Effects of Head-Up Tilt-Table Test on the QT Interval

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Background. The QT interval shortens in response to sympathetic stimulation and its response to epinephrine infusion (in healthy individuals and patients with long QT syndrome) has been thoroughly studied. Head-up tilt-table (HUT) testing is an easy way to achieve brisk sympathetic stimulation. Yet, little is known about the response of the QT interval to HUT.

Methods. We reviewed the electrocardiograms of HUT tests performed at our institution and compare the heart rate, QT, and QTc obtained immediately after HUT with the rest values.

Results. The study group consisted of 41 patients (27 females and 14 males) aged 23.9 ± 8.4 years. Head-up tilting led to a significant shortening of the RR interval (from 825 ± 128 msec at rest phase to 712 ± 130 msec in the upward tilt phase, $P < 0.001$) but only to a moderate shortening of the QT interval (from 363.7 ± 27.9 msec during rest to 355 ± 30.3 msec during upward tilt, $P = 0.001$). Since the RR interval shortened more than the QT interval, the QTc actually *increased* (from 403 ± 21.5 msec during rest phase to 423.2 ± 27.4 msec during upward tilt, $P < 0.001$). The QTc value measured for the upward tilt position was longer than the resting QTc value in 33 of 41 patients. Of those, 4 male patients and 2 female patients developed upward-tilt QTc values above what would be considered abnormal at rest.

Conclusions. During HUT the QT shortens less than the RR interval. Consequently, the QTc increases during head-up tilt.

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The QT interval on the surface electrocardiogram reflects the time course of ventricular depolarization and repolarization.¹ It is subject to substantial variability that results mainly from changes in heart rate and autonomic tone.^{2–5}

Changes in heart rate and autonomic tone induced by epinephrine^{6,7} or adenosine⁸ infusions alter the QT and the corrected QT (QTc). Because the responses of the QT and QTc often differ between patients with long QT syndrome and healthy controls, the value of challenge infusions of epinephrine or adenosine for diagnosing long QT syndrome (LQTS) has been evaluated.^{8,9} However, less is known about the effects of head-up-tilt (HUT) on the QT interval.^{10,11}

The tilt-table test is a standard and widely accepted diagnostic test for evaluating patients with

syncope. It provides a diagnostic evidence indicating susceptibility to neurally mediated syncope.¹² Upright tilt-table testing is generally performed for 30 to 45 minutes at an angle between 60 and 90 degrees. The tilt reduces venous return and the autonomic system compensates by altering the autonomic tone resulting in an increase in heart rate and constriction of blood vessels in the legs. Changes in autonomic tone may condition the QT interval both indirectly, by modulating heart rate and directly by affecting depolarization and repolarization kinetics of myocardial cells through neural and receptor-mediated mechanisms.¹³ In this article, we aimed to take advantage of the physiological change in autonomic tone during the tilt-table test and describe the changes in RR, QT, and QTc intervals during the test.

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METHODS

Study Group

Between 2003 and 2005, 73 patients underwent HUT testing at Dana Hospital, Tel Aviv Medical Center. The indications for tilt table testing were standard indications, including syncope with clinical characteristics of vagal syncope and syncope of unclear etiology. None of these patients had organic heart disease or suspected LQTS and none were receiving medications likely to affect the heart rate or QT response to HUT (like beta-blockers or QT-prolonging medications). HUT was performed using a standard two phase protocol: Phase1—horizontal lying for 10 minutes followed by 70 degrees tilt for 30 minutes with consecutive monitoring of heart rate, blood pressure, saturation, and ECG. Phase 2—which was not always performed—pharmacologic provocation with nitroglycerin. Continuous 2-lead electrocardiographic recording was performed during the test and stored electronically. Thirty-two of these patients were excluded from the present study because noisy electrocardiograms (artifact caused by patient movement) or flat T waves precluded accurate measurement of the QT interval. Thus, our study cohort consisted of 41 patients. Those 41 patients were at the ages of 13 to 48, of them, 27 females and 14 males. All patients had normal baseline electrocardiogram. About half (20) of the tests we considered positive tests and nine of the positive tests required pharmacologic provocation with nitroglycerin. However, only the first HUT, performed in the absence of pharmacologic provocation, was analyzed for this study.

Measurements

Measurements were performed on the stored 2-lead ECG records of the HUT tests. The timing of the head-up tilt was recorded in the electrocardiogram. The intervals were measured during two phases: (1) the "Resting" phase was recorded at the beginning of the test during rest in the supine position on the tilt bed; (2) the "Upward Tilt" phase in which the patient position was tilted. The "Upward-tilt" time was marked on the records within the first minute of tilt. Intervals were measured in each phase from three consecutive beats (or almost-consecutive beats when noise precluded accurate definition of the end of the T wave). An average of the three measurements was made and

the corrected QT (QTc) value was calculated according to the Bazett formula.⁶ We then repeated analysis of our results using the Fridericia¹⁴ and Framingham¹⁵ formulas.

Statistics

Data are displayed as mean (SD) for continuous variables and as number and percentage for categorical variables. To examine the hypothesis that the HUT influences the QT interval and the QTc value, paired samples *t*-test was performed three times, with RR, QT, and QTc as the dependent variables and the patient position ("rest" vs. "upward-tilt") as independent variable. Independent Sample *t*-test was then performed to compare the affect on QTc between the male and female groups in the study population. Two tailed P-value ≤ 0.05 was considered significant. The SPSS statistical package was used to perform all statistical evaluation.

RESULTS

Forty-one 2-lead ECG records were reviewed and measured in the study. The study group consisted of 41 patients (27 females and 14 males) aged 23.9 ± 8.4 years (range 13–48 years). Head-up tilting led to a significant shortening of the RR interval (from 825 ± 128 msec at rest phase to 712 ± 130 msec in the upward tilt phase, P < 0.001) but only to a moderate shortening of the QT interval (from 363.7 ± 27.9 msec during rest to 355 ± 30.3 msec during upward tilt, P = 0.001). Since the RR interval shortened more than the QT interval, the QTc actually increased (from 403 ± 21.5 msec during rest phase to 423.2 ± 27.4 msec during upward tilt, P < 0.001) (Table 1).

On average, the Upward Tilt RR interval was shorter than Rest Phase RR by 112.5 ± 108.2 msec, P < 0.001. Upward Tilt QT interval was shorter than Rest Phase by 8.8 ± 15.4 msec, P < 0.001.

Table 1. Paired Sample Statistics

		Mean	Std. Deviation	Std. Error Mean
Pair 1	RR_Rest	825.2033	148.97063	23.26530
	RR_Up	712.6829	130.33124	20.35432
Pair 2	QT_Rest	363.74	27.891	4.356
	QT_Up	354.9593	30.28680	4.73000
Pair 3	QTc_Rest	402.9496	21.51063	3.35940
	QTc_Up	423.2369	27.38126	4.27623

Table 2. Paired Samples Test

		Paired Differences							Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		t	df	
					Lower	Upper			
Pair 1	RR_Rest – RR_Up	112.52033	108.17881	16.89469	78.37488	146.66577	6.660	40	.000
Pair 2	QT_Rest – QT_Up	8.78049	15.37957	2.40189	3.92610	13.63488	3.656	40	.001
Pair 3	QTc_Rest – QTc_Up	–20.28736	23.24414	3.63013	–27.62412	–12.95060	–5.589	40	.000

Consequently, Upward Tilt QTc value was prolonged by 20 ± 23.2 msec, $P < 0.001$ versus rest QTc (Table 2). No significant differences in the response of the different electrocardiographic parameters to tilting were noticed between the male and female group in our study or between patients with positive and negative HUT.

With the Bazett formula, all the patients in our study had a resting QTc within normal QTc range (lower than 440 milliseconds for males and 460 for females). Two female patients had resting QTc of 455 milliseconds. The QTc value measured for the upward tilt position was longer than the resting QTc value in 33 of 41 patients. Of those, 4 male patients and 2 female patients developed upward-tilt QTc values above what would be considered abnormal at rest. Four more female patients had upward-tilt QTc values of between 440 and 460 milliseconds.

When we used the Fridericia correction formula for QT we found a more modest HUT-induced QT prolongation of 9.6 ± 15.8 msec, $P < 0.001$. With the Framingham correction formula, HUT induced a shortening of QTc of 8.7 ± 15.4 milliseconds $P = 0.001$.

DISCUSSION

Major Findings

We evaluated the effects of HUT on the QT interval of 41 patients (27 females and 14 males) with normal QT interval at rest. As expected, HUT led to sinus rate acceleration and QT shortening. However, the QT shortened less than the RR interval. Consequently, with the Bazett formula the QTc increased significantly in response to HUT. Indeed,

QTc prolongation during HUT was observed in 3 out of 4 patients. Moreover, "prolonged QTc" intervals were observed during HUT in 14% patients who had normal QTc at rest. Analysis of our results using the Fridericia or Framingham formulas led to less increment, or even slight shortening of the QTc, respectively. This is not surprising in view of the fact that the Bazett formula over-corrects the QTc during relatively rapid heart rate. Nonetheless, despite its imperfections, the Bazett formula is still the formula most commonly used in clinical practice. Thus, the QTc prolongation observed with this formula has important clinical implications (see below).

Previous Studies

Mizumaki et al.⁷ compared the QT-RR relationship during HUT tests in 18 patients with vasovagal syncope and 18 age and sex matched controls. They also found an inadequate adaptation of the QT interval to changes in the RR interval during HUT. QT-RR relation was the same during tilt-up in patients with vasovagal syncope. Huang et al.⁸ studied the response of QT-RR relation to abrupt postural change and found lack of fixed relationship between the heart rate and QT interval suggesting that the mechanisms that regulate the heart rate and QT may be independent.

Interpretation of the Results

The QT interval shortens during faster heart rates; however, the adaptation of the QT interval to sudden heart rate acceleration is not instantaneous.^{3,16} Indeed, following a sudden shortening of pacing cycle length it may take up to 2 minutes

for complete QT adaptation to the new pacing rate.¹⁶ During HUT, changes in the autonomic nervous system include increase of sympathetic tone, withdrawal of parasympathetic tone and changes in circulatory catecholamines. These changes may affect QT interval independently of the changes in heart rate.^{2,17} Nevertheless, the fact that shortening of the QT interval lags behind the increase in heart rate has been demonstrated also during exercise.¹⁸

Limitations

This is a retrospective study that used the records of tilt-table tests for assessing the changes in QT, RR, and QTc relations in these patients. Our study group consisted of subjects that were sent for tilt-table test to assess possible vasovagal syncope. Such subjects might not represent the general population due to their autonomic tone responses. However, Mizumaki et al.⁷ suggest that there is no difference in the QT-RR relation during the tilt up between controls and patients with vasovagal syncope.

Conclusion and Clinical Implication

The response of the QT interval to HUT is slower than the change in heart rate, leading to significance QTc prolongation when the Bazett formula is used. In our study 6 of 41 patients developed QTc intervals exceeding "normal values" in response to HUT and 4 female patients had upward-tilt values in the high normal range. This observation has three important potential implications: (1) Inadvertent "head-up tilting" may occur, for example, at the onset of exercise testing. This occurs when the tested patient awaits the onset of the test while seating only to rise up and stand for the onset of the test just as the baseline or "resting electrocardiogram" is recorded. In fact, we have encountered patients referred for evaluation following the incidental finding of "long QT" in whom all subsequent electrocardiograms were normal. The common denominator to these patients was the presence of mild QT prolongation *only* in the "baseline electrocardiogram" performed immediately prior to the onset of an exercise test. Similarly, patients may stand-up (i.e., performed an active HUT) while wearing Holter recorders. Care should be taken to avoid over-diagnosis of long QT syndrome based on electrocardiograms performed soon after active

or passive head-up tilt. (2) Patients with congenital long QT syndrome often develop exaggerated responses to sudden changes in heart rate or autonomic tone.^{6-9,19} Therefore, HUT testing could prove to be a diagnostic value for patients with LQTS. In fact, based on the results of this pilot study we performed a much larger study comparing the effects of brisk standing on the QT interval on patients with congenital LQTS and matched controls and found that the QTc prolongation is response to brisk standing is exaggerated in the LQTS.²⁰

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