

Evaluation of Tpe interval and Tpe/QT ratio in patients with slow coronary flow

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ABSTRACT

Objective: Slow coronary flow (SCF) phenomenon is described as the delayed opacification of the distal vasculature and angiographically normal coronary arteries. Considerable studies have suggested that the interval from the peak to the end of the electrocardiographic T wave (Tpe) may correspond to the transmural dispersion of repolarization and that increased Tpe interval and Tpe/QT ratio are associated with malignant ventricular arrhythmias. In this study, we intended to evaluate ventricular repolarization in patients with SCF by using the Tpe interval and Tpe/QT ratio.

Methods: The study population included 33 patients with angiographically proven SCF and 33 control patients with angiographically proven normal coronary arteries without associated SCF. Coronary flow rates of patients and the control group were documented by TIMI (Thrombolysis in Myocardial Infarction) frame count. From the electrocardiograms, Tpe interval and Tpe/QT ratio were calculated and compared between groups.

Results: No statistically significant difference was found between the two groups in terms of basic characteristics. Mean Tpe interval, Tpe/QT ratio, and Tpe/QTc ratio were prolonged in the study group compared to the control group ($p < 0.001$).

Conclusion: Tpe interval and Tpe/QT ratio were increased in SCF patients. (*Anatol J Cardiol* 2015; 15: 463-7)

Keywords: Tpe interval, Tpe/QT ratio, slow coronary flow

Introduction

Slow coronary flow (SCF) phenomenon is defined as slow antegrade progression of contrast agent to the distal vasculature and angiographically normal coronary arteries. The overall incidence of SCF is 1% among patients undergoing coronary angiography, especially those presenting with acute coronary syndrome (1).

This phenomenon has been associated with increased risk of ventricular arrhythmias and sudden cardiac death (2). Impaired myocardial blood flow in SCF may cause fatal cardiac arrhythmias by causing electrical abnormalities and altering ventricular repolarization.

Myocardial repolarization has been evaluated by various methods, including QT dispersion (QTd), corrected QT dispersion (cQTd), and transmural dispersion of repolarization. Current studies have shown that Tpe interval, which is the interval between the peak and the end of the T wave on electrocardiogram (ECG), can be used as an index of total dispersion of repolarization (TDR) (3, 4). TDR reflects the heterogeneity rather than total duration of repolarization (4). Tpe interval and Tpe/QT ratio represent valuable electrocardiographic indexes of arrhythmic risk that possibly correspond to the spatial dispersion of ventricular repolarization (5, 6).

In patients with SCF, ventricular repolarization has been evaluated by using T wave and QT interval measurements. However, the novel repolarization indexes Tpe interval and Tpe/QT ratio have not been studied in these patients. In this study, we sought to investigate ventricular repolarization in patients with SCF by using the Tpe interval and Tpe/QT ratio.

Methods

Study population

For this purpose, 2260 coronary angiographies were evaluated retrospectively, and 66 patients were suitable for study. The study group consisted of 33 patients with angiographically proven slow coronary flow in all three coronary vessels but

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Accepted Date: 19.03.2014 **Available Online Date:** 03.06.2014

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DOI:10.5152/akd.2014.5503



otherwise normal epicardial coronary arteries. The control group consisted of 33 age- and sex-matched subjects suffering from atypical chest pain but having angiographically proven normal coronary arteries without associated slow coronary flow. All patients had undergone routine diagnostic coronary angiography in our hospital due to suspected coronary artery disease between 2007 March and 2010 February. In all patients, echocardiography was performed. Patients with left ventricular dysfunction, valvular heart diseases, atrial fibrillation, bundle branch block or evidence of any other intraventricular conduction defect, prior pacemaker implantation, left ventricular hypertrophy, thyroid dysfunction, electrolyte abnormalities, and ECGs without a clearly analyzable QT segment were excluded from this study. All of the patients were in sinus rhythm, and none of them was taking medications, such as antiarrhythmics, anti-histamines, digitalis, tricyclic antidepressants, and antipsychotics. The study was approved by the local ethics committee, and informed consent was obtained from all patients.

Documentation of slow coronary flow

Coronary angiograms of all patients were analyzed by an experienced cardiologist. Coronary flow rates of all patients were documented as (TIMI) frame count (TFC) (7). TFC is a quantitative index of coronary flow velocity. The time required for contrast to reach the distal definitive points of a coronary artery was expressed as frame count. Frame counts in the left anterior descending coronary artery (LAD) were divided by a factor of 1.7 to correct for its longer length (7). Slow coronary flow was defined according to the TFC method, and individuals with a corrected TFC greater than 2 standard deviations (SDs) from the published normal range for the particular vessel were accepted as having SCF, since those whose corrected TFC fell within 2 SDs of the published normal range were labeled to have normal coronary flow (7).

Electrocardiography

All standard 12-lead ECGs were obtained at rest in the supine position simultaneously using a recorder (Nihon Kohden, Tokyo, Japan) set at 50 mm/s paper speed and 1 mV/cm standardization. Assessments of the ECG were done by 2 cardiologists, and to diminish the error measurements, QT and Tpe interval analysis was done with calipers and a magnifying glass. QT interval was assessed as the time between the first deflection of the QRS complex and the point of return of the T wave to the isoelectric line. Subjects with U waves and negative T waves on their ECGs were excluded from the study. The QT interval was measured in as many of the 12 leads as possible, whereas Tpe interval was assessed in the precordial leads (8). The Tpe interval was measured from the peak of the T wave to the end of the T wave. The end of the T wave was defined as the intersection of the tangent to the downslope of the T wave and isoelectric line. The QT interval was measured from the beginning of the QRS complex to the end of the T wave and corrected for heart rate (QTc) using Bazett's formula ($QTc=QT/RR-2$) (9). Tpe/QT

Table 1. Characteristics of the study population

	SCF n=33	Control n=33	P
Age, years	51.6±4.2	49.8±5.0	0.18
Gender, male, n, %	18 (54.5)	19 (57.6)	0.81
BMI, kg/m ²	27.7±1.6	27.1±1.7	0.17
Smokers, n, %	16 (48.5)	15 (45.5)	0.50
Systolic BP, mm Hg	119.6±9.3	116.4±10.2	0.43
Diastolic BP, mm Hg	74.3±4.9	73.6±5.2	0.52
Diabetes mellitus, n, %	9 (27.2)	7 (21.2)	0.63
Heart rate, bpm	69.7±5.5	69.0±6.8	0.87
Echocardiographic findings			
IVS, mm	0.81±0.10	0.79±0.12	0.52
PWT, mm	0.82±0.12	0.80±0.10	0.48
LV-EF, %	62.1±2.7	61.7±2.8	0.59
Thrombolysis in Myocardial Infarction (TIMI) frame counts			
LAD	47.4±8.0	23.6±2.4	<0.001
Cx	47.1±8.6	23.2±2.2	<0.001
RCA	50.3±8.9	24.9±2.0	<0.001
BMI - body mass index; BP - blood pressure; Cx - left circumflex coronary artery; IVS - interventricular septum; LAD - left anterior coronary artery; LV-EF - left ventricle ejection fraction; PW - posterior wall; RCA - right coronary artery; SCF - slow coronary flow			

ratio and Tpe/QTc were calculated from these measurements. The interobserver and intraobserver coefficients of variation were 3.6% and 3%, respectively.

Statistical analysis

Categorical and numerical variables were expressed in percentage and mean±standard deviation, respectively. Numerical variables were tested with independent samples t-test/Mann-Whitney U-test, and categorical variables were tested using Fisher's exact test or chi-square test, whichever was suitable. Spearman's test was used for the correlation analysis. A two-tailed p value <0.05 was considered significant. All analyses were performed using SPSS, version 16.0 (SPSS, Inc., Chicago, IL, USA).

Results

The baseline characteristics of the study population are presented in Table 1. There were no statistically significant differences between groups in terms of age, gender, body mass index (BMI), smoking status, presence of diabetes mellitus, systolic and diastolic blood pressure, and heart rate. Serum potassium levels were similar between SCF patients and the control group ($4.2±0.20$; $4.24±0.36$; respectively; $p=0.53$) Left ventricular ejection fraction (LV-EF), left ventricle posterior wall thickness (PWT), and thickness of the interventricular septum (IVS) were similar between the two groups ($p>0.05$). TIMI frame

Table 2. Electrocardiographic measurements of the groups

	SCF n=33	Control n=33	P
Tpe, ms	94.9±5.1	83.8±8.0	<0.001
QT, ms	384.7±14.5	390.3±21.2	0.13
QTc, ms	418.1±17.3	419.3±20.6	0.35
Tpe/QT	0.24±0.1	0.21±0.1	<0.001
Tpe/QTc, ms	0.22±0.1	0.19±0.1	<0.001

QTc - corrected QT interval; SCF - slow coronary flow

Table 3. Correlation between Tpe interval, Tpe/QT ratio, Tpe/QTc, and Thrombolysis in Myocardial Infarction (TIMI) frame count

	Tpe	Tpe/QT	Tpe/QTc
LAD	r: 0.63, p<0.001	r: 0.59, p<0.001	r: 0.51, p<0.001
Cx	r: 0.64, p<0.001	r: 0.62, p<0.001	r: 0.46, p<0.001
RCA	r: 0.58, p<0.001	r: 0.59, p<0.001	r: 0.45, p<0.001

Cx - left circumflex coronary artery; LAD - left anterior coronary artery; QTc - corrected QT interval; RCA - right coronary artery; SCF - slow coronary flow

counts of the groups are shown in Table 1. SCF patients had significantly higher TFCs than those patients for all three coronary arteries ($p<0.001$ for all). The electrocardiographic parameters of the groups are presented in Table 2. Although QT and QTc intervals were not different between groups, Tpe interval was significantly prolonged in the SCF group compared to the control group (94.9±5.1 msn, 83.8±8.0 msn, respectively; $p<0.001$). We also found that Tpe/QT ratio and Tpe/QTc ratio were significantly higher in SCF patients compared to the control group (0.24±0.1; 0.21±0.1; respectively; $p<0.001$ and 0.22±0.1; 0.19±0.1; respectively; $p<0.001$, Table 2). Furthermore, Tpe interval, Tpe/QT ratio, and Tpe/QTc ratio were found to be correlated with TFCs (all $p<0.001$, Table 3).

Discussion

The results of our study demonstrated that Tpe interval, Tpe/QT, and Tpe/QTc ratios were considerably prolonged in patients with SCF when compared to patients with normal coronary flow. Also, we found a positive correlation among the presence of coronary slow flow and these novel indices.

Ventricular myocardium is an electrically heterogeneous structure composed of 3 distinct cell types with different electrophysiological properties (endocardial layer, M cells, and epicardial layer) (10, 11). Amplification of ventricular repolarization dispersion, which indicates the heterogeneity of repolarization, has been well accepted as a substrate for ventricular arrhythmias. Even if the interval from the peak of the T wave (which coincides with end of repolarization of epicardial cells) to the end of the T wave (which coincides with the end of repolarization of endocardial cells) correlates well with TDR in animal studies (12, 13), it rather serves as an index of total dispersion of repolarization (transmural, apicobasal, and global) (4). Yan et al. (14) proposed

that changes in this parameter (Tpe interval) may forecast the risk of ventricular arrhythmia. Moreover, Tpe/QT ratio was shown to be a more sensitive index of ventricular repolarization and arrhythmogenesis, as it provided an estimate of the dispersion of repolarization relative to the total duration of repolarization. In comparison with Tpe interval, Tpe/QT ratio was found to remain constant despite dynamic changes in heart rate. These two novel indexes have been suggested to be surrogate markers of arrhythmogenesis and sudden cardiac death under conditions of short, normal, or long QT interval, as well as in congenital and acquired channelopathies (6). Also, previous studies showed that Tpe/QT ratio is increased in acute myocardial infarction, and it is associated with prognosis in patients undergoing primary percutaneous coronary intervention (15, 16). Our study is the first study to report on Tpe interval and Tpe/QT ratio in SCF.

SCF is an important angiographic entity characterized by delayed progression of contrast medium injected into the coronary tree. The presentation of this phenomenon is extremely diverse, ranging from vague chest discomfort to ST elevation myocardial infarction. Although many etiological factors, such as small-vessel disease, inflammation, and microvascular and endothelial dysfunction, have been implicated, its etiopathogenesis is still not clear. Abnormalities in coronary microcirculation, such as small-vessel structural defects and microvascular resistance, are confirmed. Endothelial dysfunction and subclinical atherosclerosis have also been shown to be responsible for the etiopathogenesis of SCF (17). Several studies showed that SCF results in myocardial ischemia, and vasodilator agents that are effective in coronary microcirculation can relieve ischemia by normalizing coronary flow (2, 17-21). Ischemia-induced Tpe is an important arrhythmogenic parameter that responds to successful reperfusion (22). Ischemia caused by microvascular dysfunction may be responsible for the heterogeneity of ventricular repolarization in SCF.

In addition, variations in cardiac autonomic neural tone and elevated sympathetic activity on the ventricular myocardium are associated with TDR and an increased risk of arrhythmia (23, 24). Korus et al. (25) settled the data showing an increase in sympathetic tonus and a decrease in vagal tonus by analyzing 24-hour Holter records in patients with SCF. Also, Yazıcı et al. (26) found higher noradrenaline and adrenaline levels in patients with SCF and suggested that increased adrenergic activity might be the manifestation of slow coronary flow. Thus, changes in autonomic neural tone may be another reason for the increase of Tpe interval and Tpe/QT ratio in patients with SCF.

Finally, Acar et al. (27) recently found that electrocardiographic ventricular repolarization indexes are correlated with systemic inflammation. Also, raised inflammatory activity is blamed in the pathogenesis of arrhythmia either by direct arrhythmogenic effects by locally activating complement or by induction of oxidative stress and apoptosis (28). Li et al. (29) showed that the plasma concentration of inflammation markers, such as high-sensitivity C-reactive protein and interleukin-6,

were increased and positively correlated with TFCs in SCF patients. Inflammation may be an explanation of the heterogeneity of ventricular repolarization in SCF patients but needs further investigation.

The measurement of Tpe interval and Tpe/QT ratio may be used to indicate increased risk of SCF-related adverse cardiovascular events. According to the current study findings, the risk of development of ventricular arrhythmia might be increased in SCF due to myocardial voltage gradients resulting from heterogeneity of repolarization. In our study, we showed for the first time that novel indices of ventricular repolarization (Tpe interval and Tpe/QT ratio) are increased in patients with SCF.

Study limitations

The primary limitation of our study is the small sample population, and follow-up of the patients could not be done. An association between ventricular arrhythmias with Tpe interval and Tp-e/QT ratio was not achieved. Therefore, we do not know whether prolongation of Tpe interval and Tpe/QT ratio predicts arrhythmias in SCF patients. Hence, long-term follow-up and large-scale prospective studies are needed to determine the predictive value of these indexes in this population.

Conclusion

Our results show that SCF is associated with prolonged Tpe interval and Tpe/QT ratio. Also, there is a positive correlation among the presence of SCF and these indexes.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - R.Z., C.Y.K., C.K.; Design - R.Z., C.Y.K.; Supervision - R.Z., A. Kalaycı., T.A.; Data collection &/or processing - A. Kalaycı., T.A., A. Kılıçgedik., C.K., R.Z., C.Y.K.; Analysis &/or interpretation - C.Y.K., T.A.; Literature search - A. Kalaycı., C.K.; Writing - R.Z., A. Kalaycı., C.Y.K., C.K.; Critical review - C.K., R.Z.

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