The Myth of QT Shortening by Weight Loss and Physical Training in Obese Subjects With Coronary Heart Disease

Luca A. Gondoni¹, Anna M. Titon¹, Mariella Montano¹, Giulia Caetani¹, Ferruccio Nibbio¹ and Peter J. Schwartz²–⁷

This study aims to describe the changes that a period of low-calorie diet and physical training determines in heart rate and in corrected QT (QTc) interval in obese patients with coronary heart disease (CHD) and to verify whether it is effective in shortening the QT interval using three different methods for QT correction. Two hundred and seventy obese white patients (162 males—60%) affected with stable CHD and treated with β-blockers were retrospectively studied in the setting of a program aimed at losing weight through training (aerobic activity + strength exercise) and diet (80% of estimated resting energy expenditure). Age was related to RR interval, QTc was related to left ventricular ejection fraction (EF) while sex exerted no effects. At the end of the study period heart rate decreased by 8.3% and noncorrected QT increased by 3.0%; QT corrected with the Bazett formula decreased by 0.7% (P = 0.007), QT corrected with the Fridericia formula increased by 0.5% (P = 0.023), whereas the modifications were nonsignificant when the Framingham correction was used. In conclusion, contrary to the current views, physical training and diet, which are effective in reducing heart rate, produced no clinically relevant change in the QT interval.

INTRODUCTION

Obesity is associated with several electrocardiographic (ECG) abnormalities and a relationship between obesity and duration of the QT interval was first described >20 years ago (1). A prolonged QT interval is an established risk factor for sudden death both in patients with coronary artery disease and in patients with genetic disorders (2–4). Therefore QT prolongation may be a contributing factor to the excess of cardiovascular mortality which has been described in obese subjects who have an increased risk of arrhythmias and sudden death, even in the absence of cardiac dysfunction (5).

Weight loss can improve or prevent many of the obesity-related comorbidities factors and can improve heart rate (6,7) and left ventricular function (8); moreover physical training determines a shortening of heart rate corrected QT (QTc) possibly as a result of an improved autonomic balance: the shortening of QTc interval may reduce the risk of cardiovascular mortality.

Given the tight relation between the QT interval and heart rate, a correction is necessary and several formulae have been tested and used (9,10): each of these formulae makes assumptions on the relationship between QT and heart rate and only a few of them completely remove the dependence of QT interval on heart rate. It has become a vexed question to decide which correction method is the most appropriate.

Here, we describe the changes in heart rate and in the QT and QTc interval in obese patients with coronary heart disease (CHD) after a short period of low-calorie diet and physical training using three different methods for the correction of the QT interval. The objective of our study was to verify whether the current belief that training in obese patients is associated with QTc shortening is indeed correct.

METHODS AND PROCEDURES

Patients

The study was conducted at San Giuseppe Hospital (Piancavallo Oggebbio VB, Italy). We retrospectively studied 270 white patients (162 males—60%) affected with obesity and stable CHD who entered a program of weight loss based on a low-calorie diet and physical activity. Obesity was defined as BMI ≥30 kg/m². CHD, was defined as a history of at least one of the following: myocardial infarction, coronary...
artery by-pass, coronary angioplasty. Patients with recent (<4 weeks) myocardial infarction, coronary artery by-pass, or coronary angioplasty were excluded. Patients were also excluded if they were not in sinus rhythm, were taking antiarrhythmic treatment, had bundle branch block or QRS duration >100 ms. Each patient was treated with β-blockers and drug treatment was not modified during the study period. The patients’ ECG was checked at the end of the program after a mean interval of 23 ± 4 days.

**Physical training**
The program entailed daily sessions (6 days a week) of aerobic activity which included 30-min sessions of cycloergometer, walking at low speed for about 45 min (at an estimated workload of 3–4 METs), and strength exercise. All patients underwent a personal interview with a physical trainer to individualize the activity program. Every week the activity level was checked and the workload was redefined on the basis of the attained results.

**Hypocaloric diet**
Resting energy expenditure was predicted by the Harris Benedict equation (11). Diet was assigned by a specialist after a personal interview with the patient. The caloric intake was set at ~80% of resting energy expenditure and was balanced with 50% of energy from carbohydrates, 30% from lipids, and 20% from proteins.

**ECG**
ECG was recorded in the morning after a light breakfast which did not include caffeinated beverages, at the beginning and at the end of the study. Calculations of heart rate and QT interval were automatically performed by the instrument (Cardiette Daedalus View; H&C Medical Devices, Sesto San, Giovanni, Italy). QT was corrected using three different formulae:

- **Bazett**: QTc = QT/RR0.5 (12);
- **Fridericia**: QTc = QT/RR0.33 (13);
- **Framingham**: QTc = QT + 0.154(1 − RR) (14).

To validate the automatic measurement of the QT interval we randomly selected 55 ECG recordings and we blindly measured QT manually and plotted it against automatic QT values of the same ECGs. The bivariate correlation index was 0.989 (P < 0.001) and the mean difference between manually and automatically measured QT was 0.6 ms.

**Echocardiogram**
Two-dimensional and two-dimensionally directed M-mode echocardiographic parameters were obtained with a GE Vivid 7 Dimension instrument (GE Medical Systems, Milwaukee, WI). The exams were conducted during quiet respiration with the patient in the left lateral recumbent position. Parasternal long- and short-axis and apical two- and four-chamber views were used for evaluating left ventricular function with a multifrequency sector transducer set on ideal frequency to obtain optimal imaging. Ejection fraction (EF) was calculated either with modified Simpson or Teichholtz method. Left ventricular mass was calculated by the Devereux formula (15) and relative diastolic wall thickness was calculated by the formula (IVSD + LVPWD)/LVDD. We corrected left ventricular mass for height 2.7 to minimize the effect that overweight would have if we corrected the mass for body surface area (16).

**Statistical analysis**
Continuous data are presented as mean ± s.d. whereas categorical variables are presented as number and percentage. EF was recoded as a categorical variable: <30% was recoded as severe reduction, 30–44% as moderate reduction, 45–54% as mild reduction, and ≥55% was considered normal (17). EF was also considered as a continuous value for bivariate correlation. The differences between QT intervals before and after weight loss were determined using t-test for paired data. Statistical analysis has been performed with SPSS 16.0 package (SPSS, Chicago, IL).

**RESULTS**
General characteristics of the study population are described in Table 1. Of the 213 patients who had left ventricular hypertrophy, 68% had concentric hypertrophy and 32% eccentric hypertrophy; moreover 11 patients (4%) had concentric remodeling of left ventricle.

Baseline noncorrected QT was strongly related to RR interval (r = 0.867; P < 0.001). It should be noted that the QT interval corrected with the Bazett formula was still strongly related to RR (r = −0.470, P < 0.001), whereas it was not significantly correlated to noncorrected QT (r = 0.022, P = 0.717). On the contrary, the other two methods of correction showed a strong relationship with noncorrected QT (P < 0.001 for both); whereas the Framingham method, that utilizes a linear correction, was not related to RR. Fridericia correction kept a positive correlation with RR (r = 0.217, P = 0.001).

Age was related to RR interval and therefore to noncorrected QT. The only method of QT correction that kept its significance with age was Fridericia.

QTc, independently of the method used for correction, was related to EF. Gender and diagnosis of hypertension exerted no effects on the study variables. The presence of diabetes was associated with a shorter RR interval and higher value of Bazett (0.917 ± 0.180 s vs. 0.977 ± 0.153 s; P = 0.006 and 0.420 ± 0.019 s vs. 0.414 ± 0.019 s; P = 0.023, respectively), but not with noncorrected QT or to QT corrected with the other methods.

BMI was positively related to heart rate (R = 0.141; P = 0.020) and to Bazett (R = 0.140; P = 0.022), but not to Fridericia or Framingham.

At the end of the study period, BMI decreased by 3.1% (from 28.1 ± 5.0 to 36.9 ± 4.7 kg/m²; P < 0.001) and heart rate by 8.3% (from 65 ± 12 to 60 ± 10 beats/min; P < 0.001). The number of patients who had heart rate >70 beats/min decreased from 70 (26%) to 33 (12%).

**Table 1 General characteristics of the study population**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>59 ± 9</td>
</tr>
<tr>
<td>Female sex</td>
<td>108 (40%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>270 (100%)</td>
</tr>
<tr>
<td>Mild (BMI = 30–34.9 kg/m²)</td>
<td>85 (32%)</td>
</tr>
<tr>
<td>Moderate (BMI = 35–39.9 kg/m²)</td>
<td>109 (40%)</td>
</tr>
<tr>
<td>Severe (BMI ≥40 kg/m²)</td>
<td>76 (28%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>225 (83%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>104 (39%)</td>
</tr>
<tr>
<td>EF</td>
<td></td>
</tr>
<tr>
<td>Normal (&gt;55%)</td>
<td>164 (61%)</td>
</tr>
<tr>
<td>Mildly reduced (45–55%)</td>
<td>71 (26%)</td>
</tr>
<tr>
<td>Moderately reduced (30–44%)</td>
<td>33 (12%)</td>
</tr>
<tr>
<td>Severely reduced (≤30%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>LVH</td>
<td>213 (79%)</td>
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</tbody>
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EF, ejection fraction; LVH, left ventricular hypertrophy.
Noncorrected QT increased by 3.0% (from 0.404 ± 0.032 to 0.416 ± 0.029 s; P < 0.001), but, even if statistically significant, only small differences emerged when QT was corrected. QT Bazett decreased by 0.7% (P = 0.007), QT Fridericia increased by 0.5% (P = 0.023), whereas the modifications were nonsignificant when the Framingham correction was used. In other words, we found only very little changes that are likely nonrelevant from a clinical standpoint. Figure 1 compares the values of QT interval, either noncorrected or corrected with the three described methods, at the beginning and at the end of the study.

DISCUSSION

The main finding of the present study is that, contrary to the current views, physical training and diet produce no relevant change in the QT interval. A small improvement (i.e., shortening) of the QTc is apparent only when the correction is made using the Bazett formula, whereas the other formulae that were tested documented either a modest prolongation in QTc (Fridericia) or no variation at all (Framingham linear method).

Weight loss increases vagal tone and reduces heart rate with an attendant prolongation of noncorrected QT interval. Several studies describe a shortening of the QTc interval which can very likely be secondary to heart rate reduction: indeed some authors recognize that QTc has a significant relation with heart rate (18,19). Other studies used the Bazett formula for correction and found a decrease in QTc, but they did not report heart rate behavior after weight loss (20,21). Also in nonobese subjects physical training determines a shortening of QTc (22), but in this population the correction was done once again with the Bazett formula and heart rate was lower after training.

Interestingly, in another study that documented a reduction in QT dispersion after a dramatic weight loss, QTc (using Bazett formula) and heart rate did not change after 12 weeks of follow-up (23). The origin of the misconception reflected in the view that QT interval shortens in obese subjects who lose weight lies in the fact that all these studies have used the Bazett formula and did not consider that the apparent shortening was actually secondary to the increase in the RR interval.

As the time interval between the two ECG measurements was relatively short, and as the patients continued with their regular medications throughout this period it is reasonable to exclude external confounding factors that might have influenced the QT interval. Our patients were all on β-blockers treatment: because current guidelines recommend the use of β-blockers for patients with chronic CHD, the relevance of our findings to clinical practice is enhanced.

The main determinants of the duration of QT interval, besides genetic factors, are heart rate and autonomic tone. After training and weight loss vagal tone is increased and sympathetic tone is decreased: a 10% increase in body weight is associated with a decline in vagal tone, accompanied by a rise in mean heart rate, and conversely heart rate declines during weight reduction. In patients of normal weight aerobic exercise increases vagal tone and reduces sympathetic tone after myocardial infarction (24). In subjects with noncomplicated obesity, regular physical activity increases vagal tone and improves autonomic balance (25).

We would like to stress that the reduction of heart rate is a relevant point of its own if we consider that a high heart rate is associated to an increased risk of mortality in many studies, being a general denominator for several pathophysiological mechanisms (26–31). We have data that suggest that reducing heart rate in patients with CHD can improve survival (32): from this standpoint the reduction of the number of patients that had a heart rate >70 beats/min can be a marker of improved prognosis, thus confirming the role of weight loss and physical training in the comprehensive approach to CHD.

Even if nonoptimal, the Bazett method for correction of the QT interval is deep-rooted in clinical practice and will probably be the more widely used method also in the future, being capable of identifying patients who are at high risk for sudden death (3).

Limitations of the study

The interval between baseline and final measurements was short, but a mean time of 23 days should be sufficient to evaluate the modifications in parameters related to the autonomic balance based on previous studies (25). Heart rate variability data were not available in an adequate number of patients.

In conclusion, QTc shortening is not a reliable tool to study improvement of autonomic balance after weight loss and physical training, heart rate reduction could be a much simpler tool to be used as a marker of an improved autonomic status (33). Previous studies indicating that the QT interval shortens after weight reduction and physical training in obese subjects should be reassessed on the basis of the interplay between heart rate changes and the QT interval: what happens is that the heart rate slows and lower heart rates are associated with a decreased mortality risk.

DISCLOSURE

The authors declared no conflict of interest.

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REFERENCES