Influence of posture and handgrip on the QT interval in left ventricular hypertrophy and in chronic heart failure

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ABSTRACT

In certain disease states prolongation of the QT interval has been shown to be arrhythmogenic. Whether QTc interval changes with position and thus whether certain positions are more arrhythmogenic than others is not known for different diseases that predispose to arrhythmias, and was therefore studied. Patients with left ventricular hypertrophy and heart failure, and the appropriate matched controls, were recruited. Subjects were studied in the lying, sitting, standing and squatting positions and had QT intervals determined by computer algorithm 2 min after each position change. After resting, QT interval was determined while the subjects performed maximum handgrip exercise with their dominant hand. QT intervals were rate-corrected using Bazett’s method. QTc interval is prolonged in heart failure patients compared with either left ventricular hypertrophy or control subjects in the lying and sitting position, but not in the standing or squatting position. The QTc intervals for heart failure and control subjects were, respectively, 443 ± 7 ms versus 421 ± 6 ms when lying (P < 0.05), 451 ± 10 ms versus 419 ± 6 ms when sitting (P < 0.05), 429 ± 10 versus 414 ± 7 ms when standing (P not significant) and 437 ± 10 versus 419 ± 8 ms when squatting (P not significant). The values for patients with hypertrophy did not differ from control values. Maximum handgrip does not affect the QTc interval in heart failure, but prolongs it in both the hypertrophy and control groups. Position and static exercise are important modifiers of QTc interval and their effect depends on the condition of the left ventricle.

INTRODUCTION

Diurnal variation, with nocturnal prolongation, of the QTc interval has been attributed to the circadian rhythm [1]. A prerequisite in interpreting whether nocturnal QT interval prolongation is due to the circadian rhythm is the assumption that changes in posture from the upright/sitting position to the supine position are not associated with changes in the QTc interval. It is possible that changes, such as in blood pressure, pre/afterload and autonomic nervous system tone, which occur with changes in posture may affect repolarization, and that part, or all, of the QTc interval lengthening that occurs at night is due to changes associated with change in posture rather than to the circadian rhythm [2,3]. This may have clinical importance, as in many disease states QTc interval prolongation is a risk factor for ventricular arrhythmias [4,5], and strategies may be developed to shorten QT interval in order to prevent sudden cardiac death. If nocturnal QT interval lengthening is due to posture change rather than to the circadian rhythm, different strategies will be needed. Previous studies have examined the effect of posture in a number of conditions [6–10]. However, these previous studies did not examine posture-related changes in the QT interval in two common conditions associated with arrhythmias, left ventricular hypertrophy and chronic heart failure. Therefore, in this study the influence of posture in these conditions was examined.

The QT interval is affected by the autonomic nervous system [3,11,12]. For example, sympathetic nerve stimulation leads to QT interval shortening [11]. Isometric
handgrip to near maximal voluntary contraction leads to sympathetic nervous system activation and one would therefore expect the QT interval to shorten in normal subjects, but in heart failure there is a down-regulation of cardiac sympathetic receptors, so one might expect hand gripping to have less effect on the QT interval [13]. As there have been no previous studies on the effect of this manoeuvre on the QTc interval in either left ventricular hypertrophy or in heart failure, this study sought to determine the effect of handgrip on the QTc interval in these conditions.

METHODS

Subjects
Subjects were recruited to the study after approval from the local ethics committee and with informed consent. The aim was to recruit subjects at high risk of ventricular arrhythmias, and two study populations were chosen: (i) subjects with left ventricular hypertrophy and normal ejection fraction, who had no clinical or investigative evidence of heart failure, and (ii) subjects with chronic heart failure, defined as typical symptoms in the presence of left ventricular systolic dysfunction [14,15]. These subjects were then age matched with a control population. No subjects had ongoing evidence of myocardial ischaemia, either on clinical grounds or through exercise ECG testing. All subjects underwent two-dimensional and M-mode echocardiography using a Hewlett Packard SONOS 2000 machine, with calculation of left ventricular mass by standard formulae [16].

Posture changes
Subjects rested supine quietly on a bed for 30 min. Subjects were then asked to sit up for a period of 2 min. They then stood up for a similar time period. Finally the subjects were asked to squat for a similar time period.

Handgrip
Subjects rested quietly on a bed until heart rate, blood pressure and QTc interval had returned to normal. Further QT, heart rate and blood pressure data were then collected. Subjects were then asked to squeeze, using their dominant hand, as hard as possible on the barrel of an empty 20-ml syringe. Further data were recorded after 2 min.

ECG recordings
ECGs were recorded at the end of each time period in each position. The QT interval was determined automatically from a commercial computer algorithm, the Marquette CASE 15, which determined, over the 12 leads of the standard ECG, the time from the earliest Q wave onset to the time of the latest T wave onset. Data on heart rate were collected simultaneously, thus allowing calculation of the Bazett rate-corrected QT interval (QTc = QT/√R–R interval). The Marquette algorithm also determined the QRS and T wave axis.

The automatic QT interval computer algorithm was validated as follows. In 38 subjects with a variety of cardiac diseases the QT interval was measured using the computer algorithm while at the same time the ECG machine produced a high-speed (50 mm/s) and high-gain (20 mm/mV) 12-lead ECG. The QT interval from each of the 12 leads of the ECG was measured manually using a magnifying graticule and compared with the computer-derived measure. The correlation between the computer-derived QT measure and the manual lead II QT interval was \( r = 0.85 \), for the mean QT it was \( r = 0.86 \) and for the longest lead QT it was \( r = 0.70 \) (all \( P < 0.0001 \)).

Statistics
Between-group comparisons were performed using ANOVA, and within-group comparisons by paired \( t \)-test. Significance was accepted at the 5% level.

RESULTS

Basic data
The basic data are shown in Table 1. This shows that mechanical function, as measured by fractional shortening, was normal in the control and hypertrophy groups and depressed in the heart failure group. Left ventricular mass was significantly increased in left ventricular hypertrophy.

Effect of posture on QT interval
As shown in Figure 1, QT interval in heart failure is significantly shorter when lying or standing compared with the hypertrophy group. The QT interval shortens in the hypertrophy and control groups when moving from the lying position. In heart failure the QT interval shortens on standing and squatting, but not when sitting.

The effect of posture on the rate-corrected QT interval is shown in Figure 2. A paired \( t \)-test showed that the QTc interval for the control group did not change with posture. This was also the case for the hypertrophy group. However, the QTc interval in heart failure shortened significantly between lying and either standing or squatting (\( P < 0.05 \)). In heart failure the QTc interval is \( 18 \pm 9 \) ms\(^{1/2} \) longer on lying compared with standing (\( P < 0.05 \)).

When between-group comparisons were made, it was found that the QTc interval in heart failure was significantly prolonged compared with either the hypertrophy or the control groups in the lying and in the sitting position, but that in both the standing and squatting
Table 1  Basic data

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Hypertrophy</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>13</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57.5 ± 2</td>
<td>56.8 ± 3</td>
<td>59.2 ± 2</td>
</tr>
<tr>
<td>LV internal dimension in diastole/systole (cm)</td>
<td>4.6/2.8</td>
<td>5.6/3.5</td>
<td>6.1*/4.9*†</td>
</tr>
<tr>
<td>Fractional shortening</td>
<td>0.38 ± 0.03</td>
<td>0.39 ± 0.03</td>
<td>0.20 ± 0.02*†</td>
</tr>
<tr>
<td>Septal thickness (cm)</td>
<td>0.98 ± 0.05</td>
<td>1.4 ± 0.10*§</td>
<td>1.1 ± 0.10</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>184 ± 16</td>
<td>432 ± 55*</td>
<td>350 ± 41*</td>
</tr>
</tbody>
</table>

Figure 1  Effect of posture on the QT interval
In heart failure the QT interval is shorter than hypertrophy in the lying and in the standing position. □, control; ■, hypertrophy; ○, heart failure.

Figure 2  Effect of posture on the QTc interval
In heart failure the QTc interval is longer in the sitting and the lying positions when compared with the standing or squatting positions. □, control; ■, hypertrophy; ○, heart failure. *P < 0.05 compared with control or hypertrophy.

Figure 3  Effect of handgrip on the QTc interval
With maximum handgrip the QTc interval is prolonged in hypertrophy and control subjects, but does not change in heart failure. □, control; ■, hypertrophy; ○, heart failure. *P < 0.05, grip compared with relaxed.

There are no differences in the QRS vector between the different disease states and different positions and no differences in the T wave vector, implying that QTc interval changes are not due to changes in the position of the heart in the thorax arising from posture change.

**Effect of handgrip on QT interval**
Handgrip increased blood pressure in the hypertrophy (P < 0.0001) and control groups (P < 0.03) but not in patients with heart failure. Heart rate was unaffected by handgrip. The QTc interval was prolonged with handgrip in the control (P < 0.02) and hypertrophy groups (P < 0.01) but not in the heart failure group (Figure 3).

**DISCUSSION**

Previous studies have examined the response of the QT interval to postural change. In normal subjects the QT interval shortens and the QTc interval lengthens on standing [6]. In atrial fibrillation standing results in shortening of the QT interval [9]. In those with QT
interval prolongation due to a variety of causes, standing has no effect on the QTc interval [7]. One study has suggested that the response of the QT interval to postural change may be useful prognostically post-myocardial infarction, and found that on moving from the supine to the sitting position the QTc interval was prolonged in those who died suddenly, but did not change in survivors [17].

This study has shown that posture has an effect on the QTc interval that is dependent on the subject’s cardiac disease status. Normal subjects show very little change in their heart-rate-corrected QT interval with any position, whereas subjects with heart failure, who show QTc prolongation at rest, normalize their QTc interval on standing or squatting such that in these positions there is no significant difference from control. This implies that QTc interval lengthening at night in normal subjects is unrelated to posture change, but that QTc changes in heart failure may be related to posture change.

This study differs from previous studies that have investigated the influence of posture on the QTc in subjects with normal left ventricular function and which have given conflicting results. Two studies have shown QTc lengthening (with either 70° upright tilting or on standing) and one study has shown QTc interval shortening [7–9]. The study reported here found no change in QTc interval with standing in subjects with normal left ventricular function.

As the QRS and T wave vectors are identical in all three groups, and as there were no significant changes with posture, this suggests that the changes in the QTc interval with posture do not relate to differing positions of the heart in the thorax with the different diseases.

The mechanism of the QTc changes in this study is not known. One possibility is that these changes are due to the differential effects of autonomic nervous system activity in different diseases. Standing results in activation of the sympathetic nervous system [18]. Adrenergic receptor stimulation, other than for very brief (< 30 s) time periods, leads to shortening of the QT interval [3].

Given the down-regulation of the β-receptor and second messenger systems that occurs in heart failure, it would be surprising if the effect of adrenergic receptor stimulation was exaggerated in heart failure, and was responsible for the excessive QTc shortening [13]. Likewise, given the fact that there is considerable down-regulation of the arterial baroreflex system, there is not much baroreflex activity to be withdrawn when standing, and therefore it is unlikely that the parasympathetic nervous system is responsible for the excessive QTc interval shortening seen in heart failure. Standing and squatting has effects other than autonomic. Afterload increases, particularly in squatting, and pre-load decreases, again particularly in squatting. It is possible that changes in loading conditions are directly responsible for the different effects of posture on the QTc interval, either directly through the mechanism of mechano-electrical feedback or possibly through the different hearts in the different conditions having a differing response to the same load changes [19,20].

The effects of isometric handgrip to near maximal voluntary contraction on the QTc interval were surprising. One would predict that handgrip, which activates the sympathetic nervous system, would lead to QT interval shortening in normal subjects, and would have little or no effect on the QT interval in subjects with down-regulated β-receptors, such as those with heart failure [3,12,21,22]. The lack of effect of handgrip on the QTc interval in heart failure is therefore not unexpected. However, paradoxically, it was found that handgrip exercise resulted in significant QTc interval prolongation in both the control population and in left ventricular hypertrophy. Why this paradoxical lengthening occurs is not clear, but in experimental situations very short (< 30 s) catecholamine stimulation has been shown to result in QT interval lengthening, and longer stimulation in QT interval shortening [3]. Although in this experiment data were collected at 2 min in a deliberate attempt to overcome this early phenomenon, this may be the explanation of the QT interval increase in the control and hypertrophy populations.

**IMPLICATIONS**

The finding of prolongation of the QTc interval at rest or when sitting, but not when standing or squatting, does have some implications for the epidemiology and prevention of sudden cardiac death.

Previous workers have reported in normal subjects a relative prolongation of the QTc interval at night, and have attributed this to factors associated with the circadian rhythm. Whether there is a similar excess prolongation of the QTc interval in heart failure at night awaits further study, but it is likely that this will be the case. This work suggests that if QTc prolongation is found at night in heart failure it may be due to change in posture rather than to changes associated with the circadian rhythm.

Whether the excess of sudden death that occurs at night is attributable to the excess QTc interval prolongation still requires further study. However, if this is found to be the case, preventative strategies may be difficult if the mechanism is related more to posture than to circadian rhythm.

**CONCLUSION**

QTc interval in heart failure is prolonged when lying or sitting but not when standing or squatting. Handgrip prolongs QTc interval in control subjects and patients with hypertrophy but not in patients with heart failure.
ACKNOWLEDGMENTS

This work was sponsored in part by funds from the British Heart Foundation. P.D. was a BHF junior research fellow.

REFERENCES

16 Troy, B. L. and Pombo, J. (1972) Measurement of left ventricular wall thickness and mass by echocardiography. Circulation 45, 602–611

Received 27 July 1998/17 November 1998; accepted 23 November 1998