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**QTc IS ASSOCIATED WITH OBESITY AND PHYSICAL ACTIVITY LEVEL FOR
AFRICAN AMERICAN FEMALES**

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ABSTRACT

QTc IS ASSOCIATED WITH OBESITY AND PHYSICAL ACTIVITY LEVEL FOR AFRICAN AMERICAN FEMALES. **C Jayne Brahler**. **JEPonline** 2004; 7(2):16-24. Long QT syndrome (LQTS) is an independent risk factor for cardiovascular or ischemic disease mortality. Obesity as a cause for acquired LQTS in otherwise healthy individuals is rapidly gaining the attention of the scientific community. African American people have a higher incidence of obesity compared to Caucasians, yet race-specific information is not available for their prevalence of LQTS. Chronic physical activity can help reduce the incidence of obesity, yet little is known about the effects of chronic physical activity on acquired LQTS. Subjects in this study were a volunteer sample of African American mothers (21-53 yr, n = 44) and daughters (5-17 yr, n = 66) recruited from the inner city Dayton, Ohio community using posters placed in a local agency that provides assistance for mothers with children. Electrocardiograph (ECG) tracings were drawn, and body weight and height were measured without shoes. Body mass index (BMI) was calculated (weight in kilograms divided by height in meters squared). Each subject completed an interviewer administered physical activity questionnaire. QTc (QT interval corrected for heart rate) data were grouped according to subject body mass index (BMI) for normal weight (BMI < 25), overweight (BMI 25 - 29.99), and obesity (BMI > 30) and statistically analyzed using an ANOVA test to determine if QTc duration was significantly different between BMI groups. Correlation tests were run between physical activity level and QTc, and between mothers' and daughters' QTc. Results indicated a longer QTc for obese mothers and daughters compared to normal-weight mothers and daughters (p = 0.003). Self-reported PA was inversely associated with QTc for mothers and daughters, but reached statistical significance (r = -0.46; p < 0.001) for the obese daughters only. Mother and daughter QTc durations were significantly and positively correlated (r = 0.42; p < 0.0001). These results indicate a positive association between obesity and QTc and an inverse association between PA and QTc.

Key Words: Electrocardiograph, Obesity, Physical Activity, LQTS

INTRODUCTION

Long QT syndrome (LQTS) is an independent cardiovascular risk factor and is predictive of cardiovascular or ischemic disease mortality. Obesity as a cause for acquired LQTS in otherwise healthy individuals is rapidly gaining the attention of the scientific community (1-5). Although it is known that African American people have a higher incidence of obesity compared to Caucasians, race-specific information is not available for the prevalence of LQTS. Furthermore, while it is well known that chronic physical activity can help reduce the incidence of obesity, little is known about the effects of chronic physical activity on acquired LQTS (6). Chronic aerobic training is associated with decreased sympathetic tone at any given work rate (7,8) and the ultimate therapy for LQTS is to reduce sympathetic activity to the heart (9). Therefore, it seems logical that chronic exercise participation may improve autonomic balance in general and have a positive effect on reducing the duration of the QT interval (6,9).

Definitions

The QT interval is an element of the electrocardiograph (ECG) tracing that includes ventricular depolarization and repolarization and is representative of ventricular function. Long QT syndrome (LQTS) extends the relative refractory period of ventricular repolarization. LQTS is an index of ventricular repolarization that is associated with an increased incidence of malignant ventricular arrhythmias, syncope and sudden death (9). QTc is the QT interval duration after being corrected for heart rate. QT dispersion (QTd) is the difference between the maximal and minimal QT intervals. LQTS and QTd are indices of ventricular repolarization that are associated with an increased incidence of malignant ventricular arrhythmias, syncope and sudden death (9). QTd reflects regional inhomogeneity of ventricular repolarization. In other words, cardiac recovery from excitation is non-uniform, reflecting ischemia, uneven autonomic innervation, or other defects (1-5). Sedentary lifestyle habits (8,10) and the incidence of childhood and adult obesity (2,11-13) are increasing at alarming rates. Currently, in the United States, approximately 35% of adult women and 31% of adult men (20 years and older) are considered obese (14). Obesity is currently the second leading cause of preventable death in the United States and is a common risk factor for many chronic health problems such as coronary heart disease, stroke, and type 2 diabetes mellitus (15). Unfortunately, obesity has proven to be quite resistant to treatment; if an individual is obese as a child, they are at an increased risk for continuing to be obese through adulthood (5,10). Furthermore, an adult with obesity, whom also had obesity as a child, is at the highest risk for developing cardiovascular and metabolic disorders (5,16). Children with obesity have conditions known to place adults at increased risk for cardiovascular disease (17). Although adult obesity and lack of physical activity have a known association with increasing numerous health risk factors in adults, less is known about the short and long term ramifications of these conditions for children (18).

African American girls are more likely to be overweight than Caucasian girls. The trend continues into adulthood, as 30% of younger (18-30 years) and 77% of older (45-65 years) black women are obese compared to 14% and 46%, respectively, for their white counterparts (19). Overall, black women are 60% more likely to become obese than are white women (16). Compounding the problem are the facts that women in minority groups are less physically active than the general American population, and the overall health status of people of color (including African American women) is lower than that of the general American population (20,21).

The proposed mechanisms for LQTS

The QT interval duration is influenced by autonomic tone but the precise mechanisms for LQTS have not been elucidated. Several explanations have been extended, including

- 1) LQTS results from an imbalanced cardiac sympathetic innervation with either an over activity of the left-sided adrenergic nerves or an under activity of the right sided nerves (9).
- 2) LQTS results from abnormal sarcolemmal membrane function whereby the membrane protein involved in the outward movement of the potassium ion during phase 3 of myocellular repolarization is defective, thus prolonging the relative refractory and vulnerable phase of the cardiac cycle (9).

- 3) Ischemic myocardial cells are known to develop a shortening of the action potential possibly due to changes in an ATP-dependent potassium channel (22).
- 4) Cells from a failing heart may have longer action potentials that may create an arrhythmogenic milieu (7). These mechanisms may result from genetic defects or acquired conditions, both of which are associated with an increased incidence of malignant ventricular arrhythmias, syncope and sudden death.

Who is at risk for LQTS?

Some people inherit LQTS and others acquire it. One type of *genetic* LQTS is Romano-Ward inherited long QT syndrome, and another is a variant, called Jervelle-Lange Nilsson long QT syndrome (LQTS) (23). *Acquired* LQTS can be due to the use of antiarrhythmic agents, psychotropic drugs, or can be due to diuretic-induced hypokalemia. *Acquired* LQTS can also be caused by very low calorie diets, which may result in biochemical changes in the myocellular membrane thus altering potassium flux. The condition has also been associated with some central nervous system disorders, and ischemia of the heart muscle following coronary heart disease may also lead to the autonomic imbalance implicated in LQTS (22). Subject age also seems to have a significant relationship with acquired LQTS as it appears more frequently with advancing age (6,24). Women appear to be at greater risk for these life-threatening events (22). Although it is known that African Americans have a higher incidence of obesity compared to Caucasians, race-specific information is not available for the prevalence of LQTS.

Association with disease conditions and mortality

Most research investigating LQTS or QTd involves patients with myocardial infarct, ischemia or genetic LQTS. The positive relationship between LQTS and mortality has been studied extensively and documented in individuals with specific autonomic or cardiovascular diseases (3,7,22,23,25-27). However, LQTS is significantly and positively correlated with cardiovascular and ischemic disease mortality in otherwise-healthy individuals (6,23), and has been established as an independent cardiovascular risk factor (6,23,27). Recently, the relationship of LQTS with cardiovascular and ischemic disease mortality was elucidated for 3,091 middle-aged, apparently healthy individuals in a 28-yr follow up study. Moderate (QTc, 420-440 ms) and extensive (QTc, >440 ms) QTc prolongations, traced in 1953-1954 in an apparently healthy middle-aged population, were significantly correlated with cardiovascular and ischemia heart disease mortality, as determined in a follow-up study conducted 28 years later in 1982, and reported in 1991 (6).

Effects of acute vs. chronic exercise on LQTS

Low levels of cardiorespiratory fitness are also associated with increased risk of disease. About 14% of young Americans report no recent light, moderate or vigorous physical activity (20). This indicator of inactivity is higher among females than males, and African American females than Caucasian females. African American girls have been shown to have a significantly lower cardiorespiratory fitness when maximal oxygen consumption was expressed relative to body weight, shorter time to exhaustion, and less ability to utilize oxygen during maximal exercises at a given fat free mass compared to white girls (28). African American women engage in less leisure-time physical activity, and spend less time standing and walking stairs compared to their white counterparts (29).

Acute Exercise

The effect of a single acute bout of exercise on LQTS and QTd has been investigated for individuals who have genetic LQTS or who are post myocardial infarct (22,25-27,30). Many individuals who have suffered myocardial infarction (MI) or ischemia have LQTS and QTd due to the electrical instability in the post MI or ischemic heart (22). This electrical imbalance is implicated in LQTS and QTd (6,7,9,22). Research reveals that acute exercise stress increases the duration of the shortest QTc. At first, this response seems unfavorable, however, it represents increased electrical stability of the myocardium owing to improved myocardial perfusion and a lengthening of the action potential in ischemic cells (7,22), which is favorable (7). An acute bout of exercise is thought to restore this autonomic imbalance but is associated with a lengthening of the shorter QT intervals thus improving QT dispersion without improving the LQTS (7,22).

Chronic Exercise

It is well known that chronic physical activity can help reduce the incidence of obesity, but little is known about the effects of chronic physical activity on acquired LQTS (6). Chronic aerobic training is associated with decreased sympathetic tone at any given work rate (7,8). As the ultimate therapy for LQTS is to reduce sympathetic activity to the heart (9), chronic exercise participation may improve autonomic balance in general and have a positive effect on reducing the duration of the QT interval (6,9).

Clearly, in the acute sense, exercise stress increases sympathetic activity (SNA) to the heart, which is contradictory with the long-term therapeutic goal for LQTS, which is to reduce sympathetic activity to the heart (22). Reduction in SNA can be accomplished pharmacologically or surgically (22), but it can also be accomplished via chronic aerobic exercise training. Will this equate to a concomitant decrease in the QT interval duration or improved QTd?

Two research teams have investigated the effect of chronic aerobic exercise training on QTd in patients with chronic heart failure or recent myocardial infarct (7,22). Results were favorable and the QTd was reduced significantly making ventricular repolarization more stable. One of the main threats in QTd is the inhomogeneity of ventricular repolarization because it is associated with fatal arrhythmias. Anything that restores the autonomic balance can be viewed as favorable.

However, to this researcher's knowledge, no one has assessed chronic aerobic exercise training as a *preventative or therapeutic measure to protect obese, but otherwise healthy, individuals from the ventricular dysrhythmias associated with acquired LQTS*. These individuals are at *increased risk* for developing cardiovascular disease. It is hypothesized that chronic aerobic exercise training may improve LQTS and QTd, thus preventing a person progressing to extensive lengthening or dispersion of the QT intervals. Although no one has tested this hypothesis, Schouten et al (6) stated;

“Because physical exercise seems to result in a favorable autonomic balance and smoking and stress appear to result in a less favorable autonomic balance, it might be speculated that preventative lifestyle changes (increased physical activity and decreased smoking and stress) may improve autonomic balance in general and thus mortality in persons with prolonged QT interval”.

Moss (9), in the Journal of the American Medical Association, reported, “ *The ultimate therapy for LQTS is to reduce sympathetic activity to the heart*”. It is known that chronic aerobic exercise training reduces sympathetic tone, and increases vagal tone, at rest and at any given work rate (7,8), which supports the use of chronic aerobic exercise as a therapeutic practice for LQTS and QTd.

It is known that an individual's resting heart rate is lower in the aerobically trained state compared to the untrained state (8). This reduction in resting heart rate is due to an increase in the vagal tone and a decrease in sympathetic tone of the heart at rest. This effect extends from rest into exercise, as it is also known that a given work rate will elicit a lesser sympathetic response for an individual in the aerobically trained state compared to the untrained state compared because any given amount of work will represent a smaller percentage of the trained individual's maximal capacity to complete work. In other words, the system perceives any given work rate as less stressful and the work rate is “easier” in the trained state, compared to the untrained state. Aerobic training diminishes the SNA for rest and any work rate, which is the long-term therapeutic goal for LQTS (22).

The purpose of this study was to determine the relationships between obesity and self-reported physical activity levels and QTc duration for 110 African American mothers and their daughters.

METHODS

The protocol and consent form for this study were approved by the University of Dayton Institutional Review Board. The University of Dayton provided transportation for the study subjects. Subjects were 12-14 hours fasted upon arrival at the university. All subjects gave written informed consent to participate before data collection began.

Subjects

Subjects were African American women (ages 21-53 years; n=44) and their biological daughters (ages 5-17 years; n = 66) who volunteered to participate via announcements placed in two Midwestern church bulletins and a local agency that provides assistance for families who earn low-incomes. A sub-sample of 82 subjects satisfactorily completed physical activity questionnaires. Eligibility criteria included premenopausal, not on estrogen therapy, not pregnant, and apparently healthy and medically stable, with no known acute heart disease complications, endocrine problems, complications from diabetes mellitus, HIV/AIDS, or other major diseases as determined by completing a health history questionnaire. Relevant subject data are displayed in Tables 1 and 2.

Measures

Trained faculty and university student technicians measured body weight, height, and waist (at the level of the superior iliac crest) and hip (at the greatest girth of the gluteus) circumferences.

BMI was calculated as weight in kilograms divided by height in meters squared. Waist to hip ratio (WHR) was calculated as waist circumference (cm) divided by hip circumference (cm). Twelve lead surface ECG tracings were drawn at a paper speed of 50 mm/s. QT interval was measured from the earliest onset of the QRS complex to the end of the T wave in lead II. Measurements from 5 consecutive beats were averaged. The QT interval was adjusted for cycle length using Bazett's formula.

Physical activity levels were estimated from questionnaire. Each subject's physical activity level was assessed by an interviewer-administered Modifiable Physical Activity Questionnaire or Modifiable Activity Questionnaire for Adolescents, developed by Kriska et al. (29,31). These questionnaires determined the average hours per week over the past year spent in occupational and leisure physical activity (29,31). Occupational physical activity was calculated according to whether light, moderate, or heavy work was involved while performing typical activities on the job. Time spent walking or biking to work was assessed as part of the occupational activity. Leisure physical activity was determined by providing a list of local leisure activities and estimating the frequency and duration of those activities performed over the past year. Each occupational activity or leisure activity was also weighted by an estimate of its relative intensity or MET value, which is the ratio of the working metabolic rate of an individual divided by the resting metabolic rate (28). One MET represents the energy expended at rest for an individual (estimated as 1 kcal/kg body weight * height), whereas a 7-MET activity requires 7 times the resting energy expenditure. Validation and reliability testing of the Modifiable Activity Questionnaires were previously published (29).

Table 1. Mean \pm SD values for selected variables for Mothers

<i>Mothers</i>	<i>NonObese</i>	<i>Overweight</i>	<i>Obese</i>
<i>Age (yrs)</i>	35.14 \pm 7.1	33.9 \pm 7.67	33.19 \pm 9.17
<i>QTc (ms)</i>	403 \pm 18.51	411.9 \pm 23.73	413.42 \pm 16.73
<i>Waist (cm)</i>	75.29 \pm 8.99	93.41 \pm 6.21	111.28 \pm 14.66
<i>Hip (cm)</i>	89.97 \pm 7.49	105.55 \pm 4.81	122.83 \pm 14.27
<i>Wt. (kg)</i>	54.52 \pm 9.19	77.82 \pm 6.69	104.33 \pm 20.99
<i>BMI</i>	20.82 \pm 2.95	27.84 \pm 1.37	39.18 \pm 6.54

Table 2. Mean \pm SD values for selected variables for Daughters

<i>Daughters</i>	<i>Nonobese</i>	<i>Overweight</i>	<i>Obese</i>
<i>Age (yrs)</i>	9.41 \pm 3.97	11.26 \pm 2.62	10.38 \pm 4.27
<i>QTc (ms)</i>	394.18 \pm 21.51	394.53 \pm 16.93	399.38 \pm 25.05
<i>Waist (cm)</i>	59.34 \pm 14.01	71.83 \pm 10.62	83.3 \pm 19.8
<i>Hip (cm)</i>	74.27 \pm 15.87	89.81 \pm 11.93	95.15 \pm 19.45
<i>Wt. (kg)</i>	34.12 \pm 14.44	52.68 \pm 16.05	61.09 \pm 31.72
<i>BMI</i>	17.62 \pm 2.36	22.59 \pm 2.78	27.48 \pm 7.12
<i>WHR</i>	0.8 \pm 0.05	0.8 \pm 0.05	0.87 \pm 0.04

Statistical Analyses

Subject data were blocked by the body mass index (BMI) for normal weight (BMI < 25), overweight (BMI 25 - 29.99), and obesity (BMI > 30), with children’s BMI values being adjusted for age and sex according to Cole et al. (Table 3) (32). ANOVA tests were run to determine if significant differences existed in QTc duration between BMI groups. Correlation tests were run between physical activity levels and QTc durations, and between mother and daughter QTc values.

RESULTS

Percentages of normal weight, overweight and obesity for mothers and daughters were 18, 23, 59, and 59, 29, and 12, respectively. Mean age, anthropometric and QTc values for non-obese, overweight and obese participants are presented in Tables 1 (mothers) and 2 (daughters). Results indicated a significantly longer QTc (p = 0.003) for obese compared to normal-weight mothers and daughters (Figure 1).

The average physical activity level for 56% of the women and 73% of the girls was less than 3.9 MET-hours/week, which is lower than the Surgeon General’s recommendation of 7.5-15 MET-hours/week. There was an inverse association between self-reported physical activity and QTc for mothers and daughters, which reached statistical significance (p < 0.001) for the obese daughters. Mother and daughter QTc durations were significantly and positively correlated (r = 0.42; p < 0.0001).

DISCUSSION

Otherwise-healthy individuals with obesity are at an increased risk for acquiring LQTS and the associated malignant ventricular arrhythmias. Chronic aerobic exercise training may protect against LQTS. The current results indicate an inverse association between self reported PA and QTc duration. Others have reported a positive association between obesity and QTc, but to our knowledge, no one has quantified the exercise intensity, duration or length of training period required to favorably affect the LQTS. The potential independent and interactive effects of obesity and participation in a controlled physical training program on QTc for African American women and their daughters should be studied. Determining the effect of a controlled exercise intervention on LQTS may have positive implications for informing healthy lifestyle habits, especially for a population at risk for developing obesity and LQTS. Combined with other risk factor indicators, information on the LQTS may have positive implications with respect to lifestyle habits because chronic aerobic exercise training is reported to have a favorable influence on LQTS (6). The effect of chronic aerobic exercise training on LQTS should be investigated further (6).

Table 3. Overweight and obesity BMI cut-off points in children and adolescents.

Age (years)	Overweight		Obese	
	Males	Females	Males	Females
2	18.4	18	20.1	20.1
2.5	18.1	17.8	19.8	19.5
3	17.9	17.6	19.6	19.4
3.5	17.7	17.4	19.4	19.2
4	17.6	17.3	19.3	19.1
4.5	17.5	17.2	19.3	19.1
5	17.4	17.1	19.3	19.2
5.5	17.5	17.2	19.5	19.3
6	17.6	17.3	19.8	19.7
6.5	17.7	17.5	20.2	20.1
7	17.9	17.8	20.6	20.5
7.5	18.2	18	21.1	21
8	18.4	18.3	21.6	21.6
8.5	18.8	18.7	22.2	22.2
9	19.1	19.1	22.8	22.8
9.5	19.5	19.5	23.4	23.5
10	19.8	19.9	24	24.1
10.5	20.2	20.3	24.6	24.8
11	20.6	20.7	25.1	25.4
11.5	20.9	21.2	25.6	26.1
12	21.2	21.7	26	26.7
12.5	21.6	22.1	26.4	27.2
13	21.9	22.6	26.8	27.8
13.5	22.3	23	27.2	28.2
14	22.6	23.3	27.6	28.6
14.5	23	23.7	28	28.9
15	23.3	23.9	28.3	29.1
15.5	23.6	24.2	28.6	29.3
16	23.9	24.4	28.9	29.4
16.5	24.2	24.5	29.1	29.6
17	24.5	24.7	29.4	29.7
17.5	24.7	24.8	29.7	29.8
18	25	25	30	30

Criteria for child obesity scores determined using Cole et al. (32) International cutoff points for body mass index for overweight and obesity by sex between 2 and 18 years, defined to pass through the body mass index of 25 and 30 kg/m² at age 18

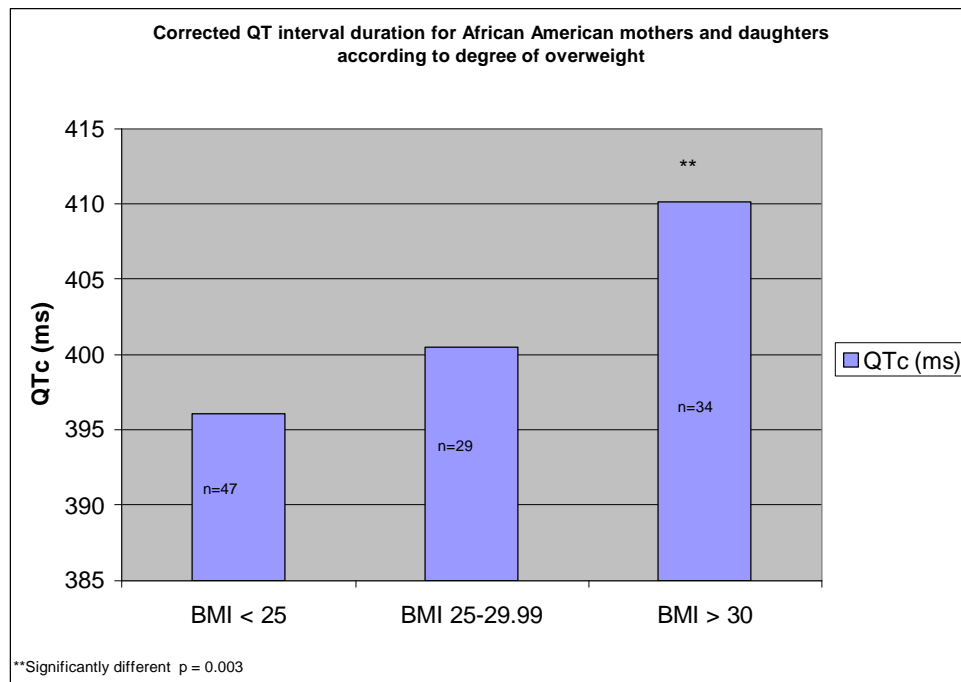


Figure 1. The QTc for the three BMI categories.

CONCLUSION

Physical activity level and QTc were inversely correlated, which indicates a need for additional research to determine the effect of a specified volume of exercise on QTc. Others have reported a positive association between obesity and QTc, but the potential independent and interactive effects of obesity and participation in a controlled physical training program on QTc for African American women and their daughters should be studied.

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