Evaluation of ventricular repolarization features with novel electrocardiographic parameters (Tp-e, Tp-e/QT) in patients with psoriasis

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ABSTRACT

Objective: Psoriasis is a chronic inflammatory disorder, which affects around 1%–3% of the human population worldwide. Cardiovascular events are the leading cause of morbidity and mortality in patients with psoriasis. Some studies have reported that psoriasis is related to increased arrhythmias. The Tp-e interval and Tp-e/QT ratio have been accepted as new markers for the assessment of myocardial repolarization and ventricular arrhythmogenesis. The aim of this study was to assess ventricular repolarization in patients with psoriasis using Tp-e interval and Tp-e/QT ratio.

Methods: The study population consisted of 74 patients with psoriasis and 74 healthy volunteers. The diagnosis of psoriasis was based on a clinical or histopathological examination of all patients. QT interval, corrected QT (QTc), QT dispersion (QTd), Tp-e interval, corrected Tp-e, and Tp-e/QT ratio were measured from the 12-lead electrocardiogram. These parameters were compared between groups.

Results: According to the electrocardiographic parameters, QT and QTc intervals and QTd were significantly higher in patients with psoriasis than in control subjects (p<0.001; p<0.001; p=0.014; respectively). The Tp-e interval, corrected Tp-e, and Tp-e/QT ratio were significantly higher in patients with psoriasis than in control subjects [93±13 milliseconds (ms) vs. 98±14 ms, p=0.040; 104±17 ms vs. 111±17 ms, p=0.008; 0.23±0.03 vs. 0.25±0.03, p<0.001; respectively]. Additionally, the CRP value was an independent predictor of an increased Tp-e/QT ratio (β=0.537, p< 0.001).

Conclusion: Our study revealed that ventricular repolarization features were impaired in patients with psoriasis. Therefore, these patients should be more closely screened for ventricular arrhythmias. *(Anatol J Cardiol 2017; 18: 397-401)*

Keywords: psoriasis, ventricular repolarization, Tp-e interval, Tp-e/QT ratio

Introduction

Psoriasis is a chronic inflammatory disorder characterized by lesions affecting the skin, nails, scalp, and joints. The disease affects around 1%–3% of the human population worldwide (1). Chronic inflammation is considered to be the most important mechanism for disease development, but the pathogenesis of this disease is still not completely understood (2). Cardiovascular events are the leading cause of morbidity and mortality in patients with psoriasis (3). Some studies have reported that psoriasis is related to increased arrhythmias and altered autonomic functions (4-7). However, there is insufficient information about ventricular repolarization features in patients with psoriasis. QT interval (QT), corrected QT (QTc) interval, and QT dispersion (QTd) are well-known markers for the prediction of ventricular arrhythmias. In addition, the Tp-e interval, the interval between the peak and the end of the T wave on an ECG, and the Tp-e/QT ratio have been accepted as new markers for the assessment of myocardial repolarization and ventricular arrhythmogenesis (8, 9). The prolongation of these intervals represents a period of potential vulnerability to re-entrant ventricular arrhythmias. In this study, ventricular repolarization features were evaluated using the QT, QTc, QTd, and Tp-e intervals and the Tp-e/QT ratio in patients with psoriasis.

Methods

Study design

This was as an observational, cross-sectional study.

Study population

The study population consisted of 74 patients with psoriasis (34 women; mean age, 41±14 years) who were followed up at

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dermatology outpatient clinic between November 2015 and May 2016. The control group consisted of 74 healthy sex- and age-matched volunteers (32 women; mean age, 37±14 years). The diagnosis of psoriasis was based on a clinical or histopathological examination of all patients. The severity of the disease was evaluated using the Psoriasis Area and Severity Index (PASI), which ranges from 0 to 72 points. The extension of skin lesions situated on the head, trunk, and upper and lower limbs were assessed (score range for each location: 0–6). The following features of skin lesions were evaluated: erythema (0–4 points), infiltration (0–4 points), and desquamation (0–4 points) (10).

Patients with coronary artery disease, left and/or right heart failure, moderate or severe valve disease, any documented arrhythmogenic diseases, thyroid dysfunction, atrial fibrillation, any bundle block or those who had pacemaker, chronic lung disease, chronic renal failure, hypertension, diabetes mellitus, and ECGs without clearly analyzable QT segment were excluded from the study. The study was approved by the local ethics committee and all subjects gave written informed consent.

Samples for the complete blood count (CBC) analysis were collected in EDTA-anticoagulated Monovette tubes (Sarstedt Monovette, Nuembrecht, Germany). An automated blood cell counter (Beckman Coulter analyzer; Beckman Coulter, California) was used for measuring CBC parameters. Also, the serum C-reactive protein (CRP) value was obtained using the immuno-turbidimetric method (Roche Diagnostics Ltd., West Sussex, UK).

Electrocardiography

A 12-lead surface ECG with 10 mm/mV amplitude and 25 mm/s paper speed was obtained for all participants at rest in the supine position (Cardiofax V; Nihon Kohden Corp., Tokyo, Japan). All of the ECGs were transferred to a PC via a scanner and then used at x400 magnification on the Adobe Photoshop software, which measurements were made on the computer. An electronic digital caliper was used to minimize error measurements on the surface ECG. All ECGs were analyzed by an independent clinician who was blinded to the clinical data of the patients. The average value of three measurements was calculated for each parameter.

The QT interval was assessed as the time between the first deflection of the QRS complex and the end of the T wave. The end of T wave was defined as an intersection between a line tangent to the descending arm of T wave and an isoelectric line. The QT interval was measured in as many 12 leads as possible and was corrected for heart rate using the Bazett formula: QTc=QT/√ (R-R interval). Subjects with U waves on their ECGs were excluded from the study. The QTd was defined as the difference between the maximum and minimum QT intervals.

The Tp-e interval was measured using the tail method. In this method, the Tp-e interval was defined as the time from the peak to the end of the T wave (9). Also, the Tp-e interval was corrected for heart rate using the following formula: Tp-ec=Tp-e/√ (R-R interval). V2 lead was used for measurements of the Tp-e interval.

Table 1. Clinical characteristics and echocardiographic and laboratory findings of the study groups

	Control (n=74)	Psoriasis (n=74)	P
Age, years	37±14	41±14	0.071
Sex, female	32	34	0.870
BMI, kg/m²	25±5	24±6	0.282
Systolic BP, mm Hg	121±21	126±15	0.113
Diastolic BP, mm Hg	77±10	79±10	0.271
Smoking, n	18	25	0.290
PASI	–	8.7 (5.0-17.8)	–
LVEDD, mm	47±5	48±4	0.154
LVESD, mm	30±4	30±6	0.918
LVEF, %	62±2	63±2	0.677
IVS, mm	8.8±0.9	9.0±1.1	0.341
PW, mm	8.2±1.2	8.3±1.1	0.435
E/A	1.40±0.23	1.43±0.22	0.382
CRP, mg/L	3.1 (3.0-8.2)	4.8 (3.4-12.1)	<0.001
ESR, mm/h	12.7±9.0	20.2±18.5	0.004
NLR	1.9±0.7	2.4±1.2	0.005

BMI-body mass index, BP-blood pressure, CRP-C reactive protein, ESR-erythrocyte sedimentation rate, IVS-interventricular septum, LVEDD-left ventricular end-diastolic diameter, LVEF- left ventricular ejection fraction, LVESD-left ventricular end-systolic diameter, NLR- neutrophil/lymphocyte ratio, PASI-Psoriasis Area and Severity Index PW-posterior wall. Data are presented as mean±SD, median (interquartile range) or n (%). Statistically significant P values shown in bold

If the height or depth of the T wave was <1.5 mm, its ECG was excluded from the analysis. The Tp-e/QT ratio was calculated from these measurements. Intraobserver and interobserver variabilities in the Tp-e interval were 4.8% and 7.2%, respectively.

Echocardiography

Transthoracic echocardiography was performed in all participants using a 2.5–3.5

MHz transducer (General Electric Vivid S5, Milwaukee, WI, USA) at the left lateral decubitus position. Basic echocardiographic measurements [Left ventricular (LV) diameter, thickness, and ejection fraction and mitral inflow EA waves and E/A ratio] were obtained using two-dimensional echocardiography.

Statistical analysis

SPSS 21.0 for Windows was used for statistical analyses (SPSS, Chicago, IL, USA). Data were tested for normality using the Kolmogorov–Smirnov test. Normally distributed continuous data were expressed as mean±standard deviation; non-normally distributed continuous variables were presented as median and interquartile range (Quartiles I–3). In statistical analysis for numeric variables, Student's t-test or Mann–Whitney U test was used, and for categorical data, chi-square test was used. In correlation analysis, Spearman's correlation test was used.

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Table 2. Electrocardiographic findings of the study groups

Variables	Control (n=74)	Psoriasis (n=74)	*P*
HR, beat/min	74±11	77±14	0.121
QT, ms	358±30	380±29	<0.001
QTc, ms	405±33	430±26	<0.001
QTd, ms	27±12	32±13	0.014
Tp-e, ms	93±13	98±14	0.040
Tp-ec, ms	104±17	111±17	0.008
Tp-e/QT	0.23±0.03	0.25±0.03	<0.001

HR-heart rate, QTc-corrected QT, QTd-QT dispersion, Tp-e-T wave peak-to-end interval, Tp-ec- corrected Tp-e, Data are presented as mean±SD. Statistically significant P values shown in bold

Table 3. Bivariate correlation and multivariate linear regression analyses between Tp-e/QT ratio and study parameters

Variables	Bivariate correlation		Multivariate linear regression	
	r	*P*	β	*P*
Age	0.077	0.365	-0.058	0.639
PASI	-0.170	0.216	-0.158	0.214
CRP	0.327	<0.001	0.537	<0.001
ESR	0.013	0.882	0.138	0.140
NLR	0.181	0.034	-0.094	0.477

CRP- C reactive protein, ESR-erythrocyte sedimentation rate, NLR-neutrophil/lymphocyte ratio, PASI-Psoriasis Area and Severity Index

Multivariate linear regression analyses were used to identify the independent predictors of Tp-e/QT ratio. A p-value of <0.05 was considered statistically significant.

Results

According to the basic clinical and demographic characteristics, both study groups were similar with regard to age, sex, body mass index, and smoking habits. All the subjects were normotensive, and no significant differences were observed in systolic or diastolic blood pressures between the two groups. Also basic echocardiographic measurements were similar in both groups with regard to LV end-diastolic diameter, LV end-systolic diameter, LV ejection fraction, interventricular septum, posterior wall thickness, and mitral inflow E/A ratio. The CRP value was higher in the psoriasis group than in the control group [3.1 (3.0–8.2) mg/L
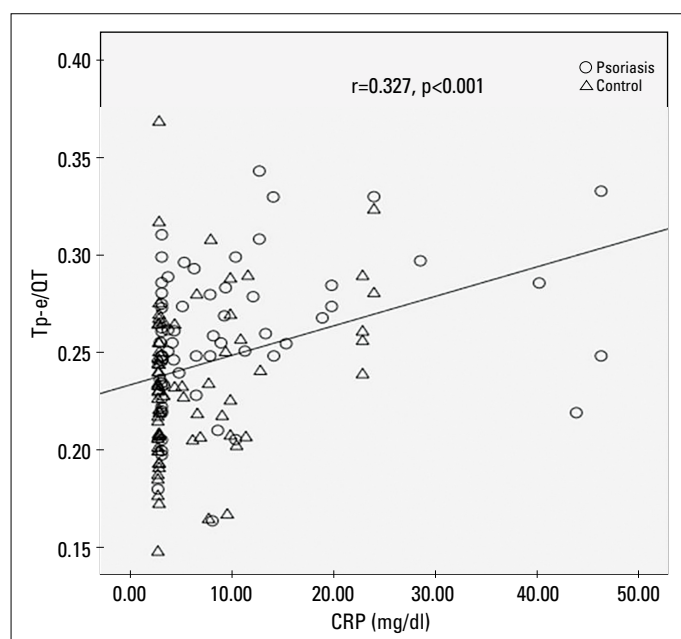
vs. 4.8 (3.4–12.1) mg/L, p<0.001]. The erythrocyte sedimentation rate (ESR) and neutrophil/lymphocyte ratio (NLR) were also higher in the psoriasis group than in the control group (12.7±9.0 mm/h vs. 20.2±18.5 mm/h, p=0.004; 1.9±0.7 vs. 2.4±1.2, p=0.005; respectively). The clinical characteristics and echocardiographic and laboratory findings of the individuals are shown in Table 1.

According to the electrocardiographic parameters, the heart rate was similar in both groups, but QT, QTc, and QTd were significantly higher in the psoriasis group (p<0.001, p<0.001, p=0,014, respectively). Additionally, Tp-e and Tp-ec intervals and Tp-e/QT ratio were significantly higher in the psoriasis group than in the control group [93±13 milliseconds (ms) vs. 98±14 ms, p=0.040; 104±17 ms vs. 111±17 ms, p=0.008; 0.23±0.03 vs. 0.25±0.03, p<0.001; respectively]. The electrocardiographic parameters of both the groups are shown in Table 2.

Table 3 presents the correlations and regression analyses between the Tp-e/QT ratio and the study parameters. There were significant correlations between the Tp-e/QT ratio and the CRP value (r=0.327, p 0.001) and NLR (r=0.181, p=0.034) (Fig. 1). Multivariate linear regression analyses demonstrated that the CRP value was an independent predictor of an increased Tp-e/QT ratio (β=0.537, p<0.001).

Discussion

In this study, we determined that ventricular repolarization features were impaired due to longer QT, QTc, Tp-e, and Tp-ec intervals, and an increased QTd and Tp-e/QT ratio in patients with psoriasis compared with controls. In addition, we found that the CRP value was an independent predictor of an increased Tp-e/QT ratio.

Psoriasis is a chronic inflammatory disorder that affects not only the skin but also the cardiovascular system. The disease has a higher mortality as a result of cardiovascular diseases , and inflammation plays an important role in the pathogenesis of this disease (11). Several studies have also suggested that there is a connection between arrhythmias and chronic inflammation (12, 13). Some chronic inflammatory diseases, including rheumatoid

Figure 1. Correlation between the Tp-e/QT ratio and the CRP value

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arthritis, systemic sclerosis, and systemic lupus erythematosus, are associated with a higher incidence of atrial and ventricular arrhythmias (14-16). Similarly, some studies have reported that psoriasis is related to increased atrial arrhythmias and altered autonomic function (4-7). Most of these studies have found a relationship between inflammation and arrhythmic parameters. These findings suggest an association between cardiac rhythm abnormalities and psoriasis.

An inflammation may lead to an alteration in cardiomyocyte electrophysiology, such as the dysregulation of ion channel function, and ultimately to myocardial repolarization heterogeneity. Kazumi et al. (17) clarified that low-grade inflammation was independently related with QTd in healthy young men. A previous large epidemiological study demonstrated that an elevated CRP value was associated with a prolonged QTc interval in middle-aged men and women (18). Lazzerini et al. (19) also reported that elevated CRP values were associated with QTc prolongation in patients with chronic inflammatory arthritis. Similar to these studies, we found a positive correlation between ventricular repolarization parameters and CRP values. Also, we found that the CRP value is an independent predictor of an increased Tp-e/QT ratio. Our study results may support the inflammatory mechanism behind arrhythmias.

Although inflammation is the most important etiological cause of repolarization heterogeneity in many inflammatory diseases, in patients with psoriasis, multiple factors may cause myocardial heterogeneity. For example, some researchers have demonstrated endothelial dysfunction and impaired coronary microvascular function in patients with psoriasis (20, 21). In addition, there is an important relationship between psoriasis and subclinical coronary atherosclerosis, independent of conventional cardiovascular disease risk factors (22). These abovementioned changes have been shown to be the cause of myocardial ischemia. Karaman et al. (23) suggested that myocardial ischemia at the microvascular level may lead to an increased Tp-e interval and Tp-e/QT ratio. Moreover, some echocardiographic studies have shown that LV mechanical function is impaired in these patients (24). Gündüz et al. (25) reported that LV diastolic dysfunction is associated with an increased QTd. The changes in ventricular mechanical function and impairment of coronary microvascular function may contribute to the heterogeneity of ventricular repolarization in patients with psoriasis.

Ventricular repolarization heterogeneity is associated with malignant arrhythmias and sudden cardiac death. QT and QTc intervals and QTd are well-known markers of ventricular arrhythmia. A prolonged QT interval and increased QTd are associated with an increased risk of ventricular tachycardia/fibrillation and sudden cardiac death (26). A recent study showed that QTd was significantly higher in patients with psoriasis (27). Also, Soylu et al. (28) recently reported that QT and QTc intervals were increased in patients with psoriasis compared with control subjects, similar to the results of our study.

The Tp-e interval and Tp-e/QT ratio are relatively new mark-

ers that also indicate repolarization features. Recent studies have reported that an increased Tp-e interval is associated with malignant ventricular arrhythmias and cardiovascular events (8, 9). However, the Tp-e interval may be affected by variations in body weight and heart rate. The Tp-e/QT ratio is independent of body weight and heart rate alterations and may be a more accurate measure for the dispersion of ventricular repolarization (29). Previous studies have indicated that some chronic inflammatory diseases, including rheumatoid arthritis and ankylosing spondylitis, are associated with an increased Tp-e interval and Tp-e/QT ratio (30, 31). Recently, Soylu et al. (28) reported that Tp-e and Tp-ec intervals and the Tp-e/QT ratio were higher in patients with psoriasis. Likewise, in our study, we found that Tp-e and Tp-ec intervals and the Tp-e/QT ratio were increased in patients with psoriasis compared with control subjects.

The PASI score is a commonly used tool for assessing psoriasis. The severity of the disease may reflect the intensity of inflammation; therefore, it may be associated with the PASI score. Many previous studies have found a relationship between disease severity and cardiovascular complications, including arrhythmias (4, 5). Interestingly, no significant relation between repolarization parameters and the PASI score were found in this study. These results may be due to the low PASI scores of the study participants. In addition, while myocardial electrical alteration is the result of chronic inflammation, the PASI score is a scoring system that reflects the current activity of psoriasis.

According to our results, the Tp-e interval and Tp-e/QT ratio may be useful for assessing ventricular repolarization and predicting ventricular arrhythmia in this population. In addition, our findings may be a basis for further studies.

Study limitations

The major limitation of this study is its cross-sectional design and lack of patient follow-up. The patients could not be prospectively followed up for arrhythmic episodes. Therefore, we could not precisely determine that an increased Tp-e interval and Tp-e/QT ratio predicts ventricular arrhythmias in patients with psoriasis. The relatively small sample size and lack of disease duration are other potential limitations of this study.

Conclusion

In this study, we determined that patients with psoriasis have impaired ventricular repolarization features, longer QT, QTc, Tp-e, and Tp-ec intervals, and increased QTd and Tp-e/QT ratios. These findings suggest that this patient population may be at an increased risk for ventricular arrhythmias. The early prediction of arrhythmias using these simple and economical methods may reduce morbidity and mortality in patients with psoriasis. Therefore, these patients should be more closely screened for ventricular arrhythmias. However, to confirm the above findings,

further studies are needed using more sensitive methods and larger patient groups.

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