The Association of QT Dispersion and QT Dispersion Ratio with Extent and Severity of Coronary Artery Disease

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Background: Although prolongation of the QT intervals in acute ischemic conditions, such as acute myocardial infarction, intracoronary balloon inflation, and exercise induced ischemia, has been shown, association of rest QT intervals with extent and severity of stable coronary artery disease (CAD) has not been assessed so far. The effects of extent and severity of stable CAD on rest QT interval were analyzed in this study.

Methods: Rest 12-lead electrocardiograms (ECG) were recorded in 162 clinically stable subjects undergoing coronary angiography before the angiography for measurement of corrected QT dispersion (cQTd) and the QT dispersion ratio (QTdR) defined as QT dispersion divided by cycle length and expressed as a percentage. Angiographic "vessel score," "diffuse score," and "Gensini score" were used to evaluate the extent and severity of coronary atherosclerosis. Subjects were grouped as follows: those with normal angiogram (Group 1), those with insignificant (<50%) coronary stenosis (Group 2), and those with 1- (Group 3), 2- (Group 4), or 3-vessel disease (Group 5).

Results: cQTd and QTdR were higher in Group 3 compared with Group 1 ($P < 0.001$ and $P = 0.001$, respectively), in Group 4 compared with Group 1 ($P < 0.001$ for both) and Group 2 ($P = 0.001$ and $P = 0.003$, respectively), and in Group 5 compared with Group 1 ($P < 0.001$ for both) and Group 2 ($P < 0.001$ and $P = 0.003$, respectively). cQTd and QTdR were positively correlated with the vessel score ($r = 0.422$, $P < 0.001$; $r = 0.358$, $P < 0.001$, respectively), diffuse score ($r = 0.401$, $P < 0.001$; $r = 0.357$, $P < 0.001$, respectively) and Gensini score ($r = 0.378$, $P < 0.001$; $r = 0.373$, $P < 0.001$, respectively). In multiple linear regression analyses, cQTd was found to be independently associated only with diffuse score ($\beta = 0.325$, $P = 0.038$). Also, QTdR was independently associated with diffuse score ($\beta = 0.416$, $P = 0.006$) and Gensini score ($\beta = 0.374$, $P = 0.011$).

Conclusions: Rest cQTd and QTdR are increased, and related to the extent and severity of coronary atherosclerosis in patients with stable CAD.

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QT dispersion; QT dispersion ratio; coronary; stenosis; atherosclerosis; angiography

Ventricular repolarization is a complex electrical phenomenon. Direct repolarization measurements obtained from epicardial monophasic action potentials and body surface mapping have been correlated with QT interval on the surface electrocardiogram (ECG).^{1,2} Simple measurements of QT interval are essential in monitoring repolarization changes. QT interval dispersion (QTd), defined as maximal minus minimal QT interval, has emerged as a noninvasive measurement for quantifying the degree of myocardial repolarization inhomogeneity.³⁻⁵ Interlead variations in QT interval reflect regional variations in ventricular repolarization,⁶⁻⁸ and increased dispersion of ventricular recovery

time is believed to provide a substrate that supports serious ventricular arrhythmias.⁹⁻¹¹ Furthermore, QTd ratio (QTdR), which is defined as QTd divided by cycle length, has been shown to be more predictive than QTd for ventricular arrhythmias.¹²

Myocardial regional ischemia may be associated with abnormalities of cardiac repolarization.^{9,13} The most pronounced electrophysiological effect of myocardial ischemia is shortening of refractoriness and slowing of conduction.⁹ It has been reported that acute myocardial ischemia induced by pacing or exercise is associated with increased QTd in patients with coronary artery disease (CAD).¹⁴⁻¹⁷ Also, prolonged QTd in patients

with syndrome X,¹⁸ vasospastic angina,¹⁹ unstable angina,⁶ myocardial infarction,^{10,12,20,21} and undergoing PTCA²² have been shown. However, no previous studies have examined rest QT intervals in patients with chronic stable CAD and their relationships with extent and severity of coronary atherosclerosis.

We hypothesized that stable CAD-related myocardial ischemia could change QT interval regionally in the area of ischemia and give rise to an increase in QTd and QTdR in the 12-lead ECG, and these changes are related to extent and severity of coronary atherosclerosis.

METHODS

Study Subjects

In all, 162 consecutive patients were collected prospectively from patients who underwent elective diagnostic coronary angiography at Harran University Hospital between November 2003 and May 2004. Clinical indication for coronary angiography was suspicion of CAD in all patients (stable effort angina or positive exercise stress test). Subjects were excluded from the study if they had acute coronary syndrome, angina pectoris even if stable within 24 hours before procedure, congenital long QT syndrome, atrial fibrillation, bundle-branch blocks, intraventricular conduction defects, atrioventricular block, sinus node dysfunction, pacemaker, cardiomyopathy, congestive heart failure and history of myocardial infarction, coronary artery bypass surgery, or coronary angioplasty. None of the patients were taking drugs, such as antiarrhythmic agents, digitalis, beta-blockers, nitrates, or calcium antagonists, which could affect the QT interval or autonomic tone.

Electrocardiographic Measurements

A 12-lead surface ECG was obtained from all subjects in the supine position immediately before the coronary angiography by using Hewlett-Packard Electrocardiograph Sanborn Series (Chine) machine. All patients were breathing freely but not allowed to speak during the ECG recordings. The ECG were recorded at a paper speed of 50 mm/s. All measurements were made by one observer who was not aware of the patients' characteristics. The QT interval was measured manually at each lead by means of a method previously described.^{12,23} The QT interval was measured in each lead from

the onset of QRS to the end of the T wave. The end of the T wave was defined as return to the TP baseline. When a U wave interrupted the T wave before return to the baseline, the QT interval was measured to the nadir of the curve between the T and U waves. Biphasic T waves were measured to the time of final return to baseline. If the T wave could not be reliably determined or if it had very low amplitude, QT measurements were not obtained and these leads were excluded from the analysis. The QT interval was measurable in at least 9 out of 12 leads (mean 10.85 ± 0.82)²⁴ in each subject. The mean QT interval was calculated as the average of all measurable leads. QTd was defined as the difference between the maximum and minimum QT intervals ($QTd = QT_{max} - QT_{min}$). The QT intervals and QTd were rate-corrected with a modification of Bazett's formula as follows: $cQT_{max} = QT_{max}/\text{square root of the R-R interval}$, $cQT_{min} = QT_{min}/\text{square root of the R-R interval}$, and corrected QT dispersion ($cQTd$) = $cQT_{max} - cQT_{min}$.²⁵ The QTdR was obtained by the formula of $(QTd/R-R\text{-ms}) \times 100$.¹² Electrocardiographic measurements (R-R interval, QT_{max} , QT_{min}) of 20 of the subjects were performed in duplicate on 2 separate days and by two independent investigators unaware of clinical and angiographic data. Linear regression analysis yielded minimal intraobserver ($r = 0.96$, $P < 0.001$) and interobserver ($r = 0.94$, $P < 0.001$) variation.

Echocardiographic Assessment

Echocardiographic examination was performed in all study subjects within 48 hours before coronary angiography. A commercially available system (Aloka Prosound SSD 5000 machine with a 3-MHz transducer) was used. Measurements were made during normal breathing at end-expiration. M mode echocardiographic measurements were obtained on the basis of the standards of the American Society of Echocardiography.²⁶ Left ventricular end-systolic and end-diastolic diameters, end-diastolic interventricular septal thickness, and end-diastolic LV posterior wall thickness were measured from the left parasternal short- and long-axis views. Left ventricular ejection fraction was obtained with Simpson's biplane methods.²⁷ All echocardiographic measurements were calculated from an average of three consecutive cardiac cycles. Echocardiographic left ventricular mass was determined by using the corrected formula

proposed by Devereux et al.²⁸ Left ventricular mass was indexed by body surface area (g/m^2).

Coronary Angiographic Scoring

Coronary angiography was performed by the femoral approach with 7Fr diagnostic catheters. Images were recorded in multiple projections for left and right coronary arteries on a digital system. The interpretation of the coronary angiograms was made by two cardiologists who were blinded for the characteristics of the patients during the interpretation. The CAD was evaluated by vessel score.²⁹ Vessel score was the number of vessels with a significant stenosis ($\geq 50\%$ reduction in lumen diameter). Scores ranged from 0 to 3, depending on the number of vessels involved. Left main artery stenosis was scored as 1-vessel disease. The intra- and interobserver correlations in this scoring system were >0.95 . In addition to the vessel score, we also used a diffuse score developed by Negri et al.³⁰ and modified by Birnie et al.³¹ In brief, the coronary circulation is divided into 15 segments, and 8 of them are classified as first-order segments: proximal and middle right coronary artery, left main coronary artery, proximal, middle, and distal left anterior descending artery, and proximal and middle circumflex artery. There are 7 second-order segments: distal right coronary artery, posterior descending branch, distal circumflex artery, obtuse marginal branch, posterolateral branch of circumflex artery, and the first 2 diagonal branches of the left anterior descending artery. The first-order segments receive a score of 1 if there is any evidence of atherosclerosis, and the second-order segments scored 0.5. The overall diffuse score is the sum of the individual segment scores and the maximum score is 11.5. The intra- and interobserver correlation were 0.94 and 0.91, respectively. The severity of CAD was assessed by using the Gensini score,³² which grades narrowing of the lumens of the coronary arteries as 1 for 1–25% narrowing, 2 for 26–50% narrowing, 4 for 51–75% narrowing, 8 for 76–90% narrowing, 16 for 91–99% narrowing, and 32 for total occlusion. This score is then multiplied by a factor that takes into account the importance of the lesion's position in the coronary arterial tree, for example, 5 for the left main coronary artery, 2.5 for the proximal left anterior descending coronary artery and proximal left circumflex coronary artery (3.5 if left circumflex coronary artery is dominant), 1.5 for the mid-region of the left anterior descending coronary

artery, 1 for the distal left anterior descending coronary artery, the first diagonal, the proximal, mid- and distal-region of the right coronary artery, the postero-descending, the mid- and distal-region of the left circumflex coronary artery (2 for both of them if left circumflex coronary artery is dominant) and the obtus margin, and 0.5 for the second diagonal and the posterolateral branch. The Gensini score was expressed as the sum of the scores for the all coronary arteries. The intra- and interobserver correlation were 0.92 and 0.89, respectively.

Statistical Analyses

Results are presented as mean $\pm$ SD or frequency expressed as a percent. Categorical variables were compared using chi-square test. Comparison among multiple groups was performed by one-way analysis of variance (ANOVA) with Bonferroni post hoc test for continuous variables. Associations of QT parameters with angiographic scores were assessed by Pearson correlation coefficient. Furthermore, associations of cQTd and QTdR with clinical, echocardiographic, and angiographic variables were also assessed by Pearson correlation coefficient. Independent predictors of cQTd and QTdR were determined by multiple linear regression analysis with candidate variables added to a model containing cQTd or QTdR as the dependent variable, and parameters that were found to be related with cQTd or QTdR in bivariate correlation as covariates. Standardized beta regression coefficients and their significance from multiple linear regression analysis are reported. A 2-tailed P value <0.05 was considered statistically significant.

RESULT

Subjects

According to coronary angiographic result, the patients were divided into 5 groups: Group 1, 69 patients who had normal coronary angiogram; Group 2, 24 patients who had insignificant ($<50\%$) coronary stenosis; Group 3, 25 patients who had 1-vessel disease ($\geq 50\%$ stenosis in one major epicardial coronary artery); Group 4, 28 patients who had 2-vessel disease ($\geq 50\%$ stenosis in two major epicardial coronary artery); and Group 5, 16 patients who had 3-vessel disease ($\geq 50\%$ stenosis in three major epicardial coronary artery). Clinical characteristics of the groups are shown in Table 1. Age, smoking, and frequency of male gender were

Table 1. Clinical, Echocardiographic and Angiographic Characteristics of the Groups

	Group 1 (n = 69)	Group 2 (n = 24)	Group 3 (n = 25)	Group 4 (n = 28)	Group 5 (n = 16)
Age (year)	51 ± 9 ^a	58 ± 9	59 ± 10	56 ± 9	57 ± 9
Male gender (%) ^b	27 (39)	12 (50)	17 (68)	18 (64)	14 (88)
Hypertension (%)	34 (49)	15 (63)	13 (52)	15 (54)	10 (63)
Diabetes (%)	9 (13)	3 (13)	4 (16)	5 (18)	3 (19)
Smoking (%) ^c	24 (35)	7 (29)	16 (64)	17 (61)	10 (63)
LVEDS (mm)	30 ± 5	29 ± 6	35 ± 9	34 ± 8	41 ± 10 ^d
LVEDD (mm)	47 ± 6	47 ± 6	51 ± 9	50 ± 7	54 ± 8 ^e
EF (%)	64 ± 7 ^f	62 ± 8 ^g	54 ± 14	54 ± 13	50 ± 14
LVMI (g/m ²)	116 ± 43	128 ± 47	139 ± 42	143 ± 38	146 ± 27
Diffuse score	–	1.7 ± 0.9 ^h	3.3 ± 1.4 ⁱ	4.4 ± 1.6 ^j	5.9 ± 1.5
Gensini score	–	4 ± 2 ^h	31 ± 23 ^h	64 ± 39 ^k	89 ± 40

EF = ejection fraction; LVEDD = left ventricular end-diastolic diameter; LVEDS = Left ventricular end-systolic diameter; LVMI = left ventricular mass index.

^aP < 0.05 versus all the other groups. ^bChi-square P = 0.002. ^cChi-square P = 0.014. ^dP < 0.007 versus Group 1 and Group 2.

^eP < 0.03 versus Group 1 and Group 2. ^fP = 0.001 versus Group 3 and Group 4, and P < 0.001 versus Group 5. ^gP = 0.022 versus Group 5. ^hP < 0.001 versus for the other groups. ⁱP < 0.001 versus Group 2 and Group 5, and P = 0.007 versus Group 4.

^jP < 0.001 versus Group 5. ^kP = 0.004 versus Group 5.

different, but frequencies of diabetes and hypertension were not different among groups.

among Group 3, Group 4, and Group 5. QTd was higher in Group 5 than in Group 3.

QT Parameters

Electrocardiographic results of the groups are shown in Table 2. There were no significant differences in R-R interval, QT_{min}, and cQT_{min} among groups. QT_{max} and cQT_{max} were higher in Group 5 compared with Group 1. QTd, cQTd, and QTdR were higher in Group 3 compared with Group 1, and in both Group 4 and Group 5 compared with both Group 1 and Group 2. Except for QTd, there were no significant differences in QT parameters

Correlation between QT Parameters and Angiographic Scores

In bivariate correlation that was performed by excluding the 69 subjects who had normal coronary angiogram, it was found that cQT_{max}, cQTd, and QTdR were significantly correlated with vessel score, diffuse score, and Gensini score (Table 3). cQT_{min} was not related to angiographic scores.

Presence of hypertension, left ventricular end-systolic diameter, left ventricular end-diastolic diameter, ejection fraction, left ventricular mass

Table 2. Electrocardiographic Results of the Groups

	Group 1 (n = 69)	Group 2 (n = 24)	Group 3 (n = 25)	Group 4 (n = 28)	Group 5 (n = 16)
tRR interval (ms)	781 ± 157	830 ± 153	795 ± 157	807 ± 180	853 ± 193
QT maximum (ms)	396 ± 37	410 ± 33	407 ± 43	416 ± 33	442 ± 35 ^a
cQT maximum (ms)	452 ± 33	453 ± 32	460 ± 46	470 ± 53	485 ± 40 ^b
QT minimum (ms)	366 ± 35	374 ± 32	362 ± 32	366 ± 32	386 ± 36
cQT minimum (ms)	417 ± 29	413 ± 28	410 ± 35	414 ± 44	424 ± 37
QT dispersion (ms)	30 ± 9	36 ± 12	45 ± 19 ^a	49 ± 10 ^c	56 ± 9 ^d
cQT dispersion (ms)	34 ± 11	40 ± 15	51 ± 20 ^a	56 ± 15 ^c	61 ± 12 ^e
QT dispersion ratio (%)	4 ± 1.5	4.5 ± 1.9	5.8 ± 2.3 ^f	6.5 ± 2.5 ^g	6.9 ± 2.0 ^g

^aP < 0.001 versus Group 1. ^bP = 0.033 versus Group 1. ^cP < 0.001 versus Group 1, and P = 0.001 versus Group 2. ^dP < 0.001 versus Group 1 and Group 2, and P = 0.045 versus Group 3. ^eP < 0.001 versus Group 1 and Group 2. ^fP = 0.001 versus Group 1. ^gP < 0.001 versus Group 1, and P = 0.003 versus Group 2.

Table 3. The Associations between QT Parameters and Angiographic Characteristics in Patients with Coronary Atherosclerosis (n = 93)

	Vessel Score		Diffuse Score		Gensini Score	
	R	P	R	P	R	P
cQT maximum	0.237	0.022	0.218	0.036	0.272	0.008
cQT minimum	0.090	0.388	0.078	0.459	0.156	0.136
cQT dispersion	0.422	<0.001	0.401	<0.001	0.378	<0.001
QT dispersion ratio	0.358	<0.001	0.357	<0.001	0.373	<0.001

index, vessel score, diffuse score, and Gensini score, which were correlated with cQTd in bivariate correlation, were included to the multiple linear regression analysis. cQTd was independently associated only with diffuse score ($\beta = 0.325$, $P = 0.038$) (Table 4). Also, presence of hypertension, left ventricular end-systolic diameter, ejection fraction, left ventricular mass index, vessel score, diffuse score, and Gensini score were correlated with QTdR in bivariate correlation. However, in multiple linear regression analysis, QTdR was independently associated only with diffuse score ($\beta = 0.416$, $P = 0.006$) and Gensini score ($\beta = 0.374$, $P = 0.011$) (Table 4). The graphs of the correlations of cQTd and QTdR with vessel score, diffuse score, and Gensini scores are shown in Figures 1 and 2.

DISCUSSION

The major findings of this study are (1) rest cQTd and QTdR are significantly increased in patients with stable CAD compared with those without; (2) in patients with coronary atherosclerosis, cQTd and QTdR are associated with extent and severity of the disease.

The interval between the onset of the Q wave and the end of the T wave of the ECG is thought to represent the time between depolarization of cells by an activating wave front and electrical recovery or repolarization. The lead of a standard ECG with the shortest QT interval indicates the area of earliest repolarization, whereas the lead with the longest QT interval represents the area of the ventricular myocardium that is last to repolarize. The difference between them is known as the QTd, a marker of the overall variability of ventricular repolarization. It has been proposed as a marker of heterogeneous repolarization and electrical instability.^{33–35} Therefore, the greater the QTd is the greater the variability in the timing of electrical recovery within

the heart. This information is of potential clinical value because experimental work has identified enhanced dispersion of repolarization as an important factor in the mechanisms underlying serious and fatal arrhythmias, particularly in the presence of cardiac ischemia.³⁶

Different studies have shown that QTd is abnormally increased in patients with acute or remote myocardial infarction, acute coronary syndrome, vasospastic angina, syndrome X, exercise induced myocardial ischemia, heart failure and ventricular hypertrophy, and during balloon angioplasty.^{15–22,37–45} Also, increased QTd is associated with malignant ventricular arrhythmias^{9–11,46} and sudden cardiac death.^{37–39,41,42,47} In a previous study of patients with 3-vessel disease,⁴³ it has been demonstrated that the severity or extent of myocardial ischemia induced by using atrial pacing was related to the degree of induced changes of the QTd. Changes in QTd associated with acute ischemic conditions raising the possibility that the acute changes in QTd related to ischemic episodes that are important. However, it has not been reported an association between rest QT parameters, and extent and severity of CAD so far. In our study, it was first described that the extent and severity of the CAD was closely related to the rest cQTd and QTdR, which are markers of heterogeneous repolarization and electrical instability within the myocardium.

The QTd and QTdR in patients with significant CAD were higher than those with normal coronary angiogram or insignificant CAD. Our results are not consistent with the findings by Sporton et al.¹⁴ In their study, QT parameters were not different at rest between controls and patients with CAD. Difference between the groups was observed only during ischemia induced by incremental atrial pacing. The differences between studies may be attributable to the differences in patients'

Table 4. Bivariate and Multivariate Relationships of the cQTd and QTdR to Clinical, Echocardiographic, and Angiographic Variables in Patients with Coronary Atherosclerosis (n = 93)

	cQT Dispersion				QT Dispersion Ratio			
	Pearson's Correlation		Standardized β Regression		Pearson's Correlation		Standardized β Regression	
	Coefficient	P value	Coefficients	P value ^a	Coefficient	P value	Coefficients ^a	P value
Age	0.102	0.33	—	—	0.032	0.757	—	—
Male gender	0.018	0.864	—	—	0.034	0.748	—	—
Hypertension	0.265	0.038	0.282	0.473	0.198	0.037	0.216	0.211
Diabetes	0.066	0.549	—	—	0.078	0.474	—	—
Smoking	-0.055	0.62	—	—	-0.036	0.746	—	—
LVESD	0.243	0.047	0.196	0.369	0.186	0.041	0.152	0.353
LVEDD	0.240	0.033	0.093	0.432	0.106	0.093	—	—
EF	-0.305	0.006	0.178	0.421	-0.324	0.004	0.247	0.067
LVMl	0.261	0.043	0.294	0.288	0.296	0.013	0.147	0.672
Vessel score	0.422	<0.001	0.285	0.113	0.358	<0.001	0.226	0.162
Diffuse score	0.401	<0.001	0.325	0.038	0.357	<0.001	0.416	0.006
Gensini score	0.378	<0.001	0.251	0.087	0.373	<0.001	0.374	0.011

^aFrom multiple linear regression.
Abbreviations as in Table 1.

characteristics. Furthermore, the number of patients in their study was too small. On the other hand, in several previous studies, it has been demonstrated that rest QT measurements were different between patients with CAD and those without. Stoletniy and Pai¹⁵ demonstrated that patients with significant CAD had wider rest cQTd compared with patients who had low probability (<5%) of CAD. In another study by Stoletniy and Pai,⁴⁴ the baseline QTd in patients with CAD was longer than those without. Likewise, in the study by Lowe et al., higher QTd at rest in patients with CAD compared with those without was reported.⁴⁸ However, in all these studies, association of extent and severity of the disease with rest QT parameters was not reported. In this aspect, a further importance of our study was the demonstration of this association.

Regional differences of repolarization mainly determine QTd. In patients with CAD, increased resting dispersion of ventricular repolarization may arise from regional myocardial ischemia, because ventricular repolarization may be more sensitive to ischemia than other myocardial functions. Hence, it may be suggested that the ischemic areas and/or regional fibrosis, which is also expected in chronic ischemia,⁴⁹ can cause heterogeneous repolarization and electrical instability within the myocardium, and therefore increased QTd and QTdR. The increase in QTd due to the effect of CAD is thought to be parallel to the degree of ischemia,^{44,45} and to result partially from an impaired response of the ischemic myocardium to catecholamines or to an abnormal flux of calcium ion.⁵⁰ In patients with extent and severe CAD, myocardial ischemia is a process affecting greater areas of the ventricular myocardium. Thus, the severity of localized ischemia would have a predominant influence on ischemia-modulated QTd even if at rest. Most of the fatal arrhythmias in patients with CAD appear to be unrelated to acute coronary occlusion,⁵¹ it is of particular relevance that QTd and QTdR were found to be increased at rest in patients with significant CAD probably due to ischemic areas, and these parameters were related to extent and severity of the disease. This finding is of potential clinical value because increased QTd and QTdR could be usable in the assessment of prognosis in patients with CAD. In our study, the more extent and severe CAD was related to higher cQTd and QTdR, probably because of larger ischemic areas. It may be suggested that observed changes of QT parameters in the patient groups are related

Figure 1. Scatter plots of correlation between (A) cQTd and vessel score, (B) cQTd and diffuse score, and (C) cQTd and Gensini score. cQTd, rate corrected QT dispersion.

to left ventricular dysfunction rather than coronary atherosclerosis and ischemia. But, in regression analyses, it was shown that the associations of cQTd and QTdR with extent and severity of coronary atherosclerosis were independent from

Figure 2. Scatter plots of correlation between (A) QTdR and vessel score, (B) QTdR and diffuse score, and (C) QTdR and Gensini score. QTdR, QT dispersion ratio = (QT dispersion/RR interval) $\times$ 100.

left ventricular ejection fraction as well as from the other clinical and echocardiographic parameters that are enrolled to the model. Although differences in cQTd and QTdR among Group 3, Group 4, and Group 5 were not statistically significant

probably because of the limited number of patients, the association of cQTd with diffuse score, and of QTdR with diffuse and Gensini score showed that ventricular repolarization inhomogeneity was independently correlated with extent and severity of CAD. Apart from this, increased cQTd and QTdR may simply be a marker of other process, such as the presence of a critical area of myocardium in jeopardy in patients with CAD without prior myocardial infarction. This point should also be assessed in the future.

LIMITATIONS

In translating our results into clinical practice, several limitations of this study must be kept in mind. First, manual measurement may be subject to errors. However, automatic techniques are less likely in practice to be able to cope with morphological and noise factors, particularly at low T wave amplitudes as often encountered in patients with CAD. Before methodological problems are resolved, many previous studies have to rely on the classical ECG intervals measured manually with all its limitations. Second, in some patients, extensive CAD disease may be present without overt evidence of ischemia. The complexities of local patterns of ischemia and their contribution to the overall dispersion of repolarization in patients need to be explored systematically. Further studies which clarify these issues may lead to useful applications of QTd in the risk stratification of patients with CAD. Third, although the exact relation between the heart rate and the dispersion of recovery times is still an unresolved issue, QT intervals were corrected for heart rate in the current study, since many studies, including large prospective ones such as the Rotterdam⁵² and the Strong Heart Study⁵³ continue to assess the "corrected" QT dispersion. Fourth, the relationships of the increased cQTd and QTdR in patients with stable CAD with the prognosis of these patients remain to be determined. Also, we did not measure the JT interval, which really reflects ventricular repolarization. QT or cQT interval is dependent on ventricular conduction time as well as ventricular repolarization. However, no significant variation in QRS interval was noted in our patients. Finally, all electrocardiographic leads were not recorded simultaneously, which affects the QT interval and QTd measurements because of variable R-R intervals.

However, the results of QT corrected for heart rate were reported.

CONCLUSIONS

cQTd and QTdR were increased, and correlated with extent and severity of CAD in patients with stable CAD, indicating that patients with extent and severe CAD had greater inhomogeneity of ventricular refractoriness, which may predispose them to life-threatening arrhythmias, even in the absence of acute ischemia. The prognostic implications should be evaluated in prospective follow-up studies.

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