Evaluation of Electrocardiographic T-Peak to T-End Interval in Patients with Cardiac Syndrome X

Kardiyak Sendrom X Hastalarının Elektrokardiografik Olarak T-Peak to T-End İntervalinin Değerlendirilmesi

Cardiac Syndrome X, Tpe Interval

Ozgur Kaplan[1], Gokhan Aksan[2]
[1]Department of Cardiology, İstanbul Bilim University School of Medicine,
[2]Department of Cardiology, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey

Özet

Amaç: Metabolik sendrom X (MSX) ile aritmi ilişkisi örneğin atrial fibrilasyon, daha önceki çalışmalarda gösterilmiştir. Bu çalışmada kardiyak sendrom X (KSX) hastalarında ventriküler repolarizasyon parameterlerinden Tp-e interval and Tp-e/QT oranı değerlendirildi. Gereç ve Yöntem: Çalışmaya 65 hasta alındı. Efor testi pozitif veya şüpheli miyokard sintigrafisi olan ve koroner arter hastalığı şüphesi olanlara koroner anjiografi yapıldı. KSX tanısı konan 35 hasta grup 1, normal koroner arter arter tanısı konan 30 hastada grup 2 olarak tanımlandı. QT parametreleri, Tp-e intervals and Tp-e/QT oranları ölçüldü. Bulgular: Tp-e interval (83.4 ± 6, 75 ± 5, p<0.001), cTp-e interval (89.9 ± 9.8 vs 84.9 ± 7.5, p =0.03), Tp-e/QT (0.21 ± 0.02 vs 0.20 ± 0.01, p = 0.003) and Tp-e/QTc oranları (0.20 ± 0.02 vs 0.17 ± 0.01, p < 0.001) grup 1 ,grup 2 den fazla bulundu. PW kalınlığı ve Tp-e interval (r = 0.308, p < 0.01) , IVS kalınlığı ve Tp-e/QTc oranı (r=0.236 p=0.05) arasında pozitif korelasyon izlendi. Bulgular: Bu çalışmada KSX hastalarında Tp-e ,cTp-e interval, Tp-e/QT ve Tp-e/QTc oranı artmış bulundu. Buda ventriküler aritmi risikini artırabilir.

Anahtar Kelimeler

Kardiyak Sendrom X; TP-E İnterval; TP-E/QT Oranı

Abstract

Aim: The relationship between metabolic syndrome X (MSX) and atrial arrhythmia such as atrial fibrillation (AF) has been shown in previous studies. The aim of this study was to evaluate ventricular repolarization by using Tp-e interval and Tp-e/QT ratio in patients with cardiac syndrome X (CSX). Material and Method: A total of 65 consecutive subjects were included in the present study. Diagnostic coronary angiography was performed on patients who had a positive stress test and suspected myocardial scintigraphy or coronary artery disease (CAD). 35 patients who were diagnosed as having CSX (Group I) and 30 patients with normal coronary angiograms (Group II) were included in this study. QT parameters, Tp-e intervals, and Tp-e/QT ratio were measured from the 12-lead electrocardiogram. Results: The Tp-e interval (83.4 ± 6 vs. 75 ± 5, p<0.001), cTp-e interval (89.9 ± 9.8 vs. 84.9 ± 7.5, p=0.03), Tp-e/QT (0.21 ± 0.02 vs. 0.20 ± 0.01, p=0.003), and Tp-e/QTc ratio (0.20 ± 0.02 vs 0.17 ± 0.01, p<0.001) were higher in Group I than in Group II. Significant positive correlations were found between PW thickness and the Tp-e interval (r=0.308, p<0.01) and between IVS thickness and the Tp-e/QTc ratios (r=0.236, p=0.05). Discussion: The present study shows that Tp-e and cTp-e interval, Tp-e/QT, and Tp-e/QTc ratios were higher in subjects with CSX, which may suggest an increased risk of ventricular arrhythmia.

Keywords

Cardiac Syndrome X; TP-E Interval; TP-E/Qt Ratio

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Corresponding Author: Ozgur Kaplan, Abidei Hürriyet Cad. No:166, 34381 Şişli, İstanbul, Turkey.
GSM: +905324609152 F.: +90 2123756565 E-Mail: drozgurkaplan@yahoo.com

Introduction

Cardiac syndrome X (CSX) is characterized by angina-like chest pain with a positive exercise stress test and myocardial perfusion scintigraphy (MPS), but where coronary arteries are detected to be normal [1]. The pathophysiology of CSX is not clearly defined. Coronary microvascular dysfunction, systemic inflammation, and arteriosclerosis of the small coronary vessel may be the principal causes of CSX [2-3].

QT interval (QT), corrected QT interval (QTc), QT dispersion, and transmural dispersion of repolarization are generally used for the evaluation of myocardial repolarization. Tp-e, which is the interval between the peak and the end of T wave as shown in an electrocardiogram (ECG), is accepted as an index of transmural dispersion of ventricular repolarization [4]. However, it is affected by variations in heart rate and body weight. Tp-e/QT and Tp-e/QTc ratios have been suggested as more accurate measures for the dispersion of ventricular repolarization compared to others parameters, and are independent from heart rate alterations [5-6].

Previous studies have consistently shown an association between metabolic syndrome X (MSX) and atrial arrhythmia such as atrial fibrillation (AF) [7-9]. However, there is not much data regarding the association between CSX and ventricular arrhythmia. Therefore, we aimed to evaluate the possible relation between CSX and ventricular repolarization, which is an indicator of risk of ventricular arrhythmia.

Material and Method

Study population

A total of 65 subjects were included in the present study. Diagnostic coronary angiography was performed on patients who had a positive stress test and suspected myocardial scintigraphy or coronary artery disease (CAD). 35 patients who were diagnosed as having CSX at coronary angiography (Group I) and 30 patients with normal coronary angiograms (Group II) were included in this study. Patients with coronary atherosclerosis, those with acute coronary syndromes, left ventricular systolic dysfunction (LVEF <50%), significant valvular heart disease, renal failure (creatinine-based estimated GFR <90 mL/min/1.73 m2 calculated by the Cockcroft-Gault formula), bundle branch block and atrioventricular conduction abnormalities on the electrocardiography (ECG), thyroid dysfunction, pulmonary disease, chronic infections or inflammatory diseases, electrolyte imbalance, and those with ECGs without clearly analyzable QT and Tp-e intervals were excluded from the study. All the patients were in sinus rhythm, and none of them was taking antiarrhythmic medications, tricyclic antidepressants, antihistamines, or antipsychotics. The study was approved by the local ethics committees and adhered to the Declaration of Helsinki, and all subjects gave written informed consent.

Coronary angiography

All patients underwent coronary angiography with Judkins technique and femoral approach. Images were recorded using a digital angiographic system (ACOM.PC; Siemens AG, Germany) at a speed of 15 frames/second. Lopromide (Ultravist 370, Schering AG, Berlin, Germany) was used as contrast material. The cine-angiograms were evaluated by two independent cardiologists. Quantitative measurements of the coronary arteries were performed using the digital angiographic system (ACOM. PC; Siemens AG, Germany).

Electrocardiography and calculation of ventricular repolarization parameters

The 12-lead ECG recording was performed after 10 minutes of rest in the supine position at 50 mm/s speed and 20 mm/mV amplitude (Nihon Kohden, Tokyo, Japan). ECG measurements of QT and Tp-e intervals were performed by two cardiologists who were blinded to the patient data. In order to lessen errors in QT and Tp-e interval analyses, each interval was measured manually with calipers and a magnifying glass. In order to improve accuracy, the average value of three readings was used. We measured the QT interval from the beginning of the QRS complex to the end of the T wave. The QT maximum (QTmax) and QT minimum (QTmin) were calculated in all leads of a 12-lead ECG. QTd was defined as the maximum minus minimum QT interval and corrected QTd (cQTd) was calculated according to Bazett's Formula adjusted according to heart rate [10]. QT peak interval was defined as the time from QRS complex onset to the peak of the T wave, whereas Tp-e interval was defined as the time from the peak to the end of the T wave. The measurements of Tp-e interval were performed from precordial leads and were corrected according to heart rate [11]. The Tp-e/QT ratios were subsequently calculated (Figure 1).

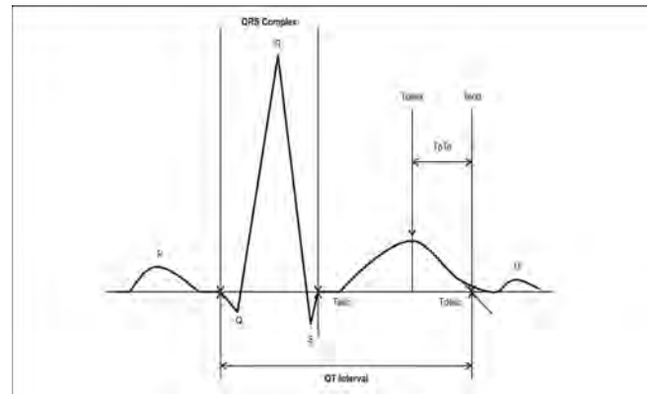


Figure 1.

The reproducibility of ECG repolarization indices was assessed by coefficients of variation (standard deviation of differences between the repeated measurements divided by the mean value and expressed as a percentage) between measurements. The intra-observer variability was calculated in 34 randomly selected study participants (18 patients with CSX and 16 control subjects) by repeating the measurements under the same basal conditions. Intra-observer and inter-observer variation was found to be <5%.

Standard echocardiography

Transthoracic echocardiography was performed in all patients at the left lateral decubitus position with a GE Vingmed Vivid 7 (GE Vingmed Ultrasound, Horten, Norway) echocardiography device. Images at the parasternal longitudinal axis, short axis, apical four chambers, and two chambers were obtained and evaluated by M-mode, 2-D, continuous wave Doppler, and

pulsed wave Doppler methods based on American Echocardiography Association criteria [12]. The following two-dimensional echocardiographic parameters were measured: left ventricular end-diastolic diameter (LVEDD, mm), left ventricular end-systolic diameter (LVESD, mm), left ventricular ejection fraction (LVEF, %), left atrium (LA), interventricular septum (IVS), and posterior wall (PW). The LVEF was estimated using Simpson's rule. Values were measured on three separate beats and then the averages were calculated for all parameters.

Statistical analysis

SPSS 17.0 statistical program (SPSS Inc., Chicago, IL, USA) was used for the statistical study. All parametric values were shown as means with standard deviation. Continuous variables were compared between groups using the Student's t test or Mann-Whitney U test, according to whether they were normally distributed or not as tested by the Kolmogorov-Smirnov test. The chi-square test was used to assess differences between categorical variables. Pearson's correlation analysis was used to examine possible associations between CSX and ventricular repolarization parameters. A p value of less than 0.05 was considered significant.

Results

Baseline clinical, demographic, and echocardiographic parameters of the study participants are listed in Table 1. Age, gender, smoking status, HT, and dyslipidemia were similar between the two groups, as were LVEDD, LVESD, and LVEF. Body mass index, LA diameter, IVS, and PW were significantly higher in Group I compared to Group II.

Table 1. Baseline characteristics and echocardiographic parameters of the study population

Variable	Patients	Controls	P value
Age, years	56.7 ± 6.1	59.6 ± 6.7	0.08
Gender, female/male	15/20	12/18	0.816
BMI,kg/m2	27.7 ± 3.3	26.2 ± 1.4	0.027
Dyslipidemia, n (%)	18(%51)	17(%56)	0.673
Hypertension, n (%)	24(%68)	18(%60)	0.471
Diabetes mellitus	8(%22)	6(%25)	0.780
Smokers, n (%)	19(54)	13(%43)	0.379
LVEDD, mm	45.7 ± 3.7	46.8 ± 2.3	0.179
LVESD, mm	30.1 ± 2.9	29.5 ± 2	0.322
LA,mm	37.3 ± 3.6	34.7 ± 2.1	0.01
IVS,mm	11.7 ± 1.2	9.9 ± 0.9	<0.001
PW,mm	10 ± 1	8.9 ±0.7	<0.001
LVEF, %	57.5 ± 1.9	56.6 ± 1.9	0.066

BMI, body mass index; IVS,intraventricular septum; LA,left atrium;LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; PW:posterior wall

The electrocardiographic parameters of the groups are shown in Table 2. The heart rates were different between the two groups (70.3 ± 9.9 vs. 79.6 ± 11.4, p=0.01). The QTmax (378 ± 23 vs. 372 ± 25ms, p=0.33), QT min (341 ± 22 vs. 334 ± 26ms, p=0.386), QTd (36 ± 5.8 vs. 35.8 ± 6, p=0.528), and corrected QTd (37.9 ± 6.5 vs. 40.9 ± 7.3, p=0.091) were not different between the two groups. The cQTmin (364 ± 25 vs. 386 ± 23ms, p=0.01) and cQTmax (403 ± 26 vs. 424 ± 28ms, p=0.03) were significantly higher in Group II than in Group I. The Tp-e interval (83.4 ± 6 vs. 75 ± 5, p<0.001), cTp-e interval (89.9 ± 9.8 vs. 84.9 ± 7.5, p=0.03), Tp-e/QT (0.21 ± 0.02 vs. 0.20 ± 0.01, p=0.003), and Tp-e/QTc ratios (0.20 ± 0.02 vs. 0.17 ± 0.01, p<0.001) were higher in Group I than in Group II. Significant positive correlations were found between PW thickness and the Tp-e interval (r=0.308, p<0.01) and between IVS thickness and Tp-e/QTc ratios (r=0.236, p=0.05).

Table 2. Electrocardiographic parameters of the study population

Variable	Patients	Controls	P value
HR (beat/min)	70.3 ± 9.9	79.6 ± 11.4	0.01
QTmax (ms)	378 ± 23	372 ± 25	0.33
cQTmax (ms)	403 ± 26	424 ± 28	0.03
QTmin (ms)	341 ± 22	334 ± 26	0.386
cQTmin (ms)	364 ± 25	386 ± 23	0.01
QTd (ms)	36 ± 5.8	35.8 ± 6.0	0.528
cQTd (ms)	37.9 ± 6.5	40.9 ± 7.3	0.091
Tp-e (ms)	83.4 ± 6	75 ± 5	<0.001
cTp-e (ms)	89.9 ± 9.8	84.9 ± 7.5	0.03
Tp-e/QT	0.21 ± 0.02	0.20 ± 0.01	0.003
Tp-e/QTc	0.20 ± 0.02	0.17 ± 0.01	<0.001

HR = Heart rate, QTmax = QTmaximum, cQTmax = corrected QT maximum, QTmin = QTminimum, cQTmin = corrected QT minimum, QTd = QT dispersion, cQTd = corrected QT dispersion, Tp-e = transmural dispersion of repolarisation, cTp-e = corrected transmural dispersion of repolarisation.

Discussion

We found that the Tp-e and cTp-e interval and the Tp-e/QT and Tp-e/QTc ratios were higher in patients with CSX compared with controls. Our finding of increased Tp-e, cTp-e, Tp-e/QT ratio, and Tp-e/QTc ratio in patients with CSX is important since this is the first study evaluating the relation between CSX and parameters of ventricular repolarization. Our results may contribute to understanding pathophysiological mechanisms of increased prevalence of ventricular arrhythmias in patients with CSX.

A previous study revealed that there is a relation among the slow coronary flow (SCF), Tpe interval, and Tpe/QT ratio [13]. Both CSX and SCF reported normal coronary angiography. Although similar etiological factors such as small-vessel disease, inflammation, and microvascular and endothelial dysfunction have a role, their etiopathogenesis are still not clear. Abnormalities in coronary microcirculation, such as small-vessel structural defects and microvascular resistance, are confirmed. Endothelial dysfunction and coronary micro-circular abnormalities have also been shown to be responsible for the etiopathogenesis of CSX [14-16].

MSX and CSX are two diseases with similarities. Both electrophysiological and observational studies showed a relationship between MSX and atrial fibrillation [7-8]. There is no data in these studies about the patients' coronary arteries. A few of the patients in these studies may have had CSX. Therefore, arrhythmias may be seen in patients with CSX. BMI and LA diameter are larger than the controls in our results. These findings support these two studies. Moreover, BMI doesn't affect myocardial repolarization parameters. In our study, Tpe interval and Tpe/

QT ratio are different from the controls. For this reason, ventricular arrhythmia may be seen in patients with CSX.

On the other hand, intravascular ultrasound studies reveal that coronary arteries with atheromatous plaques or abnormal coronary arteries with intimal thickening were detected in patients with CSX [17]. These findings suggest that CSX might be considered to be an early phase of atherosclerosis [18-19]. Also, previous studies showed that the Tpe/QT ratio is increased in acute myocardial infarction, and it is associated with the prognosis for patients who undergo primary percutaneous coronary intervention [20-21]. The other study showed that ischemia-induced Tpe is an important arrhythmogenic parameter after primary percutaneous coronary intervention [22]. Therefore, ischemia caused by microvascular dysfunction may be responsible for the heterogeneity of ventricular repolarization in patients with CSX.

Study limitations

We recognize that our study has limitations that warrant consideration. First, the cross-sectional design does not allow us to infer causation between CSX and ECG parameters. Second, the sample size of the study was relatively small and there was no longer-term follow up to detect any ventricular arrhythmias in patients with CSX.

Conclusion

The present study showed that the Tp-e interval and the Tp-e/QT and Tp-e/QTc ratios were elevated in patients with CSX, which might imply they are an indicator of risk of ventricular arrhythmias in this group of patients.

Competing interests

The authors declare that they have no competing interests.

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