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# Novel Ventricular Repolarization Indices in Patients with Coronary Slow Flow

Murat Sucu[1], Berzal Ucaman[2], Orhan Ozer[1], Yakup Altas[2], Esra Polat[1]

*[1]Gaziantep University School of Medicine, Department of Cardiology, Gaziantep Turkey. [2]Gazi Yasargil Training and Research Hospital, Department of Cardiology, Diyarbakır Turkey.*

## Abstract

**Background:** Coronary slow flow (CSF) phenomenon is described angiographically as delayed progression of the injected contrast agents through the coronary arteries. Aim of this study was to analyze ventricular repolarization in CSF patients by using Tpeak-Tend interval, Tpeak-Tend/QT ratio, Tpeak-Tend/QTc ratio and other repolarization parameters since these parameters are used as predictors for ventricular arrhythmogenesis.

**Materials and Methods:** We have retrospectively analyzed diagnostic coronary angiography results of 160 patients between 2010 and 2014. Patients were divided into two groups according to coronary flow results. CSF group consisted of 33 female, 82 male patients with mean age 51,9±11,5 years. Control group included patients with normal coronary flow; 13 female, 32 male with mean age 50,8±11,7 years. In all patients, ventricular repolarization parameters as well as other associated electrocardiographic intervals were measured on the twelve-lead surface electrocardiogram.

**Results:** The ventricular repolarization parameters: QTmax interval, QTmin interval, QTc, QTI, QTcI, JTmax interval, JTmin interval, JTdispersion and JTIndex were not significantly different between the groups. However followings parameters differed significantly between patients and controls; QRS (92,8±11,5 msn versus 78,3±16,713,40 msn, respectively; p=0.001), T wave (89±20,2 msn vs. 73,3±13,3 msn respectively, p=0.001), QT dispersion (26,8±17,5 msn vs. 13,5±20,4 msn respectively, p=0.002), JTcorrected (331,6±39,8%; vs. 350,1±39,7% respectively; p=0.01). Furthermore; Tpeak-Tend duration (89±20,2 msn vs. 73,3±13,9 msn respectively; p=0.001), T wave (204±34,9 msn vs. 189,2±24,8 msn respectively; p=0.003), Tpeak-Tend/QT ratio (0,22±0,05 msn vs. 0,19±0,03 msn respectively, p=0.001) were significantly higher in patients compared to controls. Tpeak-Tend/QTc ratio was also significantly higher in the CSF group compared to the controls. (0,21±0,05 msn vs. 0,17±0,03 msn respectively, p =0.001).

**Conclusion:** Ventricular repolarization parameters are prolonged in patients with CSF.

## Introduction

The coronary slow flow (CSF) is an important coronary angiographic entity characterised by delayed progression of the injected contrast agents through the coronary arteries. It is a frequent finding, typically observed in patients with acute coronary syndromes. Myocardial repolarization can be evaluated with QT interval (QT), corrected QT interval (QTc), QT dispersion (QTd), and transmural dispersion of repolarization. The Tpeak-Tend interval, which is the interval between the peak and the end of the T wave on twelve-lead electrocardiogram (ECG), could be used as an index of transmural dispersion of repolarization.[1] Saya et al. reported a case with CSF and increased QTc dispersion which was associated with ventricular tachycardia.[2] Tpeak-Tend interval, which is the interval between the peak and the end of T wave on electrocardiogram (ECG), is accepted as an index of transmural dispersion of ventricular repolarization.[3] JT dispersion (JTd), corrected JT (JTc), corrected JT index (JTcI), Tpeak-Tend/QT ratio, Tpeak-Tend/QTc ratio are also used as an electrocardiographic index of ventricular arrhythmogenesis.[1] In this study, we assessed ventricular repolarization patterns in order to reveal any possible arrhythmogenic substrate in patients with CSF.

## Key Words:

Electrocardiography, Coronary Slow Flow, Ventricular Arrhythmia.

**Disclosures:**
None.

**Corresponding Author:**
Murat Sucu,
Gaziantep University School of Medicine,
Department of Cardiology,
Gaziantep, Turkey.

## Methods

### Study Population

One hundred-sixty patients who were admitted to the cardiology outpatient clinics with complaints of chest pain between January 2010 and December 2014, aged between 18 and 70 years, and who underwent coronary angiography for diagnostic purposes were included in the study. The patients were divided into two groups according to coronary flow characteristics. One hundred fifteen patients with CSF (33 female, 82 male patients; mean age 51,9±11,5 years) and 45 patients with normal coronary flow (13 female, 32 male; mean age 50,8±11,7 years) were included in the study. The exclusion

**Table 1: Characteristics of the Study Population**

| Patients (n=115) | Control(n=45) | P(value) | % |
|---|---|---|---|
| Sex(Female/Male) | 33/82 | 13/32 | 0,563 |
| Age(years) | 51,9±11,5 | 50,8±11,7 | 0,571 |

Values are presented as mean±SD.p<0.05

criteria were arterial hypertension, left ventricular wall anomalies, ejection fraction (EF) below 50%, primary cardiomyopathy, valvular heart disease, rhythm other than sinus on the ECG, bundle branch block and atrioventricular block, thyroid dysfunction, renal failure, and a history of drug abuse.

### Electrocardiography

We used a standard twelve-lead surface ECG tracing at 25 mm/s paper speed and 10 mm/mV amplitude. Measurements were taken manually by two independent investigators. If possible, parameters were determined in all 12 leads and mean results were calculated from three consecutive cardiac cycles. RR interval distance between two consecutive R waves, PR interval distance from the beginning of the P wave to the beginning of the Q wave, T wave duration and amplitude was measured. If the T-wave amplitude was <1.5 mm in a particular lead, that lead was excluded from analysis. The QT interval was measured from the onset of the QRS interval to the end of the T-wave in all leads where the end of the T-wave could be clearly defined.[4] All of the QT intervals in each lead were analysed, and the highest values of three consecutive intervals were used for the analysis. The QT interval was corrected for heart rate using the Bazett formula.[5] The dispersion of the corrected QT interval (QTcd) was defined as the difference between the maximum and the minimum of the corrected QT intervals measured in any of the leads. QTc=measured QT interval(s)=√RRinterval. The QT interval index (QTI) was measured by the following formula: QTI% =(QT/656) x(HR+100).[4,6]

The JT interval was measured in each of the 12 leads in three consecutive intervals in milliseconds, from the J point to the terminal inscription of the T wave. The U wave was not taken into consideration. When U wave was present, the JT interval was measured to the nadir of the curve between the T and U waves. The corrected JT (JTc) interval calculated by subtracting the QRS duration from the QTc interval in leads II, and V5. The dispersion of the corrected JT interval (JTcd) was defined as the difference between the maximum and the minimum of the measured corrected JT intervals in ms in any of the measured D2 and V5 leads. The JT interval index (JTI) was calculated by the following formula: JTI =(JT/518)x(HR+100).[4,6]

**Table 2: Electrocardiographic Measurements of the Between Groups**

| | Patients(n=115) | Control(-)(n=45) | P(value) |
|---|---|---|---|
| RR(msn) | 838,7±158,1 | 794,0±155,2 | 0,022 |
| Heart Rate(beat/min) | 71,8±15,5 | 78,3±15,4 | 0,020 |
| QRS(msn) | 92,8±11,5 | 78,3±16,7 | 0,001 |
| T wave duration (msn) | 204,0±34,9 | 189,2±24,8 | 0,003 |
| Tpeak-Tend (msn) | 89,0±20,2 | 73,3±13,9 | 0,001 |
| QTmax(msn) | 392,2±36,9 | 381,3±35,8 | 0,091 |
| QTmin(msn) | 365,2±37,8 | 365,5±36,5 | 0,959 |
| QTc(msn) | 424,5±38,1 | 428,4±39,5 | 0,564 |
| QTd(msn) | 26,8±17,5 | 15,5±20,4 | 0,002 |
| QTI(%) | 102,2±8,6 | 103,1±8,7 | 0,544 |
| QTcI (%) | 111,6±18,6 | 116,8±17,6 | 0,092 |
| JTmax(msn) | 296,4±40,2 | 292,6±41,9 | 0,566 |
| JTmin(msn) | 273,7±39,3 | 281,2±41,1 | 0,299 |
| JTd(msn) | 25,2±15,9 | 18,7±46,5 | 0,369 |
| JTc(msn) | 331,6±39,8 | 350,1±39,7 | 0,010 |
| JTI(%) | 97,8±11,9 | 99,9±11,5 | 0,293 |
| JTcI(%) | 98,7±10,3 | 105,1±10,7 | 0,001 |
| Tpeak-Tend/QT(msn) | 0,22±0,05 | 0,19±0,03 | 0,001 |
| Tpeak-Tend/QTc(msn) | 0,21±0,05 | 0,17±0,03 | 0,001 |

QTd: QT interval dispersion, QTI: QT interval index, QTc: Corrected QT interval, QTcI: QTc interval index, JTd: JT interval dispersion, JTc: Corrected JT, JTcI: Corrected JT interval index. NS:not significant. Values are presented as mean±SD:p<0.05

The Tpeak–Tend is the interval from the summit of the T-wave to the end of the QT interval. Tpeak-Tend and QT intervals were measured in leads D2 and V5. If V5 was not suitable, leads V4 and V6 in that order were measured.[1,7]

Tpeak-Tend/QT interval as well as Tpeak-Tend/QTc interval ratios (Tpeak-Tend interval divided by a QTc) were also calculated as indexes of repolarization. The Tpeak-Tend/QT ratio was calculated as the ratio of Tpeak-Tend in that lead to the corresponding QT interval.[8] All ECG measurements were performed by two independent cardiologists, who were blinded to patient information. When measurements were not identical, the mean of the values was calculated.

### Coronary Angiography

Coronary angiography is the only tool for the diagnosis and evaluation of CSF. All patients had been referred to diagnostic coronary angiography for evaluation of exertional chest pain suggestive of angina pectoris or positive treadmill testing. The diagnostic coronary angiography was performed via transfemoral approach with the Judkins technique. Coronary flow rates of all subjects were documented by Thrombolysis in Myocardial Infarction (TIMI) frame count. TIMI frame count method is a simple, reproducible, objective, and quantitative index of coronary flow velocity.[9] Initial frame count is defined as the frame in which concentrated dye occupies the full width of the proximal coronary artery lumen, touching both borders of the lumen, and forward motion down the artery. Distal end was defined as the distal bifurcation for the left anterior descending artery (LAD), the distal bifurcation of the segment with the longest total distance for the circumflex artery (Cx), and the first branch of the posterolateral artery for the right coronary artery (RCA).[9] For objective quantification of the coronary flow, two independent observers, blinded to the clinical data of the study subjects, assessed the coronary flow in coronary arteries using TIMI frame count method.

### Statistical Analysis

The SPSS software package (Version 15.0 for Windows, Inc.,Chicago, IL, USA) was used for statistical analysis. Data are expressed as mean values+standard deviation. Categorical data were analysed by the Pearson $x^2$ test. The mean differences between the study groups were evaluated by calculating Student's t-test. Categorical data were expressed as count and percentages. Multivariate logistic regression was used to identify the independent predictors of CSF. P-value <0.05 was considered significant. A P-value of, 0.05 was considered to be statistically significant.

## Results

Demographic and clinical characteristics of the SCF patients and control group are presented in Table 1. The mean age was 51,9±11,5

years in the SCF patients and 50,8±11,7 years in the control group (p>0.05). There were 33 female and 82 male patients in the SCF group, and 33 male and 12 female in the control group (p<0,05). The average heart rate for the CSF group and the control group was 71,8±15,5 and 78,3±15,4 beats/min, respectively (p=0,02). P wave amplitude, PR interval and QT interval were not significantly different between the groups but T wave duration and QRS complex duration were significantly longer in CSF group compared to controls (Table 2). Furthermore; Tpeak-Tend interval was significantly prolonged in the CSF group compared to control group (89,0±20,2 msn vs. 73,3±13,9 msn respectively; p<0.001). Tpeak-Tend/QT ratio was significantly higher in the CSF group compared to the control group (0,22±0,05 vs. 0,19±0,03 msn respectively; p<0.001). Tpeak-Tend/QTc ratio was also significantly higher in the CSF group compared to the control group (0,21±0,05 vs. 0,17±0,03 msn respectively; p<0.001). JTc (331,6±39,8% vs. 350,1±39,7%; p=0.010) and JTcI (98,7±10,3 vs. 105,1±10,7%; p=0,001) was significantly higher in the CSF group compared to the control group. The difference in JTd between the groups did not reach statistical significance (25,2±18,7 vs. 18,7±46,5 msn; p=0,369).

## Discussion

We investigated the ventricular repolarization parameters in patients with CSF and in healthy controls with normal coronary flow pattern. The clinical series and individual case reports have shown that CSF may be associated with typical angina, infarction, ischemia, and even sudden cardiac death.[2,10,11]

In a recent study, CSF was found to be associated with microvolt T-wave alternans positivity.[12] The QT and QTc dispersion and associated parameters are measures of cardiac electrical heterogeneity.[12] They may be of prognostic value in CSF patients. In our study, we revealed that the mean values of the QT dispersion were longer, and the JTc and corrected JT interval index were longer than QTcI. Zhou et al reported that in normal conduction, the JT interval may reflect the closest action potential durations in the basal portion of the heart and the corrected QT interval has no distinct electrophysiological meaning at the cellular level.[14] They stated that the JT rather than QT interval is the proper measure of the repolarization duration and that the JT parameter should be used as a single parameter, without QRS duration, which is also compatible with our findings. Rautaharju et al showed that JT adjustment obtained as QTc - QRS retained a strong residual correlation with ventricular rate.[15] Prolonged transmural dispersion of repolarization (TDR) is associated with inducibility as well as spontaneous development of VT in higher risk patients. TDR may be a useful index for predicting ventricular tachyarrhythmias.[16] Antzelevich reported an association between ventricular arrhythmogenesis and Tpeak-Tend prolongation.[17] In our study, we observed that the mean values of the Tpeak-Tend interval was longer in CSF patients. Yan et.al. demonstrated that dispersion in repolarization may arise from differences in the action potential durations between cells situated in different myocardial layers.[18] They showed that the M cells are characterized by prolonged repolarization compared with the epicardial or endocardial layer cells. The peak of the T wave in a transmural ECG was found to reflect the termination of action potentials from the epicardial layer. In addition, the T wave offset was found to represent the termination of repolarization in the M cells. The Tpeak –Tend/QT ratio is a new index of ventricular repolarization that remains constant despite dynamic changes in heart rate. The Tpeak–Tend/QT ratio is considered as a more sensitive index of arrhythmogenesis compared to Tpeak–Tend interval as it provides an estimate of dispersion of repolarization relative to total duration of repolarization.[19] This ratio varies from 0.15 to 0.25 in adults. The Tpeak –Tend interval was measured in precordial leads that are considered to reflect the transmural axis of the left ventricle, and therefore to provide an index of transmural dispersion of repolarization1. Prolonged transmural dispersion of ventricular repolarization is associated with inducibility as well as spontaneous development of VT in higher risk patients. Tpeak–Tend interval has been evaluated in congenital long QT syndrome (LQTS) patients, short QT syndrome, Brugada syndrome, hypertrophic cardiomyopathy and myocardial infarction.[19,20] An increased Tpeak–Tend interval has been associated with the development of ventricular tachyarrhythmias and thus may be considered as a non-invasive marker of arrhythmogenesis. Transmural dispersion of ventricular repolarization may be a useful parameter for predicting ventricular tachyarrhythmias.[16] Increased QT dispersion of repolarization is known to be an important factor in the development of ventricular arrhythmias.[21]

QTc dispersion, indicating increased risk for ventricular arrhythmias and cardiovascular mortality, was found to be significantly higher in patients with slow coronary artery flow.[22]

The QTc dispersion of more then 60 msec has been correlated with increased risk for sudden cardiac death in the elderly.[21] In our study, we found that patients with CSF had increased QTd compared to subjects with normal coronary artery flow.

Recently published studies reported that Tpeak-Tend interval and Tpe/QT ratio were increased in CSF patients.[23,24] The number of patients in both studies was too small and the results showed a single institution records. We have shown that T wave duration Tpeak-Tend interval, Tpe/QT ratio and Tpe/QTc ratio were increased in patients with CSF in a much bigger patient population.

Amasyali et.al. reported a young man with aborted sudden cardiac death. His coronary angiography revealed slow coronary flow phenomenon as a possible cause of this condition.[11] In Tatlı E. opinion, CSF is not purely an incidental angiographic finding; on the contrary, it may lead to angina pectoris and true myocardial ischemia.[25]

## Conclusions

In conclusion, Our results show that SF is associated with prolonged T wave duration, Tpeak-Tend interval and increased Tpeak-Tend/QT and Tpeak-Tend/QTc ratio. The findings of our study support a possible association between CSF and ventricular arrhythmias, which needs to be studied further.

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