Analysis the Incidence and Clinical Significance of Long and Short Corrected QT Interval in Electrocardiogram in Healthy Population of Changsha in China

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ABSTRACT

Objectives: To analyse the incidence of long and short corrected QT (QTc) in healthy population of Changsha in China.

Methods: Standard 12-leads electrocardiogram (ECG) were performed on 4025 subjects in Changsha of China, who aged from six minutes after birth to 83 years old, between January 1993 to December 2012. Heart rate and QT interval were measured and recorded, Corrected QT (QTc) was calculated with Bazett´s formula ($QTc = QT/RR^{0.5}$). All recruited individuals had taken healthy examination, ruling out general health issue, in the Second Xiangya Hospital of Central South University. Statistical analyses were performed with the SPSS 16.0 software.

Results: The incidence of short QTc was 6.88% (127/4 025 cases). The peak values of incidence were in the 30–40 years old group (15.71%). The low values were in the 1–3 month group, 3–6 month group (0.76%), respectively. The incidence of long QTc was 3.16% (127/4 025 cases). The values diminished significantly after adulthood. The low values were in the 18–30 years old group, 30–40 years old group (0.86%，0.71%), respectively. After the age of 50, the incidence of long QTc increased with age (7.89%，9.06%，14.06%), respectively. There was no statistically significant difference between genders ($p > 0.05$).

Conclusions: The peak incidences of long and short QTc existed in two separate age groups in healthy population. The peak incidence of short QTc was in 18–40 years old group, the peak incidence of long QTc was in the group beyond 50 years old groups. For these two age groups, it was recommended to pay close attention to the changes of QTc in order to prevent cardiovascular events.

Keywords: Electrocardiography, long corrected QT interval, short corrected QT interval

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INTRODUCTION

QT interval of standard 12-leads electrocardiogram (ECG) represents the time from the onset of ventricular depolarization (onset of the Q wave) to the completion of ventricular repolarization [end of the T-wave] (1), ventricular electrical contraction time as well. In the pathologic condition, electrical contraction changes much earlier and more sensitively than mechanical one. Abnormal ventricular repolarization may induce the shortening or extending of QT interval, which indicates the instability of ventricular electrical conduction, causing ventricular arrhythmia, syncope, spasm and even sudden death (2). Algra *et al* (3) discovered that the risk of sudden death exist in the patients with long and short QT interval (< 400 ms). The QTc extension and shortening would bring average 2 times more risk of sudden death than the normal QTc (400–440 ms). Relative risk of QT interval extension was 2.3, while QT interval diminishing was 2.4. QT interval is affected mostly by various factors, such as heart rate, age, gender, adrenaline, autonomic nerve tension and so on (4).

Most significant of which is the heart rate. In order to rectify the influence of heart rate of QT interval, the Bazett′s square root correction formula ($QTc = QT/RR^{0.5}$) is adopted since Bazett put it forward in 1920 (5). Autonomic nerve system is the important regulatory mechanism of ventricular repolarization, whose function declines with age, impaired baroreceptor caused by arterial wall stiffness and so on (6). The QT interval is also regulated by autonomic nerve. The function of autonomic nerve through the activity of

sympathetic and parasympathetic nerve on QT interval is complex. The clinical researches also showed that long QT interval syndrome (LQTS) and short QT interval syndrome (SQTS) could result in malignant arrhythmia, that always associated with autonomic nerve function changing and the rise of ventricular repolarization heterogeneity (7). Cardiac automatic nerve matured in childhood, reaching to its fastigium in puberty, contrary, the carotid artery elasticity declines with the age (8). So we assume that the incidence of short and long QTc interval was obviously different in certain subgroups of age group.

Therefore the aim of this study is to find the high incidence of long and short QTc age groups in healthy population before they have clinical symptoms, and appealed to focus on those high incidence age groups to prevent the cardiovascular events.

Participants

We recruited Changsha's people who taking physical examinations in Second Xiangya Hospital of Central South University in Changsha of China from January 1993 to December 2012, including government functionaries, workers, students (college, high school, primary school), kindergarteners and newborn infants from obstetrics department.

All the objects have been excluded from the cardiovascular diseases through detailed medical history collecting and physical examinations. The research objects over 60 years old need to meet the following criteria: move with ease, no history of cardiovascular

drugs, no abnormal signs in cardiac examinations, normal blood pressure, no cardiomegaly in echocardiography and heart X-ray tests, left ventricular and aorta contract normally, normal serum electrolytes, normal serum lipid and normal blood glucose. In all, we collected 4025 cases, including 2207 cases of male, 1818 cases of female, aged from newborn in six minutes to 83 years old. They were classified into eleven age groups (9) accordingly: newborn, 1 m, one year, five years, 10 years, 14 years, 18 years, 30 years, 40years, 50 years, 60–83 years. Each age group was further divided into subgroups of male and female. The distribution characteristics of age, gender and group cases are listed in Table 1.

Table 1: Age and gender distributions of long and short QTc in ECG among Changsha healthy people (cases)

Age group	**Total (case)**	**Man (case)**	**Female (case)**
newborn	457	393	850
1 month	89	66	155
3 month	75	57	132
6 month	66	63	128
1 year	152	100	252
3 years	74	84	158

5 years	104	69	173
8 years	170	183	351
12 years	239	209	448
18 years	122	110	232
30 years	142	138	280
40 years	129	115	244
50 years	153	151	304
60 years–83 years	235	83	318
Total	**4025**	**2207**	**1818**

Electrocardiogram

Siemens and Japan photoelectrical electrocardiographs were adopt to record body surface ECG. The subjects took a 15 minutes rest to minimize the tension interference. Electrocardiogram electrodes were placed routinely, and the electrode diameter varies according to ages, in order to avoid local interference. The gain was 10 mm/mV, speed was 25 mm/s, filter unit was not applied. Each record of ECG should have smooth baseline, without significant interference and clear graphics. QT interval of ECG was measured by two specialists independently. A third person would make the final judgment when different

opinion occur. The QT interval was the time from the beginning of QRS wave to the end of T wave of ECG.

Diagnostic criteria

We calculated QTc with the Bazett′s square root correction formula ($QTc=QT/RR^{0.5}$). QTc ＜360 ms indicated that QTc was shortened (10), and QTc ≥ 450 ms of man or QTc ≥460 ms of female indicated that QTc was prolonged (11).

Statistical analysis

Each measured value was stored in computer respectively according to gender, age (minute, hour, day, month, year), number and feature, SPSS 16.0 software was used to calculate descriptive parameter, *eg*, ages were compared with F test, two-by-two were compared with *Q*-test, man and female were compared with *t*-test; $p < 0.05$ indicated there was a significant statistical difference.

RESULTS

The incidences of long and short QTc of each age group were not changing linearly.

Short QTc incidence

The total incidence of short QTc was 6.88% (127 in 4025 cases), reaching to its maximum in these three age groups: 18–30 years, 30–40 years, 40–50 years, in which it was 15.09% (35 in 232 cases), 15.71% (44 in 280 cases) and 13.11% (32 in 244 cases), respectively; However, the rates of the following two age groups: 1–3 month and 3–6 month were the lowest, 0% (0 in 155 cases) and 0.76% (1 in 132cases), respectively; The incidence of children (＜18years) was 5.89% (156 in 2647 cases), which (≥ 18years) was 9.51% (131 in 1378 cases) in adult.

Long QTc incidence

The total incidence of long QTc was 3.16% (127 in 4025 cases), and there was no obvious difference in all age groups of childhood. However, it diminished dramatically in adulthood, reaching to the trough in 18–30 years and 30–40 years groups, in which it was 0.86% (2 in 232 cases) and 0.71% (2 in 280 cases) respectively, It gradually rose with the age from 50 years old, reaching to the peak in groups of 50–60 years, 60–70 years and 70–83years, in which it was 7.89% (24 in 304 cases), 9.06% (23 in 254 cases), 14.06（9 in 64 cases), respectively. The incidence of the children (< 18years) was 2.34% (62 in 2 647 cases). The incidence of the adult (≥ 18years) was 4.72% (65 in 1 378 cases), See Figure 1.

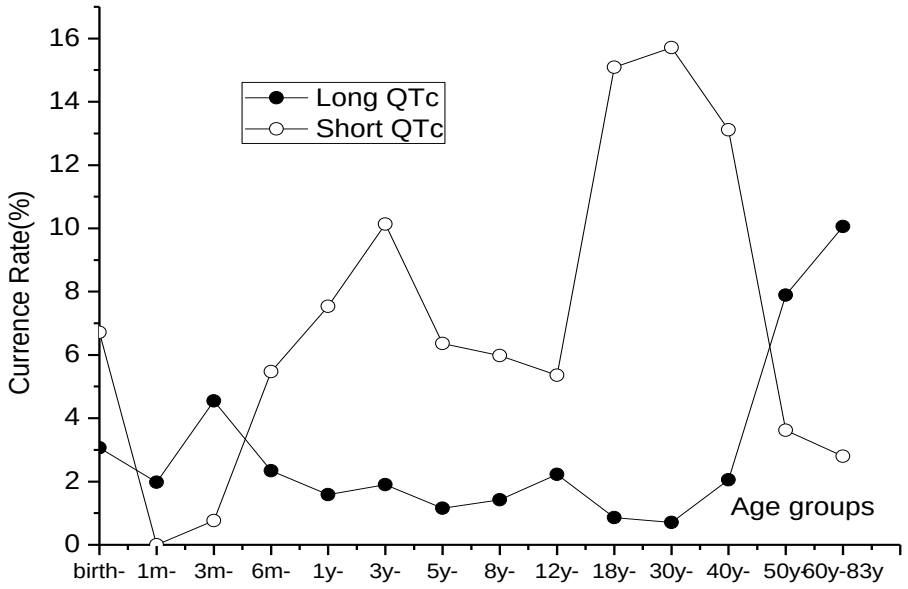

Figure 1: The incidence of long and short QTc of different age and gender of health people in Changsha.

Gender difference

The comparison of the incidences between man and woman of all the subjects and between each group had no statistically significant difference.

DISCUSSION

In this study, the total incidence of short QTc was 6.88%, the incidences between man and female of all the objects and each group had no statistically significant difference. Anttonen *et al* (12) followed-up 10822 cases of people of middle age (5658 cases of man, from

30–59 years old, average age 44 ± 8.4years), the percentage of QTc＜ 360 ms was 2.9% (man 4.4%, female 1.3%, p ＜ 0.01). There was no statistically significant difference of sudden death caused by all kinds of reason or cardiovascular factor between short QTc group and normal QTc group. This study showed the incidence of 30–59 years old was 9.42%, the data was higher than the Anttonen's. Consideration should be given to possibility of small sample size and racial differences. Viskin *et al* (10) defined male ≤ 360 ms, female ≤ 370 ms as short QTc, finding that in patients with idiopathic ventricular fibrillation, men's short QTc accounted for 35% (6/17 cases), no one in female. They considered that QTc intervals shorter than 360 ms may entail some arrhythmic risk and are commonly seen in male patients with idiopathic VF. However, "short" QTc values are not rare among healthy adults, especially at slow heart rates. Our study showed that the high incidence of short QTc value was in 30–40 years groups (15.71%, 44/280). Gallaqher et al (13) reported a study of 12 500 cases of health men and found the incidence of QTc< 335ms was 0.4% (54/12 500 cases), no one was dead after 7.9 ± 4.5 years' following-up. But other researchers Gollob *et al* (14) reported 62 cases of patients with short QTc, 75.4% were men, 35 cases of them (57.4%) suffered sudden cardiac death, or had been rescued from cardiopulmonary arrest, syncope, and atrial fibrillation. Thus, the healthy people with short QTc might require regular follow-up, and the risk of death would be significantly increased if this population complicate with other diseases. The incidence rate of children's short QTc was rarely reported in current literatures. In this study, the incidence of children

(＜18years) was 5.89%, reaching to its low values in 1–3 month and 3–6 month age groups, which were 0% and 0.76%, respectively. Pearl (15) have taken ECG on 781 healthy children from 10–18 years of age. They found QTc intervals were significantly ($p < 0.0005$) greater for each age group over 14 years. QTc interval varied inversely with age and directly with heart rate. In our study, the incidence of short QTc interval in younger than 6 m groups is low, so we deduce that the low incidence of short QTc values was correlated with the higher average heart rates of younger babies. Rijinbeek *et al* (9) recruited 1912 children aged from 11 days to 16 years to record their ECG, and taken the 2nd percentiles as the lower limits of normal. In their study, they found the lower QTc limits of 1–3 months group and 3–6 months group apparent higher than others age groups, the values were 396 ms and 391 ms, respectively, which was consistent with our study.

Antelmi *et al* (16) conducted a test of heart rate variability (HRV) in different age groups (＜19 years, 20–29 years, 30–39 years, 40–49 years, 50–59 years, ≥ 60 years), analysing the influence of age to autonomic nerve function. It was discovered that all time- and frequency-domain indexes including low frequency (LF), very low frequency (VLF), the standard deviation of average value of normal heartbeats (SDANA) in all 5 minutes sections, high frequency (HF), root mean square of successive differences between normal adjacent heartbeat (rMSSN), the number of heartbeat interval more than 50 ms (PNN50) were decreased significantly with age until the fourth decade of life and decreased

non-significantly in the older age groups. But the ratio of LF/HF increased with age in the group 20–50 years. Indicating that the tension of sympathetic nerve and parasympathetic nerve attenuated with the augmentation of age, of which the activity of parasympathetic nerve reduced more remarkably, and the age group 30–39 years was the most significant. In this study, the incidence of short QTc reached its maximum in the age groups (18–30 years, 30–40 years, 40–50 years), were [15.09% (35/232 cases), 15.71% (44/280 cases), 13.11% (32/244 cases), respectively of which the group 30–40 years was the most remarkable, so we deduce that it was the vagus that reduced more intensively, resulting in the highest incidence of short QT. QT interval is one of the most sensitive index that reflect state of local cardiac muscle repolarization.

Prolonged QT interval was related to myocardial electrical activity dyssynchrony and myocardial cell extension. Any factors causing the outflow of potassium ions weakened or calcium influx strengthened could prolong action potential duration (APD). There are much more studies about the drug caused QT interval lengthening at present, showing that the most common cause of it is that the fast delayed rectifier potassium current being affected (17). The incidence of long QTc in this study was 3.16%. The incidence of long QTc had no remarkable difference in all age groups of childhood, and decreased rapidly in adult, reaching to its trough in age groups 18–30 years and 30–40 years, which were 0.86% and 0.71%, respectively. QTc extended was related to sudden infant death syndrome or risk of babies' life danger (18). Schwartz *et al* (19) studied

44 596 cases of infants aged from 12 days to 25 days, finding that the incidence of long QTc was 11.85%. Twenty-eight cases of those newborn infants whose QTc were longer than 470 ms getting gene tests, 12 cases of them had gene mutation of LQTS. In the 28 cases of newborn infants whose QTc between 460 to 470 ms, 12 cases of them had conducted DNA tests and four of them had the gene mutation of long QTc syndrome. In our study, the incidence of infants aged one month was 3.07%, the difference might due to the wider age range and ethnic differences. It reminded us that for the newborn infants' long QT interval, especially those longer than 470 ms, we needed to make a detailed inquiry of their family history and made the genetic diagnosis of LQTS. In this study, the incidence of children was 2.34%, and no statistically significant difference between man and female, the same as Dickinson (20) report. Pearl (15) reported 781 cases of healthy children aged from 10 to 18 years old, the incidence of their long QT interval was 2.3%, of which female was 1.9% and man was 2.5%, there was no statistically significant difference between gender ($p > 0.05$). In this study, the occurrence rate of long QTc in age groups 8–10 years and 12–18 years were 1.42% and 2.23%, respectively the same as Pearl's conclusion.

In our study, the incidence of adult was 4.72%. Anttonen *et al* (12) had made a follow-up about 10 822 case of people of middle age, the incidence of QTc longer than 450 ms was 6.5%, and for various reasons, the cardiovascular mortality in the people with long QTc (longer than 450 ms) had significant difference compared with the people with

normal QTc and short QTc (56.76% *vs* 51.8% *vs* 37.2%, $p < 0.05$). So the people of middle age needed regular follow-up to prevent cardiovascular events. Ashim *et al* (21) carried out an one-year retrospective study about 384 cases of syncope patients caused by various reasons. All the patients had excluded atrial fibrillation, left bundle branch block, cardiac pacemaker and cardioverter-defibrillator installed. QTc > 440 ms had been regarded as QTc extension, and the endpoint event of the research was death. After 30 months' follow-up, 58 cases of patients were dead (16%), the mortality was much higher than the group of normal QTc (22% *vs* 11%, $p < 0.01$). Age over 65 years old and QTc longer than 500 ms were the predictive markers of mortality of syncope patients. In this study, the incidence of long QTc gradually increased over 50 years old, reaching to the maximum in age groups 50–60 years, 60–70 years and 70–83 years, were 7.89%, 9.06%, 14.06%, respectively. So for the older people, especially in the syncope people, we should pay close attention to the extension of QTc to prevent cardiovascular accidence. For the aged, their cardiac structure and function are gradually getting worse. Some studies showed that the abnormal cardiac structure could also change QT interval (22). The factors like left ventricular hypertrophy (23), myocardial infarction or myocardial ischemia (24), abnormal electrolyte [like hypokalemia, hypomagnesaemia, hypocalcemia] (25) and diabetic ketoacidosis or ketosis might contribute to the extension of QT interval (26). In addition, neurohumoral systems relevant to cardiovascular regulation are affected by ageing. In the elderly, an exaggerated shift towards sympathetic activity has been reported (27), and such

sympathetic over-activity has been proved to be an important factor to cause the prolongation of QT interval and the increase of QT dispersion (28, 29). Hence, the imbalance of sympathetic and parasympathetic tones in the elderly may be another explanation for the increased QT interval. But the patients would still need to take tests of ECG, heart Doppler ultrasound and electrolyte regularly in order to discover the symptoms early, so as to prevent cardiovascular events as the QT interval extended progressively.

CONCLUSION

In conclusion, the short and long QTc interval existed in healthy people, the high incidence of short QTc was in aged 18–40 years, the high incidence of long QTc was in over 50 years old, which may because the activity of sympathetic nerve and parasympathetic nerve changed with age. As for these period of age, we need to follow-up high risk people (*eg*: syncope, palpitation, metabolism disorder and so on) with ECG.

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