QT interval and P wave dispersion in slow coronary flow phenomenon

Ali Eshraghi[1], Emadoddin Hoseinjani[2], Majid Jalalyazdi[3], Mohammad Vojdanparast[4], Reza Jafarzadeh-Esfehani[5]

Original Article

Abstract

BACKGROUND: Slow coronary flow (SCF) phenomenon is an angiographic finding which is defined as slow contrast passage through coronary arteries which may predispose patients to serious cardiac complications such as fatal arrhythmias. P-wave and QT-interval dispersion are electrocardiographic findings which are related to atrial fibrillation and ventricular tachyarrhythmias. In the present study, the relation between SCF and presence of P-wave and QT-interval dispersion in electrocardiography has been evaluated.

METHODS: 47 patients with normal coronary arteries and SCF and 40 patients with normal coronary artery flow without SCF were enrolled in this case control study. Standard electrocardiogram (ECG) was analyzed for P-wave and QT-interval dispersion. SCF was identified in normal coronary vessels by use of Thrombolysis in Myocardial Infarction (TIMI) frame count (TFC) method (TFC > 27). Corrected TIMI frame count (CTFC) of coronary vessels as well as mean CTFC along with QT-interval and P-wave dispersion were compared between 2 groups. The study data were analyzed by SPSS software and P value less than 0.050 was considered to be significant.

RESULTS: QT-interval [76.17 (35.23) ms versus 39.25 (19.26) ms] and P-wave [39.74 (17.48) ms versus 19.50 (8.54) ms] dispersion were significantly higher among patients with SCF phenomenon (P < 0.050). In addition, there was a positive significant linear correlation between TFC and P-wave and QT-dispersion (r = 0.857, r = 0.861, respectively, P < 0.050).

CONCLUSION: According to the results, increasing TFC among patients with SCF will result in P wave and QT interval dispersion and therefore this finding can be considered as an indicative marker for cardiac events.

Keywords: Coronary Angiography, Electrocardiography, Cardiac Arrhythmias

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Introduction

Slow coronary flow (SCF) phenomenon was first described by Tambe et al. and was defined as slow velocity of dye in coronary arteries.[1] A recent study in Iran showed that approximately 2% of patients who are scheduled for coronary angiography have the characteristics of SCF phenomenon.[2] While exact pathophysiology of this phenomenon is not clearly understood, thrombogenesis and enhancement of inflammation status are two possible mechanisms.[3] This phenomenon is seen in some cardiac effects such as ST elevation myocardial infarction (MI) and arrhythmias.[4,5] While patients with vulnerable myocardium such as those with ischemic heart disease are more susceptible to developing arrhythmias, patients with patent arteries are even at risk.[6,7] Dispersion in QT interval and P wave are 2 electrocardiographic findings which can predict predisposing of individuals for developing fatal arrhythmia.[6,8,9] P wave dispersion (PWD) is considered as an electrocardiographic marker for prediction of idiopathic paroxysmal atrial fibrillation and even its recurrence.[10,11] In addition to PWD, QT interval dispersion is also related to increased ventricular arrhythmias, cardiac death, and total mortality.[9,12] The P wave and QT interval dispersion

1- Associate Professor, Department of Cardiovascular Diseases, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2- Resident, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran
3- Associate Professor, Department of Cardiovascular Diseases, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
4- Cardiologist, Department of Cardiovascular Diseases, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
5- PhD Candidate, Department of Medical Genetics, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
Correspondence to: Reza Jafarzadeh-Esfehani, Email: drrezajafarzadeh@yahoo.com

is an interesting area of research and there is not enough evidence available for evaluation of these electrocardiographic findings among patients undergoing SCF phenomenon. According to prevalence of arrhythmias in SCF and predicting role of electrocardiographic findings such as P wave and QT interval dispersion for arrhythmias, possible relation between SCF and P wave and QT interval dispersion will be evaluated in this case control study.

Materials and Methods

The present case control study received approval from the research and ethics committee of Mashhad University of Medical sciences, Mashhad, Iran, in July 2012 and registered as a thesis (Code:7171) in the degree of Doctor of Medicine. Two groups of patients who were referred to Imam Reza Hospital angiography unit of Mashhad City enrolled in this study and the study was performed from August 2012 to August 2013. 47 patients who had documented SCF and 40 patients who had normal coronary artery flow filled an informed contest. The SCF phenomenon was documented angiographically as normal or near normal coronary arteries with less than 40% stenosis and Thrombolysis in Myocardial Infarction (TIMI)-2 flow in at least one major coronary arteries despite specific provocative maneuvere.[13] According to individual matching protocol, some confounding factors were matched between both groups. Confounding factors were defined as age, sex, diabetes mellitus (DM), hypertension, smoking, and systolic and diastolic function of left and right ventricles. Patients with significant valvular heart disease were excluded from the study. The patients who were presented with stable angina and did not respond to therapy had undergone angiography by femoral method (with non-ionized contrast agent and without using nitroglycerine) under the impression of typical angina and had normal coronary arteries. Stable angina was defined as chest discomfort occuring predictably and reproducibly at a certain level of exertion and was relieved with rest or nitroglycerin.

All the angiographies were performed by two expert interventional cardiologists who were blinded to the clinical details of the study. SCF was identified in normal coronary vessels by use of TIMI frame count (TFC) method in at least one of the main coronary vessels. TFC value greater than 27 was considered as SCF.[14] While normal frames for left anterior descending artery (LAD) were 1.7 times more than mean value of right coronary artery (RCA) and left circumflex artery (LCX), the mean corrected TFC (CTFC) values were calculated as follow:

$$\text{CTFC mean} = 1/3\ (\text{LAD}/1.7 + \text{RCA} + \text{LCX})$$

Every patient underwent a resting 12 lead ECG recorded at a paper speed of 50 ms and voltage of 1 mV. QT dispersion (based on the difference between maximum and minimum QT) and P dispersion (based on the difference between maximum and minimum P wave duration) were calculated based on patient's ECG.[7] All standard 12-lead ECGs for every patient were obtained in a quiet room after 15 minutes of adjustment in supine position with the same recorder. Wave measurements were conducted blindly by a trained cardiologist. Patients who had evidence of obstructive coronary artery disease (more than 20% stenosis of luminal area), coronary ectasia, myocardial bridging, major coronary spasm, atrial fibrillation, branch blocks, connective tissue disease, uncontrolled hypertension and systemic disease, were not included in the study groups.

Study data including TFC of the three main coronary arteries, maximum and minimum of QT and P wave duration in both groups were analyzed by SPSS software (version 20, IBM Corporation, Armonk, NY, USA). The Kolmogorov-Simonov (K-S) test was used in order for examination of the normality of data distribution. Categorical variables such as smoking, blood glucose, blood pressure, and lipid profile in both groups were analyzed by chi-square test. Continuous variables were presented as mean and standard deviation (SD), while categorical variables were presented as frequency and percentage. Moreover, variables with normal and without normal distribution were analyzed by t-test and Mann Whitney test, respectively. The correlation between variables was evaluated by Spearman's correlation coefficient. P-value less than 0.050 was considered as "statistically significant".

Results

A total of 87 patients (47 patients in case group and 40 patients in control group) were participated in this study. Mean ± SD of age in normal and SCF groups were 53.78 ± 9.72 and 51.62 ± 7.35, respectively (P = 0.252). The age distribution in both groups was normal and groups were homogenous for gender based on K-S and chi-square tests. Smoking, having DM, hypertension, or hyperlipidemia were not significantly different between both groups (P = 0.640, P = 0.777, P = 0.990, and P = 0.990, respectively). Left ventricular systolic function in both groups was

within normal range (55 to 65%). CTFC of 3 main coronary vessels are shown in table 1.

Table 1. Comparison of baseline characteristics of study groups

Variable	Case group (n = 47) Rate (%)	Control group (n = 40) Rate (%)	P
Smoking	14 (29.8)	10 (25.0)	0.640
DM	9 (19.1)	6 (15.0)	0.777
Hypertension	17 (36.2)	15 (37.5)	0.990
Hyperlipidemia	15 (31.9)	13 (32.5)	0.990

DM: Diabetes mellitus

Mann-Whitney test showed that QT interval and PWD, mean CTFC, and TFC in 3 coronary vessels were significantly different in both groups (P < 0.001) (Table 2). These variables were not normally distributed in groups based on the K-S test.

The mean CTFC and QT disturbance were significantly correlated in SCF group (P < 0.001, correlation coefficient: 0.857), which was absent in normal flow group (P = 0.536, correlation coefficient: -0.101) (Figure 1).

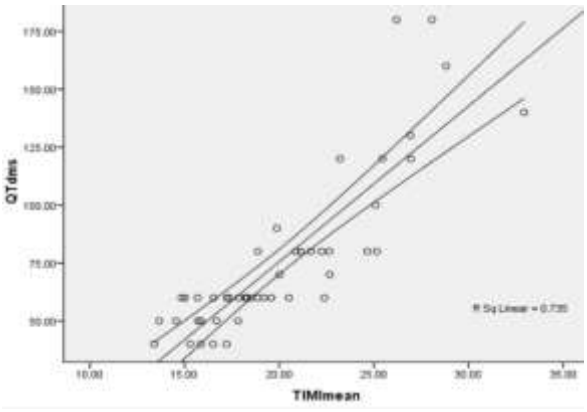

Figure 1. Corrected Thrombolysis in Myocardial Infarction (TIMI) frame count (TFC) mean and QT disturbance with a linear relation in slow coronary flow (SCF) group which was absent in normal flow group

The CTFC and PWD were significantly correlated in SCF group (P < 0.0001, correlation coefficient: 0.861), which was absent in normal flow group (P = 0.522, correlation coefficient: -0.104) (Figure 2). The correlation between P wave and QT dispersion with CTFC in study groups are shown in table 3. These results indicated that QT interval and PWD significantly increased with increasing the CTFC among patients with SCF (P < 0.001).

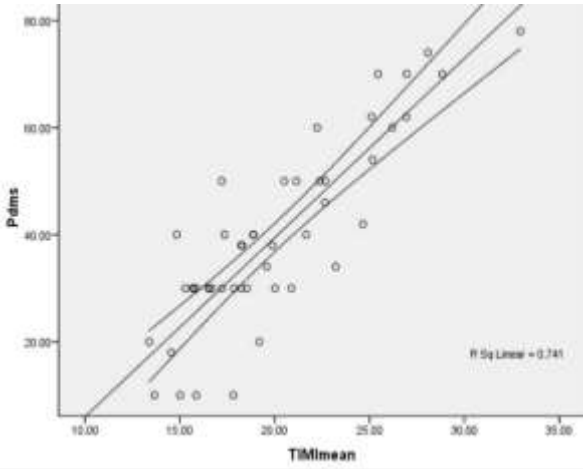

Figure 2. Corrected Thrombolysis in Myocardial Infarction (TIMI) frame count (TFC) mean and P wave disturbance with a linear relation in slow coronary flow (SCF) group which was absent in normal flow group

Discussion

The results of the present study showed that P wave and QT interval dispersion were electrocardiographic findings indicating good correlation with SCF phenomenon. Exact prevalence of SCF varied from 1 to approximately 6% in literature because of using different populations and study design.[2,13,15] While SCF is related to various clinical conditions such as ventricular dysfunction and acute coronary syndrome, serious arrhythmias are also considered to be a common finding in this phenomenon.[16,17]

Table 2. Mean of corrected TIMI frame count (CTFC) values in coronary vessels and dispersion of QT interval and P waves in study groups

	Case group (n = 47) (mean ± SD)	Control group (n = 470) (mean ± SD)	P
CTFC (LAD)(30f/s)	29.48 ± 8.25	17.50 ± 2.48	< 0.001*
CTFC (LCX) (30f/s)	21.89 ± 6.56	12.67 ± 2.50	< 0.001*
CTFC (RCA) (30f/s)	21.04 ± 9.46	12.05 ± 2.57	< 0.001*
CTFC mean (30f/s)	20.09 ± 4.49	11.68 ± 1.16	< 0.001*
QT interval dispersion (ms)	76.17 ± 35.23	39.25 ± 19.26	< 0.001*
PWD (ms)	39.74 ± 17.48	19.50 ± 8.54	< 0.001*

SD: Standard deviation; CTFC: Corrected TIMI frame count; PWD: P wave dispersion; LAD: Left anterior descending artery; CTFC: Corrected TIMI frame count; LCX: Left circumflex artery; RCA: Right coronary artery

* The Mann-Whitney test was used for the comparison.

Table 3. Correlation of P wave and QT segment dispersion in case and control groups

ECG parameter	Involved vessel	Case group (n = 47)		Control group (n = 40)	
		P	Correlation coefficient *	P value	Correlation coefficient*
QT dispersion	LAD	< 0.001	0.489	0.319	0.162
	LCX	< 0.001	0.668	0.846	-0.032
	RCA	< 0.001	0.508	0.220	-0.198
P dispersion	LAD	< 0.001	0.444	0.935	-0.013
	LCX	< 0.001	0.556	0.869	-0.027
	RCA	< 0.001	0.613	0.277	-0.176

ECG: electrocardiogram; LAD: Left Anterior Descending artery; LCX: Left circumflex artery; RCA: Right coronary artery
* Spearman's correlation coefficient

P wave and QT interval dispersion are 2 major electrocardiographic findings which are associated with serious arrhythmias. QT interval dispersion indicates ventricular electrical instability and variable ventricular repolarization.[6] PWD is also a marker for atrial remodeling and is considered to be related to paroxysmal atrial fibrillation.[18] Among arrhythmias, ventricular arrhythmias are reported to be associated with SCF.[19] P wave and QT interval dispersion can be seen with SCF. Similar to the results of the present study, Mahmoud with smaller study population had found that SCF phenomenon was associated with dispersion of P wave and QT interval.[20] Unlike the current study, Mahmoud had evaluated urea and creatinine levels and had found that SCF was related to increase of these values.[20] Mahfouz et al. with larger sample size has also approved that QT interval and PWD were associated with SCF.[21] According to these similar studies from different countries, a significant relation between SCF and certain electrocardiographic findings can be concluded. However, there are some clinical conditions with significant impact on electrocardiographic findings, especially QT interval dispersion. As an example, there are some environmental causes for QT dispersion such as smoking. Akbarzadeh et al. reported that even smoking a single cigarette among nonsmokers will increase QT dispersion.[22] Moreover, a meta-analysis study had shown that anxiety in clinically healthy patients would affect QT interval dispersion and predispose patients to develop arrhythmias.[23] According to these wide range of cofounding results on measuring QT interval dispersion, conducting a study to cover healthy individuals with SCF and without confounders for P wave or QT interval dispersion seems difficult but necessary.

The other concern was the factors influencing developing SCF phenomenon and the unknown underlying etiology. Given the present results, smoking, hypertension, and DM were not related to SCF phenomenon. Unlike this study, Ramakrishnan et al. reported that dyslipidemia, smoking, and hypertension were significantly associated with SCF and recommended endothelial dysfunction as a significant contributor in SCF phenomenon.[24] Similarly, in a study by Sanati et al., it was concluded that low level of high hyperalphalipoproteinemia (HDL-c) and hypertension were independent predictors of SCF phenomenon.[2] Some authors have evaluated the relation of more parameters and SCF phenomenon. Naing et al. reported uric acid level as an independent predictor of SCF phenomenon.[25] Hawkins et al. in a study reported obesity as an independent predictor of this phenomenon.[15]

Heterogeneous nature of this phenomenon might be the explanation of its association with different comorbidities.[15] As Sanati et al. suggested, a possible reason for different predictors in different studies could be an unknown confounder which is not addressed in any specific study.[2] Sezgin et al. reported that low coronary flow will increase QT dispersion and prolong QT interval duration and suggested that ventricular heterogeneity, autonomic neural tone changes or micro vascular ischemia may be responsible for QT dispersion.[6]

Limitations: Confounding factors such as autonomous disorders, electrolyte disturbances such as potassium, magnesium and calcium disturbances, congenital heart disease, anemia or chronic infections are believed to impact patient's electrocardiography. Although the cases in this study were matched and a study protocol was developed which included many of other confounding factors; however, due to various effective factors on electrocardiogram (ECG), considering an exact conclusion about the effect of SCF on P wave and QT interval is difficult.

Conclusion

The results of this study showed that QT interval and PWD were significantly related with SCF. Conducting further studies on healthy individuals with SCF phenomenon and without these

mentioned confounders for electrocardiographic findings seems necessary.

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Conflict of Interests

Authors have no conflict of interests.

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