Evaluation of left ventricular myocardial deformation parameters in individuals with electrocardiographic early repolarization pattern

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Abstract

Objective: Although an early repolarization (ER) pattern was considered to be a benign electrocardiographic variant, several studies have shown that it is associated with an increased risk of idiopathic ventricular fibrillation and death. The aim of the present study was to determine whether there is any abnormality in myocardial deformation parameters (strain, strain rate, rotation, and twist) of the left ventricle obtained by speckle-tracking echocardiography (STE) in subjects with ER pattern.
Methods: There were two groups in this prospective case-control study. The first group consisted of subjects with ER pattern (n=35). The other group was control without ER pattern (n=25). Subjects with poor echocardiographic image quality and history of cardiovascular, pulmonary, systemic, or metabolic disease were excluded from the study. For STE of the left ventricle, two-dimensional images from apical long-axis, two-chamber, and four-chamber views and from parasternal short-axis views were obtained.
Results: We did not observe significant differences between the groups for left ventricular (LV) longitudinal deformation parameters, rotation, and twist. When LV circumferential deformation parameters were analyzed, early diastolic strain rate value at the level of apex was higher in subjects with ER pattern (2.3±0.7 s^{-1} vs. 1.9±0.4 s^{-1}, p=0.01). Among LV radial deformation parameters, only peak strain (42.5±16.1% in the ER group vs. 56.9±21.1% in controls, p=0.004) and early diastolic strain rate (–2.0±0.7 s^{-1} in the ER group vs. –2.3±0.7 s^{-1} in controls, p=0.03) values at the level of papillary muscle were different.
Conclusion: In subjects with ER pattern, LV myocardial deformation evaluated by STE is normal with a few regional exceptions. STE does not provide much information about risk stratification of these subjects. *(Anatol J Cardiol 2016; 16: 850-4)*
Keywords: Electrocardiography, early repolarization, speckle-tracking echocardiography, strain, strain rate, rotation

Introduction

The prevalence of early repolarization (ER) pattern in standard 12-lead electrocardiography is as high as 13% in the general population, and it is relatively common in young adults, males, African descents, and athletes (1). Although ER pattern was considered to be a benign electrocardiographic variant, several case–control and epidemiological studies have shown that it is associated with an increased risk of idiopathic ventricular fibrillation and death (2, 3). A meta-analysis of these studies showed that the risk ratio was 1.70 (95% confidence interval [CI]: 1.19–2.42; p=0.003) for arrhythmic death in patients with ER (4).

Speckle-tracking echocardiography (STE) is a relatively new imaging technique that is increasingly used in the evaluation of global and regional myocardial functions. It is largely independent from ultrasound beam angle and cardiac translational movements (5). It allows the assessment of myocardial deformation parameters in different spatial directions (i.e., longitudinal, radial, and circumferential). These parameters include displacement, velocity, strain, strain rate, and rotation (6). Recent studies have shown that STE can be used in different clinical situations to evaluate cardiac mechanics in a feasible, reproducible, and accurate way (7).

The aim of the present study is to determine whether there is any abnormality in myocardial deformation parameters (strain, strain rate, rotation, and twist) of the left ventricle obtained by STE in subjects with ER pattern.

Methods

Study population

ER pattern in standard 12-lead electrocardiography is defined as a J-point elevation of ≥0.1 mV in at least two contiguous leads with either a QRS slurring or notching (8, 9). This was a prospective case–control study with two groups. The first group

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Accepted Date: 29.01.2016 **Available Online Date:** 25.04.2016

DOI:10.14744/AnatolJCardiol.2016.6912

consisted of subjects with ER pattern (n=35). The other group was control without ER pattern (n=25). Subjects in both groups did not have a history of cardiovascular, pulmonary, systemic, or metabolic disease, and their physical examinations were normal.

Exclusion criteria of the study were atrial fibrillation, advanced atrioventricular block, left or right bundle branch block, paced rhythm, moderate to severe valvular heart disease, prosthetic heart valve, systolic heart failure, segmental wall motion abnormality, pericardial disease, acute coronary syndrome, liver or renal failure, malignancy, pregnancy, poor echocardiographic image quality, age <18 years or >45 years, and regular medication use (i.e., antihypertensives, statins, anticoagulants, antiarrhythmics, antibiotics, steroids, and antipsychotics).

The study complied with the Declaration of Helsinki and was approved by the local Ethical Committee, and each patient gave written informed consent.

Echocardiographic analysis

All echocardiographic examinations were performed by a single experienced operator blinded to clinical data of the subjects using a Vivid E9 echocardiography machine (GE Vingmed Ultrasound, Horten, Norway). Measurements of standard transthoracic echocardiography, Doppler analysis, and STE were performed according to the guidelines and statements (6, 10). Strain is the fractional change in the length of a segment relative to its original length. Strain rate is the rate of strain per unit time. Rotation is the relative clockwise or counterclockwise displacement of myocardium in the short axis of the left ventricle around the long-axis of the heart. Twist is the net difference between apical and basal rotation (11).

For STE of the left ventricle, two-dimensional images from apical long-axis, two-chamber, and four-chamber views and from parasternal short-axis views at the level of mitral valve, papillary muscle, and apex were obtained. For each view, three consecutive cardiac cycles were recorded at end-expiration. Offline analysis of digitally recorded images was performed by using commercially available software (EchoPac PC, version 110.1.2, GE Vingmed Ultrasound, Horten, Norway). The software is a semi-automated program. The endocardial border was manually traced, and then a region of interest was automatically drawn by the software. If needed, a region of interest was adjusted to cover the entire myocardium without including the pericardium. After tracking, each left ventricular (LV) plane was divided into six equidistant segments, and speckle-tracking analysis was performed on a frame-to-frame basis by the program. The segments with poor tracking quality were excluded from the analysis. Aortic valve motion in apical long-axis view was used to determine aortic valve closure time. While apical two-chamber and four-chamber views were used for the measurement of longitudinal deformation parameters, parasternal short-axis views were used for the measurement of radial and circumferential deformation parameters and twist. All parameters were calculated as the average of three measurements. The values at each plane were combined and averaged to obtain mean values.

Nine subjects who were intended to be included into the study were excluded due to poor echocardiographic image quality. Suboptimal quality of a region of interest during speckle-tracking analysis led to exclusion of 18 segments in subjects with ER pattern (1.7%) and of 12 segments in controls (1.6%).

Statistics

All data were reported as a mean±standard deviation for continuous variables and as a percentage for categorical variables. Shapiro–Wilk test was used to test the accordance of the data with normal distribution. Continuous variables were compared using Student's t-test or Mann–Whitney U test, where appropriate. Chi-square test was used to compare categorical variables. A difference was considered significant when the p value was <0.05. A sample size of 19 for each group was determined to achieve a power of 80% with an alpha error level of 5% for detecting significant change in ratio of peak velocity of early mitral inflow to peak early diastolic velocity of mitral annulus. SPSS v21 Base (IBM Corp., New York, USA) was used for all statistical analyses.

Results

Patients

Baseline clinical characteristics of the two study groups are shown in Table 1. In the ER group, there were 29 males and 6 females. In controls, there were 16 males and 9 females. Mean

Table 1. Baseline clinical characteristics and standard two-dimensional and Doppler echocardiographic measurements of the study subjects

	ER group (n=35)	Control group (n=25)	*P*
Males, n	29	16	0.09
Age, years	25.5±6.2	26.1±5.3	0.50
BMI, kg/m^2	23.1±3.6	24.5±3.1	0.12
Heart rate, per/m	78.9±12.1	71.2±11.0	0.01
IVS, mm	10.3±1.6	10.3±2.1	0.99
PW, mm	8.8±1.3	9.2±1.8	0.41
LVEDD, mm	43.9±4.2	45.4±4.4	0.19
LVESD, mm	29.5±3.2	28.6±3.2	0.31
LV mass index, g/m^2	76.7±16.0	81.4±19.5	0.31
EF, %	64.2±2.8	65.6±3.1	0.07
LA, mm	31.9±4.6	32.9±4.4	0.43
Aorta, mm	29.0±3.2	30.0±3.2	0.25
E/A	1.4±0.2	1.5±0.3	0.12
E/E′	5.7±1.0	6.7±1.2	0.001

Chi-square test and Student's t-test or Mann–Whitney U test were used.
BMI - body mass index; E/A - ratio of peak velocity of early mitral inflow to peak velocity of late mitral inflow; E/E′ - ratio of peak velocity of early mitral inflow to peak early diastolic velocity of mitral annulus; EF - ejection fraction; ER - early repolarization; IVS - interventricular septum; LA - left atrium; LV mass - left ventricular mass; LVEDD - left ventricular end-diastolic diameter; LVESD - left ventricular end-systolic diameter; PW - posterior wall

Table 2. Left ventricular longitudinal deformation parameters of the study groups

	ER group (n=35)	Control group (n=25)	*P*
Apical four-chamber view			
Strain, %	-20.8±2.8	-21.5±2.6	0.39
SR_S, 1/s	-1.3±0.1	-1.2±0.1	0.24
SR_E, 1/s	1.9±0.3	1.9±0.4	0.84
SR_A, 1/s	0.8±0.2	0.8±0.1	0.23
Apical two-chamber view			
Strain, %	-20.4±2.6	-21.3±2.6	0.17
SR_S, 1/s	-1.2±0.1	-1.2±0.1	0.91
SR_E, 1/s	1.7±0.2	1.7±0.3	0.57
SR_A, 1/s	0.8±0.2	0.8±0.1	0.72
Global			
Strain, %	-20.6±2.4	-21.4±2.4	0.22
SR_S, 1/s	-1.2±0.1	-1.2±0.1	0.59
SR_E, 1/s	1.8±0.2	1.8±0.3	0.74
SR_A, 1/s	0.8±0.2	0.8±0.1	0.93

Student's t-test or Mann–Whitney U test
ER - early repolarization; SRA - late diastolic strain rate; SRE - early diastolic strain rate; SRS - systolic strain rate

age was 25.5±6.2 years in subjects with ER pattern and 26.1±5.3 years in controls. There was no significant difference between the groups according to sex, age, and body mass index. Heart rate was higher in subjects with ER pattern (Table 1). Among the ER group, there were 18 subjects with inferior ER pattern, 13 with lateral ER pattern, and 4 with inferolateral ER pattern.

Standard two-dimensional and Doppler echocardiographic measurements

These measurements are shown in Table 1. There was no significant difference between the groups according to LV dimensions, LV wall thicknesses, LV mass, left atrial diameter, and ascending aortic diameter. Doppler ratio of peak velocity of early mitral inflow to peak early diastolic velocity of mitral annulus (E/E′) was within normal limits, but was lower in subjects with ER pattern.

Speckle-tracking echocardiography measurements

We did not observe significant differences between the groups for LV longitudinal deformation parameters. Peak strain, systolic strain rate, early diastolic strain rate, and late diastolic strain rate values were all similar (Table 2).

When LV circumferential deformation parameters were analyzed, early diastolic strain rate at the level of apex and global early diastolic strain rate were higher in subjects with ER pattern compared to the control group (2.3±0.7 s^{-1} vs. 1.9±0.4 s^{-1}, p=0.01 and 2.0±0.4 s^{-1} vs. 1.7±0.2 s^{-1}, p=0.01, respectively). All other measured parameters were similar between the groups (Table 3).

Table 3. Left ventricular circumferential deformation parameters of the study groups

	ER group (n=35)	Control group (n=25)	*P*
At the level of mitral valve			
Strain, %	-16.7±3.7	-16.5±2.7	0.89
SR_S, 1/s	-1.4±0.3	-1.4±0.2	0.75
SR_E, 1/s	1.7±0.4	1.7±0.3	0.48
SR_A, 1/s	0.6±0.2	0.6±0.1	0.85
At the level of papillary muscle			
Strain, %	-19.7±4.7	-18.0±3.0	0.08
SR_S, 1/s	-1.5±0.3	-1.4±0.2	0.13
SR_E, 1/s	1.9±0.4	1.6±0.3	0.06
SR_A, 1/s	0.6±0.2	0.5±0.1	0.12
At the level of apex			
Strain, %	-24.8±7.0	-23.1±4.5	0.21
SR_S, 1/s	-1.9±0.5	-1.7±0.3	0.09
SR_E, 1/s	2.3±0.7	1.9±0.4	0.01
SR_A, 1/s	0.7±0.3	0.7±0.2	0.42
Global			
Strain, %	-20.4±4.0	-19.2±2.4	0.19
SR_S, 1/s	-1.6±0.3	-1.5±0.1	0.24
SR_E, 1/s	2.0±0.4	1.7±0.2	0.01
SR_A, 1/s	0.7±0.2	0.6±0.1	0.25

Student's t-test or Mann–Whitney U test
ER - early repolarization; SRA - late diastolic strain rate; SRE - early diastolic strain rate; SRS - systolic strain rate

Among LV radial deformation parameters, only peak strain (42.5±16.1% in the ER group vs. 56.9±21.1% in controls, p=0.004) and early diastolic strain rate (–2.0±0.7 s^{-1} in the ER group vs. –2.3±0.7 s^{-1} in controls, p=0.03) at the level of papillary muscle were different between the groups. However, all other parameters, including global values, were similar (Table 4).

There was no significant difference between the groups for LV rotation and twist values (Table 5).

Discussion

In this study, we found that LV myocardial deformation parameters obtained by STE were normal with a few regional exceptions in subjects with ER pattern. This is the first study in medical literature evaluating the possible abnormalities in subjects with ER pattern by STE in three spatial directions.

In many clinical studies, STE was shown to allow the preclinical detection of cardiac dysfunction before deterioration of traditional echocardiographic parameters. Angle independency, semiautomatic nature, lack of geometric assumptions, and ability to obtain information regarding global and regional cardiac functions in different spatial directions are the major advantages of this technique (11).

Table 4. Left ventricular radial deformation parameters of the study groups

	ER group (n=35)	Control group (n=25)	*P*
At the level of mitral valve			
Strain, %	43.1±18.5	39.8±14.5	0.46
SR_S, 1/s	2.1±0.7	1.8±0.4	0.23
SR_E, 1/s	-1.7±0.7	-1.4±0.4	0.10
SR_A, 1/s	-0.9±0.5	-0.9±0.4	0.82
At the level of papillary muscle			
Strain, %	42.5±16.1	56.9±21.1	0.004
SR_S, 1/s	1.7±0.5	1.9±0.4	0.12
SR_E, 1/s	-2.0±0.7	-2.3±0.7	0.03
SR_A, 1/s	-0.8±0.3	-0.8±0.3	0.92
At the level of apex			
Strain, %	27.5±16.4	33.2±15.8	0.11
SR_S, 1/s	1.5±0.6	1.7±0.6	0.21
SR_E, 1/s	-2.0±1.0	-2.0±0.6	0.92
SR_A, 1/s	-0.7±0.6	-0.6±0.4	0.98
Global			
Strain, %	37.6±11.7	43.3±11.0	0.06
SR_S, 1/s	1.8±0.5	1.8±0.3	0.54
SR_E, 1/s	-1.9±0.5	-1.9±0.3	0.86
SR_A, 1/s	-0.8±0.3	-0.8±0.2	0.92

Continuous variables were compared using Student's t-test or Mann–Whitney U test, where appropriate. ER - early repolarization; SRA - late diastolic strain rate; SRE - early diastolic strain rate; SRS - systolic strain rate

Table 5. Left ventricular rotation and twist values of the study groups

	ER group (n=35)	Control group (n=25)	*P*
Basal rotation, degree	-1.8±5.9	-3.3±5.4	0.29
Apical rotation, degree	7.4±7.3	7.7±3.9	0.87
Twist, degree	9.3±10.5	11.1±5.5	0.44

Continuous variables were compared using Student's t-test or Mann–Whitney U test, where appropriate. ER - early repolarization

ER pattern in a standard 12-lead electrocardiography is not a rare finding in general population and has been accepted as a benign electrocardiographic variant for many years. However, the association of ER pattern with an increased risk of idiopathic ventricular fibrillation and death has been shown in many studies. Additionally, there is an increased risk of experiencing syncope or sudden cardiac arrest if idiopathic ventricular fibrillation patients have ER pattern in their electrocardiographies (2, 3). These findings have raised great interest among physicians and researchers, and possible triggers of the increased risk have been tried to be found. Different electrocardiographic and demographic variables have been suggested to predict arrhythmic risk in ER pattern with predictive value of one compared with the other not clearly established (8). Although there is no effective risk stratification strategy for asymptomatic individuals with ER pattern, close follow-up is recommended if they have a personal history of unexplained syncope or a family history of unexplained sudden death (1).

In medical literature, unfortunately, there are too few echocardiographic studies done in individuals with electrocardiographic ER pattern. Wilhelm et al. (12) investigated the influence of ER pattern on diastolic function and left atrial size in professional soccer players. Among 54 players, 24 showed an ER pattern. Players with ER pattern had a lower heart rate (54±9 vs. 62±11 beats/min, p=0.024), a higher E/E′ ratio (6.1±1.2 vs. 5.1±1.0, p=0.002), and larger left atrial volumes (25.6±7.3 vs. 21.8±5.0 mL/m^2, p=0.031) compared to players without ER pattern. In our study, however, individuals with ER pattern had a higher heart rate, decreased E/E′ ratio, and similar left atrial dimension compared to those without ER pattern. This discrepancy may be partly explained by the fact that professional soccer players have a higher vagal tone causing lower heart rate and higher LV filling pressure. Wilhelm et al. (12) also evaluated LV longitudinal deformation parameters. They found that there was no difference between the groups for global longitudinal strain, systolic strain rate, and diastolic strain rate values, as in our study.

Stankovic et al. (13) presented a 56-year-old male with chest pain, persistent ST-segment elevation in inferolateral leads, and suspected hypokinesia of the inferior wall. They evaluated the value of two-dimensional speckle-tracking-derived strain to distinguish acute coronary syndrome from a marked early repolarization. Speckle-tracking strain analysis revealed normal longitudinal peak systolic strain in all segments of inferior wall, ruling out wall-motion abnormalities in that region. At follow-up, no evolution of ECG findings was detected. In addition, coronary angiogram and serial cardiac biomarkers were normal. ER pattern was responsible for ECG findings of the patient and quantification of regional LV function was successfully performed by speckle-tracking analysis.

Aagaard et al. (14) conducted a study with the aim of assessing prevalence and patterns of ER in middle-aged long-distance runners, its relation to cardiac structure and function, and its response to strenuous physical activity. Among 151 runners, 67 had an ER pattern. There was no difference between the subjects with versus without ER pattern for interventricular and posterior wall thicknesses, LV dimensions, mass, and ejection fraction, as in our study. However, the E/A ratio was higher in runners with ER pattern. In addition, there were differences in the vectorcardiographic parameters between the subjects. For this, the authors explained that exercise training led to an increase in parasympathetic modulation.

In our study, some LV myocardial deformation parameters (i.e., circumferential early diastolic strain rate value at the level of apex, global circumferential early diastolic strain rate value, and radial peak systolic strain and radial early diastolic strain rate values at the level of papillary muscle) obtained by STE were different between the groups. Since our study is the first in medical literature to evaluate possible abnormalities in subjects with ER pattern by STE in three spatial directions, it is difficult to interpret these results. These findings may be a chance phenomenon due to limitations of the study. However, these findings may also indicate abnormal regional myocardial mechanics in subjects with ER pattern. The study of Sauer et al. (15) supports this hypothesis. They evaluated the repolarization heterogeneity in 82 outpatients referred for echocardiography and found an independent relationship between heterogeneity of electrical repolarization and that of contraction duration in the radial direction by strain imaging. This may be the case in subjects with ER pattern, causing regional alterations in LV myocardial deformation parameters. Further research is required to investigate this point.

Study limitations

Our study has some limitations. The sample size was low, which may lead to a statistical type I error. Segmental analysis of LV longitudinal deformation parameters was not performed. In addition, there are inherent problems related to STE (i.e., sensitivity to acoustic shadowing or reverberations, suboptimal tracking of endocardial border in case of poor image quality, relatively low temporal resolution, and postprocessing time).

Conclusion

In subjects with ER pattern, LV myocardial deformation evaluated by STE is normal with a few regional exceptions. STE does not provide much information about risk stratification of these subjects. Further studies are required to show the potential clinical value of STE in this special population.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept- O.G.; Design – O.G.; Supervision – G.D., M.Ş.; Materials – O.G., S.Y.; Data collection &/or processing – O.G., G.D.; Analysis &/or interpretation – O.G., K.S.; Literature search – O.G., G.D.; Writing – O.G., S.Y.; Critical review – M.Ş., K.S.

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