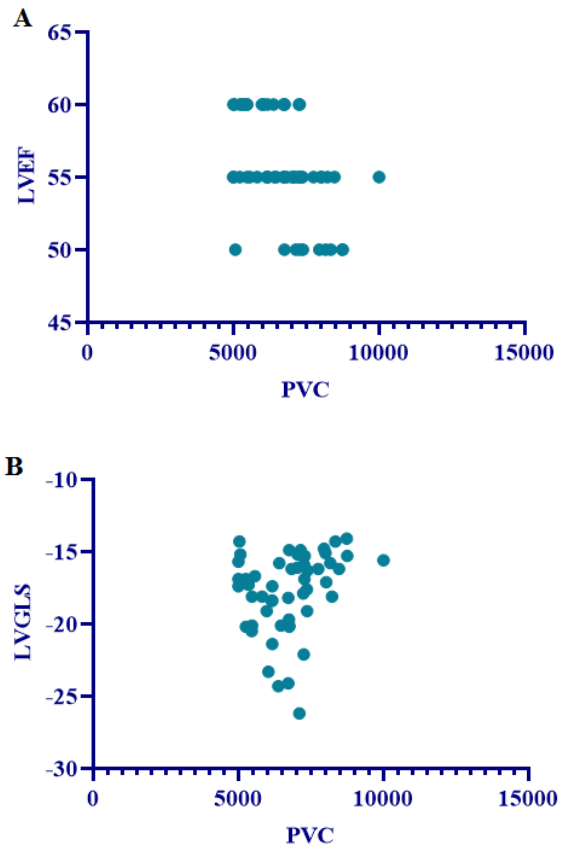

Figure 3: The images illustrate correlations between PVCs at 24 hours with A: LVEF and B: LVGLS.

PVCs: premature ventricular contractions; LVGLS: left ventricular global longitudinal strain; LVEF: left ventricular ejection fraction

Subsequently, the patients were divided into 2 subgroups considering a cutoff value of −18 for LVGLS. Accordingly, 21 patients had LVGLS > −18 and 32 patients < −18. A comparison of the rate of PVC events in 24 hours between the 2 subgroups revealed no significant difference between the subgroups (*P*=0.07).

DISCUSSION

Although PVCs are often considered a benign condition, long-term recurrent PVCs may lead to PVC-CM in some patients. However, there is uncertainty regarding the exact diagnostic criteria for PVC-CM diagnosis, so the diagnosis is mostly established retrospectively by excluding high-risk cases. It is also debated whether intervention is necessary in patients with recurrent PVCs who are asymptomatic with regular LVEFs. In this study, we used 2D-STE and evaluated strain values to detect cardiac dysfunction in patients with recurrent PVCs but without structural heart disease. It should be kept in mind that varying degrees of cardiac dysfunction exist even in patients without abnormal findings on conventional echocardiography. [31]

Based on the results of this study, our patient and control groups were well-matched in terms of age, sex, and LVEF and had no significant differences. Therefore, we can be certain that the difference observed between the groups was not influenced by other effective factors. LVGLS showed a significant difference between the PVC and control groups: LVGLS was significantly lower in the former group. Our ROC curve evaluation also demonstrated that the diagnostic value of LVGLS in identifying patients with PVCs was acceptable (AUC, 0.82; *P*=0.0001), with a sensitivity of 71.7% and a specificity of 84.9%.

Recent studies have reported that LVGLS was reduced significantly in patients with recurrent PVCs and preserved LVEFs. [23,25] In a recent study, Koca et al [32] reported that radiofrequency ablation increased LV longitudinal strain values. Uhm et al [33] showed the positive effects of radiofrequency ablation on right ventricular GLS in patients with recurrent PVCs.

Another study demonstrated that LVGLS disrupted the pre-PVC sinus rhythm, suggesting that disturbances in cellular physiological processes may contribute to the generation of recurrent PVCs. [34] Another investigation reported a significant rise in LVGLS value after radiofrequency ablation in patients with normal LVEFs. The increase was statistically significant in patients with LVGLS >16 before ablation. Additionally, in the group of patients whose LVGLS was within the normal range, a slight improvement trend was observed, especially in those whose values were close to the reference value, which was not statistically significant. [35] Nevertheless, a larger study sample is necessary to determine the exact cutoff values. Although the mechanism of PVC-CM is not known, there is general agreement that higher PVC rates per day correlate with a higher risk of CM development. [9] In addition to PVC burden, some other risk factors for progression to CM have been identified, but inconsistencies exist between different studies. Patient characteristics, such as increasing age and male sex, were associated with PVC-CM in some research. [36, 37] We detected no significant differences between the groups in terms of these characteristics. Based on our exclusion criteria, patients with ECG features such as more than 1 morphology in PVCs and unstable ventricular tachycardia (which may increase CM) were excluded from the study.

We sought to evaluate LV systolic function in patients with PVCs but without structural heart disease. Via 2D-STE, we also aimed to evaluate early detection of subtle dysfunction. LVGLS was significantly lower

in the patient group than in the control subjects, suggesting that PVCs may cause early LV dysfunction that may not be detected by conventional echocardiographic measurements. This finding is consistent with those reported by other studies. [15, 26] The findings of our study revealed an inverse and significant correlation between the PVC rate and LVEF, such that with an increasing PVC load, LVEF decreased. On the other hand, we observed no significant correlation between PVC load and LVGLS. Be that as it may, some studies have reported a significant inverse correlation between PVC load and LVEF and LVGLS. [38, 39] Of course, the correlation can be affected easily by the number of samples. Thus, at the subclinical level and normal LVEFs, LVGLS may not decrease rapidly with an increasing PVC burden. In line with our conclusion, a prior study also showed that the frequency of PVCs was at least moderately related to the level of LV dysfunction. However, no cutoff point determines the frequency of the inevitability of CM. Some studies have suggested a cutoff point of 24%, with a sensitivity of 79% and a specificity of 78.5% for predicting CM. Nonetheless, we cannot currently assume a definite cutoff value because PVC-CM can be observed even in patients with a lower PVC burden (10%). [40,41] Lie et al [25] concluded that more than 8% of PVCs were associated with myocardial dysfunction by GLS, a significantly lower threshold than that previously reported. This finding suggests that patients with more than 8000 PVCs in 24 hours should undergo strain echocardiography for cardiac function evaluation, and PVC inhibitor therapy should be considered if necessary. In a study with ROC analysis, a PVC rate >12.5% optimally identified patients with GLS worse than −18%, with a sensitivity of 80%, a specificity of 67%, and an area under the ROC curve of 0.79. Our results are in line with the mentioned studies. Thus, although load was a significant predictor, it was not the only factor contributing to LV systolic dysfunction. [42]

The interpretation of the findings of this study is limited due to several factors. We had a limited sample size, preventing the definition of PVC-CM predictors and a valuable strain cutoff to determine the need for ablation intervention. We were unable to examine variables useful in identifying subclinical LV dysfunction in patients with normal LVEFs, such as the BNP level, the Kansas City Cardiomyopathy Questionnaire, and the 6-minute walk test. Long-term follow-up is needed to confirm the results of the present study and evaluate the recovery of cardiac function in patients with recurrent PVCs undergoing clinical intervention. Moreover, 2D-STE requires high-quality images, and the possibility of comparing echocardiographic results is limited because parameters vary between different echocardiographic devices and the software used. Future studies with large sample sizes are necessary to determine accurate reference values.

CONCLUSIONS

In light of the results of the present study, we conclude that recurrent PVCs may cause LV dysfunction and CM independently of any underlying heart disease despite normal LVEFs. In addition, subtle LV dysfunction is detectable with STE methods other than conventional echocardiographic procedures. Further, STE is valuable as a critical adjunct in systolic function assessment, especially in patients whose LV function is expected to progressively deteriorate.

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