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Evaluation of the relationship between speckle tracking echocardiography and arrhythmia markers Tp-e interval and Tp-e/QTc in patients with arterial hypertension

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Abstract. – OBJECTIVE: The prolongation of the Tp-e interval, which is defined as the interval from the peak to the end of the T wave on electrocardiography (ECG), is considered a non-invasive predictor of malignant ventricular arrhythmia development. In our study, we aimed to compare the Tp-e interval and Tp-e/QTc ratios on ECG and subclinical myocardial dysfunction evaluated by left ventricular global longitudinal strain (LV-GLS) imaging in patients receiving treatment for hypertension.

PATIENTS AND METHODS: Two-dimensional speckle tracking echocardiography was performed in 102 consecutive hypertensive patients with blood pressure values regulated by treatment. The normal left ventricular global longitudinal strain (LV-GLS) limit was accepted as < -18%. The patients were divided into two groups: those with normal (≥ -18%) LV-GLS and those with impaired LV-GLS (< -18%). Comparisons between the groups were made by measuring ventricular repolarization parameters, such as QT, QTc, and Tp-e intervals, and Tp-e/QT and Tp-e/QTc ratios.

RESULTS: While the mean age of the patients with impaired LV-GLS was 55±6 years, the mean age of the normal LV-GLS group was 58±9 years (*p*=0.101). The Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios were significantly higher in the impaired LV-GLS group than in the normal LV-GLS group (*p*<0.05 for all). A positive correlation was observed between the ventricular repolarization parameters and LV-GLS values. This positive correlation was statistically significant in terms of the Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios.

CONCLUSIONS: The Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios were increased in hypertensive patients with impaired LV-GLS, and therefore a close follow-up in terms of increased arrhythmia risk is required in this patient group.

Key Words:
Hypertension, Tp-e interval, Tp-e/QTc ratio, Left ventricular global longitudinal strain, Transthoracic echocardiography.

Introduction

Arterial hypertension is an important risk factor for cardiovascular morbidity and mortality worldwide[1-3]. Impaired left ventricular (LV) function, left ventricular hypertrophy, and the presence of myocardial fibrosis measured by transthoracic echocardiography are known indicators of target organ damage[4]. Speckle tracking echocardiography (STE) is used to identify yearly regional and global myocardial dysfunction that cannot be detected by routine transthoracic echocardiography in both asymptomatic and symptomatic patients with cardiovascular disease[5]. Global longitudinal strain (GLS) has been reported[6] to be a more sensitive indicator than ejection fraction in demonstrating LV systolic dysfunction and cardiovascular prognosis. There are studies[7] showing that there may be subclinical myocardial damage in LV-GLS measurements even if the ejection fraction is normal in patients with hypertension.

It has been shown[8] that arterial hypertension is associated with cardiac arrhythmias, which can significantly affect prognosis. The Tp-e interval is the interval between the peak and the end of the T wave measured on electrocardiography (ECG). Various studies[9] have indicated that the Tp-e interval can be used as an index of the total (transmural, apicobasal, and global) repolarization dispersion. The prolongation of the Tp-e interval

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is considered a non-invasive predictor of malign ventricular arrhythmias[10]. It has also been shown[11] that the Tp-e interval is prolonged in hypertensive patients compared to the normal population.

To our knowledge, there are no literature data presenting arrhythmia risk in hypertensive patients with subclinical myocardial dysfunction. Therefore, in this study, we aimed to compare the Tp-e interval and Tp-e/QT, and Tp-e/QTc ratios, which are markers of malignant ventricular arrhythmias, in patients with controlled hypertension according to the LV-GLS status.

Patients and Methods

Study Population

Patients with arterial hypertension and regulated blood pressure values were consecutively included in the study between January and April 2022. Unregulated hypertension, history of the presence of arrhythmia, the presence of branch block, the history of the use of drugs that have an effect on the QT/QTc, Tp-e interval, the presence of valvular heart disease, coronary artery disease, heart failure (LVEF <50%), atrial fibrillation, diabetes mellitus, beta-blocker use, renal failure (eGFR <30 ml/min/1.73 m2), poor echogenicity, and an age under 18 years were determined as exclusion criteria. Accordingly, 11 patients with unregulated hypertension, 24 with coronary artery disease, six with heart failure, seven with atrial fibrillation, 10 with diabetes mellitus, nine using beta-blockers, five with renal failure, 14 with poor echogenicity, and 19 without optimal ECG measurements (interference) were excluded from the study. As a result, the sample consisted of 102 patients. LV-GLS measurements were performed with speckle-tracking echocardiography in all the patients participating in the study. The patients' LV-GLS values were calculated by an experienced cardiologist blinded to the study data. Taking the normal LV-GLS limit as < -18%, the patients were divided into two groups: normal (≤ -18%) LV-GLS and impaired LV-GLS (> -18%). The ECGs of the patients were evaluated by two cardiologists. Ventricular repolarization parameters (QT and QTc intervals, QT and QTc distributions, Tp-e interval, and Tp-e/QT and Tp-e/QTc ratios) were measured, and the average of two measurements was recorded for each parameter. The study was conducted by following the principles of the Declaration of Helsinki after receiving approval from the Local Ethics Committee (No.: 2022-32) Informed consent was obtained from all the patients included in the study.

Echocardiography

Echocardiographic examinations were performed on all the patients during their routine cardiology outpatient clinic controls using the X5 transducer (Philips Affiniti 50C; Philips Healthcare, Inc., Andover, MA, USA). For this examination, standard parasternal long and short axis, apical two-chamber, three-chamber, and four-chamber images were obtained. LV end-systolic and diastolic diameters, left atrium diameter, LV posterior wall thickness, and interventricular septum thickness were measured following the recommendations of the American Society of Echocardiography guidelines[12]. The ejection fraction (LVEF), end-systolic volume, and end-diastolic volume of LV were measured using the modified Simpson's method[13].

LV-GLS was measured by an experienced cardiologist blinded to the study data using the Qlab13 software (Philips Healthcare, Andover, MA, USA). The end of the diastole was considered as the peak of the R wave on ECG, while the end of the systole was considered as aortic valve closure. The mean LV-GLS was calculated by averaging the peak LV-GLS values of the apical two-chamber, three-chamber, and four-chamber images. Automatic endocardial borders were observed at the end of the systole. Manual adjustments were made where necessary to ensure accurate monitoring and include the LV wall thickness. The normal LV-GLS value was accepted as ≤ -18%[14].

Electrocardiography

ECG measurements were evaluated manually by two cardiologists using calipers and magnifying lenses. The coefficient of variation between the observers was 2.7%. The baseline heart rate (HR), PR interval, QT interval, and QTc interval [corrected by the Bazett Formula: cQT=QT∞ (R-R interval)] values were calculated manually. The Tp-e interval was defined as the distance between the peak and end of the T-wave (Figure 1)[15]. The measurements were calculated by averaging the values obtained separately from each lead of the 12-lead ECG. One measurement was made for each lead, but at least two consecutive measurements were averaged to improve accuracy in any lead where the image quality was not good. ECGs

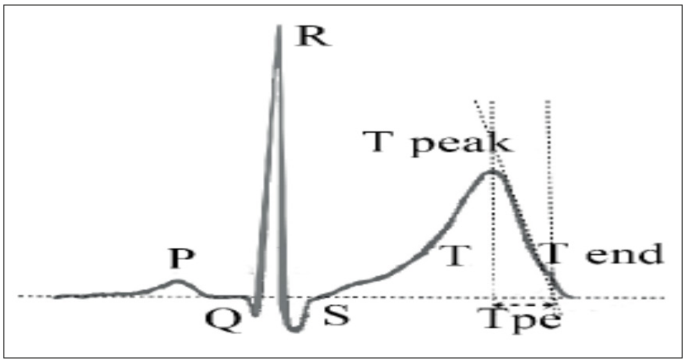

Figure 1. T-wave end defined as the intersecting point of a tangent on the terminal T wave and the T-p baseline. Tp-e: T-wave peak to end.

were included in the study data if at least nine of the 12 leads could be measured. Ventricular repolarization parameters included the QT and QTc intervals, QT and QTc distributions, Tp-e interval, and Tp-e/QT and Tp-e/QTc ratios.

Statistical Analysis

Continuous variables were presented as mean±standard deviation and categorical data as frequencies and percentages in descriptive tests. The Kolmogorov-Smirnov test was used to evaluate the normality of the distribution of continuous variables. The Chi-square test was used for categorical variables. The statistical comparison of clinical data between the two groups was performed using Student's *t*-test. Pearson's correlation coefficient was used to determine correlations between the strain values and ventricular repolarization parameters. Scatter plots were obtained to evaluate the relation-

Table I. Demographic and laboratory findings of the study group.

Variables	Impaired LV-GLS (n=32, 31.4%)	Normal LV-GLS (n=70, 68.6%)	*p*-value
Age (years)	55±6	58±9	0.101
Gender, female (%)	24 (75%)	50 (71.4%)	0.708
BMI (kg/m^2)	26.4±1.21	27.8±1.18	0.476
SBP (mmHg)	136±8	133±7	0.072
DBP (mmHg)	84±4	81±3	0.128
EF (%)	56±3	58±2	0.298
LA size (cm)	3.42±0.39	3.54±0.48	0.532
IVSd (cm)	0.89±0.10	0.96±0.57	0.232
LVPWd (cm)	0.88±0.23	0.94±0.12	0.356
LVEDD (cm)	4.76±0.42	4.84±0.54	0.316
LVESD (cm)	3.16±0.44	3.23±0.52	0.402
BUN, mg/dl	17±4	18±6	0.586
Creatinine, mg/dl	0.8±0.2	0.8±0.2	0.722
eGFR, mL/min/1.73 m^2	75±5	72±3	0.787
Sodium, mEq/L	141±2	142±1	0.510
Potassium, mEq/L	4.4±0.3	4.6±0.3	0.256
Glucose (mg/dl)	96±3	94±2	0.262
Hemoglobin, g/dl	13.1±1.6	12.7±1.4	0.336
Total cholesterol (mg/dl)	183.2±11.7	173.26±11.76	0.221
LDL (mg/dl)	111.2±31.2	101.21±31.23	0.123
HDL (mg/dl)	47.5±6.4	45.51±6.59	0.502
Strain Scale Point	-15.67±1.97	-19.94±1.15	<0.001

Numerical data are expressed as mean±standard deviation. BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, EF: Ejection Fraction, LA size: left atrial size, IVSd: interventricular septal thickness, LVEDD: left ventricular end-diastolic diameter, LVESD: left ventricular end-systolic diameter, LVPWd: left ventricular posterior wall thickness at diastole, BUN: Blood Urea Nitrogen, eGFR: Estimated glomerular filtration, LDL: Low-density lipoprotein, HDL: High-density lipoprotein.

Table II. Electrocardiographic measurements of the study groups.

Variables	Impaired LV-GLS (n=32, 31.4%)	Normal LV-GLS (n=70, 68.6%)	*p*-value
HR (bpm)	72±5	70±4	0.132
PR interval (ms)	188±16	191±4	0.067
PR dispersion (ms)	35±14	33±10	0.096
QT interval (ms)	421.56±25.25	387.85±28.82	<0.001
QT dispersion (ms)	40.19±17.36	32.36±12.16	0.024
QTc (ms)	432.21±17.25	383.42±15.04	<0.001
QTc dispersion (ms)	39.14±15.63	33.54±10.02	0.019
Tp-e (ms)	76.09±7.80	64.64±7.48	<0.001
Tp-e/QT	0.180±0.018	0.167±0.020	0.002
Tp-e/QTc	0.177±0.020	0.168±0.021	0.041

Numerical data are expressed as mean±standard deviation. LV-GLS: left ventricular global longitudinal strain; HR: heart rate, QTc: QT corrected by the Bazett formula, Tp-e: T-wave peak-to-end interval.

ship between the strain values and ventricular repolarization parameters. Statistical analyses were performed using SPSS v. 22 (IBM Corp., Armonk, NY, USA), and a *p*-value <0.05 was considered statistically significant.

Results

The mean age of the 32 patients with impaired LV-GLS was 55±6 years, and 75% (n=24) were female. In the normal LV-GLS group, the mean age was 58±9 years, and 71.4% (n=50) were women. There was no significant difference between the two groups in terms of the remaining demographic data, laboratory test results, systolic and diastolic blood pressure values, glomerular filtration, and mean ejection fraction. The LV-GLS score was -15.67±1.97 in the impaired LV-GLS group and -19.94±1.15 in the normal LV-GLS group (*p*<0.001), which is an expected finding considering that hypertension was our inclusion criterion. The laboratory results and demographic characteristics of our study are presented in (Table I).

The ECG measurements of the groups are presented in Table II. The QT and QTc intervals and dispersions were found to be significantly higher in the impaired LV-GLS group (*p*<0.05 for all). The Tp-e interval and Tp-e/QT and Tp-e/QTc ratios were also significantly higher in the impaired LV-GLS group than in the normal LV-GLS group (*p*<0.05 for all).

A positive correlation was observed between the ventricular repolarization parameters and LV-GLS. It was determined that this correlation was statistically significant in terms of the Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios. Among the ventricular repolarization parameters, Tp-e interval had the highest correlation coefficient (r: 0.564, *p*<0.001) (Table III).

There was a positive correlation between the ventricular repolarization parameters and LV-GLS, which is presented in (Figure 2) with a scatterplot.

Discussion

This study provides information about the ECG and STE evaluations of patients with arterial hypertension and regulated blood pressure. As a result of our study, it was observed that the Tp-e interval and Tp-e/QT and Tp-e/QTc ratios, which are associated with malignant ventricular arrhythmia risk, were significantly increased in the patients with impaired LV-GLS compared to those with normal LV-GLS values. A positive correlation was detected between the ventricular repolarization parameters and LV-GLS. These results suggest that among patients with controlled hypertension, those with impaired LV-GLS are at

Table III. Correlation analysis results of the left ventricular global longitudinal strain point and electrocardiography findings.

Variables	LV- GLS point R	*p*-value
Tp-e	0.564	0.000
Tp-e/QT	0.422	0.000
Tp-e/QTc	0.196	0.048

LV-GLS: Left ventricular global longitudinal strain, Tp-e: T-wave peak-end interval, QTc: QT corrected by the Bazett formula.

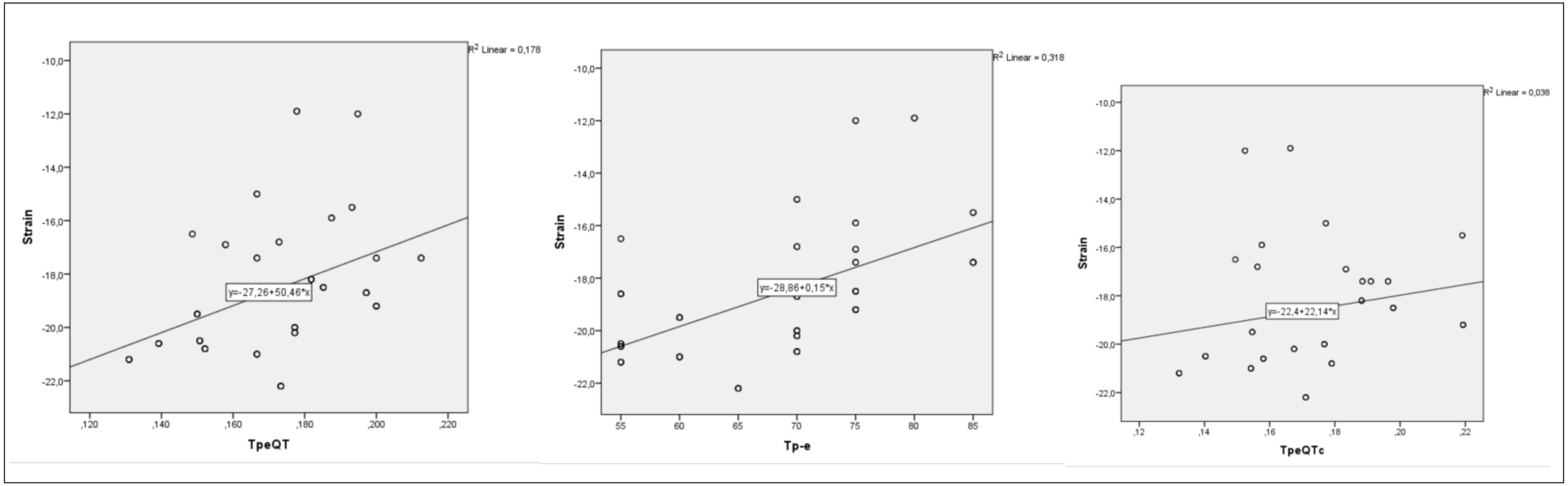

Figure 2. Scatter plot of the positive correlation between ventricular repolarization markers and strain scale point, Strain: Speckle tracking echocardiography, Tp-e: T-wave peak-to-end interval, QTc: QT corrected by the Bazett formula.

higher risk of malignant ventricular arrhythmias.

STE is a better method for evaluating regional and global myocardial deformation and predicting cardiovascular outcomes compared to transthoracic echocardiography[16]. Studies[17,18] have shown that LV-GLS is impaired in patients with arterial hypertension without any decrease in systolic ejection fraction. It was observed that approximately 29% of the patients with arterial hypertension included in our study had impaired LV-GLS. Previous studies[16-19] have determined that impaired LV-GLS is a strong predictor of major adverse cardiac events, including heart failure, stroke, myocardial infarction, and all-cause mortality.

In the literature[8], it has been reported that arterial hypertension is associated with cardiac arrhythmias, which have an effect on cardiovascular morbidity and mortality in hypertensive patients and may have important effects on prognosis. It has also been shown[10,20,21] that an increased Tp-e interval is associated with death, cardiac death, major adverse cardiac events, and malignant ventricular arrhythmias. Increased Tp-e/QT ratios have been associated with cardiovascular mortality and malignant ventricular arrhythmias[20,21]. It has been shown[11,22] that the Tp-e interval is increased in patients with non-dipper hypertension compared to those with dipper hypertension, and an increase in the Tp-e time is associated with sudden cardiac death and malignant ventricular arrhythmia. It has been shown[23,24] that there is an increase in Tp-e interval, QTc interval and Tp-e/QTc ratios in hypertension patients compared to healthy individuals, regardless of the geometry of the left ventricle. In various studies[24], the progression of left ventricular diastolic dysfunction is associated with an increase in Tp-e interval and Tp-e/QTc ratios. During the COVID-19 pandemic, an increase in Tp-e interval and Tp-e/QTc ratios from ventricular repolarization parameters were shown[25] to be associated with increased mortality in COVID-19 patients. In our study evaluating asymptomatic patients with arterial hypertension controlled by medical treatment, we found that the Tp-e interval and Tp-e/QT, and Tp-e/QTc ratios were increased significantly in the impaired LV-GLS group compared to the normal LV-GLS group.

In our study, we evaluated the malignant ventricular arrhythmia parameters Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios in asymptomatic arterial hypertension patients under medical treatment and compared them between patients with normal and impaired LV-GLS. As a result of our study, it was observed that there was a significant increase in the Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios, in patients with impaired LV-GLS compared to patients with normal. It was observed that there was a positive correlation between the ventricular repolarization parameters Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios and LV-GLS. The results suggest that among asymptomatic patients with hypertension receiving medical treatment, patients with impaired LV-GLS have an increased risk of developing sudden cardiac death and malignant ventricular arrhythmia. It is recommended to consider a close follow-up of this patient group.

Limitations

Our study includes several limitations. First, due to its single-center design, the number of patients was relatively low. Secondly, the patients included in the study were not followed up for long-term arrhythmia, and the absence of Holter recordings, and wearable or implanted device interrogation records are among our limitations. However, in literature, it has been shown that markers of ventricular repolarization are associated with the risk of sudden death and the development of malignant ventricular arrhythmia. In this context, our study suggests that the deterioration in LV-GLS values is related to the prolongation of ventricular repolarization parameters, and this result may be associated with an increased risk of developing malignant ventricular arrhythmia. Thirdly, our exclusion of patients with unregulated hypertension, coronary artery disease, heart failure (LVEF <50%), atrial fibrillation, diabetes mellitus, gastrointestinal problems, beta-blocker use, and kidney failure may affect LV-GLS and ventricular repolarization parameters reducing the ability of our results to reflect the situation in the general population. However, we consider that by applying the specified exclusion criteria, we were able to determine better the risk of sudden death and malignant ventricular arrhythmias among isolated asymptomatic arterial hypertension cases with or without impaired LV-GLS.

Conclusions

The Tp-e interval and Tp-e/QT and Tp-e/QTc ratios, which are accepted as malignant ventricular arrhythmia markers, were significantly increased in patients with arterial hypertension presenting with impaired LV-GLS values. This result suggests that asymptomatic hypertensive patients with impaired LV-GLS have an increased risk of malignant ventricular arrhythmias.

Conflict of Interest

All the authors declared that they have no conflict of interest.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' Contributions

S. Ozer and E. Aydın designed the study, S. Ozer and E. Aydın collected the data and S. Ozer and E.Aydın analyzed the data and wrote the manuscript. S. Ozer, E. Aydın and M. Sahin contributed to the study design and wrote the manuscript. All authors read and approved the final manuscript.

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Ethics Approval

Ethics Committee approval was released from Trabzon Kanuni Research and Treatment Hospital (No. 2022-32).

Informed Consent

An informed consent form was obtained from the patients before participating in the study.

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