An Evaluation of the Impact of Gender and Age on QT Dispersion in Healthy Subjects

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Objectives: To determine if gender, age, and gender per age category, have an impact on QT and QTc dispersion in healthy volunteers.

Methods: This study was undertaken in 150 patients (50 per age group, 75 males, 75 females). The age groups included young (20-40 years), middle-aged (41-69 years) and elderly (> 70 years) subjects. The QT intervals on a 12 lead ECG were determined and Bazett's formula was used to derive the QTc intervals. The QT and QTc dispersion were determined by subtracting the shortest QTc interval from the longest on each 12-lead recording.

Results: Males had higher QT dispersion than females (50 ± 22 vs 42 ± 18 ms, P = 0.017) but QTc dispersion was not significantly changed. No significant differences were seen among the different age categories for QT or QTc dispersion. In elderly subjects, males had higher QT and QTc dispersion than females (54 ± 23 vs 42 ±15 ms, P = 0.039 and 63 ± 23.7 vs 48 ± 21 ms, P = 0.032, respectively).

Conclusions: When evaluating the effect of gender in different age categories, elderly males have significantly greater QT and QTc dispersion than elderly female subjects. No other gender differences were noted for QT or QTc dispersion in the other two age categories. When evaluating a population of healthy volunteers, regardless of age, gender has an impact on QT dispersion but no significant interaction with QTc dispersion. Evaluating age without dividing the data by gender yields no significant differences in QT or QTc dispersion. **A.N.E. 2001;6(2):129–133**

QT dispersion; gender; age; normal population

The interlead variation of the QT interval provides an index of ventricular repolarization heterogeneity within the ventricles of the heart.[1] The difference between the longest and shortest QT interval on a 12 lead ECG (QT dispersion) is primarily due to changes in T-wave duration. Hence, changes in QT dispersion reflect a prolongation of repolarization within one region of the heart but not within another region.[1] Enhanced heterogeneity, measured as an increase in QT dispersion, may increase the risk for re-entry and thus ventricular tachyarrhythmias.[2]

Disease or disease sequelae such as hypertension induced left ventricular hypertrophy,[3-5] myocardial infarction,[3,6-8] and dilated cardiomyopathy [9,10] have all been shown to significantly increase QT dispersion from this baseline. However, in a population without known underlying disease, the impact of age and gender on QT dispersion has not been well evaluated. Hence, we sought to determine the impact of age and gender on QT dispersion in an apparently healthy population.

METHODS

Study Population and Design

This was a blinded study approved by the Hartford Hospital Institutional Review Board. Subjects' medical histories and medication profiles were

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screened during routine annual "wellness visits" of primary care physicians affiliated with Hartford Hospital. Only subjects living independently, free of prespecified diseases (coronary artery disease, heart failure, arrhythmic events, hypertension or COPD), and not taking concurrent medications except acetaminophen, nonsteroidal antiinflammatory agents, oral antibiotics (except macrolides), and sedatives were eligible for inclusion. Subjects not in sinus rhythm, experiencing bundle branch block, having electrocardiographic evidence of intraventricular conduction abnormalities, having a QRS interval greater than 100 ms, and without at least 10 evaluable leads with which to measure the QT interval were excluded from participation.

ECG Interval Measurements

All patients had a standard 12-lead electrocardiogram (ECG) recorded at 25 mm/sec during their routine "wellness visit." A single blinded observer measured the RR, QRS, and QT intervals in each of the 12 leads using a 0.5 mm scale precision ruler (Schaedler Instruments, Parsippany, NJ, USA). This ruler method was previously found to be superior to a caliper and computer method.[11] The QT interval was measured in all leads from the earliest QRS deflection to the end of the T wave. The beginning of the Q wave was identified by visual inspection and the point of T-wave offset was defined by return of the terminal part of the T wave to the TP baseline. When a U wave was present and interrupted the T wave, the terminal portion of the visible T wave was extrapolated to the TP baseline to identify the point of T-wave offset. When the end of the T wave could not be identified with certainty, that lead was excluded from the analysis. Each interval (RR, QRS, QT) was the average of three consecutive complexes measured from the 12-lead ECG. QT intervals were also corrected for heart rate using Bazett's formula: [QTc = QT/RR1/2]. QT and QTc dispersion were calculated by subtracting the shortest interval from the longest interval measured on the ECG. The intraobserver variability in this study was 8.0 ± 8.1 ms.

Study Variables and Statistical Analysis

Electrocardiographic comparisons for age: young (20-40 years), middle (41-69 years), and elderly (> 70 years) were performed using Analysis of Variance with posthoc Bonferroni corrected *t*-tests, if applicable. Electrocardiographic comparisons for gender groups were performed using a Student *t*-test. Patients of different gender were then subdivided by age and intergroup comparisons were performed using a Student *t*-test. All data is presented as means ± SD. A P value < 0.05 was considered significant for the Student *t*-tests while a P value of < 0.017 was considered significant for Bonferroni corrected *t*-tests.

RESULTS

QTc Dispersion

A total of 150 subjects were enrolled (75 males and 75 females) with 50 subjects per age group (25 subjects per age-gender group). No QT or QTc dispersion differences were observed among the three age groups (Table 1). The mean QT dispersion in males was larger than that of females ($P = 0.017$) but the QTc dispersion was not different (Table 2). When age categories were compared between males and females, only the elderly had higher QT and QTc dispersions among males ($P = 0.039$ and 0.032, respectively) (Table 3).

QTc Interval

Age category, regardless of gender, did not elucidate any difference in the QT or QTc interval (Table 1). The QT interval was similar between males and females, regardless of age, but the QTc

Table 1. Electrocardiographic Comparison Irrespective of Gender

Age (Years)	RR (ms)	QT (ms)	QTc (ms)	QT Disp (ms)	QTc Disp (ms)
20–40	885 ± 120	372 ± 26	397 ± 27	45 ± 19	55 ± 24
41–69	910 ± 127	381 ± 29	401 ± 28	46 ± 22	55 ± 27
≥ 70	877 ± 109	384 ± 28	412 ± 28	48 ± 20	56 ± 23
Total	891 ± 119	379 ± 28	403 ± 28	46 ± 21	55 ± 25

No significant differences found between age groups. Disp = dispersion.

Table 2. Electrocardiographic Comparison Irrespective of Age

Gender	RR (ms)	QT (ms)	QTc (ms)	QT Disp (ms)	QTc Disp (ms)
Male	913 ± 122	378 ± 30	397 ± 27	50 ± 22	58 ± 24
Female	869 ± 116†	380 ± 30	410 ± 28†	42 ± 18*	53 ± 26

* $P < 0.05$; † $P < 0.01$, male vs female; disp = dispersion.

interval was longer in females (Table 2). When age categories were compared between males and females, the QTc interval was larger in the 20—40 year and 41—69 year old females but not differences in the QT interval was noted (Table 3). The lack of significant QT interval differences but significant QTc interval differences between genders in each age category are due, in part, to the larger RR intervals in each age category for the males (Table 3).

DISCUSSION

QTc Dispersion

In our study, no differences in QT or QTc dispersion were observed among patients from different age groups. QT dispersion was 16% higher in males than females but the QTc dispersion was only 9% higher and did not achieve statistical significance. Elderly subjects had the greatest disparity in QT and QTc dispersion between men and women with men having 22% and 24% higher values, respectively. The QT intervals were not different for men and women but women had higher QTc intervals than men predominantly from a shorter RR interval.

The QT and/or QTc dispersion of normal volunteers have been evaluated in several studies (averaging 24 subjects) where the normal population served as the control group.[10, 12-18] In these studies, most subjects (80%) were male and the average age was 40 years. The average QT and QTc dispersion in these studies were 42 ms and 46 ms, respectively.[10, 12-18] One small study of 13 male (average age 33 years) and 12 female (average age 29 years) normal subjects found that the QT dispersion was 24% higher among males.[19] QTc dispersion was not evaluated in this study but the QT dispersion difference is consistent with our present study.

In the largest study to evaluate normal volunteers (n = 1000, 41% male) no significant QT dispersion differences were observed between the sexes (QTc not performed, actual differences or percent differences not given).[20] In addition, no significant correlation was found between age and QT dispersion. Our study also found that subjects in older age categories did not have higher QT dispersion than younger categories. These investigators did not compare the QT dispersion between genders in different age categories. This may be because the average age in their study was 46 years and the standard deviation was 16 years, giving only limited number of elderly subjects. It was in the elderly subjects that we found the largest QT dispersion differential in males and females. Since both males and females had equal representation (25 subjects per sex) in the elderly group in our study, our data is unique and may represent an early marker of the greater subclinical atherosclerotic burden in asymptomatic males for the same age distribution as females.[21] If so, this may be a useful non-invasive screening tool in the elderly and should be explored further.

Table 3. Electrocardiographic Comparison for Gender with Varying Ages

Age (Years)	RR Male	RR Female	QT Male	QT Female	QTc Male	QTc Female	QT Disp Male	QT Disp Female	QTc Disp Male	QTc Disp Female
20–40	906 ± 132†	864 ± 110	367 ± 28†	377 ± 24	387 ± 25†	408 ± 28	45 ± 19	44 ± 20	53 ± 20	58 ± 27
41–69	941 ± 127†	879 ± 128	381 ± 31	380 ± 26	395 ± 27†	408 ± 30	52 ± 24	40 ± 19	59 ± 26	51 ± 28
≥ 70	892 ± 107†	863 ± 110	385 ± 32	384 ± 24	408 ± 28	415 ± 28	54 ± 23*	42 ± 15	63 ± 24*	48 ± 21

* $P < 0.05$; † $P < 0.01$ male vs female; data in ms; disp = dispersion.

QTc Interval

In this study, the QT interval was similar in different age categories, gender categories, or age by gender categories. However, the QTc was 3.3% higher in females (the group with lower QT and QTc dispersion (QTc dispersion was not significantly different)). Females had significantly higher QTc intervals in those patients less than 70 years of age (5.4 and 3.3% among patients 20—40 years and 41—69 years, respectively).

Previous studies have shown that females, without regard to age, had higher QTc interval values than in males.[22,23,24] One study in normal volunteers shows females to have a QTc interval 20 ms (5%) higher than males (n = 40).[22] The most recent and one of the largest evaluations of normal volunteers (n = 2,894) demonstrated that females had QTc intervals that were 6 ms (1.6%) higher than males.[24] Not only do females have higher QTc intervals than males but also show greater increases in the QTc interval when exposed to the class IA antiarrhythmic agent quinidine.[25] In one study (n = 24), the baseline QTc was 12 ms larger in females (3%) and after quinidine (4 mg/kg), females had an increase in the QTc interval/serum quinidine concentration of 42.2 ms/mL versus only 29.3 ms/mL in males.

Clinical Implications of Study Findings

Males have a higher risk of developing sudden cardiac death but a lower risk of torsade de pointes as compared to females.[23,26] In one evaluation, patients (n = 27) with a history of ventricular fibrillation did not have differences in the QTc interval as compared to controls but the QT dispersion was 29 ms higher.[27] Hence, our elderly male groups with elevated QTc dispersion may be at elevated risk of subsequent ventricular fibrillation than their female counterparts. An elevated QTc interval has been shown to increase the risk for torsade de pointes in several investigations[23] including an in vitro animal model.[28] Hence, our female patients less than 70 years of age may be at a higher risk of torsade de pointes than their age matched counterparts.

CONCLUSION

When evaluating the effect of gender in different age categories, elderly males have significantly greater QT and QTc dispersion than elderly female subjects. No other gender differences were noted for QT or QTc dispersion in the other two age categories. When evaluating a population of healthy volunteers, regardless of age, male gender has an impact on QT dispersion but no significant interaction with QTc dispersion. Evaluating age without dividing the data by gender yields no significant differences in QT or QTc dispersion. Finally, women who are less than 70 years of age have a larger QTc interval than age matched males.

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