Published in final edited form as:

Appl Nurs Res. 2012 August ; 25(3): 218–221. doi:10.1016/j.apnr.2010.11.003.

A Pilot Study of QT Interval Analysis in Overweight and Obese Youth

Shirleatha Lee, Ph.D.^{*}, Patricia Ann Cowan, Ph.D.[†], and Pedro Velasquez-Mieyer, M.D.

^{*} The University of Memphis

[†] The University of Tennessee Health Science Center Memphis

Introduction

The risk for cardiovascular disease increases when obesity is present and in the past 30 years childhood obesity has more than tripled (Centers for Disease Control and Prevention, 2010). One cardiovascular risk factor that has become increasing more prevalent when obesity is present is prolongation of the QT Interval (Lee, Cowan, Wetzel, & Velasquez, In Press). The “QT” is a time interval on the electrocardiogram (ECG) that represents depolarization and repolarization of the ventricles (Furukawa, Shimizu, Hiromoto, Kanemori et al., 2006; Hunt, 2005), and is measured from the onset of the QRS complex to the end deflection of the T wave (Furukawa et al., 2006; Hunt, 2005). The QT Interval is modulated by autonomic function (Viitasalo, Karjalainen, Makijarvi, & Toivonen, 1998) and therefore is often corrected (QTc) to be independent of heart rate with Bazett’s formula ($QTc = QT / \sqrt{RR}$) used most often (Malik, Färholm, Batchvarov, Hnatkova et al., 2002). Normally ranging from 0.2–0.4 seconds (Barone, 1996; Moss & Allen, 2001) measures in excess of 0.440(sec) in males and 0.460(sec) in females are considered as prolonged (Crotti, Celano, Degradì & Schwartz, 2008). Accurate measurement is essential and clinically relevant, because prolongation of the QTc Interval is associated with life threatening arrhythmias and an increased risk of sudden cardiac death (Antzelevitch, 2005; Lanjewar, Pathak, & Lokhandwala, 2004; Kligfield, Tyl, Maarek, and Maison-Blanche, 2007; QT Syndrome, 2005; Texas Heart Institute, 2007; Toivonen, 2002). Researchers have indicated a positive association exists between body mass index (BMI) and QT Interval duration (Poirier, Giles, Bray, Hong et al., 2006), and while prolonged QT syndrome has been studied in youth, there is a paucity of information on measurement techniques used to determine QT interval duration in obese youth.

The preferred method to derive QT measures is from the 12-lead ECG using visual interpretations with calipers (Goldenberg, Moss, & Zareba, 2006). However, autonomic dysfunction develops in youth when obesity is present (Nagai, Matsumoto, Kita, & Moritan, 2003) that influences the QT Interval (Ishida, Nakagawa, Fujino, Yonemochi et al., 1997; Yeragani, Berger, Pohl, & Balon, 2005). These unpredictable autonomic variations

Corresponding Author: Shirleatha Lee, Ph.D., RN, CNE, The University of Memphis, Newport Hall 210, 610 Goodman, Memphis, TN 38152, sntaylr1@memphis.edu, Phone: (901) 678–2036.

Patricia A. Cowan, PhD, RN, University of Tennessee Health Science Center, 920 Madison Avenue, Suite 507N, Memphis, TN 38139, pcowan@uthsc.edu, Phone: (901) 448–3318

Pedro Velasquez-Mieyer, M.D., University of Tennessee Medical Group, 777 Washington Ave # P110, Memphis, TN 38105, velasquez493@gmail.com, Phone: (901) 448–2040

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

throughout the day and nighttime hours often cannot be identified using a standard 12-lead ECG. An alternative, the automated 24-hour Ambulatory Holter provides measures over varied time periods and can assess QTc duration during these unpredictable times.

Both the 12-lead manual ECG and automated 24-hour Ambulatory Holter methods have pros and cons when used to obtain QTc measures. It has been suggested that inter-operator differences for standard 12-lead manual ECG measurement of QTc Intervals are both imprecise and poorly reproducible and automatic measurements are more stable and reproducible, but risk being reproduced incorrectly (Hunt, 2005). Therefore, automated 24-hour Ambulatory Holter QTc measures have longed been questioned. In addition, Ambulatory Holter measures have a lower frequency response that contributes to an unsteady baseline (Christiansen, Guccione, & Garson, 1996) and manufacturer variations (Goldenberg et al., 2006) may decrease consistency in reported measures. The controversial ability of automated Ambulatory Holters to obtain accurate measures, has led to a suggestion that this method not be used for the primary assessment of QTc analysis (Goldenberg et al., 2006). Despite this argument researchers identified a two-fold risk of sudden cardiac death was associated with prolonged QTc mean over 24-hours (Algra, Tijssen, Roelandt, & Lubson, 1993).

Identification of the most effective method to determine QTc Interval prolongation in youth that are obese is important in the assessment of cardiovascular risk. The risks for cardiac arrhythmias increase during periods of sympathetic stimulation that increase heart rate with QTc prolongation (Haapalahti, Viitasalo, Perhonen, Makijarvi et al., 2006). In addition, Pater (2005) reported that during sleep hours the QT and QTc are longer and peak shortly after awakening. These high risk periods for arrhythmias and during physical activity and emotional arousal may not be identified with a standard 12-lead ECG (Chauhan, Krahn, Mitoff, Klein et al., 2004). The automated 24-hour Ambulatory Holter measures of QTc duration can provide meaningful data during unconventional time periods when performing a standard 12-lead ECG is not practical.

The purpose of this pilot study was to examine if manual QTc Interval measures obtained from a standard 12-lead ECG at rest correlated with automated 24-hour Ambulatory Holter QTc measures in overweight and obese youth. In addition, this study sought to determine if a significant difference exists between manual 12-lead ECG and automated 24-hour Ambulatory QTc measures in overweight and obese youth.

Sample

A convenience sample of 30 overweight and obese youth was included for this ancillary pilot study. Participants were aged 12–17 years of age with a mean age (years) of 15.07 ± 1.48 with 66.7 % female. Institutional Review Board Approval was obtained. During the original study procedures that examined autonomic function and lifestyle behaviors in overweight and obese youth informed consent was obtained from parents/legal guardians and assent from participants. Individuals were eligible to participate in the study if they were: 12–18 years of age, overweight or obese according to Centers for Disease Control age/gender percentiles, had a resting 12-lead ECG, and at least 18 hours of analyzable 24-hour Ambulatory Holter monitor recording data available for analysis. Despite being overweight or obese participants were otherwise considered healthy.

Procedures

Body Mass Index

Body mass index (BMI) [(weight (kg)/height² (m²))] was calculated using the Department of Health and Human Services Centers for Disease Control and Prevention Body Mass Index (BMI) Calculator for Children and Teens (Centers for Disease Control and Prevention, 2010). Age and gender percentiles were used to determine if youth were overweight or obese (85th or 95th percentile) respectively.

Manual 12 Lead ECG “QTc”

A 12-lead ECG was performed at rest on all participants at a standard paper speed of 25mm/sec and a sensitivity of 10mm/mv. The recording was manually analyzed in lead II by a single blinded observer certified in ECG analysis. Each QT interval was measured from the beginning of the QRS complex to the end deflection of the T wave. The preceding RR interval was obtained for each QT interval. Three distinct corrected QT intervals (QTc) were determined according to Bazett’s formula, correcting for variations in heart rate. The average of the three QTc calculations was used to determine the QTc for each participant for data analysis. QTc measures in excess of 0.440 sec in males and 0.460 sec in females were considered prolonged.

Automated 24-hour Ambulatory Holter “QTc”

The 24-hour Ambulatory Holter data was obtained for each participant. During the original study procedures subjects were instructed to engage in normal daily activities during the data collection period excluding activities that would subject the Holter monitor to water. Upon receipt of the Holter monitor, data were submitted to the Mars PC Unity Workstation Analysis and Editing system with software version 5.8 for processing and examination of Holter recorded data for automated high resolution QT analysis. The average oriented approach was utilized in which QT intervals are measured on 15-second incremental medians (GE Medical Information Technologies, n.d.). The analysis and editing system utilized the Bazett QT correction formula and mean $\pm$ standard deviations of the QT variable are provided. The QT algorithm includes re-sampling the PQRS, high-pass filtering, QRS (onset) detection, low pass filtering, detection of the isoelectric level, and T wave detection (apex and offset). Lead I backward inspection starting at the QRS peak was utilized. The QTc was obtained from automated analysis for comparison to manually measured QTc measurements obtained from the standard 12-lead electrocardiogram. Gender specific guidelines for QTc prolongation were also used for automated analysis to determine prolongation (> 0.440sec in males and >0.460 sec in females).

Statistical Analysis

We used Statistical Software for the Social Sciences (SPSS) version 18.0 with a p-value 0.05 set for statistical significance. Descriptive statistics and Spearman rho correlation coefficient was obtained. In addition, the nonparametric Wilcoxin Signed Rank Test for paired data was used to examine the hypothesis that there is no significant difference in the means of manual 12-lead ECG QTc measurements in comparison to QTc measures obtained from the 24-hour Ambulatory Holter using the automated analysis. All data is expressed as the mean $\pm$ the standard deviation.

Results

The sample means and demographics are displayed (Table 1). Spearman rho correlation coefficient was obtained in this sample of obese youth and there was little if any correlation identified for manual 12-lead ECG QTc measures and 24-hour Ambulatory Holter QTc

measures obtained from automated analysis ($r = 0.179$, $p = 0.345$). Wilcoxin Signed Rank Tests indicated a significant difference existed ($p = 0.01$) in the means of automated 24-hour Ambulatory Holter QTc measures in comparison to the manual 12-lead ECG QTc measurements.

Discussion

In our sample although the prevalence of QTc prolongation was 10% for both the manual 12-lead ECG and the automated 24-hour Ambulatory Holter QTc measures (Table 1) the results indicate there was little if any correlation between actual measures. We hypothesized that measures obtained from both the manual 12-lead ECG and automated 24-hour Ambulatory Holter analysis would not display a significant difference. However, a significant difference did exist between the means of QTc measures manually derived from the 12-lead ECG and those obtained from the automated 24-hour Ambulatory Holter analysis. Findings from our study are intriguing and several factors could have contributed to the results. First, periods of sympathetic stimulation and parasympathetic stimulation reflect high variations in QTc data. Because, the 24-hour Ambulatory Holter recording has an increased ability to capture these moments unlike the 12-lead ECG this could have contributed to the significant difference between the measures. Next, within our study 66.7% of participants were female. Studies indicate that prior to puberty, QTc Interval duration is similar between genders; however, at puberty, the QTc Interval shortens in boys, and a variation in the pattern of ventricular repolarization is seen between genders (Surawicz & Parikh, 2003). In a sample of 781 healthy 10–18 year olds, Pearl (1996) found that QTc Intervals were greater in girls than boys across age ranges, and QTc varied inversely with age and directly with heart rate. Therefore, small variations between genders could have also contributed to our study findings. Next, divergent measurements could have resulted from low frequency content of the T wave, low signal, or due to merging of the U wave and T wave when utilizing automated 24-hour Ambulatory Holter QTc analysis (Hunt, 2005). This factor is of particular concern because in obese youth increased subcutaneous tissue could further contribute to low frequency waveforms during Holter recording and impact QTc analysis. Lastly, during the automated 24-hour analysis youth had the ability to engage in movement and periods of activity in comparison to the resting 12-lead ECG that could have increased noise and artifact during the 24-hour recording. This could have also impacted automated 24-hour Ambulatory Holter interpretation for comparison to the manual 12-lead ECG.

Implications for Practice and Research

Several factor can contribute to prolonged QTc duration, however obesity may be one of the most common causes of prolonged QTc duration (Poirier et al., 2006). Therefore, it is very important that clinicians and researchers accurately assess QTc status in obese youth with special attention to autonomic alterations to identify increased cardiovascular risk for arrhythmias and sudden cardiac death. The 12-lead ECG is performed more frequently than 24-hour Ambulatory Holter analysis and can be easily interpreted in the clinical setting. Data collection when using the 24-hour Ambulatory Holter analysis takes longer but, it can provide more data over varied time periods with particularly fast interpretation using automated analysis. Clinicians and researchers should consider the impact of autonomic nervous system function on QTc duration when considering a measurement technique to assess QTc status and cardiovascular risk in overweight and obese youth.

Conclusion

In conclusion, findings from our study do not suggest a lack of reliability of either QTc analysis method, but rather suggests that these methods not be used for comparison of QTc

measures in overweight and obese youth. Although a small sample size is indeed a limitation within our study. Additional research is needed to determine which QTc measurement technique; manual 12-lead ECG or automated 24-hour Ambulatory Holter more strongly correlates with increased cardiac arrhythmias and sudden cardiac death risk in overweight and obese youth for cardiovascular risk stratification.

Acknowledgments

This research study was funded with support from The National Institute of Health and Sigma Theta Tau International Beta Theta Chapter at large

References

- Algra A, Tijssen JG, Roelandt JR, Pool J, Lubsen J. QT interval variables from 24 hour electrocardiography and the two year risk of sudden death. *Br Heart J*. 1993; 70(1):43–48. [PubMed: 8037997]
- Antzelevitch C. Role of transmural dispersion of repolarization in the genesis of drug-induced torsades de pointes. *Heart Rhythm*. 2005; 2(2 Supplement):S9–15. [PubMed: 16253930]
- Barone, M. *Cardiology*. 14. St. Louis, MO: Mosby; 1996. The Harriet Lane Handbook; p. 127-154.
- Centers for Disease Control and Prevention. BMI Calculator for Child and Teen English Version. 2010. Retrieved October 18, 2010 from <http://apps.nccd.cdc.gov/dnpabmi/>
- Centers for Disease Control and Prevention. Healthy Youth-Childhood Obesity. 2010. Retrieved October 18, 2010 from <http://www.cdc.gov/HealthyYouth/obesity/>
- Chauhan VS, Krahn AD, Mitoff P, Klein GJ, Skanes AC, Yee R. Sudden intense exercise increases QT heart rate slope and T wave complexity in long QT syndrome and normal subjects. *Pacing Clin Electrophysiol*. 2004; 27(10):1415–1423. [PubMed: 15511252]
- Christiansen JL, Guccione P, Garson A Jr. Difference in QT interval measurement on ambulatory ECG compared with standard ECG. *Pacing Clin Electrophysiol*. 1996; 19(9):1296–1303. [PubMed: 8880793]
- Crotti L, Celano G, Dagradi F, Schwartz PJ. Congenital long QT syndrome. *Orphanet Journal of Rare Diseases*. 2008; 3:18. [PubMed: 18606002]
- Furukawa Y, Shimizu H, Hiromoto K, Kanemori T, Masuyama T, Ohyanagi M. Circadian variation of beat-to-beat QT Interval variability in patients with prior myocardial infarction and the effect of beta-blocker therapy. *Pacing Clinical Electrophysiology*. 2006; 29:479–486.
- GE Medical Information Technology. QT Intervals in MARS Unity Workstation. n.d..
- Goldenberg I, Moss AJ, Zareba W. QT interval: how to measure it and what is “normal”. *J Cardiovasc Electrophysiol*. 2006; 17(3):333–336. [PubMed: 16643414]
- Haapalahti P, Viitasalo M, Perhonen M, Makijarvi M, Vaananen H, Oikarinen L, Hekkala A, Salorinne Y, Swan H, Toivonen L. Ventricular repolarization and heart rate responses during cardiovascular autonomic function testing in LQT1 subtype of long QT syndrome. *Pacing Clinical Electrophysiology*. 2006; 29(10):1122–1129.
- Hunt A. Accuracy of popular automatic QT Interval algorithms assessed by a ‘gold standard’ and comparison with a Novel method: computer simulation study. *BMC Cardiovascular Disorders*. 2005; 5:29. [PubMed: 16185361]
- Ishida S, Nakagawa M, Fujino T, Yonemochi H, Saikawa T, Ito M. Circadian variation of QT Interval dispersion: correlation with heart rate variability. *Journal of Electrocardiology*. 1997; 30(3):205–210. [PubMed: 9261728]
- Kligfield P, Tyl B, Maarek M, Maison-Blanche P. Magnitude, mechanism, and reproducibility of QT interval differences between superimposed global and individual lead ECG complexes. *Ann Noninvasive Electrocardiol*. 2007; 12(2):145–152. [PubMed: 17593183]
- Lanjewar P, Pathak V, Lokhandwala Y. Issues in QT Interval measurement. *Indian Pacing Electrophysiology Journal*. 2004; 4:156–161.

- Lee S, Cowan P, Wetzel G, Velasquez P. Prediabetes and Blood Pressure Effects on Heart Rate Variability, QT Interval Duration, and Left Ventricular Hypertrophy in Overweight-Obese Adolescents. *Journal of Pediatric Nursing*. In Press. 10.1016/j.pedn.2010.08.008
- Malik M, Farbom P, Batchvarov V, Hnatkova K, Camm A. Relation between QT and RR Intervals is highly individual among healthy subjects: implications for heart rate correction of the QT Interval. *Heart*. 2002; 87(3):220–228. [PubMed: 11847158]
- Moss, A.; Allen, H. Moss and Adams' heart disease in infants children, and adolescents including the fetus and the young adult. 6. Philadelphia, PA: Lippincott, Williams, & Wilkins; 2001. p. 58-342.
- Nagai N, Matsumoto T, Kita H, Moritani T. Autonomic nervous system activity and the state and development of obesity in Japanese school children. *Obesity Research*. 2003; 11(1):25–32. [PubMed: 12529482]
- Pater C. Methodological considerations in the design of trials for safety assessment of new drugs and chemical entities. *Current Control Trials in Cardiovascular Medicine*. 2005; 6(1):1–13.
- Pearl W. Effects of gender, age, and heart rate on QT Intervals in children. *Pediatric Cardiology*. 1996; 17(3):135–136. [PubMed: 8662028]
- Poirier P, Giles T, Bray G, Hong Y, Stern J, Pi-Sunyer F, Eckel R. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2006; 26(5):968–976.
- QT Syndrome. 2005. Retrieved March 23, 2008, from, <http://www.qtsyndrome.ch/faq.html>
- Surawicz B, Parikh S. Differences between ventricular repolarization in men and women: description, mechanism and implications. *Annals of Noninvasive Electrocardiology*. 2003; 8(4):333–340. [PubMed: 14516290]
- Texas Heart Institute. Long Q-T Syndrome. 2007. Retrieved March 24, 2008, from <http://www.texasheartinstitute.org/HIC/Topics/Cond/longqts.cfm>
- Toivonen L. More light on QT Interval measurement. *Heart*. 2002; 87(3):193–194. [PubMed: 11847147]
- Viitasalo M, Karjalainen J, Makijarvi M, Toivonen L. Autonomic modulation of QT Intervals in post-myocardial infarction patients with and without ventricular fibrillation. *American Journal of Cardiology*. 1998; 82:154–159. [PubMed: 9678284]
- Yeragani V, Berger R, Pohl R, Balon R. Effect of age on diurnal changes of 24-hour QT Interval variability. *Pediatric Cardiology*. 2005; 26(1):39–44. [PubMed: 15793652]

Table 1

Demographics and QTc Measures *

Measures	Total Group
Gender: % Female	66.7
Race: % Black	50.0
Age: years; mean $\pm$ SD	15.07 $\pm$ 1.48
Body Mass Index: mean $\pm$ SD	37.20 $\pm$ 7.58
Manual 12-Lead ECG	0.410 $\pm$ 0.034
Average QTc duration: sec; mean $\pm$ SD 24-hour Automated Ambulatory Holter	0.429 $\pm$ 0.018
Average QTc; sec; mean $\pm$ SD Manual 12 Lead ECG QTc Prolonged: %	10.0
Automated 24-hour Ambulatory Holter QTc Prolonged: %	10.0

Note. ECG = Electrocardiogram; QTc = corrected QT;

* N = 30.