Published in final edited form as:

Am J Cardiol. 2015 July 01; 116(1): 74–78. doi:10.1016/j.amjcard.2015.03.038.

Risk of Mortality Associated with QT and JT Intervals at Different Levels of QRS Duration (from *the Third National Health and Nutrition Examination Survey [NHANES III]*)

Muhammad A. Zulqarnain, MD^{1,*}, Waqas T. Qureshi, MD^{2,*}, Wesley T O'Neal, MD, MPH³, Amit J. Shah, MD⁴, and Elsayed Z. Soliman, MD, MSc, MS^{2,5}

¹Department of Internal Medicine, Division of Hospitalist Medicine, Wake Forest School of Medicine, Winston Salem, NC

²Department of Internal Medicine, Section on Cardiovascular Medicine, Wake Forest School of Medicine, Winston Salem, NC

³Department of Internal Medicine, Wake Forest School of Medicine, Winston Salem, NC

⁴Department of Internal Medicine, Division of Cardiology, Emory University School of Medicine, Atlanta, GA

⁵Epidemiological Cardiology Research Center (EPICARE), Department of Epidemiology and Prevention, Wake Forest School of Medicine, Winston-Salem, NC

Abstract

QT prolongation in the setting of QRS>120 ms is believed to be triggered by prolonged depolarization rather than repolarization. Hence, JT interval is suggested as an alternative to QT interval when QRS duration is prolonged. It is unclear, however, if JT and QT intervals portend similar risk of mortality for different durations of QRS. We examined the association between QT and JT, separately, with all-cause mortality across different levels of QRS duration in 8,025 participants (60±13 years, 41% white, and 54% women) from the Third National Health and Nutrition Examination Survey. At baseline (1986–1994), 486 (6%) participants had QRS duration ≥120 ms. During a follow-up of up to 18 years, 3,045 (38%) deaths occurred. There were significant non-linear relationships of QT and JT intervals with mortality ($p < 0.001$). Hence, QT and JT were categorized as prolonged (>95th percentile), shortened (<5th percentile) and normal (reference group). In multivariate adjusted Cox regression models, prolonged JT [HR (95% CI): 4.75, (1.86, 12.11)] was associated with increased risk of mortality more than prolonged QT [HR (95% CI): 1.50 (1.03, 2.17)] in participants with QRS ≥120 ms (Interaction $p=0.02$). In participants with QRS duration <120ms, prolonged QT and JT were equally predictive of all-cause mortality [HR (95% CI): 1.27(1.06, 1.54)] and [1.31 (1.10, 1.55)], respectively. Similar patterns were observed with shortened QT and JT intervals. In conclusion, although both QT and JT intervals are

Correspondence: Waqas T Qureshi, MD, Division of Cardiovascular Medicine, Department of Internal Medicine, Wake Forest School of Medicine, Medical Center Boulevard, Winston Salem, NC 27157 Phone: 3367137129 Fax: 3367169188 (wqureshi@wakehealth.edu).

*Contributed equally

DISCLOSURES

None

predictive of mortality, JT is more predictive in the setting of QRS duration >120 ms supporting the use of JT interval in individuals with prolonged QRS.

Keywords

JT interval; QT interval; NHANES; mortality

INTRODUCTION

Prolonged QT interval has been shown to be one of the strongest risk factors of mortality in various populations.^{1–4} Prolonged QT interval is routinely encountered by clinicians and is present in 8.7% of the general population.⁵ In patients with QRS duration ≥ 120 ms, QT interval increases due to prolonged duration of QRS and thus, JT interval is recommended to be used for identifying patients at higher risk of torsades de pointes.⁶ Since QT interval is considered primarily as a measure of repolarization more than the depolarization abnormality, special considerations must be taken in the presence of QRS >120 ms where depolarization abnormality becomes a significant part of QT interval. Therefore, JT interval is thought to convey better prognostic information regarding mortality risk specifically attributable to repolarization abnormalities. Because of this, the American College of Cardiology and American Heart Association recommend measuring JT interval instead of QT interval when QRS is >120 ms.⁷ Both QT and JT interval are known to be associated with mortality.^{7, 8} However, it is not well established if QT interval mortality risk is similar for individuals with QRS duration ≥ 120 ms and <120 ms. If both JT and QT intervals provide similar prognostic information regardless of QRS duration, this will suggest they can interchangeably be used for risk stratification in patients with both normal and prolonged QRS duration. This may also help to simplify risk management of such patients. Thus, we aimed to examine the risk of mortality associated with QT and JT intervals in community-dwelling adults at different levels of QRS duration.

METHODS

The *National Health and Nutrition Examination (NHANES)* III survey was conducted using a representative sample of the non-institutionalized United States (US) population which included individuals who participated in the survey both during an in-home interview as well as subsequent visit to a mobile examination center for a period of six years from 1988 to 1994. As part of the in-home interview, data were obtained which included complete medical history encompassing individual's smoking history and medications, demographics, body mass index, blood pressure measurements and total serum cholesterol levels. Blood pressure readings were taken during the in house evaluation and again during their visit at the mobile examination center. These blood pressure measurements were averaged for each individual for this study. Elements of history were obtained by self-report. Prior history of heart failure, prior history of cerebrovascular accident and coronary artery disease were categorized as prior history of cardiovascular disease. NHANES III participants who were 40–90 years of age with quality ECGs and had medical, anthropometric measurements and mortality data available by 2006 were included in this particular study. Trained technicians

recorded standard 12-lead ECG (using Marquette Medical Systems, Milwaukee, Wisconsin) during the study visit at mobile examination center. These ECG recordings were then analyzed digitally using computerized automated analysis of the electrocardiographic data with classification of ECG abnormalities using Minnesota ECG Code Classification. All the ECG abnormalities detected by the software were later on confirmed by an ECG coder visually. The individuals who participated in the NHANES III survey were followed up until December 31, 2006 for mortality. Probabilistic matching method was utilized as a link between the NHANES III participants and the National Death Index for identification of vital status and the cause of death in individuals who died. Gender, date of birth and social security number were part of twelve identifiers which were used to match the participating individuals. The time period between NHANES III examination and December 31, 2006 or date of death with whichever occurring first was defined as the follow up duration.

Categorical variables were reported as frequency and percentage while continuous variables were reported as mean $\pm$ standard deviation (SD). Statistical significance for differences in the baseline characteristics between individuals with <120 ms and ≥ 120 ms of QRS duration were tested using the chi-square for categorical data and t-test for continuous data. Due to nonlinear relationship of QT and JT intervals as evidenced by restricted cubic spline models adjusted for model 2 covariates, QT and JT intervals were divided into three groups; $>95^{\text{th}}$ percentile (prolonged), $5 - 95^{\text{th}}$ percentile (normal) and $<5^{\text{th}}$ percentile (shortened). In the Cox regression models, we used $5 - 95^{\text{th}}$ percentile group as the reference group. Adjusted and unadjusted Cox proportional hazard regression models were used to compute hazard ratios (HR) and 95% confidence intervals (CI) for the association between QT and JT intervals with mortality. Multivariable models were adjusted as follows: Model 1 adjusted for age, sex, race, and heart rate; Model 2 adjusted for covariates in Model 1 with the addition of antihypertensive medication use, systolic blood pressure, HDL-cholesterol, total cholesterol, body mass index, smoking status, diabetes, history of previous cardiovascular disease (composite of prior history of congestive heart failure, prior history of cerebrovascular accident, prior history of coronary heart disease). Mortality rates were calculated per 1000 person years. Statistical significance was defined as $p < 0.05$. SAS v 9.2 (SAS Inc. Cary, NC, USA) was used for all analyses.

RESULTS

A total of 8,025 individuals were included in the analysis. The mean age was 60 ± 13 years. There were 41% white, 27% black, and 54% women. The mean QT interval was 407 ± 32 ms and mean JT interval was 309 ± 31 ms. The mean QRS duration was 98 ± 14 ms with 486 (6%) participants having QRS duration ≥ 120 ms. Participants with QRS duration ≥ 120 ms were more likely to be older, white, males, diabetic, ever smoker, hypertensive, had history of prior cardiovascular disease, and have higher systolic blood pressure while less likely to be black, and lower cholesterol, high density lipoprotein and heart rate (Table 1). There were no differences in BMI and diastolic blood pressure between the two groups. During a follow-up of up to 18 (median 14, interquartile range= 12–16) years, 3,045 (38%) deaths occurred, of which 286 (59%) occurred in individuals with QRS duration ≥ 120 ms. The mortality rate per 1000 person years for participants with normal, prolonged and shortened QT interval were 2.3, 3.5 and 4.0, respectively. For normal, prolonged and shortened JT interval, the mortality

rates were 2.3, 3.3 and 4.1 per 1000 person years, respectively. There were significant non-linear relationships of QT and JT intervals with mortality (Figure 1 and Figure 2). In multivariable adjusted Cox proportional hazard models, prolonged and shortened QT and JT intervals (compared to normal) were associated with increased risk of mortality (Table 2). However, the magnitude for association of mortality with prolonged JT was greater than prolonged QT interval in individuals with QRS ≥ 120 ms vs. QRS < 120 ms, with $p=0.02$ for the interaction between the two groups.

DISCUSSION

In this study, we examined the risk of mortality associated with QT and JT intervals in individuals with QRS duration ≥ 120 ms and < 120 ms. We observed that prolongation of both QT and JT intervals was associated with mortality regardless of the QRS duration. However, prolonged JT interval was a stronger risk factor for mortality than prolonged QT interval in individuals with QRS ≥ 120 ms. We also demonstrated that there is non-linear relationship of both QT and JT intervals with risk of mortality, with shortening of JT and QT being also associated with mortality. Our findings add support to using JT instead of QT in the setting of prolonged QRS duration.

QT interval prolongation has been shown to be an independent predictor of mortality in different populations^{9–12}, in patients with metabolic syndrome¹³, end stage renal disease¹⁴ and as a predictor of sudden cardiac death in patients with left ventricular hypertrophy¹⁵ and myocardial infarction¹⁶. Another study evaluated 11,739 subjects with normal conduction and 1,251 subjects with ventricular conduction defects¹⁷. This particular study included men and women from three population studies including the Cardiovascular Health Study¹⁸, Atherosclerosis Research in Communities Study¹⁹ and the Third National Health and Nutrition Examination Survey, and concluded that assessment of prolonged repolarization abnormalities requires the use of JT interval or a bivariate model for QT, with utilizing RR and QRS intervals as covariates. JT has shown to have a prognostic value in a group of patients with Wolff-Parkinsons-White syndrome pre- and post-ablation²⁰. Surface ECGs of 29 patients including 16 males and 13 females with WPW pre and post ablation were assessed. Both the QRS and the QT intervals were found to have shortened on the post ablation ECGs compared to preablation ECGs (QRS: 115 ± 23 ms vs 89 ± 15 ms, respectively; $P < 0.001$), QT: 454 ± 26 ms vs 423 ± 23 ms, respectively; $P < 0.001$). The preablation JT interval did not change, post ablation (319 ± 21 ms vs 323 ± 23 ms, respectively; $P > 0.05$). Another study evaluated QT and JT intervals as monitoring tools for drug induced repolarization changes in the setting of ventricular pacing²¹. Results revealed that mean percent increase in peak QT interval during native conduction was significantly greater than during ventricular pacing (12% vs 7%, $P = .003$). In contrast, peak JT interval during drug loading was not significantly different between native conduction and ventricular pacing ($P = .67$). This showed that JT interval is a valid assessment for repolarization changes as the JT interval during ventricular pacing correlated with JT interval during native conduction.

The influence of QRS duration on the QT and JT intervals was evaluated by Zhou *et. al.* in 20,687 normal individuals and 2,865 individuals with various ventricular conduction defects.

Variation in QRS duration resulted in 16% of total QT variation but had a negligible effect on JT interval²². It is proposed that if the QRS complex duration is increased, it will result in an increase in QT interval but JT interval will remain unaffected as it does not involve ventricular depolarization.

Prolonged QT interval in individuals with wide QRS complex can be associated with normal repolarization or prolonged repolarization times,²³ and is therefore non-specific. Prolonged QT interval results in abnormal depolarization before the completion of repolarization resulting in premature action potentials²⁴. As a result, altered ventricular repolarization dynamics predispose to serious ventricular arrhythmias and sudden cardiac death²⁵. These observations support the idea that JT interval is the true measure of ventricular repolarization²⁶.

Normal QT interval corrected for heart rate in men ranges from 350–450 ms and in women from 360 to 460 ms²⁷. QRS duration impacts the QT interval and as a result the prediction of all-cause mortality. An analysis of QT and JT intervals in patients with QRS intervals of more than 120, 120 to 150 and more than 150 ms revealed that JT interval remained relatively stable over a wide range of QRS durations, however QT interval increased with increased QRS duration²⁸. This creates a potential dilemma as to the validity of the prolonged QT interval in predicting all-cause mortality in the presence of prolonged QRS duration. Our study highlights that both QT and JT intervals are associated with all-cause mortality regardless of QRS duration, with some advantage of using JT in the setting of prolonged QRS duration. In addition, we also observed an increased risk of mortality associated with shortened QT interval (<359 ms) and JT interval (<261 ms). This suggests that shortened repolarization is also associated with increased risk of mortality. Previously this was only observed for individuals with short QT syndromes. The present study establishes the importance of JT interval in community dwelling individuals. It also suggests its inclusion in risk stratification algorithms for all-cause mortality.

The strengths of our study include centralized interpretation of ECGs, long term follow up which in turn increases the reliability of the results, large sample size with better generalizability of the United States population. Limitations of our study include self-report of several variables and thus there is a potential for recall or interviewer bias. Single ECG measurements were taken and these intervals may change with subsequent measurements. Information regarding use of QT prolonging medications was not included in the analysis, in which case there might a differential effect of JT and QT intervals in predicting mortality risk.

Acknowledgments

WTQ is funded by Ruth L. Kirschstein NRSA Institutional Training Grant 5T32HL076132-10. AJS was supported, in part, by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR000454 and KL2TR000455.

References

1. Fagher K, Nilsson A, Londahl M. Heart rate-corrected qt interval prolongation as a prognostic marker for 3-year survival in people with type 2 diabetes undergoing above-ankle amputation. *Diab Med.* 2015; 32:679–685.
2. Zhang Y, Post WS, Blasco-Colmenares E, Dalal D, Tomaselli GF, Guallar E. Electrocardiographic QT interval and mortality: A meta-analysis. *Epidemiol.* 2011; 22:660–670.
3. Villa A, Bacchetta A, Milani O, Omboni E. Qt interval prolongation as predictor of early mortality in acute ischemic stroke patients. *Am J Emerg Med.* 2001; 19:332–333. [PubMed: 11447538]
4. Veglio M, Sivieri R, Chinaglia A, Scaglione L, Cavallo-Perin P. Qt interval prolongation and mortality in type 1 diabetic patients: A 5-year cohort prospective study. Neuropathy study group of the italian society of the study of diabetes, piemonte affiliate. *Diab Care.* 2000; 23:1381–1383.
5. Montanez A, Ruskin JN, Hebert PR, Lamas GA, Hennekens CH. Prolonged qtc interval and risks of total and cardiovascular mortality and sudden death in the general population: A review and qualitative overview of the prospective cohort studies. *Arch Intern Med.* 2004; 164:943–948. [PubMed: 15136301]
6. Berul CI, Sweeten TL, Dubin AM, Shah MJ, Vetter VL. Use of the rate-corrected jt interval for prediction of repolarization abnormalities in children. *Am J Cardiol.* 1994; 74:1254–1257. [PubMed: 7977100]
7. Crow RS, Hannan PJ, Folsom AR. Prognostic significance of corrected qt and corrected jt interval for incident coronary heart disease in a general population sample stratified by presence or absence of wide qrs complex: The aric study with 13 years of follow-up. *Circulation.* 2003; 108:1985–1989. [PubMed: 14517173]
8. Pelliccia F, Critelli G. Evidence for a prognostic role of the jt interval. *Am J Cardiol.* 1993; 71:758. [PubMed: 8447280]
9. Schouten EG, Dekker JM, Meppelink P, Kok FJ, Vandenbroucke JP, Pool J. QT interval prolongation predicts cardiovascular mortality in an apparently healthy population. *Circulation.* 1991; 84:1516–1523. [PubMed: 1914093]
10. de Bruyne MC, Hoes AW, Kors JA, Hofman A, van Bommel JH, Grobbee DE. Prolonged QT interval predicts cardiac and all-cause mortality in the elderly. The rotterdam study. *Eur Heart J.* 1999; 20:278–284. [PubMed: 10099922]
11. Elming H, Holm E, Jun L, Torp-Pedersen C, Kober L, Kircshoff M, Malik M, Camm J. The prognostic value of the qt interval and qt interval dispersion in all-cause and cardiac mortality and morbidity in a population of danish citizens. *Eur Heart J.* 1998; 19:1391–1400. [PubMed: 9792266]
12. Algra A, Tijssen JG, Roelandt JR, Pool J, Lubsen J. Qtc prolongation measured by standard 12-lead electrocardiography is an independent risk factor for sudden death due to cardiac arrest. *Circulation.* 1991; 83:1888–1894. [PubMed: 2040041]
13. Li W, Bai Y, Sun K, Xue H, Wang Y, Song X, Fan X, Song H, Han Y, Hui R. Patients with metabolic syndrome have prolonged corrected qt interval (QTC). *Clin Cardiol.* 2009; 32:E93–99. [PubMed: 20014212]
14. Hage FG, de Mattos AM, Khamash H, Mehta S, Warnock D, Iskandrian AE. Qt prolongation is an independent predictor of mortality in end-stage renal disease. *Clin Cardiol.* 2010; 33:361–366. [PubMed: 20556806]
15. Panikath R, Reinier K, Uy-Evanado A, Teodorescu C, Gunson K, Jui J, Chugh SS. Electrocardiographic predictors of sudden cardiac death in patients with left ventricular hypertrophy. *Ann Noninvasive Electrocardiol.* 2013; 18:225–229. [PubMed: 23714080]
16. Schwartz PJ, Wolf S. Qt interval prolongation as predictor of sudden death in patients with myocardial infarction. *Circulation.* 1978; 57:1074–1077. [PubMed: 639227]
17. Rautaharju PM, Zhang ZM, Prineas R, Heiss G. Assessment of prolonged qt and jt intervals in ventricular conduction defects. *Am J Cardiol.* 2004; 93:1017–1021. [PubMed: 15081446]
18. Fried LP, Borhani NO, Enright P, Furberg CD, Gardin JM, Kronmal RA, Kuller LH, Manolio TA, Mittelmark MB, Newman A. The cardiovascular health study: Design and rationale. *Ann Epidemiol.* 1991; 1:263–276. [PubMed: 1669507]

19. The aric investigators. The atherosclerosis risk in communities (aric) study: Design and objectives. *Am J Epidemiol.* 1989; 129:687–702. [PubMed: 2646917]
20. Salim MA, Case CL, Gillette PC. The jt interval as a depolarization independent measurement of repolarization: Lessons from catheter ablation of the wolff-parkinson-white syndrome. *PACE.* 1995; 18:2158–2162. [PubMed: 8771128]
21. Tsai SF, Houmsse M, Dakhil B, Augostini R, Hummel JD, Kalbfleisch SJ, Liu Z, Love C, Rhodes T, Tyler J, Weiss R, Hamam I, Winner M, Daoud EG. Qtc compared to jtc for monitoring drug-induced repolarization changes in the setting of ventricular pacing. *Heart rhythm.* 2014; 11:485–491. [PubMed: 24252288]
22. Zhou SH, Wong S, Rautaharju PM, Karnik N, Calhoun HP. Should the jt rather than the qt interval be used to detect prolongation of ventricular repolarization? An assessment in normal conduction and in ventricular conduction defects. *J Electrocardiol.* 1992; 25(Suppl):131–136. [PubMed: 1297679]
23. Das G. Qt interval and repolarization time in patients with intraventricular conduction delay. *J Electrocardiol.* 1990; 23:49–52. [PubMed: 2406360]
24. Zabel M, Hohnloser SH, Behrens S, Li YG, Woosley RL, Franz MR. Electrophysiologic features of torsades de pointes: Insights from a new isolated rabbit heart model. *J Cardiovasc Electrophysiol.* 1997; 8:1148–1158. [PubMed: 9363818]
25. Singh JP, Johnston J, Sleight P, Bird R, Ryder K, Hart G. Left ventricular hypertrophy in hypertensive patients is associated with abnormal rate adaptation of qt interval. *J Am Coll Cardiol.* 1997; 29:778–784. [PubMed: 9091524]
26. Salik J, Muskin PR. Consideration of the jt interval rather than the qt interval. *Psychosomatics.* 2013; 54:502.
27. Viskin S. The QT interval: Too long, too short or just right. *Heart rhythm.* 2009; 6:711–715. [PubMed: 19389656]
28. Piotrowicz K, Zareba W, McNitt S, Moss AJ. Repolarization duration in patients with conduction disturbances after myocardial infarction. *Am J Cardiol.* 2007; 99:163–168. [PubMed: 17223412]

Figure 1. Risk of mortality across JT interval

Cubic regression model adjusted for age, sex, race, heart rate, systolic blood pressure, anti-hypertensive medications, diabetes, HDL, body mass index, total cholesterol, ever smoker, history of cardiovascular disease (history of congestive heart failure, previous stroke, and previous coronary artery disease). Knots were placed at 5th, 50th and 95th percentiles. The non-linear relationship was significant ($p < 0.001$)

Figure 2. Risk of mortality across QT interval

Cubic regression model adjusted for age, sex, race, heart rate, systolic blood pressure, anti-hypertensive medications, diabetes, HDL, body mass index, total cholesterol, ever smoker, history of cardiovascular disease (history of congestive heart failure, previous stroke, and previous coronary artery disease). Knots were placed at 5th, 50th and 95th percentiles. The non-linear relationship was significant ($p < 0.001$)

Table 1

Baseline characteristics of the study cohort

Characteristics	QRS duration (ms)		p-value
	<120 (n = 7539)	120 (n = 486)	
Age (years)	60±13	67±12	<0.001
Males	3369 (45%)	313 (64%)	<0.001
White	2916 (39%)	301 (62%)	<0.001
Black	2007 (27%)	112 (23%)	<0.001
Mexican	2394 (32%)	69 (14%)	<0.001
Antihypertensive medication use	1720 (23%)	145 (29%)	<0.001
Systolic blood pressure (mmHg)	133±20	139±21	<0.001
Diastolic blood pressure (mmHg)	75±9	74±11	0.06
Total Cholesterol (mg/dl)	217±44	211±42	0.007
High Density Lipoprotein Cholesterol (mg/dl)	51±16	48±15	<0.001
Body mass index (kg/m ²)	28±6	28±6	0.56
Heart Rate (beats per minute)	68±12	67±11	0.02
Diabetes mellitus	855 (11%)	73 (15%)	0.02
Ever smoker	4541 (60%)	319 (65%)	0.02
Previous cardiovascular disease *	238 (3.2%)	62 (13%)	<0.001

* Previous cardiovascular disease includes history of congestive heart failure, previous stroke and previous coronary artery disease; Continuous variables are expressed as mean ± standard deviations, while categorical as frequency (percentages)

Table 2

Risk of mortality associated with QT and JT intervals stratified by QRS duration

Events	Models	QRS duration (ms)	
		<120	120
		(2759/7539)	(286/486)
Prolonged QT interval (>462 ms)	Model 1 [*]	1.34(1.13,1.60)	1.48(1.04,2.12)
	Model 2 [†]	1.27(1.06,1.54)	1.50(1.03,2.17)
Prolonged JT interval (>362 ms)	Model 1 [*]	1.36(1.16,1.60)	5.53(2.21,13.87)
	Model 2 [†]	1.31(1.10,1.55)	4.75(1.86,12.11)
Shortened QT interval (<359 ms)	Model 1 [*]	1.30(1.09,1.53)	1.64(1.32,2.05)
	Model 2 [†]	1.26(1.06,1.50)	1.65(1.31,2.07)
Shortened JT interval (<261 ms)	Model 1 [*]	1.42(1.22,1.66)	1.16(0.85,1.57)
	Model 2 [†]	1.41(1.21,1.66)	1.18(0.85,1.63)

QT and JT were categorized as prolonged (>95th percentile), shortened (<5th percentile) and normal (reference group in the models).

^{*} Model 1: adjusted for heart rate, age, sex and race

[†] Model 2: adjusted for model 1 variables and systolic blood pressure, anti-hypertensive medications, diabetes, HDL, body mass index, total cholesterol, ever smoker, and history of cardiovascular disease (history of congestive heart failure, previous stroke, and previous coronary artery disease)