Analysis of QT Interval during Passive Tilt Test: Comparison of Different Correction Formula

F Badilini, P Maison-Blanche, R Spaulding*, M Palma*, P Coumel

Hôpital Lariboisiére, Paris, France
*Marquette Medical Systems, Milwaukee, WI, USA

Abstract

We analyzed the QT and RR interval time series continuously recorded during 90 degrees passive Tilt test in 10 young healthy subjects (age 26±5 years, 5 females). Changes in QT interval were assessed on 1 minute time related templates and on rate-independent waveforms obtained by averaging beats preceded by the same RR interval. Following Tilt, the mean RR interval shortened from 927±73 ms to 733±118 ms, p<0.01); Bazett corrected QT increased (QTb : from 403±12 ms to 413±21 ms, p=0.058) whereas exponential QTe did not change significantly. Conversely, QTf and QTl (respectively Fridericia and linear rate-corrected QT), decreased after Tilt (e.g. QTf: 398±11 ms vs 391±14 ms, p<0.05). Comparison at identical heart rate confirmed a QT shortening (QTrr: 387±14 ms vs 363±15 ms, p<0.01). Thus, rate-correction formula are inconsistent and should be used with caution when assessing autonomic nervous system changes.

1. Introduction

Tilt test is an autonomic experiment clinically used in various settings mainly to diagnose neurocardiogenic syncope [1]. In physiologic studies, it is a well-known model of sympathetic stimulation [2].

The effects of sympathetic stimulation and blockade on ventricular repolarization have been extensively described in experimental studies (cells, AP, animal). However, much less is known on the influences of this stimulation in humans. Due to the increase on heart rate associated with this procedure, the overall effect of Tilt on the non-corrected QT interval is that of a shortening (see Fig 1). The challenging question would actually be on whether this shortening is purely an heart rate effect or rather the reflexion of the sympathetic stimulation on the ventricle. Thus, this experiment may represent the ideal setting to test the extensibility of classical correction formula in continuous ECG monitoring.

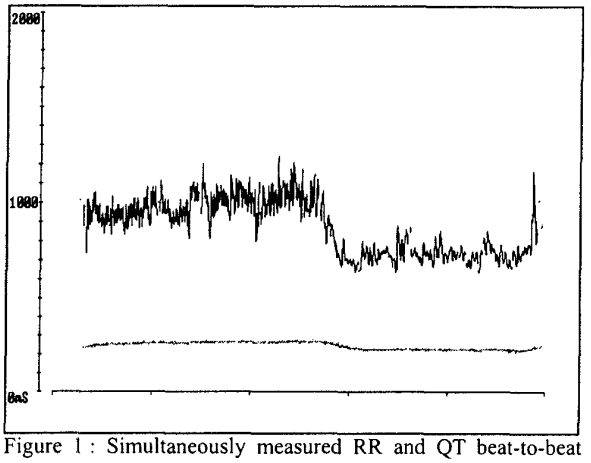

Figure 1 : Simultaneously measured RR and QT beat-to-beat time series.

2. Methods

2.1. The MARS research project

In general, the development or research applications in the field of Holter recordings relies on a proper interface with a commercial system. Thus, the achievement of a specific study is conditioned to the obtainment of internal files format and often to their transfer on a different computer platform.

The MARS ambulatory system (Marquette Medical Systems, Milwaukee, WI, USA) permits a direct implementation of research applications on the same environment of the commercial product. This is possible thanks to the complete open-architecture philosophy of this system which is based on object-oriented

0276-6547/98 $10.00 © 1998 IEEE

programming. All C++ interfaces to the classes used in the MARS are available, both for user-interface graphic objects and Holter specific objects such as annotation lists, ECG waveforms, trends, histograms and so for. The access to internal database is thus achieved with standard calls to specific class handlers. In this way the researcher has complete access to the whole set of internal data. As part of a supported project, we have developed the Lariboisiere ATREC system directly inside the MARS environment. Main goal of this project consisted in the development of a package of routines for analysis of repolarization and in particular to the measurement of QT intervals from single beats or from P-QRS-T complexes obtained after averaging techniques. The results here reported are part of this project.

2.2. Study population

The study population consisted of 10 young healthy subjects (age 26 +/- 5 years, 5 females) extracted from a larger database previously described [3]. No subject had history of cardiac disease, hypertension or diabetes mellitus. None had prior history of syncope and none were receiving medications known to affect the autonomic nervous system. Inclusion criteria required a normal physical examination, normal blood pressure and resting ECG in sinus rhythm. All volunteers provided a written informed consent.

2.3. Data acquisition and analysis

All tests were performed at about 3:00 pm and all subjects were instructed to consume a light lunch without alcohol or caffeine absorption and to avoid smoking. The temperature of the room was between 22° and 24°C. Subjects were placed on an electrically driven tilt-table and ECG was monitored by a three-lead analog Holter recorder (Marquette 8500) with an XYZ configuration. During the entire procedure, subjects were instructed to breathe concurrently with an auditory signal sound at a fixed rate of 15 cycles per minute (0.25 Hz). After approximately 15 minutes in supine position, the table was rotated to a 90° upright position that was maintained for another 15 minutes. None of the volunteers experienced syncope or any symptom.

Analog data was successively digitized on the MARS system at 128 Hz and with a resolution of 12 bits. ECG digital files were processed by an algorithm which identified each QRS complex with first-derivative adaptive threshold algorithm and estimated the apex of the R wave after parabolic interpolation. The continuous series of RR interval were then visualized and stable 5 minute segments before and after the transition were selected for analysis. In particular, post-tilt data segments always started within 30 seconds after tilt onset and range of interindividual variations was very small (in the range of seconds). No premature beats were observed in the complete set of ECGs and consequently there was no need of RR interpolation.

To assess the rate-independent effect of Tilt on QT interval, averaged beats were obtained for each minute and four different rate-correction formula were applied to the 5 averaged templates (see Table 1): QTb (Bazett square-root), QTf (Fridericia cubic-root), QTl (Framingham linear fit) and QTe (Sarma exponential fit). In addition, for each subject, all individual sinus beats with preceding RR intervals common to the two positions were averaged to allow a comparison at identical heart rate (QTrr). In all templates, the QT interval was automatically determined by a dedicated program which determines QRS onset after high-pass filtering and T offset on the basis of smoothed first and second derivatives of low-pass filtered ECG waveform (4th order recursive Butterworth filter) [4]. The algorithm independently processes each of the 3 recorded leads; however, results of this study were obtained from analysis of Lead X.

2.4. Rate-correcting the QT interval

The four correction formula implemented are reported in Table 1. QT correction formula are derived from the correspondent prediction formulas by defining the QT when RR=1 sec as the corrected QTc and solving for one of the parameters [5]. Thus, monoparametric prediction formula yield to parameter-free correction formula (Bazett and Fridericia), whereas prediction formula with 2 or three parameters (linear and Exponential) yield respectively to corrected QT dependent on 1 and 2 parameters which need to be set.

Table 1. Prediction and Correction formula used

	Prediction	Correction
Bazett	$QT = a\sqrt{RR}$	$QTb = QT/\sqrt{RR}$
Fridericia	$QT = a\sqrt[3]{RR}$	$QTf = QT/\sqrt[3]{RR}$
Linear	$QT = aRR + b$	$QTl = QT + a(1 - RR)$
Expon.	$QT = a - be^{-kRR}$	$QTe = QT - b(e^{-k} - e^{-kRR})$

Correction formula shown in Table 1 are derived considering the RR interval expressed in seconds. Slightly different expressions (only for Linear and Exponential) are obtained when considering the RR interval in msec.

The most popular implementation of Linear correction formula is certainly the Framinghmam Heart Study [6]. In this population of 5018 subjects the parameter a was found to be 0.154. Exponential formula was initially introduced by Sarma [7]. However the largest cohort of patients on which this formula has been applied is the database of Seven Country Study which consisted of 881 middle-aged men [8] where the b and k parameters were found to be -0.431 and 2.3 respectively.

3. Results

Results are summarized in Table 2. All values reported are expressed in mean±standard deviation and units are msec. Last column indicates the p-value after comparison by Wilcoxon paired test.

Table 2. Comparisons of corrected QT intervals

	Supine	Tilt	Δ (S-T)	p
RR	927±73	733±118	194±99	<0.01
QTb	403±12	413±21	-10±15	0.058
QTf	398±11	392±14	6±8	<0.05
QTl	399±10	393±13	6±8	<0.05
QTe	397±10	391±13	5±9	NS
QTrr	387±14	363±15	25±12	<0.01

Figure 2 shows the X and Y Leads of two overlapped 1-minute templates before and after tilting for one representative subject. In this case, the RR interval changed from 963 to 717 msec and the raw QT interval from 387 to 348 msec (on Lead X). QTb actually augmented from 394 to 411 msec whereas all other corrected intervals indicated a slight decrease.

Among the 10 subjects analyzed, there was one case for which the mean RR interval did not change after tilt (970 vs 977 msec). Nevertheless, the presence of a sympathetic stimulation was confirmed from power spectral analysis by the typical increase of LF/HF ratio. Despite the lack of change of RR interval, the raw QT interval of this subject shortened from 391 to 370 msec.

4. Discussion

Limitations of correction formula, and particularly the under- and over-correction of Bazett (respectively for slow and fast heart rates) are well-known. Results of this study seem to indicate that even at moderate and short-term changes, the use of these formula is inadequate.

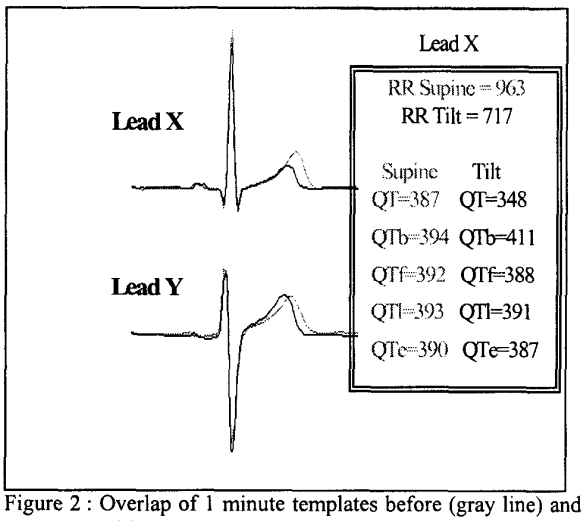

Figure 2 : Overlap of 1 minute templates before (gray line) and after tilting (black line).

Thus, QT rate-correction should only be employed to the field of resting ECG.

The major limitation in determining a QT interval "free" of the heart rate is that we still lack knowledge on the transfer function between RR and QT, and in particular of its memory (i.e. on how many beats it takes to obtain a stable QT given an abrupt change in RR). What we also know is that the characteristics of this system change rather frequently and are most likely affected by autonomic nervous system long-term modulations. Experiments at the cellular level have shown that the response of monophasic action potential to step-changes in heart rate are similar to those of a 1st order system (or maybe to those of a 2nd order with dumped overshoots) [9]. In this regard, even the QTrr values here reported have to be taken with caution, as the identical RR intervals used for the comparison represent two different dynamic instances of the hypothetical transfer function.

Figure 3 shows 2 overlapped templates before and after tilt for the subject with no heart rate change after tilt described in previous paragraph. As we have said, despite an unchanged RR interval, the QT interval still shortened. Thus, this example supports the hypothesis of a QT shortening associated with Tilt and seems to indicate a different action of sympathetic stimulation at the atrial and ventricular levels. This is in accordance with the only similar experiment previously performed (to our knowledge) where Tilt was evaluated after double blockade [10].

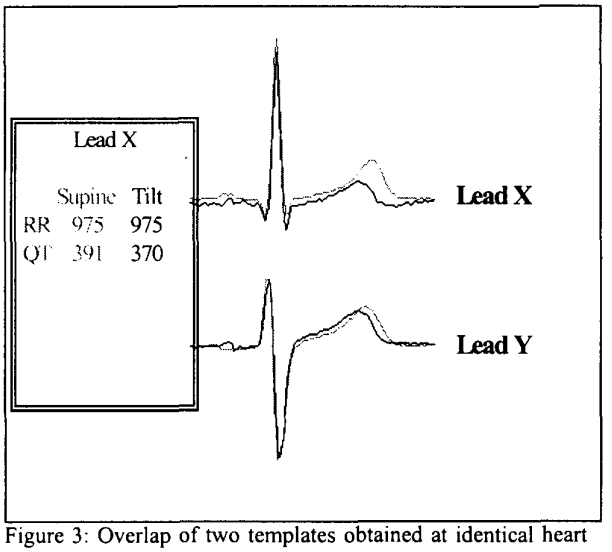

Figure 3: Overlap of two templates obtained at identical heart rate (RR=975 in both tilt and supine positions).

4.1. Limitations

The methodology described, and in particular the comparison at identical heart rate requires the existence of an overlap in RR interval. Thus, an intrinsic limitation is the exclusion of experiments for which this condition was not satisfied.

5. Conclusion

Even in the context of a very simple test, the rate-independent effect on QT interval is not simple to assess. In particular, the use of classical correction formula is clearly contradictory. Comparison of QT interval obtained at identical heart rate (identical preceding RR interval) seems to suggest an effect of QT shortening after tilt maneuver.

References

[1] Natale A, Akhtar M, Jazayeri M *et al.* Provocation of hypotension during head-up tilt testting in patients with unexplained syncope. *Circulation* 1995; **92**: 54-8.

[2] Montano N, Gnecchi Ruscone T, Porta A *et al.* Power spectrum analysis of heart rate variability to assess the changes in sympathovagal balance during graded orthostatic tilt. *Circulation* 1994;**90**:1826-31.

[3] Jasson S, Médigue C, Maison-Blanche P *et al.* Instant power spectrum analysis of heart rate variability during orthostatic tilt using a time-/frequency-domain method. *Circulation* 1997;**96**:3521-36.

[4] Badilini F, Maison-Blanche P, Childers R *et al.* QT Interval analysis on ambulatory ECG recordings: a selective beat averaging approach. *Med & Biol Eng & Comp*, in press.

[5] Molnar J, Weiss J, Zhang F *et at.* Evaluation of five QT correction formulas using a software-assisted method of continuous QT measurement from 24-Hour Holter recordings. *Am J Cardiol* 1996;**78**:920-6.

[6] Sagie A, Larson MG, Goldberg RJ, Bengston JR, Levy D. An improved method for adjusting the QT interval for heart rate (The Framingham Heart Study). *Am J Cardiol* 1992;**70**:797-801.

[7] Sarma JSM, Sarma RJ, Bilitch M *et al.* An exponential formula for heart rate dependence of QT interval during exercise and cardiac pacing in humans: reevaluation of Bazett's formula *Am J Cardiol* 1984; **54**: 103-8.

[8] Puddu PE, Jouve R, Mariotti S *et al.* Evaluation of 10 QT prediction formulas in 881 middle-aged men from the seven countries study: emphasis on the cubic root Fridericia's equation. *J Electrocardiol* 1988; **21**: 219-29.

[9] Franz MR, Swerdlow CD, Liem BL et *al.* Cycle-length dependence of human action potential duration in vivo: effects of single extrastimuli, sudden sustained rate acceleration and deceleration, and different steady-state frequencies. *J Cin Invest.* 1988; **82**: 972-9.

[10]Ahmed M, Kadish AH, Goldberger JJ. Autonomic effects on the QT Interval. *A.N.E.* 1996 ; **1**(1) 44-53.

Address for correspondence:
F Badilini, via Paolo VI 25018 Montichiari (BS), Italy
E-mail: badilini@aol.com