

## The Effect of Coronary Risk Factors on QT Dispersion

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**Abstract:** It is known that in patients with ischemic heart disease, QT dispersion (QTd) predicts ventricular arrhythmia and sudden cardiac death and that major coronary risk factors such as smoking, diabetes mellitus, hypertension increase QTd. It is not clear whether, in coronary artery disease, QTd increases because of ischemia or co-existence of coronary risk factors. In this study, we aimed to investigate the independent effect of coronary risk factors on QTd by examining patients with just one major coronary risk factor. 133 (111 patient, 22 healthy people, average age (52±10; 49±11) patients were included in our study. The patients were divided into 5 groups according to existence of diabetes mellitus (19 patients), hypertension (24 patients), hyperlipidemia (17 patients), a positive family history (21 patients), smokers (30 patients). The control group consists of completely healthy subjects without any risk factors (22 patients). 12 derivations ECG of all patients were recorded at 50 mm sec<sup>1</sup>. QT intervals were measured after the ECG recordings were transferred to a computer and magnified by 400-600 times with Adobe photoshop program on a high resolution monitor. QTd and QTcd (QT corrected dispersion) of all groups with one risk factor were significantly higher than the control group (p< 0.01). In addition, each coronary risk factor had an independent and significant increasing effect on QT interval (p<0.01). QTd and QTcd intervals are affected by coronary risk factors as well as ischemia and this finding should be taken into account in studies concerning QT intervals.

**Key words:** QT dispersion, coronary risk factors

### INTRODUCTION

Ischemic heart disease is the most important cause of mortality in the adult population and these patients frequently die as a result of malignant ventricular arrhythmias<sup>[1]</sup>.

As new clinical studies have shown, QT dispersion (QTd) measured on a surface electrocardiogram (ECG) is an important variable predicting ventricular arrhythmia, sudden cardiac death and other cardiac events<sup>[2]</sup>. It has also been shown that in ischemic heart disease.

QTd is related to acute ischemia; can be used as a non-invasive marker of ischemic injury and is a promising parameter which predicts ventricular arrhythmia<sup>[3,4]</sup>. Major risk factors of Coronary Artery Disease (CAD) are age, hypertension, diabetes mellitus, smoking, hyperlipidemia, male sex, and positive family history<sup>[5]</sup>.

Effects of some coronary risk factors (age, Hypertension, Diabetes mellitus and smoking) on QTd have been investigated<sup>[6-9]</sup>. However, effect of hyperlipidemia, positive family history and independent effects of all coronary risk factors on QTd have not been studied.

We sought to study how QTd is affected in patients with only one known coronary risk factor.

### MATERIALS AND METHODS

133 subjects (111 patients and 22 healthy people) who were admitted to Izzet Baysal University Izzet Baysal Medical Faculty internal medicine and cardiology outpatient clinics were included in the study. Among the patients with one coronary risk factor: 19 (13 female/ 6 male) had diabetes mellitus (type II ); 24 (19 female/ 5 male) had hypertension; 17 (12 female/ 5 male) had hyperlipidemia; 30 (11 female/19 male) were smoker and 21 (9 female/12 male) had a positive family history. In addition 22 healthy people (16 female/ 6 male) were included as a control group.

Age, sex, Body Mass Index (BMI), systolic and diastolic blood pressures, levels of serum total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol were taken into account. Of the patients using Oral Antidiabetic Drugs (OAD) and insulin or ones with a 2 hour blood sugar over 200 mg dLG<sup>1</sup> on an oral glucose tolerance test were diagnosed as diabetic. Patients with

total cholesterol over 200 mg dLG<sup>1</sup> were diagnosed as hyperlipidemia. Patients who had systolic blood pressure over 140 mmHg or/ and diastolic blood pressure over 90 mmHg on physical examination were defined as hypertensive. Patients using medication for the treatment of hypertension who were diagnosed before were also included in this group. Smoking was quantitatively measured as pack/year. A positive family history was defined as existence of coronary artery disease before the age of 55 for males and before the age of 65 for female relatives. Control group consisted of healthy people without any coronary risk factors.

Patients with anemia, thyroid dysfunction, electrolyte imbalance, known ischemic or valvular heart disease, cardiac heart failure and arrhythmias, left bundle branch block on ECG, patients using anti-psychotics, antidepressants,  $\beta$  blockers; anti-hyperlipidemics and anti-arrhythmic drugs were excluded.

All subjects underwent a routine standard 12-lead surface ECG recorded at 50 mm sG<sup>1</sup> at rest. ECG's of all patients were obtained in a quiet room. ECG's were transferred to a personnel computer via a scanner and then used for magnification of 400 times by Adobe Photoshop software. QT interval which is the duration between beginning of QRS complex to the end of T wave was measured in all derivations in which T wave was clearly seen and not mixed with a U wave. In all patients derivations in which the beginning and endpoint of QT could not be distinguished were excluded.

Cases of which at least 8 derivations and at least 3 precordial derivations could be measured were included in the study. These measurements repeated three times and average values were accepted for QT measurements. QTd was defined as the difference between the longest QT interval (QT max) and shortest QT interval (QT min). Measured QT intervals were corrected by Bazett's formula and defined corrected QT interval (QTc). The difference between the longest QTc (QTc max) and shortest QTc (QTc min) was defined as corrected QTd (QTcd).

The QT values of patients and control cases were compared. Also the subgroup of patients according to the CAD risk factors were compared with the control cases.

For statistical analysis; SPSS 10.0 software was used. Quantitative variables of two groups were given as arithmetic average  $\pm$  standard deviation. In comparison of quantitative and qualitative values of two groups, student's t test and chi-square tests were applied. One way ANOVA was used in analysis of clinical; laboratory and ECG variables of more than one group. P values < 0.05 was considered statistically significant. In addition; multiple logistic regression method was used to compare coronary risk factors with QT intervals.

## RESULTS AND DISCUSSION

133 patients were included in the study (111 patients and 22 control cases; with mean ages of 52 $\pm$ 10 years and 49 $\pm$ 11 years, respectively). Clinical, laboratory and ECG values of all groups are shown on Table 1.

Statistically significant differences were present between total cholesterol, triglyceride, LDL cholesterol, QT max, QTd and QTcd values (p<0.05). Mean BMI and age was not statistically different between the two groups.

The values of QT intervals of the patients are summarized in Table 2. Mean QTc min in the smokers group, QT max and QTc max in hyperlipidemic group and QT max in the group with a positive family history were significantly different than the control group. Multivariate logistic regression analysis was used to identify independent risks on QTcd. Statistical analysis is summarized in Table 3. The most important factor that can alter QTd and QTcd was found to be hypertension.

Table 1: Comparison of the characteristics of the clinical, laboratory and ECG findings of the patients with control cases

		Patients	Control group	P
Age	(year)	52 $\pm$ 10	49 $\pm$ 11	NS
Gender	(F/M)	64/47	16/6	NS
BMI*	kg mG <sup>2</sup>	27 $\pm$ 4	26 $\pm$ 3	NS
Systolic blood pressure	mmHg	131 $\pm$ 18	124 $\pm$ 13	NS
Diastolic blood pressure	mmHg	83 $\pm$ 10	77 $\pm$ 6	P<0.05
Triglyceride	mg dLG <sup>1</sup>	136 $\pm$ 49	108 $\pm$ 36	P<0.05
Total cholesterol	mg dLG <sup>1</sup>	202 $\pm$ 36	184 $\pm$ 28	P<0.05
LDL cholesterol	mg dLG <sup>1</sup>	125 $\pm$ 31	109 $\pm$ 27	P<0.05
HDL cholesterol	mg dLG <sup>1</sup>	51 $\pm$ 11	55 $\pm$ 12	NS
QT minimum	ms	335 $\pm$ 24	33 $\pm$ 29	NS
QTc minimum	ms	370 $\pm$ 26	377 $\pm$ 19	NS
QT maximum	ms	367 $\pm$ 23	354 $\pm$ 27	P<0.05
QTc maximum	ms	404 $\pm$ 25	399 $\pm$ 18	NS
QT Dispersion	ms	31 $\pm$ 11	19 $\pm$ 9	p<0.05
QTc Dispersion	ms	34 $\pm$ 14	21 $\pm$ 9	p<0.05

\* Body Mass Index ms: millisecond NS: p> 0.05

Table 2: Characteristics of the clinical, laboratory and ECG findings of the patients

	Patients with HL	Smokers	Patients with HT	Patients with DM	Patients with a positive CAD history
Age (years)	56 $\pm$ 9	46 $\pm$ 10	55 $\pm$ 10	54 $\pm$ 9	44 $\pm$ 7
Gender (F/M)	12/5	11/19	19/5	13/6	9/12
BMI kg/m <sup>2</sup>	28 $\pm$ 3	25 $\pm$ 2	28 $\pm$ 3	26 $\pm$ 3	26 $\pm$ 3
SBP	126 $\pm$ 11	119 $\pm$ 12	151 $\pm$ 20	131 $\pm$ 13	128 $\pm$ 9
DBP	79 $\pm$ 6	78 $\pm$ 8	96 $\pm$ 10	78 $\pm$ 6	81 $\pm$ 2
Total cholesterol	251 $\pm$ 34	182 $\pm$ 27	195 $\pm$ 22	188 $\pm$ 22	196 $\pm$ 16
Triglyceride	203 $\pm$ 99	125 $\pm$ 39	130 $\pm$ 43	120 $\pm$ 37	144 $\pm$ 54
HDL	56 $\pm$ 12	47 $\pm$ 11	54 $\pm$ 12	50 $\pm$ 9	50 $\pm$ 6
LDL	160 $\pm$ 46	115 $\pm$ 26	115 $\pm$ 19	113 $\pm$ 23	117 $\pm$ 10
QT minimum ms	345 $\pm$ 18	337 $\pm$ 25	334 $\pm$ 26	334 $\pm$ 23	336 $\pm$ 13
QT maksimum ms	377 $\pm$ 22	367 $\pm$ 23	366 $\pm$ 22	353 $\pm$ 23	370 $\pm$ 17
QT Dispersion ms	32 $\pm$ 12	29 $\pm$ 13	32 $\pm$ 10	29 $\pm$ 9	32 $\pm$ 8
QTc minimum ms	377 $\pm$ 24	363 $\pm$ 29	377 $\pm$ 21	364 $\pm$ 24	369 $\pm$ 25
QTc maximum ms	413 $\pm$ 26	395 $\pm$ 26	412 $\pm$ 17	397 $\pm$ 28	403 $\pm$ 16
QTc Dispersion ms	36 $\pm$ 15	32 $\pm$ 15	35 $\pm$ 12	33 $\pm$ 11	33 $\pm$ 13

Table 3: The effect of coronary risk factors on QTd and QTcd

Risk Factors	QT dispersion			QT c dispersion		
	Odds ratio	%95 CI	p	Odds ratio	%95 CI	P
Diabetes mellitus	3.17	4.08-17.5	0.002	2.94	4.01-20.4	0.004
Smoking	3.61	4.98-17.08	0.000	3.06	4.04-18.8	0.003
Hypertension	4.18	7.08-19.80	0.000	3.59	6.3-21.8	0.001
Hyperlipidemia	3.90	6.75-20.6	0.000	3.63	7.07-24.04	0.001
Family history of CAD	3.55	6.1-21.5	0.001	2.60	2.99-21.8	0.010
Age	1.02	-.09-0.302	0.306	-.258	-.275-0.212	0.797

Ischemic heart disease increases QT interval and QTd. An increase in QT interval and QTd is an independent predictor of cardiovascular mortality<sup>[10]</sup>. Several cardiovascular risk factors are known to effect the QTd. Studies have also shown that in ischemic heart disease QTd increases and this increase is correlated to the duration and severity of ischemia or presence of scar tissue<sup>[11]</sup>. Therefore; it was noted that; QTd is a promising noninvasive parameter predicting ischemic injury and ventricular arrhythmias in patients with acute or chronic ischemia<sup>[3,12]</sup>.

Hypertension was shown to increase QTd<sup>[13,14]</sup>. Akhobadze *et al.*<sup>[15]</sup> demonstrated that this increase is present in case of left ventricular hypertrophy. Furthermore; ramipril, felodipin and irbesartan can inhibit the increase in QTd<sup>[16,17]</sup>. Kaftan *et al.*<sup>[18]</sup> found that hypertension can effect the QTd by causing left ventricular hypertrophy and altering heart rate. The present study showed that QTd as well as QTcd increases in patients with hypertension, where this increase is independent to heart rate. The odds ratio for QTd is 4,18 (p<0.01) and 3.59 (p< 0.01) for QTcd.

In patients with type II diabetes mellitus, QTd was found to be an independent predictor of cardiac death<sup>[18]</sup>. Previous studies deonstrated a high prevelance of QTd abnormalities in type II diabetes mellitus patients<sup>[19,20]</sup>. An increased QTd is associated with presence of diabetic cardiovascular complications<sup>[8,21,22]</sup>. In our study; QTd (p<0.01 ) and QTcd (p<0.01) of diabetic patients were significantly higher than the control cases, where odds ratios of QTd and QTcd were 3.17 and 2.94, respectively.

Cigarette smoking increases QTd. In our study; QTd (p< 0.01) and QTcd (p< 0.01) were significantly increased in smokers. It was observed that smoking has an important effect on QTd (odds ratio = 3.61, p<0.01) and QTcd (odds ratio =3.06 p< 0.01). This data is in concordance with other studies that reported an increase in heart rate and QTd of smokers which can be caused by the effects of smoking on autonomic nervous system and endothelium<sup>[9,23]</sup>

Hyperlipidemia is a major risk factor for ischemic heart disease. A study investigating the relation of

hyperlipidemia and QTd is not present in the medical literature. Only Laszio *et al.*<sup>[24]</sup> demonstrated that fluvastatin can significantly decrease QTd by correcting the homogeneity during ventricular recovery after cardiac injury. In our study; when normal individuals and hyperlipidemic patients were compared, it was seen that QTd (p<0.01) and QTcd (p<0.01) is prolonged significantly in the patients and the presence of hyperlipidemia has a role on the prolongation of QTd (odds ratio = 3.90, p<0.01) and QTcd (odds ratio =3.63, p<0.01). On theoretical basis it can be speculated that this effect is due to altered coronary blood flow, endothelial dysfunction or disorder in ventricular homogeneity as stated in the previously mentioned study. A study conducted on rabbits showed that a diet rich in cholesterol increase action-potential durations and QTd<sup>[25]</sup>. The present study is the first one in the English medical literature conducted with human population that showed a relation between hyperlipidemia and QTd.

Family history is a known major coronary risk factor. The effect of this known risk factor on QTd was not studied before. In our study, when normal individuals and individuals with a family history were compared; individuals with a family history had a significantly longer QTd (p<0.01) and QTcd (p<0.01). It was shown that family history of CAD has a role on prolongation of QTd (odds ratio = 3.55, p<0.01) and QTcd (odds ratio =2.60, p< 0.05). It is not very easy to describe the mechanism causing this effect. Genetically predisposition on QTd is not clear. There are several inherited electrical abnormalities affecting the heart such as familial dysautonomy and long QT syndrome that increases QTd. There can be a similar but more benign mechanism underlying the relation between CAD history and QTd.

## CONCLUSIONS

Our findings show that; apart from ischemia, the presence of coronary risk factors has a role in prolongation of QT interval. We found that QTd is increased in individuals with hyperlipidemia and family history. Therefore it can be concluded that in future

studies concerning QT dispersion, our findings should be taken into account and it should be kept in mind that coronary risk factors; even just one of them, can increase QTd. Although our findings show that QTd and QTcd is higher in patients with only one coronary risk factor compared to controls, studies with a larger number of patients are needed.

#### **Limitations of the present study:**

- C The diagnosis of coronary artery disease was reached by history, physical examination and evaluation of the ECG, where as coronary artery angiography was not routinely performed.
- C The patients were not screened by transthoracic echocardiography to detect left ventricular hypertrophy.
- C The effect of antihypertensive medication was omitted.
- C Interobserver variability was not studied.

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