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Does Premature Ventricular Complex Impair Left Ventricular Diastolic Functions?

ABSTRACT

Background: A higher frequency of premature ventricular complexes is associated with a higher risk of premature ventricular complex-induced cardiomyopathy. Although there are several studies on the systolic functions of the left ventricle in this patient group, it is clearly not known how the diastolic functions of the left ventricle are affected. This study examined the effect of premature ventricular complex on left ventricle diastolic functions using diastolic strain rate.

Methods: The trial included 57 patients with frequent premature ventricular complexes and 54 healthy volunteers. The patient was evaluated using echocardiography in its entirety. The vendor-independent software system determined systolic and diastolic strain parameters via 2-dimensional speckle tracking analysis. Using the auto strain 3P semi-automated endocardial boundary tracking instrument, the global longitudinal strain was measured from the apical 4-chamber, 2-chamber, and long axis. The diastolic strain rate was determined by averaging the strain rates of 17 cardiac segments at 2 distinct periods of diastole.

Results: In the patient group, early diastolic strain rate was significantly lower than that in the control group (1.62 ± 0.58 vs. 1.25 ± 0.38, $P < .001$). There were found to be significant negative connections between PVC's electrocardiographic QRS wave length and early diastolic strain rate and coupling interval and early diastolic strain rate. Significant positive associations between coupling interval and early diastolic strain rate were discovered ($P < .001$ and $P < .001$, respectively).

Conclusions: Patients with premature ventricular complex exhibited a lower early diastolic strain rate than healthy individuals. The early diastolic strain rate can be used to predict left ventricle diastolic dysfunction, and persons with premature ventricular complex may have a higher risk of left ventricle diastolic dysfunction than the general population.

Keywords: Longitudinal early diastolic strain rate, premature ventricular complex, left ventricular diastolic function, a speckle tracking echocardiography

ORIGINAL INVESTIGATION

Nurşen Keleş[1]
Erkan Kahraman[1]
Kemal Emrecan Parsova[2]
Murat Baştopçu[3]
Mesut Karataş[4]
Nizamettin Selçuk Yelgeç[1]

[1]*Department of Cardiology, University of Health Sciences, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, İstanbul, Turkey*
[2]*Department of Cardiology, Zile State Hospital, Tokat, Turkey*
[3]*Department of Cardiovascular Surgery, University of Health Sciences, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, İstanbul, Turkey*
[4]*Department of Cardiology, University of Health Sciences, Kartal Koşuyolu Yüksek İhtisas Training and Research Hospital, İstanbul, Turkey*

Corresponding author:
Nurşen Keleş
✉ drnursenkeles@yahoo.com.tr

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INTRODUCTION

Premature ventricular complex (PVC) is the most prevalent kind of ventricular arrhythmia. PVCs were traditionally thought to be benign in the absence of structural heart disease; however, recent research reveals that PVC-induced cardiomyopathy can arise in individuals without structural heart disease who have a high number of PVCs. With medical treatment or ablation for PVC, PVC-induced cardiomyopathy may improve. In cases when PVCs exacerbate a preexisting cardiomyopathy, suppression of PVCs may result in a partial recovery of left ventricular dysfunction.[1,2]

Although there are several studies on the systolic functions of the left ventricle (LV) in PVC patients, it is not clear how the diastolic functions are affected.[3] Conventional LV diastolic measures, such as septal and lateral mitral annular early diastolic peak velocity assessed by pulsed tissue Doppler imaging (TDI) and maximum left atrial volume index (LAVI), are now used to evaluate LV diastolic performance. However, these annular and volumetric measurements have severe drawbacks, such as angle dependency and difficulty to evaluate the LV accurately. Moreover, the current guidelines for left ventricular diastolic dysfunction

(LVDD) underscore the limits of these evaluations. A recent study has demonstrated a unique (angle-independent) diastolic indicator. For the diastolic function of the LV, the early diastolic strain rate (SRe) may be a more suitable measure.[4,5]

This study aimed to determine how PVC impacts the diastolic functions of the LV in patients using a novel diastolic measure named the SRe.

METHODS

Study Groups

The study comprised 57 patients with more than 10 000 PVCs during 24-hour Holter monitoring and 54 healthy volunteers as a control group. Holter monitoring indicated no arrhythmia in the 24-hour ambulatory rhythm of the control group. Exclusion criteria included decreased left ventricular ejection fraction (LVEF <50%), LV hypertrophy, moderate or severe valvular heart disease, coronary artery disease, significant congenital heart disease, other arrhythmias (including supraventricular tachycardia, atrial fibrillation, and atrial flutter), grade 2 or grade 3 arterial hypertension, smoking, or hyperlipidemia. The study was approved by the Local Ethics Committee. Each participant in the study provided informed consent.

Echocardiography

Two-dimensional (2D), M-mode, and TDI tests were conducted with a GE vivid E95 ultrasonic diagnostic system (GE Healthcare; Vingmed Ultrasound, Horten, Norway) equipped with an M5S probe (frequency: 1.5-4.6 MHz). All subjects received a single-lead electrocardiogram (ECG) recording during echocardiography. On the parasternal long-axis view, the left ventricle end-diastolic diameter (LVEDD), left ventricle end-systolic diameter (LVESD), end-diastolic interventricular septal (IVS), and posterior wall thicknesses were measured using M-mode. The LVEF was computed by modifying the Simpson's biplane technique. The early diastolic peak flow velocity (*E*), the late diastolic peak flow velocity (*A*), and the E-wave deceleration time were measured using transmitral Doppler imaging. Pulsed-wave Doppler mode was utilized for TDI. At a velocity range of 15-20 cm/s, the Nyquist limit was established, and high-frequency signals were filtered away. Reduced gains produced the lowest background noise achievable. When the subject's breathing was normal, all TDI recordings were taken. The velocities were obtained by placing a 5-mm sample volume on the lateral and medial sides of the mitral annulus and sweeping the sample volume at 100 mm/s for 5-10 cardiac cycles. The temporal velocity integral of the cardiac systolic (Sm) wave and diastolic function parameters including mitral inflow early diastolic tissue velocity (Em) and mitral inflow late diastolic tissue velocity (Am) were calculated. Using 2D speckle tracking analysis, the vendor-independent software system (EchoPAC version 202) was used to quantify systolic and diastolic strain parameters. Global longitudinal strain (GLS) was defined as the average peak strain across all 17 myocardium segments and was expressed as absolute values. The greater the systolic strain value, the more the tissue deforms during systole. From the apical 4-chamber, apical 2-chamber, and apical long axis, GLS was computed using the semi-automated auto strain 3P endocardial boundary tracking approach. The moment of aortic valve closure (end systole) was used to determine the maximum systolic pressure. Using Pulsed-wave Doppler, the time interval between the onset of the R-wave on the ECG and the end of the LV outflow tract signal was estimated. The diastolic strain rate was determined using an average of 17 myocardial segments during 2 separate phases of diastole: isovolumic relaxation (SRivr) and SRe. During mitral valve opening, SRivr timing was established. Mitral valve opening timing was determined as the interval between the beginning of the R-wave on the ECG and the beginning of the mitral E-wave in the Pulsed-wave Doppler mitral inflow signal. At the apex of the ECG's positive signal waveform following systole and preceding the P-wave, the diastolic strain rate was determined[6,7] (Figure 1).

Statistical Analysis

For statistical analysis, the IBM Statistical Package for Social Sciences Statistics 22 application was used. Normality was tested using the Shapiro–Wilk test. Normally distributed continuous variables are given as mean and SD, whereas categorical variables are presented as numbers and percentages. For comparing groups, the chi-squared test or Fisher's exact test was implemented to categorical variables, the Student's *t*-test was applied to normally distributed continuous variables, and non-normally distributed continuous variables were analyzed with the Mann–Whitney *U*-test. Kendall rank correlation was utilized to examine the connection between ordinal variables. A *P*-value of less than .05 was statistically significant.

HIGHLIGHTS

- Patients with premature ventricular complex had a decreased early diastolic strain rate (SRe).
- SRe measures can be used to predict left ventricle diastolic dysfunction.
- A significant negative association was found between QRS duration and SRe, but a significant positive correlation was found between coupling interval and SRe.

RESULTS

The study comprised 57 patients (mean age 46.4 ± 13.6 years, 43.9% male) and 54 healthy controls (mean age 41.6 ± 10.4 years, 61.1% male). Table 1 displays the baseline demographic and clinical characteristics of the patient and control groups. The study groups shared similar initial features.

Table 2 lists the typical 2D transthoracic echocardiographic parameters of the study group. The patient group had significantly larger left atrial anterior–posterior dimensions, LVESD, and *E*/Em ratio ($P < .001$, $P = .001$, and $P = .001$, respectively). A wave was larger in the patient group, but Em was greater in the control group. Other echocardiographic parameters did not change substantially between patient and control groups. The longitudinal strain parameters for each research group are listed in Table 3. In the patient group,

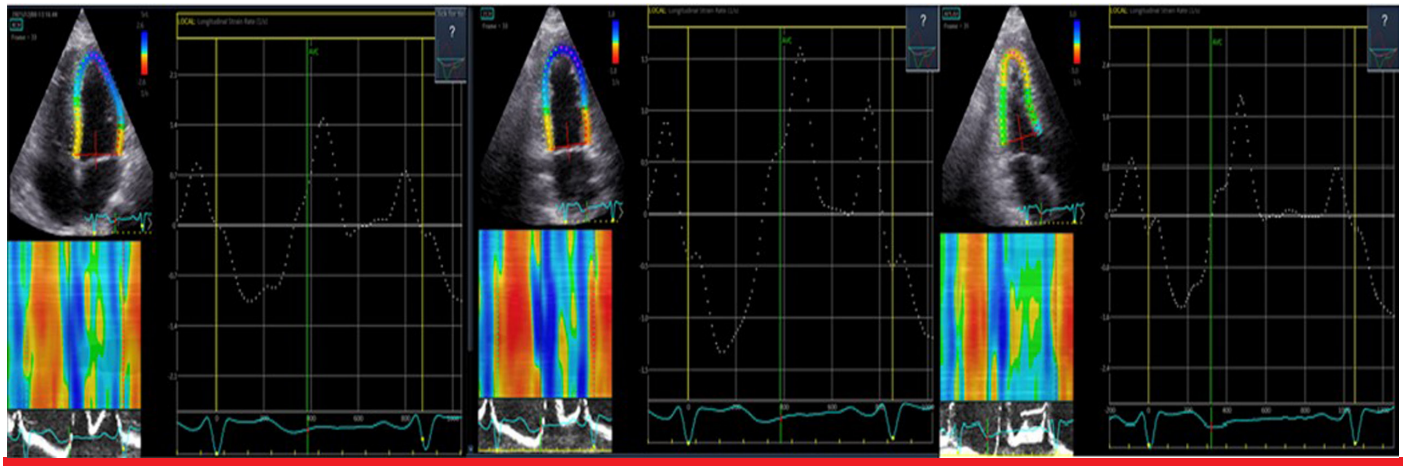

Figure 1. Left ventricular longitudinal diastolic strain data. The diastolic strain rate was determined using an average of the 17 myocardial segments during isovolumic relaxation and early diastole. The diastolic strain rate was determined during the peak positive signal waveform following systole and prior to the P-wave on the electrocardiogram.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population

	Control Group (n = 54)	Patient Group (n = 57)	*P*
Age	41.6 ± 10.4	46.4 ± 13.6	.037
Gender			.069
Male	33 (61.1%)	25 (43.9%)	
Female	21 (38.9%)	32 (56.1%)	
BMI	26.22 ± 3.93	28.08 ± 4.73	.052
HT	11 (20.4%)	20 (35.1%)	.084
DM	5 (9.3%)	6 (10.5%)	.823

P-value of less than .05 was statistically significant. BMI, body mass index; DM, diabetes mellitus; HT, hypertension.

SRe decreased dramatically ($P < .001$). In the patient group, the late diastolic strain rate and maximum LAVI were raised ($P = .043$ and $P = .002$, respectively). Even while the *E*/Em ratio (5.58 ± 1.71) and the maximum LAVI (24.75 ± 6.02) were greater in the patient group, they did not meet the criteria for diastolic dysfunction. SRe was significantly reduced in patients whose PVCs originated in the right ventricle (RV) or epicardial region, as determined by an examination of patients based on the origin of their PVCs ($P < .001$ and $P < .001$, respectively) (Table 4). In the study group, the SRe values of women with PVC were larger than those of men with PVC. However, there were no statistically significant differences between the genders (Table 5).

In the correlation analysis, a significant negative association was found between QRS duration and SRe, but a significant positive correlation was found between coupling interval and SRe ($P < .001$ afterward, $P < .001$) (Table 6).

DISCUSSION

This study aims to compare the risk of LV diastolic dysfunction that may lead to heart failure with preserved ejection fraction between patients with PVC and the general population by analyzing the SRe, a unique diastolic parameter.

Table 2. 2-Dimensional Transthoracic Echocardiographic Parameters of the Study Group

	Control Group (n = 54)	Patient Group (n = 57)	*P*
LVEDD (mm)	4.55 ± 0.33	4.58 ± 0.38	.613
LVESD (mm)	2.74 ± 0.30	2.93 ± 0.30	**.001**
LAD-AP (mm)	2.97 ± 0.35	3.26 ± 0.39	**<.001**
IVS (mm)	1.04 ± 0.13	1.01 ± 0.13	.143
PW (mm)	1.01 ± 0.11	1.12 ± 0.80	.630
E (cm/s)	0.70 ± 0.14	0.70 ± 0.18	.866
A (cm/s)	0.61 ± 0.13	0.67 ± 0.15	**.013**
E/*A* ratio	1.19 ± 0.34	1.09 ± 0.31	.135
Em (cm/s)	0.19 ± 0.20	0.14 ± 0.05	**.021**
Am (cm/s)	0.15 ± 0.13	0.13 ± 0.08	.780
E/Em ratio	4.57 ± 1.23	5.58 ± 1.71	**.001**
IVRT (ms)	90.50 ± 17.85	92.12 ± 12.87	.582
IVCT (ms)	90.46 ± 16.67	89.97 ± 14.89	.869
DT (ms)	154.85 ± 28.54	166.33 ± 44.00	.237
TAPSE (mm)	2.42 ± 0.33	2.44 ± 0.35	.713
LVEDV (mL)	94.36 ± 27.88	98.42 ± 21.74	.142
LVESV (mL)	37.09 ± 11.94	41.12 ± 11.83	.061
LVEF (2D biplane Simpson's method) (%)	60.04 ± 3.25	59.19 ± 3.83	.104
LAV maximum index (left atrial maximum volume/BMI)	21.36 ± 5.05	24.75 ± 6.02	**.002**

P-value of less than .05 was statistically significant. *A*, mitral inflow late diastolic velocity; Am, mitral inflow late diastolic tissue velocity; BMI, body mass index; DT, left ventricular deceleration time; *E*, mitral inflow early diastolic velocity; EF, ejection fraction; Em, mitral inflow early diastolic tissue velocity; IVCT, the isovolumic contraction time; IVRT, isovolumic relaxation time; IVS, interventricular septum thickness; LAD-AP, left atrium anterior–posterior diameter; LAV; left atrial volume; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVESV, left ventricular end-systolic volume; PW, posterior wall thickness; TAPSE, tricuspid annular plane systolic excursion.

Table 3. Longitudinal Strain Parameters of the Study Group

	Control Group (n = 54)	Patient Group (n = 57)	*P*
LV-LS 4 chamber (%)	−18.41 ± 1.81	−18.18 ± 1.68	.864
LV-LS 2 chamber (%)	−20.43 ± 2.86	−19.45 ± 2.36	.197
LV-LS 3 chamber (%)	−18.74 ± 2.67	−17.94 ± 2.63	.098
LV-GLS (%)	−19.24 ± 2.07	−18.46 ± 1.73	.119
SRe (/s)	1.62 ± 0.58	1.25 ± 0.38	**<.001**
SRa (/s)	0.90 ± 0.24	0.99 ± 0.28	**.043**
SRs (/s)	0.48 ± 1.09	1.01 ± 0.33	.107

P-value of less than .05 was statistically significant. GLS, global longitudinal strain; LS, longitudinal strain; LV, left ventricle; SRa, late diastolic strain rate; SRe, early diastolic strain rate; SRs, systolic strain rate.

Table 4. Comparison of Strain Rates by PVC Origin

	Probable Left Ventricle Origin (n = 11)	Probable Right Ventricle Origin (n = 46)	*P*
SRe (/s)	1.73 ± 0.27	1.14 ± 0.31	**<.001**
SRa (/s)	1.02 ± 0.25	0.98 ± 0.30	.655
SRs (/s)	1.02 ± 0.12	1.01 ± 0.36	.675
	Probable Endocardial Origin (n = 21)	**Probable Epicardial Origin (n = 37)**	***P***
SRe (/s)	1.54 ± 0.31	1.07 ± 0.30	**<.001**
SRa (/s)	0.95 ± 0.29	1.01 ± 0.28	.410
SRs (/s)	1.02 ± 0.20	1.00 ± 0.39	.441

P-value of less than .05 was statistically significant. PVC, premature ventricular complex; SRa, late diastolic strain rate; SRe, early diastolic strain rate; SRs, systolic strain rate.

Table 5. Comparison of Longitudinal Diastolic Strain Rate by Sex

	Men (n = 25)	Women (n = 32)	*P*
SRe (/s)	1.17 ± 0.33	1.31 ± 0.41	.092
SRa (/s)	1.00 ± 0.24	0.98 ± 0.32	.462
SRs (/s)	0.99 ± 0.47	1.03 ± 1.16	.591

SRa, late diastolic strain rate; SRe, early diastolic strain rate; SRs, systolic strain rate.

A link has been shown between PVC and the onset of cardiomyopathy, commonly known as PVC-induced cardiomyopathy.[8] The cardiomyopathy typically takes months or even years to develop rather than just a few weeks. This has significant effects on how high PVC burden patients are managed and followed up.[9] However, while there are several studies on the systolic functions of the LV in patients with PVC, it is clearly not known how the diastolic activities of the LV are affected. In this study, we determined that the LVEF, LV volumes, LV GLS, and conventional diastolic and tissue Doppler parameters were comparable to those seen in the healthy population. Patients with PVC had a much lower SRe than the overall population. As a result of this observation, patients with PVC may have an increased risk of diastolic dysfunction of the LV.

Table 6. Correlation Analysis

	Kendall's tau *b*	*P*
QRS duration		
SRe (/s)	−0.911	**<.001**
SRa (/s)	0.306	.306
SRs (/s)	0.003	.977
Coupling interval		
SRe (/s)	0.959	**<.001**
SRa (/s)	0.064	.508
SRs (/s)	−0.006	.950

P-value of less than .05 was statistically significant. SRa, late diastolic strain rate; SRe, early diastolic strain rate; SRs, systolic strain rate.

In the literature, there is a study that included 39 patients with PVC. In this study, diastolic function was assessed by echocardiographic mitral inflow pattern and TDI.[10] The patients with PVC had a lower *E*/*A* ratio, mean values of systolic tissue velocity (Sm), Em, and Em/Am ratio. The Am velocity and *E*/Em ratio were significantly greater in the patient group. However, the values of the patients included in the study did not meet the criteria for diastolic dysfunction.[6] In our study, we also found that the patients with PVC had greater *E*/Em ratio compared to the healthy population.

The following 2016 European Association of Cardiovascular Imaging (EACVI) criteria for LVDD were used to evaluate abnormal values of traditional LV diastolic parameters: (i) LAVI > 34 mL/m^2; (ii) tricuspid regurgitation jet peak velocity > 2.8 m/s; (iii) septal Em < 7 cm/s or lateral Em < 10 cm/s using TDI; and (iv) mitral average septal−lateral *E*/Em ratio > 14. In line with this, LVDD was determined when >50% of the aforementioned criteria were positives and normal LV diastolic function was determined when <50% of these criteria were positives.[6] However, in our study, there were no patients who met the recent 2016 criteria for LVDD of the EACVI. Unfortunately, most of the 2D and tissue Doppler measurements of these criteria are angle dependent. On the other hand, in this study, we measured a unique (angle-independent) diastolic indicator named as the SRe, and the SRe values were significantly lower in patients with PVC compared to healthy volunteers.

The QRS duration is a strong predictor of PVC-induced cardiomyopathy. Numerous investigations have shown that extended QRS duration increases the incidence of PVC-induced cardiomyopathy from 3% to 12%. A PVC with a QRS length greater than 140 ms that is more likely to originate from the free walls and outflow tracts of the ventricles has been found as a predictor of LVEF decline.[1,11-13] The length of the PVC QRS complex was inversely related to the amplitude of the SRe, as determined by our analysis. This suggests that those with a longer PVC QRS complex may be at an increased risk for LV diastolic dysfunctions.

A PVC coupling interval of less than 600 ms is related with a reduced LVEF, which may be caused by aberrant LV filling and decreased stroke volume.[1,14,15] In addition, we discovered that the PVC coupling interval greater than 600 ms is associated with a higher SRe value in individuals with PVC.

Del Carpio et al[11] showed that PVCs originating from the RV are more likely to decrease LVEF than those originating from the LV, although having a lower daily occurrence. This may be because RV PVCs are linked with a larger likelihood of LV dyssynchrony than LV PVCs. In our study, patients with right ventricular PVC had decreased SRe values. Patients with a shorter PVC coupling interval and RV-originated PVC may be at a greater risk for LV diastolic dysfunction based on these results.

Recent research indicates that an epicardial origin of PVCs may be associated with an elevated risk of cardiomyopathy.[16] It may be owing to the increased atrio-ventricular mechanical dyssynchrony of epicardial PVCs. Patients with PVC coming from the epicardium were shown to have a lower SRe. This data may give insight on the increased risk of LV diastolic dysfunctions in individuals with epicardial PVC.

Men are more likely to be asymptomatic, a condition that can delay diagnosis and increase the risk of developing cardiomyopathy. The lower risk of cardiomyopathy in women may be attributed to early intervention.[17,18] In addition, our study revealed that women with PVC had a greater SRe than males with PVC. However, there were no statistically significant differences between the genders.

Study Limitations

A small number of patients were included in this study. Although the number of patients participating in the study was low, statistically significant results were obtained supporting our hypothesis. Although this is consistent with data from the general population, in which two-thirds of idiopathic PVCs originate from the right ventricular outflow tract, the number of individuals whose PVC originated from the RV is greater than the number whose PVC originated from the LV. Another problem is that the PVC was not assessed utilizing electrophysiological study. The individuals in the study were not monitored for the development of cardiomyopathy.

CONCLUSIONS

Even though the *E*/Em ratio and maximum LAVI were higher in the patient group, these results did not meet the threshold for diastolic dysfunction. It is vital to evaluate the SRe when diagnosing diastolic dysfunction. Patients with PVC showed a decreased SRe compared to those who were healthy. SRe can be used to predict LV diastolic dysfunction, and patients with frequent PVC may have a higher risk of LV diastolic dysfunction than the general population.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Haydarpaşa Numune Training and Research Hospital (04.01.2021, approval No: HNEAH-KAEK 2020/268-3073).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

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