QT Dispersion Increases with Aging

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Background: Age-related changes in cardiovascular system are well-known. Arrhythmias in elderly patients constitute most of the urgencies, consultations, or hospitalizations. QT dispersion (QTd) is a simple noninvasive arrhythmogenic marker to demonstrate the electrical instability of the heart. The aim of this study was to investigate how QTd changes with increasing age by calculating the QTd in the elderly and younger subjects.

Methods: One hundred and forty-six consecutive subjects (62 males and 84 females; age range: 18–82 years) were enrolled in the study. Sixty-seven of the subjects were 65 years and over (mean age, 70 ± 4), 79 were younger than 65 (mean age, 37 ± 11). A 12-lead ECG was recorded. The longest and the shortest QT intervals were measured manually on these ECG recordings. QTd was calculated from the formula, $QTd = QT_{max} - QT_{min}$.

Results: Demographic features were similar between the two groups. QTd of the elderly group was found to be significantly higher than the younger group (35.6 ± 15.6 in elderly, 24.2 ± 12.4 in younger group, $P < 0.001$). A positive relationship was found between QTd and age ($r = 0.415$, $P < 0.001$). QTd was greater in female than in male (31.9 ± 16.7 ms vs 26.0 ± 11.3 ms, respectively, $P = 0.018$).

Conclusions: Our study shows that QTd increases with advancing age. We think that long-term follow-up of these patients would be useful to show if there is any relationship between the clinical outcomes and the increase in QTd.

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Age-related changes in cardiovascular system are well-known. Significant changes have been noted in the structure and function of the cardiovascular system in elderly people, which are considered to be the result of aging. These changes can be regarded as either adaptive or early preclinical disease, but they occur in the absence of clinically manifest dysfunction.¹ Arrhythmias in elderly patients constitute most of the urgencies, consultations, or hospitalizations.² QT dispersion (QTd) is a simple noninvasive arrhythmogenic marker which is defined as the difference between the maximum and minimum QT interval in the standard ECG. It reflects nonhomogeneous recovery of excitability or heterogeneity of ventricular repolarization.^{3,4}

The aim of this study was to investigate how QTd changes with increasing age by calculating the QTd in the elderly and younger subjects.

METHODS

One hundred and forty-six consecutive subjects (62 males and 84 females; age range: 18–82 years) who were seen at the outpatient clinic of the Hacettepe University, Faculty of Medicine, Department of Cardiology and Division of Geriatric Medicine, between 2003 and 2004 were selected for this study. The subjects were divided into two groups according to their age: (a) group 1: those who are over 65 years (67 subjects, mean age: 70.5

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Table 1. Clinical Characteristics of Subjects

	Group 1 (n = 67) (Younger Subjects)	Group 2 (n = 79) (Elderly Subjects)	P Value
Age (years)	37.9 ± 11.5	70.5 ± 4.5	<0.001
Gender (females/males)	45/34	39/28	NS
Systolic blood pressure (mmHg)	123 ± 11	122 ± 9	NS
Diastolic blood pressure (mmHg)	81 ± 9	79 ± 8	NS
Heart rate (beats/min)	73 ± 2	75 ± 3	NS
Smokers	11%	12%	NS
High density lipoprotein (mg/dL)	44 ± 7	45 ± 6	NS
Low density lipoprotein (mg/dL)	129 ± 9	127 ± 10	NS
Diabetes mellitus	5%	6%	NS
Hypertension	15%	15%	NS

NS = nonsignificant.

± 4.5, range: 65–82 years), (b) group 2: those who are younger than 65 years (79 subjects, mean age: 37.9 ± 11.5, range: 18–54 years). All subjects had normal cardiac physical examination findings. The inclusion criteria were: (1) no drugs that would potentially influence QT duration; (2) no history and laboratory findings of ischemic heart disease, congestive heart failure, atrial fibrillation, bundle branch block, or abnormal serum electrolytes; and (3) a good quality ECG recording for measurement of the QT interval. Subjects were excluded from the study if the end of the T wave of their ECG could not be determined reliably.

The patients who had risk factors for coronary artery disease underwent a treadmill exercise test with Bruce protocol. The patients who had positive exercise test were also excluded from the study. Transthoracic echocardiographic examination was performed to all subjects by using a System Five (GE Vingmed Ultrasound, Horten, Norway) cardiac ultrasound scanner and 2.5–3.5 MHz transducers to rule out severe heart failure and cardiac valvular disease.

Electrocardiographic Measurements

A 12-lead ECG was recorded in all patients at a paper speed of 25 mm/s. None of the patients were taking any drugs which potentially may alter the results of QT analysis. QT intervals were measured manually from the onset of QRS to end of the T wave, defined as a return to the T–P baseline. If U waves were present, subjects were excluded from the study. Four consecutive cycles in each of the 12 leads were measured. All ECG measurements were made by two blinded (without knowledge of age,

gender, clinical status) experienced cardiologists. From the four cycles, maximum QT and minimum QT were calculated. QTd was calculated from the formula, $QTd = QT_{max} - QT_{min}$.⁵ Blinded inter-observer and intraobserver reproducibility of measurement were evaluated, and comparison revealed a Spearman correlation coefficient of 0.92 and 0.94, respectively.

In this study we did not calculate corrected QTd, because it has been shown that a rate correction of parameters of dispersion of repolarization is probably unnecessary and may even distort the values and predictive value of QTd.^{6,7}

Statistical Analyses

Data of numeric values are reported as mean ± standard deviation. Categorical variables are

Figure 1. Linear regression curve of QTd and age.

Table 2. QT Length and QT Dispersion

	Young	Elderly	P Value
QT max (ms) (mean $\pm$ SD)	387.6 $\pm$ 23.9	400.8 $\pm$ 30.1	0.01
QT min (ms) (mean $\pm$ SD)	362.5 $\pm$ 23.5	364.9 $\pm$ 30.2	0.79
QT dispersion (ms) (mean $\pm$ SD)	24.2 $\pm$ 12.4	35.6 $\pm$ 15.3	<0.001

reported in percentages. The Pearson chi-square test was used to compare categorical variables. Systolic blood pressure, diastolic blood pressure, heart rate, low density lipoprotein (LDL), and high density lipoprotein (HDL) levels distribution between groups were tested by using one-way analysis of variance method (ANOVA). Gender, smoking status, diabetes, and hypertension ratio distribution between groups were tested by using Pearson chi-square test. Means were compared by ANOVA. The relationship between numeric QTd data and age was tested using one-way ANOVA. The significance of correlations between the QTd data and age was assessed by Pearson correlation analysis. SPSS for Windows version 10.0 statistical package was used.

RESULTS

We studied 67 elderly and 79 younger subjects. In the elderly and younger groups, mean age were 70.5 ± 4.5 and 37.9 ± 11.5 , respectively ($P < 0.001$). Baseline characteristics of the elderly and younger groups are shown in Table 1. There were no significant differences with respect to gender distribution, systolic blood pressure, diastolic blood pressure, heart rate, smoking status, LDL and HDL levels, diabetes, and hypertension ratio. No subject had positive exercise test. Transthoracic echocardiography revealed that none of the elderly and the younger age group of subjects had heart valve disease and left ventricular dysfunction.

We found that QTd was significantly greater in the elderly group than in the younger group (35.6 ± 15.6 ms vs 24.2 ± 12.4 ms, respectively, $P < 0.001$). A positive relationship was found between QTd and age ($r = 0.415$, $P < 0.001$). Figure 1 shows the linear regression curve of QTd and age. QTmax was found to be greater in the elderly group than in the younger group (400.8 ± 30.1 ms vs 387.6 ± 23.9 ms, respectively, $P = 0.01$). The minimum–maximum values of QT interval are given in Table 2. There was no correlation between the QTd and baseline characteristics of the subjects except gender. QTd

was greater in female than in male (31.9 ± 16.7 ms vs 26.0 ± 11.3 ms, respectively, $P = 0.018$). We analyzed QTd in the elderly and the younger groups with respect to sex and we found that QTd was greater in female than in male in the elderly group (39.0 ± 16.5 ms vs 31.0 ± 12.7 ms, respectively, $P = 0.037$; Fig. 2). There was no difference in QTd between female and male in the younger group.

DISCUSSION

Our data showed an increased QTd with aging. QTd reflects increased heterogeneity of repolarization and it is associated with increased risk of ventricular tachyarrhythmias.⁸ QTd has been demonstrated to be increased in several cardiovascular conditions such as coronary artery disease, congestive heart failure, and cardiomyopathies.^{9,10}

Age-related changes of QTd have been reported in some studies. Savelieva et al.¹¹ showed that QTd was increasing with aging on healthy subjects. Macfarlane et al.¹² found no significant age differences in QTd. Consequently, data about age-related changes of QTd remain controversial.

There are some explanations for increased QTd with advanced aging. One cause of increased QTd may be related to myocardial fibrosis, which may prolong the ventricular recovery time or increase its dispersion. Myocardial fibrosis is one of the consequences of aging,^{13,14} together with a reduction

Figure 2. Mean QT dispersion of the elderly male and female groups.

of capillary density¹⁵ and of energy available for ventricular pump function.¹⁶ The mechanisms of myocardial fibrosis may be related to the remodeling of cardiac interstitium and intrinsic age-related cardiac modifications. Remodeling of cardiac interstitium is induced by coronary atherosclerosis that increases with aging.

Another possible explanation is related to the autonomic dysfunction, which is present in the elderly patients. Cardiovascular autonomic function declines with aging, which is partly because of gradual impairment of baroreflex function.¹⁷ It has been established by a number of investigators that cardiovascular baroreflex sensitivity (BRS) starts to decline from the age of 20s and is reduced to almost 0 in the 70s and 80s.^{18–20} With advancing age, both BRS and carotid compliance were found to be decreased, and the reduction in BRS was explained in part by stiffening of the arterial wall.²¹

Gender was only a weak predictor of QTd in our study; the women showed slightly increased dispersion. Previous studies showed either no statistically significant difference in QTd between genders or marginally greater values in men. Macfarlane et al.¹² showed that male and female subjects had similar QTd values obtained from adult healthy subjects. Tran et al.²² measured QTd in 150 healthy subjects and observed that male subjects had higher QTd than female subjects. Saba et al.²³ by measuring QTd in healthy adult women, have shown that QTd is significantly prolonged (54 ms) in the postmenopausal group as compared to premenopausal women (30 ms). In our study, the majority of female subjects were in the postmenopausal state. Probably, this was one reason for QTd prolongation in women in our study. It might suggest that hormonal factors effect QTd.

Several limitations of our study should be noted. Although there are a lot of studies, there is no standard method for the measurement of QTd yet. Determination of the end of T wave is an important problem. It may be very difficult to determine the end of T wave in some lead derivations. There are different suggestions about the paper speed of ECG. Current measurement of QTd involves manual measurement of the QT interval with a standard ECG recorded at 25 mm/s. There is considerable interobserver and intraobserver variability reported in the manual measurement of QTd. We attempted to minimize this error by having all measurements performed by two operators using the same standardized technique.

CONCLUSIONS

Our study shows that QTd increases with advancing age. We think that long-term follow-up of these patients would be useful to show if there is any relationship between the clinical outcomes and the increase in QTd.

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