# Relationship between QT Interval Dispersion and Degree of Coronary Artery Disease

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## Abstract

**Background:** It has been shown that QT dispersion (QTD) increases during episodes. Currentstudyhas been done in order to determine QTD in patients with stable angina, assess myocardial ischemia and infarction.

**Aims of Study:** This study aiming to determine the relationship between severity of coronary artery disease (CAD) and degree of QTD.

**Patients and Method**: A 214 patients (177 men and 37 women) underwent diagnostic coronary angiography because of suspected CAD. Standard resting 12 lead electrocardiogram (ECG) were recorded within 24hrs before coronary angiography. QT intervals were measured manually by ruler method and QTD were gauged as (QT maximum – QT minimum).

A 184 patients had CAD and control group (30 persons) had a normal coronary angiogram

Interestingly, QTD has increased significantly as there was sever increment of CAD. QTD was in 1 vessel disease, 2 vessel disease, in 3 vessel disease, and in left main stem disease.

Left ventricular dysfunction has raised QTD significantly in patients with 1,2 vessels, as well as left main stem disease.

QTD clearly elevated as Gensini score increased. Involvement of proximal left anterior descending artery did not increase QTD significantly in patients with CAD.

Multiple regression analysis demonstrated that severity of CAD, left ventricular dysfunction and previous myocardial infarction were independently associated with increased QTD.

QTD increased significantly in patients with stable angina compared to the controls.Severity increase of CAD resulted in significant increase in QTD, and presence of LV dysfunction has caused further increase.

## Introduction

QT dispersion (QTD) has been defined as difference between maximum and minimum QT intervals in any number of Electrocardiography (ECG) leads [1, 2] and related to electrical instability and risk of ventricular arrhythmogenesis[2].

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QTD increased in patients with coronary artery disease (CAD) [3-5] and it especially prolonged during active ischemia [6, 7].

In present study we tried to determine QTD in patients with chronic stable angina as measured by surface ECG at rest. As well as, to assess the relationship between severity of CAD as assessed by coronary angiography and the degree of QTD.

## Patients and Method

Between April 2001-2002, 2106 patients underwent cardiac catheterization and coronary angiography for definite or suspected Ischemic Heart Disease (IHD) in Ibn Albitar Hospital for Cardiac Surgery. Of those patients 214 (177 men and 37 women) fulfilled the following criteria.

**1.** Coronary angiography because of suspected CAD.

**2.** No valvular disease.

**3.** No sign of LV hypertrophy on LV angiogram or Echo study.

**4.** No evidence of unstable angina or acute myocardial infarction (MI).

**5.** ECG: sinus rhythm, no bundle branch block, with a well-defined T wave in all or most (10 or more of the 12 leads ECG) leads that make accurate measurement of QT interval possible.

**6.** Normal levels of serum potassium and calcium.

**7.** No medication, known to induce prolongation or shortening of QT interval or change QTD.

Detailed history and careful physical examination have been applied for all patients.

Standard resting 12-lead ECG with simultaneous lead acquisition were recorded with Mac 500, version 2.2 (Marquette Hellige GmbH, Freiburg, Germany) at speed 25 mm/second.

Diagnostic coronary angiography and left ventriculography were done within 24 hours of the ECG recording.

### Coronary Angiography

Left heart catheterization was done using Judkin's technique (percutaneous tansfemoral) [9]. Coronary angiography has been done in multiple views. Coronary artery lesions were considered significant in cases when stenosis was at least 70% (or 50% left main coronary artery) [10].

Furthermore, coronary angiography was evaluated as single, double or triple vessel disease [8, 11] by quantification of the lesions according to Gensiniscore [12].

In addition, left ventricular function was assessed by single plane left ventricular angiogram in the 300 right anterior oblique positions [13], as well as by two D and M modes Echocardiography[14]. Moreover, normal LV function was defined as ejection fraction of 55% or more [15].

Mild LV dysfunction was defined as ejection fraction (EF) between 40-55%. Finally, moderate LV dysfunction 30-40% and severe LV dysfunction < 30% [15].

### Analysis of ECG

Einthoven lead II [8] was analyzed in order to measure QT and corrected QT (QTc) intervals.

QT intervals were measured manually (ruler method) [16] in all limb and chest leads by two observers and were measured from the onset ofQRS complex (from the first deflection of QRS complex) to the point of return of the T wave to the isoelectric line [3, 8, 17]. More specifically, when a U wave followed the T wave, the end of the T wave was taken as the nadir between the T and U waves [6]. In case that the end of the T wave could not be identified assuredly, that lead was excluded from the analysis.

Notably, the QT interval was measured in three consecutive complexes in each lead and the average value was relied [6].

QTD was calculated as the difference in ms between longest and shortest measured QT intervals [3, 6, 16 & 18].

No attempt was made to correct for missing leads.

For the measurement of QTc interval of lead II modified Bazett's formula was applied QTc=QT/RR [1, 8].

Patients were considered normal in term of coronary arteries when there was no angiographic stenosis, no clinical, as well as ECG or angiographic evidence of previous myocardial infarction [6].

## Statistical Analysis

All data were given as mean ± standard deviation. Analysis of variance (ANOVA) was used for comparison among variances.

$P \leq 0.05$ was considered significant.

## Results

The study population was composed of 184 patients with CAD with a mean of age (54.75± 9.19 years) and 30 patients with normal coronary angiogram (control group) with a mean of age (Table 1).

No significant difference was found between the two groups in term of age; however hypertension, diabetes mellitus (D.M.) and smoking were more common among those with CAD. Interestingly, male: female ratio was significantly higher in CAD patients.

Among patients with CAD, ECG evidence of Q wave MI was present in 90 patients that represent (48.9%).

Patients with CAD have been classified according to the severity of their diseaseas single, two, three- vessel or left main stem (LMS) disease (Table 2). Moreover, those with more extensive disease tended to be older with most common hypertension and D.M. In contrast, there was no significant difference in relative to gender or smoking within the different groups of CAD patients.

No significant difference in the incidence of Q wave MI or LV dysfunction in all groups of CAD patients was detected. In addition, our results have illustrated that QTD significantly increased as severity of CAD elevated (Fig. 1). However, no significant difference in QTD was found between those with three vessels disease and LMS disease.

Patients with CAD (one, two, three vessels or LMS disease) are further stratified according to their LV function (Table 3). LV dysfunction induced QTD significantly in patients with one, two vessels and LMS disease.

We noticed that the occurrence of Q wave MI among those with LV dysfunction was significantly higher than those with normal LV function in patients with one, two vessels and LMS disease.

If Gensini score is used to assess the severity of CAD (Fig.2), so the QTD is clearly raised as the score increased.

We also found that there was no significant difference in QTc interval when compare normal subjects to those with CAD, or among different groups of patients with CAD (Table 3).

In the current study, when patients with CAD are stratified according to LV function and involvement of proximal left anterior descending (LAD) artery (Table 4).

**Table 1. Characteristics of study population.**

| | Control group | IHD patients | P value |
|---|---|---|---|
| Number | 30 | 184 | |
| Age (year) | 51.5±11.2 | 54.75±9.19 | NS |
| Male gender (%) | 19(63.2%) | 158(85.87%) | <0.02 |
| Hypertension (%) | 12(40%) | 108(58.69%) | <0.05 |
| D.M(%) | 1(3.3%) | 66(35.87%) | <0.001 |
| Smoking (%) | 8(26.7) | 109(59.245) | <0.01 |

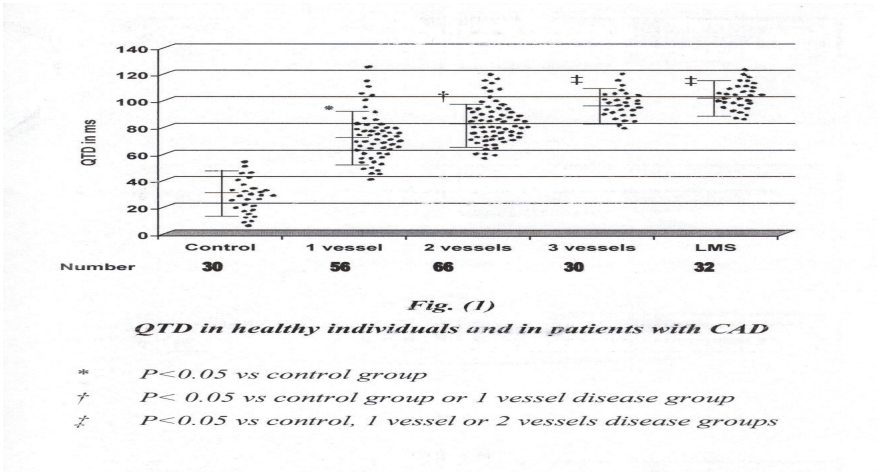


*Fig. (1)*
*QTD in healthy individuals and in patients with CAD*

* *P≤0.05 vs control group*
† *P≤ 0.05 vs control group or 1 vessel disease group*
‡ *P≤0.05 vs control, 1 vessel or 2 vessels disease groups*

**Fig 1: QTD in healthy individuals and in patients with CAD**

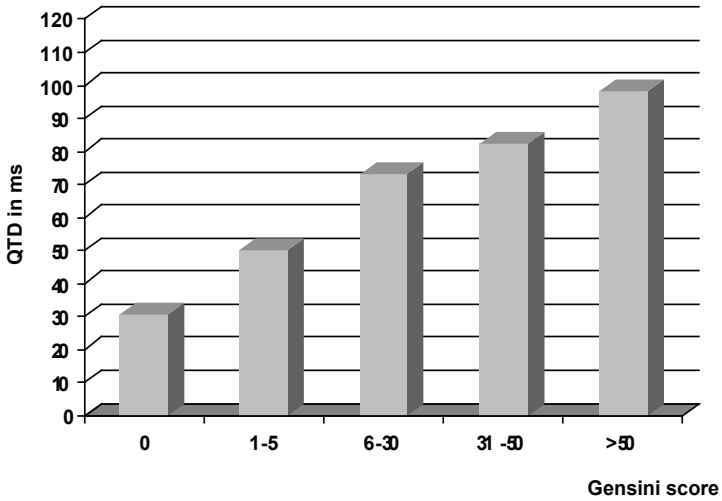


**Fig. 2 QTD data for patients classified using Gensini Score**

**Table 2. Characteristics of patients with IHD.**

| | 1 vessel | 2 vessels | 3 vessels | LMS |
|---|---|---|---|---|
| **number** | **56** | **66** | **30** | **32** |
| Age (years) | 50.05±8.91 * | 54.82±7.76PNS | †56.7±9.0* | 61±8.47 |
| Male gender(%) | 44(78.57)PNS | 60(90.91)PNS | 24(80)PNS | ‡30(93.75) |
| Hypertension(%) | 30(53.57)PNS | 35(53.03)* | **23(76.67) | **20(62.5) |
| D.M.(%) | 14(25)PNS | 20(30.3)* | **16(53.33)PNS | **16(50) |
| Smoking(%) | 29(51.79)PNS | 42(63.64)PNS | 14(46.67)* | †24(75) |
| Q-wave MI(%) | 28(50)PNS | 30(45.45) PNS | 14(46.67)PNS | ‡18(56.25) |
| LV dysfunction(%) | 14(25)PNS | 18(27.3)PNS | 2(6.7) * | ‡8(25) |

**Table 3. ECG variables of control group and patients with CAD.**

| | **1vessel** | **2 vessels** | **3 vessels** | **LMS** | **Normal** | ***stratified*** | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **EF>50** | **EF<50EF>50** | **EF<50EF>50** | **EF<50** | **EF>50** | **EF<50** | | | |
| Number | 30 | 42 | 14 | 48 | 18 | 28 | **2** | 24 | 8 |
| _Q-MI(%) | 0 | 17(40)* | 11(78.57) | 19(39.58)* | 11(61.6) | 12(42.86) | 2(100) | 10(41.66)* | 8(100) |
| QTc | 415.2? ±30.9 | 405.93 ±33.35? | 414.28 ? ±52.11 | 417.75 ±43.67 ? | 447.28 ? ±70.47 | 411.78 ±49.26 ? | 414.0 ±2.83 | 402.42 ±42.32 | 440.75 ±35.84 |
| _QTD | 30.67 ±16.39 | 65.62 ±22.93* | 84.57 ±28.52 | 77.17 ±20.61* | 89.77 ±29.26 | 95.71 ±11.36NS | 95 ±7.07 | 94.17 ±12.83* | 115.0 ±27.7* |

**Table 4. QTD and QTc in patients with CAD classified according to LV function and involvement of proximal LAD artery.**

| | **1 vessel** | **2 vessels** | **3 vessels** | | | |
|---|---|---|---|---|---|---|
| | +LAD | LAD+LAD | LAD+LAD | -LAD | | |
| **Good LV** | | | | | | |
| Number | 10 | 32 | 12 | 36 | 16 | 12 |
| QTc | 407.9 ±20.56 * | 405.3 ±36.74 | 431.58 ±39.83 * | 410.69 ±39.39 | 401.63 ±57.31 * | 429.08 ±36.4 |
| QTD | 74±20.65 * | 63 ±23.28 | 81.58 ±14.35 – * – | 75.7 ±22.31 | 95 ±8.94* – | 96.67 ±14.35 |
| **LV dysfunct.** | | | | | | |
| Number | 8 | 6 | 2 | 16 | 2 | 0 |
| QTc | 388.75 ±37.89 * | 448 ±51.93 | 329 ±1.41 ** | 462.06 ±59.41 | 414 ±2.38 | |
| QTD | 78.77 ±31.51* | 80.3 ±20.65 | 87 ±2.83 * – | 90.1 ±25.17 | 95 ±7.07 | |

** P <0.0 5*

*-LAD No proximal LAD critical lesion*

*+LAD Proximal LAD critical lesion*

## Discussion

Present study has appraised relationship between QTD and severity of CAD in patients with angina pectoris. Observations of our study have showed that hypertension, diabetes mellitus, smoking and male gender were more prevalent among patients with CAD in comparison to control group. This prevalence indicates the impact of these risk factors in increasing coronary atherosclerosis [11, 19].

Among patients with CAD, we found that those with more extensive disease tended to be older, with most common hypertension and diabetes mellitus. Previous study has revealed that prevalence and severity of coronary artery atherosclerosis increase dramatically with age advance [11]. Our interpretation is that may reflect the cumulative nature of atherogenesis [20]. In addition, it has been demonstrated that aging is associated with higher incidence of hypertension, diabetes mellitus, disturbed lipid profile and obesity [11].

We also found that QTD is significantly increased among patients with stable angina than healthy controls. In agreement with our observations, Tikiz et al [21] has showed that patients with single vessel disease had wider baseline QTD.

Numerous studies have evaluated QTD in patients with CAD during active ischemia either induced by atrial pacing [6], exercise test [23], spontaneous anginal episodes [23] or after acute MI [3].

Transient myocardial ischemia followed by reperfusion, or chronically ischemic and hypo perfused myocardium may result in increased production of superoxide and hydroxyl radicals[24], this leads to impaired sarcolemmal Na+, K+-ATPase and calcium-stimulated ATPase with resultant impaired excitation-contraction coupling and calcium overload which can also activate enzymes that causes further damage in the sarcolemma and sarcoplasmic reticulum[24]. Actually, these changes may persist after resolution of active ischemia [24].

In the current study, we evaluated the relationship between severity of CAD and QTD. We classified the patients into those with single, two, three vessels disease or left main stem disease, furthermore Gensini score was also used in order to getseverity assessment. We showed that QTD increased with more severe CAD, and patients with higher Gensini score had higher QTD. Patients with left main stem disease or three vessels disease had QTD higher than those with two vessels disease who in turn have higher QTD than those with one vessel disease.

Notably, the relationship between severity of CAD and QTD has been demonstrated in post MI patients [25].

This study also assessed the effect of LV dysfunction or proximal LAD artery involvement on QTD in patients with CAD.

QTD did not increase significantly as severity of LV dysfunction increased LV dysfunction in patients with CAD may be due to myocardial stunning, hibernation [24] or scar due to previous MI.

In patients with previous MI, infracted areas are associated with prolonged recovery times that, in the end, may lead to increased dispersion of repolarization compared with the base line state [24].

In TEAM-3 study [27] LV dysfunction was independently associated with increased QTD in patients with acute MI. However, Bodi et al [28] has revealed that QTD was not related to ejection fraction in patients within six months after an acute MI.

In fact, this contradictionsmyy resulted from the differences in patients characteristics in diverse studies, as the study by Bodi and his Colleagues [28] has evaluated the effect of LV dysfunction on QTD in patients who have MI only, whereas the present study involves those with previous MI and those without history of MI.

The absence of significant increment of QTD in patients.

LAD artery supplies anterosuperior two thirds and the entire apical one third of ventricular septum, anterior LV free wall and the medial third of the anterior right ventricular free wall [33]. So critical stenosis in the proximal segment of this artery jeopardizes substantial area of myocardium.

Previously, Tikiz et al [21] showed that there is no relation between QTD and the pattern of CAD or the lesion localization in 119 patients with single vessel disease.

In our study, we used multiple regression analysis to identify variables independently affecting QTD. We included six variables: Age, hypertension, D.M., previous MI, severity of CAD and LV dysfunction.

Among these features, severity of CAD, LV dysfunction and previous MI are independently associated with increased QTD.

The impact of MI on QTD has been demonstrated also by Van de Loo et al [3] and Higham et al [29] who have revealed that QTD was higher in patients with acute MI than in those with unstable angina.

## Conclusions

QTD is a simple ECG parameter, (which could be calculated easily at bed side) is significantly higher in patients with IHD in comparison to the normal persons and it increases with increased severity of CAD.

**Source of Funding-** Self

**Ethical Clearance** – Not required

**Conflict of Interest:** None

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