

# Could Premature Ventricular Contractions Lead to Atrial Remodeling?

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February 22, 2024

## Abstract

**Background** Premature ventricular contraction (PVC) is a frequent kind of arrhythmia that affects around %1 of the general population. While PVC most frequently impairs ventricular function in structurally normal heart, retrograde ventriculo-atrial conduction can occur in people with PVC. These retrograde atrial activations may mimic pulmonary vein-derived atrial ectopies. As a result, PVC may raise the risk of AF by retrograde ventriculo-atrial conduction. The Four-Dimensional Automated Left Atrial Quantification (4D Auto LAQ) tool is a left atrial analytical approach that utilizes three-dimensional volume data to quantify the volume, as well as LA longitudinal and circumferential strains. The purpose of this study was to determine if clinical diagnosis of PVC is connected with abnormal LA function as determined by LA strain evaluation utilizing a 4D Auto LAQ compared to the healthy population. **Methods** The 58 patients with frequent PVCs and 53 healthy volunteers as a control group were enrolled in the study. Imaging was performed using the GE Vivid E95 echocardiography equipment (GE Healthcare; Vingmed Ultrasound, Horten, Norway) equipped with an M5S probe (frequency range: 1.5–4.6 MHz) and a 4V probe (frequency range: 1.5–4.0 MHz). Images were imported into and were selected for analysis using the EchoPAC203 software (GE Healthcare). The analysis mode was selected, followed by the volume and 4D Auto LAQ submodes. Following that, the sample point was positioned in the center of the mitral orifice in each of the three planes. The review function was used to acquire the LA parameters measured by 4D Auto LAQ, including volume and strain parameters. **Results** The maximum left atrial volume (LAVmax) and minimal left atrial volume (LAVmin) were significantly higher in the patient group ( $38.91 \pm 9.72$  vs.  $46.31 \pm 10.22$ ,  $17.75 \pm 4.52$  vs.  $23.10 \pm 7.13$  respectively, all p values <0,001). On the other hand left atrial reservoir longitudinal strain (LASr), conduit longitudinal strain (LAScd), contraction longitudinal strain (LASct), reservoir circumferential strain (LASr-c), conduit circumferential strain (LAScd-c), and contraction circumferential strain (LASct-c) were significantly lower in patient group ( $26.64 \pm 5.64$  vs.  $19.16 \pm 4.58$ ,  $-19.53 \pm 3.72$  vs.  $-11.28 \pm 3.47$ ,  $-10.34 \pm 1.56$  vs.  $-4.59 \pm 1.49$ ,  $30.72 \pm 4.04$  vs.  $19.31 \pm 2.60$ ,  $-19.91 \pm 1.78$  vs.  $-13.38 \pm 2.85$ ,  $-15.89 \pm 6.37$  vs.  $-9.24 \pm 1.63$ , respectively, all p values <0,001). **Conclusions** The present study found that premature ventricular complexes can lead to atrial remodeling as well as ventricular remodeling in patients with PVC and 4D LAQ technology can quantitatively examine left atrial function and determine these alterations early.

## Could Premature Ventricular Contractions Lead to Atrial Remodeling?

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**Running Title:** Worsened Left Atrial Strain Values in Frequent Premature Ventricular Contractions

**Keywords:** a speckle tracking echocardiography; left atrial function; premature ventricular contraction

**Source of Funding:** None

**Conflict of Interest/Disclosure:** None

**Data Availability Statement:** Authors can confirm that all relevant data are included in the article and/or its supplementary information files

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The Four-Dimensional Automated Left Atrial Quantification (4D Auto LAQ) tool is a left atrial analytical approach that utilizes three-dimensional volume data to quantify the volume, as well as LA longitudinal and circumferential strains. The purpose of this study was to determine if clinical diagnosis of PVC is connected with abnormal LA function as determined by LA strain evaluation utilizing a 4D Auto LAQ compared to the healthy population.

### Methods

The 58 patients with frequent PVCs and 53 healthy volunteers as a control group were enrolled in the study. Imaging was performed using the GE Vivid E95 echocardiography equipment (GE Healthcare; Vingmed Ultrasound, Horten, Norway) equipped with an M5S probe (frequency range: 1.5–4.6 MHz) and a 4V probe (frequency range: 1.5–4.0 MHz). Images were imported into and were selected for analysis using the EchoPAC203 software (GE Healthcare). The analysis mode was selected, followed by the volume and 4D Auto LAQ submodes. Following that, the sample point was positioned in the center of the mitral orifice in each of the three planes. The review function was used to acquire the LA parameters measured by 4D Auto LAQ, including volume and strain parameters.

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## Conclusions

The present study found that premature ventricular complexes can lead to atrial remodeling as well as ventricular remodeling in patients with PVC and 4D LAQ technology can quantitatively examine left atrial function and determine these alterations early.

## Introduction

Premature ventricular contraction (PVC) is a common arrhythmia affecting around 1% of the population. PVC is typically asymptomatic, but it can also cause palpitations, the sense of a skipped beat, chest discomfort, dyspnea, fatigue, presyncope, or syncope. Although PVC is mostly benign, it may increase the risk of cardiomyopathy or ventricular tachyarrhythmias such as ventricular tachycardia and ventricular fibrillation. [1-3]

PVC can affect ventricular function in a structurally normal heart, and retrograde ventriculo-atrial conduction can also occur in PVC patients. These retrograde atrial activations may resemble pulmonary vein-derived atrial ectopies and raise the risk of atrial fibrillation (AF). [4-6]

Numerous researchers have used speckle tracking echocardiography (STE) to measure left atrial strain (LAS). Despite its effectiveness, the therapeutic value of STE is limited by its thin-walled design, irregular organization of myocytes in the LA, and interobserver variability. The four-dimensional automated left atrial quantification (4D Auto LAQ) tool is an analytical method that uses three-dimensional volume data to quantify the left atrial (LA) volume and left atrial longitudinal and circumferential strains. [7-9]

This study aims to examine the relationship between PVC and abnormal LA function as measured by LA strain evaluation using a 4D Auto LAQ.

## Methods

### Study Population

In the trial, 58 patients with more than 10,000 PVCs during 24-hour ambulatory rhythm Holter monitoring were compared to 53 healthy persons who served as the control group. Participants were excluded if they had a left ventricular ejection fraction (LVEF) of less than 50 percent, LV hypertrophy, more than mild valvular heart disease, coronary artery disease, significant congenital heart disease, other arrhythmias (such as atrial flutter, atrial fibrillation, supraventricular tachycardia), uncontrolled or more than grade 1 arterial hypertension, dyslipidemia, obstructive sleep apnea, or a history of smoking. The local ethics committee approved of the research. All participants who participated in the study provided their informed permission.

### Echocardiography

For imaging, a GE Vivid E95 echocardiography system (GE Healthcare; Vingmed Ultrasound, Horten, Norway) with an M5S probe (frequency range: 1.5-4.6 MHz) and a 4V probe was employed (frequency range: 1.5-4.0 MHz). During echocardiography, a single lead rhythm recording was collected from all subjects. All of the subjects had normal sinus rhythm. According to the current standards of the American Society of Echocardiography, a comprehensive transthoracic echocardiographic examination was performed to evaluate heart anatomy, chamber size, and cardiac function. We calculated the LVEF using the biplane Simpson technique with enhancements. A transducer with a 4V output was used to perform a three-dimensional echocardiographic examination on each participant. On the apical four-chamber view, volumetric data for the whole LA was acquired by adjusting the pictures. The dataset was acquired using five distinct heartbeat acquisition settings, with the frame rate set to 40% of the heart rate. At the end of inhalation or exhalation, participants were instructed to hold their breath. At least four datasets have been collected. The three

picture data sets with the highest quality were chosen for examination. A dataset was eliminated if the LA endocardial boundary was missing or ambiguous. To enhance the precision and repeatability of the measurements, high-resolution pictures were acquired. [9-11]

## Standards for 4D Auto LAQ

### Principles for 4D Auto LAQ

For volume computation, a semi-automated segmentation approach was applied. At the annular level, a mark was inserted in the center of the mitral valve (MV) to initiate the algorithm. Using an extended Kalman filter that incorporates the LA motion model, geometry, and edge detection techniques, the segmentation procedure determines the deformation of the three-dimensional model. Using differences in the lengths of several lines perpendicular to each anatomical direction, strain was assessed. Using a triangular mesh, eight longitudinal lines, each connecting two opposing LA base points, were used to calculate longitudinal strain. Seven circumferential lines are uniformly positioned between the LA base and LA apex in order to compute the circumferential strain. The strain duration for each frame was then determined using the formula  $s(t) = (L(t) - L(tr)) / L(tr) \times 100$  percent, where  $L(t)$  is the line length at time  $t$  and  $tr$  is the end diastolic time of the left ventricle. To determine the global strain, the strains of all significant directional lines were averaged. [9, 12, 13]

### Automated LAQ Assessments in 4D

The program EchoPac-203 from GE Healthcare was used to import the images and evaluate their suitability for analysis. The analytical volume, and 4D Auto LAQ submodes were employed sequentially. Beginning the sampling technique, a location in the middle of the mitral orifice was selected in each of the three planes. The review function was used to create the LA strain and volume parameters. The end diastole of the left ventricle was used as a reference point. The LA wall grew during the reservoir phase, resulting in a positive strain value. In the last two steps of the length decrease of the LA wall, the strains had negative values. This method generated LA longitudinal strain parameters, including LA conduit strain (LAScd), LA reservoir strain (LASr), and LA contraction strain (LASct), as well as LA circumferential strain parameters, including LA conduit circumferential strain (LAScd-c), LA reservoir circumferential strain (LASr-c), and LA contraction circumferential strain (LASct-c) (LASct-c). [9, 12, 13] (Figure 1)

### Statistical Analysis

Using IBM SPSS Statistics 22 software, statistical analysis was done. Continuous variables are provided as mean and standard deviation, while nominal variables are presented as numbers and percentages. For nominal variables, the Chi-squared test or Fisher's exact test, the Student's t-test for continuous parametric variables, and the Mann Whitney U test for continuous non-parametric variables were used. group comparison. Kendall rank correlation was used to evaluate the correlation between non-parametric variables. variables. A p-value less than 0.05 was considered statistically significant.

### Results

58 patients (mean age 45.9 13.50 years, 52.2% female) and 53 control participants (mean age 41.8 10.3 years, 62.3% male) enrolled in the study. Table 1 presents the clinical characteristics of the study group. Comparable baseline characteristics existed amongst the study groups.

Table 2 displays the 2D transthoracic echocardiographic characteristics of the research group. In the patient group, the left atrial anterior-posterior dimension was substantially greater ( $p=0.001$ ). The left ventricular end-systolic diameter (LVESD) and the left ventricular end-systolic were greater in the patient group ( $p=0.002$ ,  $p=0.033$ , respectively), as were the mitral inflow late diastolic velocity (A) and the E/Em ratio (E; mitral inflow early diastolic tissue velocity; Em; mitral inflow early diastolic tissue velocity). In the control group, the mitral inflow early diastolic tissue velocity (Em) was greater. ( $p=0.040$ ) Other echocardiographic parameters did not differ significantly between the patient and control groups. Table 3 provides the longitudinal and circumferential strain values of the study group for LA. The maximum LA volume (LAVmax), the minimal

LA volume (LAVmin), and the LA maximum volume index were substantially greater in the patient group (p=0.001, p=0.001, and p=0.001, respectively). In the patient group, the longitudinal and circumferential strain values of LA were considerably lower. (all p values <0.001) LASr, LAScd, LASct, LASr-c, LASct-c, LASr-c, LAScd-c, LASct-c were shown to be considerably lower (p=0.004, p=0.002, p=0.007, p< 0.001, p=0.001, p0.001, p=0.001, p< 0.001, respectively) in individuals with PVC coming from the right ventricle. The longitudinal and circumferential strain values of LA were shown to be considerably lower in individuals with epicardial PVC. (all p values <0.001) (Table 4)

In the correlation study, negative relationships between QRS duration and the circumferential and longitudinal strain values of LA were shown to be statistically significant (all p values< 0.001). (Table 5)

Conversely, substantial positive relationships were found between coupling interval and the circumferential and longitudinal strain values of LA (all p values < 0.001). (Table 6)

## Discussion

The longitudinal and circumferential strain values of the LA were considerably lower in the patient group compared to the control group. In compared to healthy volunteers, individuals with PVC exhibited impaired LA function, according to our findings.

Increased PVC frequency (>10,000/day or >10/hour) might negatively impact the left atrial and left ventricular functions of a structurally normal heart. Frequent PVC may result in an aberrant LV filling pressure, leading in a change in LV shape and systolic dysfunction or PVC-induced cardiomyopathy. Depending on the degree and duration of the aberrant LV filling pressure, frequent PVC may lead to atrial overload and pathological alterations of the LA. These structural modifications to the LA have the potential to affect its functions and degrade longitudinal and circumferential strain values. In recent research analyzing patients with normal LVEF and frequent PVCs, individuals with PVCs had an elevated LA volume index. [14, 15] Prior research investigating the effect of PVC ablation on atrial and ventricular architecture demonstrated that effective PVC ablation can prevent LA dilatation. [15, 16] In our study, it was also shown that the LA volumes increased in patients with PVC.

The relationship between PVC and atrial arrhythmias is not clear. Age, hypertension, and diabetes are common risk factors for both PVC and atrial arrhythmias. PVC may generate retrograde ventriculo-atrial conduction and behave like atrial ectopic beats originating from the pulmonary vein. Consequently, PVC may enhance the incidence of atrial ectopies via retrograde ventriculo-atrial conduction [4-6].

As LA may contract against a closed mitral valve, PVC can result in atrioventricular dyssynchrony. This may raise LA pressure and atrial wall tension. Occasionally, PVC cannot conduct retrogradely to the LA, but it might render the AV node resistant to the subsequent sinus beat. Due to the postextrasystolic compensatory pause, the beat following a PVC may result in a LA volume overload. Depending on the cause of the PVC, the QRS duration and coupling interval may be lengthened and shortened, respectively. In this situation, atrioventricular dyssynchrony may increase. An increase in atrioventricular dyssynchrony may result in a deterioration of LA functions and strain levels. [15, 18-20] In our investigation, LA strain metrics were worse in patients with epicardial origin PVC whose QRS length was predicted to be longer. PVC coupling intervals were also shown to be closely associated with LASrc, LASr, LASct, LAScd, LAScdc and LASctc.

Del Cardipo et al. observed that PVCs originating from the right ventricle (RV) may result in a more serious reduce in LVEF than those coming from the left ventricle (LV). [21] A deteriorating LVEF will likewise have significant effects on LA functioning. LASrc, LASr, LASct, LAScd, LAScdc and LASctc were considerably lower in individuals with PVC coming from the right ventricle, according to our study. Our data indicate that PVCs affect the quantities and functioning of LA. Patients with PVC of epicardial and right ventricular origin and longer QRS durations have more significant alterations in LA characteristics.

## Study Limitations

The research only included a small number of patients. Patients whose PVC originated from the right

ventricle were more prevalent than those whose PVC originated from the left ventricle, however this is consistent with findings from the general population, in which two-thirds of idiopathic PVCs originate from the right ventricular outflow tract (RVOT). (cümle düşük gibi abla) Electrophysiological evaluation of PVC has not been undertaken. Patients were not monitored for the development of cardiomyopathy or atrial arrhythmias, such as atrial fibrillation, over the long term.

## Conclusions

PVC can cause remodeling of the atrium and ventricle in patients with frequent PVC. 4D LAQ technology can objectively assess the myocardial function of the left atrium and can be utilized to detect LA alterations in patients with recurrent PVC.

## Consent

The authors affirm that the patient has provided written consent for the submission and publishing of this study, including photos and supporting text, in accordance with COPE guidelines.

## Source of Finances

None

## Interest Conflict/Disclosure

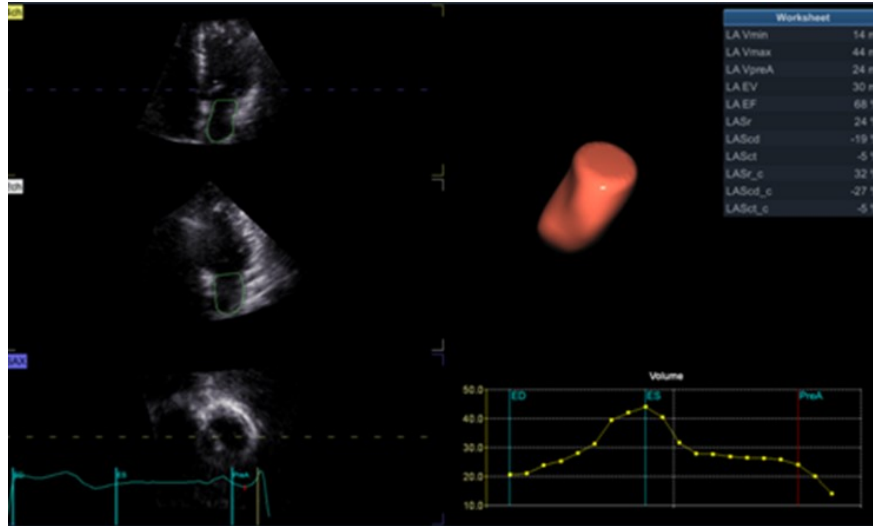
The work will be presented at the "European Society of Cardiology (ESC) Congress 2022, Barselona" as an oral moderated poster presentation and will be published as an abstract in the supplement of the European Heart Journal.

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**Figure Legend****Figure 1:** Measurement of left atrial strain parameters. LA volume curve and strain curve measured by the 4-Dimensional Automated Left Atrial Quantification (4D Auto LAQ) tool.



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