Original Article

Association of QT Interval with Blood Pressure in 80-Year-Old Subjects


Few data are available on the association between the prolonged heart rate-adjusted QT (QTc) interval and high blood pressure in elderly individuals, particularly in subjects over 80 years old. The aim of the present study was to determine the association between the QTc interval and blood pressure in 80-year-old subjects. This study was part of the 8020 Data Bank Survey, which was designed to collect the baseline data of systemic and dental health conditions in 80-year-old subjects. We studied the cross-sectional association of the QTc interval with blood pressure in 642 Japanese (257 men and 385 women), all 80 years old. Mean systolic blood pressure (SBP) rose from 146.0 mmHg in the first quartile of QTc interval to 149.1 mmHg in the second, 154.6 mmHg in the third, and 152.3 mmHg in the fourth quartile (test for trend, \( p \leq 0.008 \)). Mean diastolic blood pressure (DBP) also rose from 76.9 mmHg in the first quartile of QTc interval to 77.7 mmHg in the second, 81.8 mmHg in the third, and 79.0 mmHg in the fourth quartile (test for trend, \( p \leq 0.003 \)). We performed multiple regression analysis, controlling for factors known to influence the QTc intervals—e.g., SBP, heart rate, sex, and left ventricular hypertrophy assessed by the voltage amplitudes recorded in the precordial leads of the electrocardiogram. The association between the QTc interval and SBP was highly statistically significant in all analyses. These results show that SBP by itself may influence the QTc interval in very old subjects. (Hypertens Res 2004; 27: 387–391)

Key Words: aged, QT interval, blood pressure, eighty years old, Japanese

Introduction

The QT interval from the standard 12-lead electrocardiogram reflects the depolarization and repolarization of myocardial cells. Factors that augment the depolarization or delay repolarization of myocardial cells can increase the QT interval length. A prolonged heart rate-adjusted QT (QTc) interval is regarded as an indicator of the imbalanced distribution of the sympathetic nervous system activity on the heart (1, 2), and it has been suggested that a prolonged QTc interval increases the risk of either ventricular arrhythmias or sudden cardiac death, even in apparently healthy subjects (3, 4). Although aging and left ventricular hypertrophy have been shown to prolong the QTc interval (5, 6), the effect of blood pressure by itself on the QTc interval has not been determined. It seems difficult to separately evaluate the roles of blood pressure and left ventricular hypertrophy on the QTc interval, because high blood pressure induces cardiac hypertrophy (7).

Hypertension is associated with an increased overall risk for mortality as well as with coronary heart disease mortality and stroke mortality (8, 9). High blood pressure levels are significant risk factors for cardiovascular disease in the elderly (10, 11). However, at present, few data are available not only on the actual QTc interval, but also on the association between the QTc interval and blood pressure by itself in elderly individuals, particularly in subjects more than 80 years old. It seems important to explore these relationships,
because elderly essential hypertensive subjects with left ventricular hypertrophy could have a prolonged QTc interval (5, 6), resulting in an increased risk of ventricular arrhythmia or sudden cardiac death. In the present study, we hypothesized that blood pressure levels by themselves may influence the QTc interval independently of left ventricular hypertrophy in very elderly subjects. Blood pressure, particularly systolic blood pressure (SBP), tends to increase progressively with age (12), and elderly people with hypertension have a greater risk of cardiovascular disease.

Given that the age distribution of the general population in Japan is rapidly shifting towards an elderly majority, the number of elderly hypertensive patients is increasing. The 8020 Data Bank Survey, a unique cross-sectional survey conducted in Japan, was a study originally designed to explore the relationship between the systemic and dental health conditions of very aged subjects. The participants in our study were all 80 years old; thus, we did not consider the effect of age on the changes in blood pressure and QTc interval. Accordingly, the aim of the present study was to determine the actual QTc interval values, and to elucidate the relationship between the QTc interval and blood pressure in the very old Japanese population by using the data from this survey.

Methods

Study Population

This study is part of a community-based cross-sectional survey of the 8020 Data Bank Survey, which was conducted in four prefectures in Japan. The 8020 Data Bank Survey was designed to collect the baseline data of systemic and dental health conditions in 80-year-old subjects, and to promote the idea that everyone should still have at least 20 original teeth by the age of 80. All participants were born in 1917, and were 80 years old when the survey was conducted. In the present study, we analyzed the data from nine districts (Munakata City, Yukuhashi City, Buzen City, Tobata Ward in Kitakyushu City, Katsuyama Town, Toyotsu Town, Tsuiki Town, Kanda Town, and Shinyoshitomi Village) in Fukuoka Prefecture. Among these nine districts, 1,244 people were born in 1917, and 642 residents (257 men and 385 women) completed the physical, blood, and electrocardiography examinations performed in this survey. All participants were ambulatory, and their activities of daily living were well preserved. The details of the study protocol were explained to the subjects, and informed consent was obtained prior to participation.

Data Collection

The examination included completion of a medical questionnaire which contained questions regarding smoking history, physical activity, and alcohol consumption. All subjects were asked about their current medications, except those who lived in two cities (Buzen City and Yukuhashi City; 185 subjects). Fasting serum glucose, total cholesterol, and creatinine concentrations were measured. Height and weight were measured, and the body mass index (BMI) was calculated. BMI was defined as weight (in kg) divided by height (in m²).

The subjects were kept in a sitting position for at least 10 min in a quiet room, and then sitting blood pressure was measured by an oscillometric method using an automatic device (BP-103; Nippon Colin, Komaki, Japan). Standard 12-lead electrocardiography was recorded (Alpha 500BX; Fukuda ME Kogyo Co., Tokyo, Japan). The QT interval was taken from the onset of the QRS complex to the end of the T wave. QT intervals of 12-leads were automatically measured, and the median value of these intervals was used for further data analysis. The amplitudes of the S wave in V1 (SV1) and the R wave in V5 (RV5) were also automatically measured. To adjust QT for the heart rate, we calculated the QTc according to Bazett’s formula (13): QTc = QT/RR¹⁄², with RR being the R-R interval in seconds. SV1 + RV5 was calculated and was used as an index of left ventricular hypertrophy.

Data Analysis

The subjects were divided into quartiles of the QTc interval. In order to analyze the effects of blood pressure on the QTc interval, a one-way ANOVA was performed. In addition, we performed multiple regression analyses to establish the association of the QTc interval with blood pressure. p values <0.05 were considered statistically significant.

Results

The subjects were divided into quartiles on the basis of the QTc interval (Table 1). The mean QTc interval was prolonged from 391.5 ms in the shortest quartile to 458.9 ms in the longest. Table 1 also shows the mean values (and SEM for continuous variables) of potentially confounding variables by the quartiles of the QTc interval. Habitual alcohol intake was defined as alcohol intake of more than 3 times per week. A relatively large number of subjects were treated with antihypertensive agents in the longest quartile of the QTc interval.

Figure 1 shows the mean SBP by quartiles of the QTc interval. The mean SBP rose from 146.0 mmHg in the first quartile to 154.6 mmHg in the third, and to 152.3 mmHg in the fourth quartile (test for trend, p = 0.008). The mean diastolic blood pressure (DBP) also rose from 76.9 mmHg in the first quartile to 81.8 mmHg in the third, and to 79.0 mmHg in the fourth quartile (test for trend, p = 0.003) (Fig. 1).

SBP was significantly correlated with the amplitude of SV1 + RV5 (r = 0.2125, p < 0.0001), but DBP failed to correlate with it. Figure 2 shows the simple correlation between
the QTc interval and the amplitude of SV1 + RV5. The QTc interval was also significantly correlated with the amplitude of SV1 + RV5 ($r = 0.0915$, $p = 0.026$).

Table 2 indicates the results of the multiple regression analysis on the QTc interval in association with SBP and other confounding factors, including heart rate, sex, voltage amplitude of SV1 + RV5, and BMI, known to influence the QTc interval and blood pressure. SBP was independently
Table 3. Multiple Regression Analysis for QTc Interval in Subjects without Antihypertensive Drugs

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>β</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>0.144</td>
<td>0.024</td>
</tr>
<tr>
<td>Heart rate (l/min)</td>
<td>0.623</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sex (men 0, women 1)</td>
<td>4.078</td>
<td>0.18</td>
</tr>
<tr>
<td>SV₁ + RV₅ (mV)</td>
<td>0.202</td>
<td>0.23</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>-0.757</td>
<td>0.096</td>
</tr>
</tbody>
</table>

QTc, heart rate-adjusted QT; β, regression coefficient; SBP, systolic blood pressure; SV₁, RV₅, amplitudes of S wave in V₅ and R wave in V₅, respectively; BMI, body mass index.

and significantly associated with the QTc interval (p = 0.006). The QTc interval was also significantly associated with heart rate (p < 0.0001) and sex (p = 0.04), but not with the voltage amplitude of SV₁ + RV₅, or BMI. Multiple regression analysis on the QTc interval in association with DBP and other confounding factors was also applied; however, DBP was not associated with the QTc interval (p = 0.11).

In order to evaluate the effect of antihypertensive treatment on the results of the present study, subjects who had been taking antihypertensive drugs or whose medications were unknown were excluded, and multiple regression analysis for the QTc interval was performed again. After these exclusions, 149 men and 216 women remained to be studied. Table 3 indicates the results of the multiple regression analysis on the QTc interval in association with SBP and other confounding factors, including heart rate, sex, voltage amplitude of SV₁ + RV₅, and BMI, in subjects without antihypertensive drugs. SBP was still found to be significantly and independently associated with the QTc interval (p = 0.024).

Discussion

The QTc interval has been shown to be modulated by the autonomic nervous system (1, 2), and blockade of the autonomic nervous system can increase the QTc interval, even in normal subjects (14). The principal finding of the present study is that SBP is significantly and independently associated with the QTc interval in aged individuals in Japan. Although both the QTc interval and blood pressure are influenced by aging (5, 12), the advantage of the present study is that the subjects participating in the survey were all 80 years old. Accordingly, the effect of aging on the changes in blood pressure and the QTc interval did not need to be considered. To the best of our knowledge, this is the first study to demonstrate that a close relationship between SBP and the QTc interval exists in very old subjects.

Blood pressure tends to increase progressively with age (8, 12), and hypertension, one of the most common chronic conditions in the elderly population, remains strongly associated with cardiovascular morbidity and mortality (8). Given that the age distribution of the general population in Japan is rapidly shifting toward an elderly majority, it is important to determine the cardiovascular risks associated with high blood pressure in aged subjects. A prolonged QTc interval has been shown to be related to the increased risk of either ventricular arrhythmia or sudden cardiac death, even in apparently healthy subjects (3, 4). Therefore, treatment with antihypertensive agents may influence the QTc interval in elderly hypertensive subjects. Further studies will be necessary to determine whether antihypertensive treatment improves the prolonged QTc interval, resulting in the reduction of cardiovascular events.

In the present study, SBP was significantly correlated with the QTc interval (r = 0.131, p = 0.0009). Quartiles of the QTc interval also had significant positive trends with respect to SBP and DBP (Fig. 1). However, Kulan et al. (6) reported that the QTc interval correlates well with the left ventricular mass index determined by echocardiography, which is extremely influenced by blood pressure values. Furthermore, Passino et al. (15) suggested that left ventricular hypertrophy was associated with prolongation of the QTc interval in nondipper hypertensive subjects. In order to evaluate the relation between blood pressure and the QTc interval, therefore, left ventricular hypertrophy secondary to hypertension needs to be considered. In the present study, we have attempted to evaluate left ventricular hypertrophy by using the voltage amplitude of SV₁ + RV₅ recorded by standard electrocardiography. Left ventricular hypertrophy determined by echocardiography is superior to that by electrocardiography. Since left ventricular mass assessed by echocardiography was not available in the present study, the voltage amplitude of SV₁ + RV₅ recorded by electrocardiography was used to evaluate left ventricular hypertrophy. SBP significantly correlated with the voltage amplitude of SV₁ + RV₅ (r = 0.213, p < 0.0001), suggesting that SV₁ + RV₅ was likely to be a good reflection of the left ventricular hypertrophy secondary to hypertension. After adjusting for confounding factors, including heart rate, sex, the voltage amplitude of SV₁ + RV₅, and BMI, multiple regression analysis revealed that the QTc interval was significantly associated with SBP. These findings suggest that SBP by itself is directly associated with the QTc interval in elderly individuals. Pressure overload of the left ventricle may influence the depolarization or repolarization of myocardial cells in these subjects. Furthermore, it has been reported that a prolonged QTc interval and morning sympathetic overactivity coexist in hypertensive patients who show an acute rise of blood pressure in the early morning (16). These previous findings also support the idea that a close relationship exists among prolongation of the cardiac repolarization time, sympathetic activity, and blood pressure.

The limitations of the present study is that data on the medications used were available in 71% of the subjects studied, and 20% of the subjects studied were being treated with antihypertensive agents (Table 1). Many subjects treated...
with antihypertensive agents were included in the longest quartile of the QTc interval. The peak value of the SBP or DBP was found in subjects in the third quartile of the QTc interval, not in the fourth quartile (Fig. 1), which may be explained by the fact that a greater number of hypertensive subjects in the fourth quartile were receiving antihypertensive agents. However, SBP was still found to be significantly independently associated with the QTc interval after the exclusion of subjects taking antihypertensive drugs, and those whose medications were unknown. That is, the data regarding antihypertensive medication and antihypertensive treatment would, in and of itself, have minimum effects on the results of the present study.

In conclusion, a positive relationship was found between SBP and the QTc interval in 80-year-old Japanese subjects. After adjusting for factors including heart rate, sex, left ventricular hypertrophy evaluated by electrocardiogram, and BMI, the association between SBP and the QTc interval remained highly statistically significant. SBP by itself might directly influence the QTc interval in very elderly individuals. Further studies will be necessary to determine whether this association is specific to elderly individuals.

References