Correlation of QT Interval Correction Method in Patients with Atrial Fibrillation

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บทคัดย่อ: การศึกษาความสัมพันธ์ของวิธีคำนวณระยะ corrected QT ในผู้ป่วยที่มีหัวใจห้องบนสั่นพลิ้ว

คมสิงห์ เมธาวีกุล พ.บ.,รติกร เมธาวีกุล พ.บ.
กลุ่มงานอายุรศาสตร์หัวใจ สถาบันโรคทรวงอก ตำบลบางกระสอ อำเภอเมือง จังหวัดนนทบุรี 11000

ภูมิหลัง: การวัดค่าระยะ corrected QT ยังคงเป็นปัญหาในผู้ป่วยที่มีโรคหัวใจห้องบนสั่นพลิ้ว เนื่องจากการเต้นไม่สม่ำเสมอของหัวใจทำให้มีผลต่อความแม่นยำลดลง วัตถุประสงค์เพื่อศึกษาความสัมพันธ์ของวิธีคำนวณระยะ corrected QT ในผู้ป่วยที่มีหัวใจห้องบนสั่นพลิ้วแต่ละวิธีเทียบระหว่างตอนเป็นหัวใจห้องบนสั่นพลิ้วและ sinus rhythm (SR) **วิธีการ:** การศึกษานี้เป็นการศึกษาแบบย้อนหลังในผู้ป่วยหัวใจห้องบนสั่นพลิ้วที่ได้รับการรักษาในสถาบันโรคทรวงอกในปี พ.ศ. 2543 - 2558 ค่า corrected QT interval ตอนเป็นหัวใจห้องบนสั่นพลิ้วและ SR จะคำนวณมาจาก Bazett's formula, Fridericia formula และ Framingham linear formula หลังจากนั้นหาความสัมพันธ์ของวิธีคำนวณระยะ corrected QT ตอนเป็นหัวใจห้องบนสั่นพลิ้วเทียบกับตอนเป็น SR โดยใช้ Pearson's correlation และยืนยันการมี agreement ด้วย Bland-Altman plot **ผล:** การศึกษานี้เก็บข้อมูลในผู้ป่วยหัวใจห้องบนสั่นพลิ้วจำนวน 90 ราย ส่วนใหญ่เป็นหัวใจห้องบนสั่นพลิ้วเป็นครั้งคราว พบว่า corrected QT interval ที่คำนวณโดย Bazett's formula, Fridericia formula และ Framingham linear formula ตอนเป็นหัวใจห้องบนสั่นพลิ้วกับ SR มีความสัมพันธ์ปานกลาง (r = 0.32, 0.40 และ 0.40 ตามลำดับ) เมื่อหัวใจเต้นเร็ว พบว่า ระยะ corrected QT ที่คำนวณโดย Bazett's formula จะมากกว่าปกติตอนเป็นหัวใจห้องบนสั่นพลิ้วเทียบกับตอนเป็น SR ในขณะที่ระยะ corrected QT ที่คำนวณโดย Fridericia formula และ Framingham linear formula จะน้อยกว่าปกติตอนเป็นหัวใจห้องบนสั่นพลิ้วเทียบกับตอนเป็น SR อัตราการเต้นของหัวใจมีผลต่อระยะ corrected QT ที่คำนวณโดย Fridericia formula (r = 0.20, p = 0.06) น้อยกว่า Bazett's formula (r = -0.32, p = 0.002) และ Framingham linear formula (r = 0.35, p = 0.001) **สรุป:** ระยะ corrected QT ที่คำนวณโดย Bazett's formula, Fridericia formula และ Framingham linear formula ตอนเป็นหัวใจห้องบนสั่นพลิ้วกับตอนเป็น SR มีความสัมพันธ์ปานกลาง แต่อัตราการเต้นของหัวใจมีผลต่อระยะ corrected QT ที่คำนวณโดย Fridericia formula น้อยกว่า Bazett's formula และ Framingham linear formula

คำสำคัญ: หัวใจห้องบนสั่นพลิ้ว ระยะ corrected QT, Bazett's formula, Fridericia formula, Framingham linear formula

Abstract

Background: The measurement of QT interval is the problem in patients with atrial fibrillation (AF) because of irregularity leads to the inaccuracy of this interval. This study aims to determine the correlation of each QT interval correction method in AF patients compared with sinus rhythm (SR). **Methods:** This retrospective study recruited the AF patients treated at Central Chest Institute of Thailand. The corrected QT intervals (QTc) during AF and SR were calculated by using Bazett's formula, Fridericia formula and Framingham linear formula. The correlation of corrected QT interval (QTc) in AF and SR was performed by a Pearson's correlation. The Bland-Altman plot was used to assess the agreement of QTc for the individual patients using each method in AF to SR. **Results**: Ninety patients were recruited. Most patients were paroxysmal AF. QTc calculated by using Bazett's formula, Fridericia formula and Framingham linear formula in AF and SR had fair correlation (r = 0.32, 0.40, 0.40, respectively). During rapid heart rate, Bazett's formula overestimated the QTc, in contrast, Fridericia formula and Framingham linear formula underestimated it. The QTc calculated by using Fridericia formula was less dependent on heart rate (r = 0.20, p = 0.06) than Bazett's formula (r = -0.32, p = 0.002) and Framingham linear formula (r = 0.35, p = 0.001). **Conclusions:** QTc calculated by using Bazett's formula, Fridericia formula and Framingham linear formula had the fair correlation in patients with AF compared with SR, but Fridericia formula was less dependent on heart rate than Bazett's formula and Framingham linear formula.

Keywords: Atrial fibrillation, Corrected QT interval, Bazett's formula, Fridericia formula, Framingham linear formula

Introduction

Atrial fibrillation (AF) is the common cardiac arrhythmia in our clinical practice. It can lead to the heart failure because of its rapid rate and irregularity[1]. The QT interval is dependent on heart rate. It shortens at faster heart rate, but it lengthens at slower heart rate. So the RR interval is used to correct the QT interval[2-3]. Presently, there are several QT correction methods such as Bazett's formula[4], Fridericia formula[5], Framingham linear formula[6], etc. The measurement of the QT interval is a problem in AF patients because of its irregularity leading to the inaccuracy of this interval.

Musat[7] studied the QT interval correction methods in patients with persistent AF terminated with dofetilide. But that study had some limitations such as the dofetilide could prolong QT interval and there was small sample size. The corrected QT intervals (QTc) should be used to assess the AF patients before prescribing the QT prolonging drugs and reducing the risk of Torsades de Pointes. So the present study was conducted to determine the correlation of QT interval correction method in patients with AF compared with sinus rhythm (SR).

Materials and Methods

This retrospective study recruited the AF patients who were 18 years old or more that had electrocardiograms (ECGs) done between 2000 and 2015 and showing the AF and SR within six months. The present study excluded the patients using QT prolonging drugs (e.g. amiodarone, quinolone, macrolide, etc) or QT shortening drugs (e.g. lidocaine, etc) within 1 week or for amiodarone within 1 month. The AF patients with recent acute coronary syndrome (ACS) within 1 month, abnormal electrolyte or conditions affecting QT prolongation (e.g. hypocalcemia, hypokalemia, hypomagnesemia, overt hypothyroidism, intracranial bleeding, etc) or affecting QT shortening (e.g. hypercalcemia, hyperkalemia, etc), intraventricular conduction disturbance with QRS duration in lead II of 110 milliseconds or more, Wolff-Parkinson-White (WPW) pattern, complete AV block, long QT syndrome or short QT syndrome were excluded. The patients with history of maze operation or permanent pacemaker implantation with atrial or ventricular paced rhythm 50% or more were also excluded. The study protocol was approved by the Institutional Review Board. The present study complied with the Declaration of Helsinki.

The corrected QT interval was calculated according to the 3 following formulas:

1. Bazett's formula = $\frac{\text{QT interval}}{(\text{RR interval})^{1/2}}$

2. Fridericia formula = $\frac{\text{QT interval}}{(\text{RR interval})^{1/3}}$

3. Framingham linear formula = QT interval + [0.154 x (1 - RR interval)]

The QT interval was measured in lead II from the beginning of the QRS complex to the end of T wave, as previously described[8]. The QT and RR intervals in AF were averaged over 10 beats or all beats if they were less than 10 beats. Two cardiologists (Methavigul K and Methavigul R) independently assessed the QT interval on the 20 random sampling ECGs. There was high reproducibility as reflected by a correlation coefficient of 0.87.

The author determined 0.05 for type I error, 0.20 for type II error with 80% power and 0.3 for correlation coefficient value. A sample size of 85 patients or more was calculated by sample size estimation for correlation. The categorical data were presented as frequency and percentage. The continuous variables were presented as mean ± SD The Pearson's correlation was used to assess in relation of QTc during AF to SR and assess in relation of QTc during AF to RR interval.[9-10] The Bland-Altman plot was used to assess the agreement of QTc for the individual patients using each method in AF to SR. A p-value < 0.05 was considered the statistical significance.

Results

A total of 90 patients with AF were recruited. The average age was 64 years. A half of the patients were male and most patients were paroxysmal AF. Of the 90 patients, two-third of patients had hypertension, a half of patients had hypercholesterolemia, one-third of the patients had a history of coronary artery disease and one-fourth of the patients had a history of valvular heart disease. The baseline characteristics of the patients were shown in Table 1.

Table1 Baseline characteristics of the patients

Characteristics	Total n = 90 n (%) or mean ± SD
Age (years)	64.52 ± 12.22
Male gender	46 (51.1)
Paroxysmal AF	86 (95.6)
Heart rate (beats/minute)	
During AF	112.61 ± 28.82
During SR	68.62 ± 16.7
Medical history	
Diabetes mellitus	19 (21)
Hypertension	58 (64.44)
Hypercholesterolemia	46 (51.11)
Coronary artery disease	28 (31.11)
Valvular heart disease	23 (25.56)
Chronic kidney disease	6 (6.67)
History of previous ischemic stroke or TIA	9 (10)
LVEF (%)	60.66 ± 14.10

Table1 Baseline characteristics of the patients (Continued)

Characteristics	Total n = 90 n (%) or mean ± SD
Medications	
Beta-blockers	62 (68.89)
Nondihydropyridine CCB	6 (6.67)
Digoxin	23 (25.56)
Warfarin	41 (45.56)
Aspirin	48 (53.33)
Clopidogrel	16 (17.78)
Flecainide	2 (2.22)

SD = standard deviation, n = numbers, AF = atrial fibrillation, SR = sinus rhythm, TIA = transient ischemic attack, LVEF = left ventricular ejection fraction, CCB = calcium channel blockers

The QTc calculated using Bazett's formula, Fridericia formula and Framingham linear formula on the ECGs taken during AF were analyzed compared with it taken during SR. The average QTc during AF and SR were shown in Table 2.

Table 2 Comparison between the QTc during AF and SR

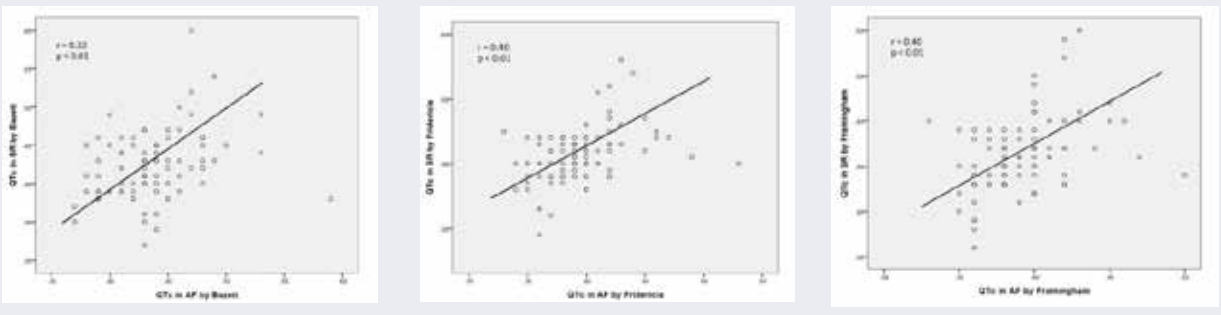
QT interval correction methods	QTc during AF (msec) Mean ± SD	QTc during SR (msec) Mean ± SD
Bazett's formula	435 ± 37	422 ± 44
Fridericia formula	395 ± 34	413 ± 43
Framingham linear formula	392 ± 29	413 ± 41

QTc = corrected QT interval, AF = atrial fibrillation, SR = sinus rhythm, msec = milliseconds, SD = standard deviation

The QTc during AF were analyzed by using Pearson's correlation relative to that during SR. The QTc calculated by using Bazett's formula, Fridericia formula and Framingham linear formula during AF had the fair correlation compared with that during SR (r = 0.32, 0.40 and 0.40, respectively) (Fig. 1).

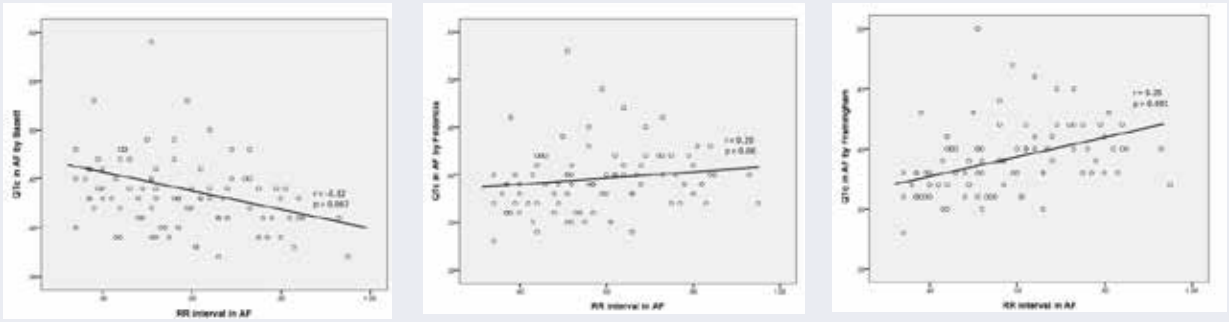
The QTc during AF were also analyzed by using Pearson's correlation relative to concurrent RR interval showed the correlation coefficients according to Bazett's formula, Fridericia formula and Framingham linear formula were -0.32, 0.20 and 0.35 seconds, respectively. During rapid heart rate, Bazett's formula overestimated the QTc, in contrast, Fridericia formula and Framingham linear formula underestimated it, respectively (Fig. 2). Fridericia formula was less dependent on heart rate (r = 0.20, p = 0.06) than Bazett's formula (r = -0.32, p = 0.002) and Framingham linear formula (r = 0.35, p = 0.001).

The Bland-Altman plot was performed to confirm the agreement of QTc calculated by using Bazett's formula, Fridericia formula and Framingham linear formula for individual patients in AF to SR (Fig. 3).



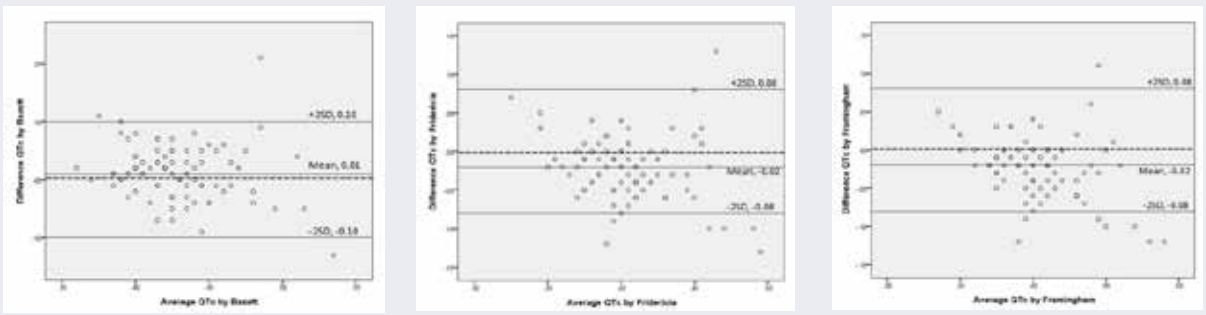
A B C

Figure 1 Relationship between QTc during AF and SR as assess by Bazett's formula (A), Fridericia formula (B) and Framingham linear formula (C)



A B C

Figure 2 Relationship between QTc during AF and RR interval as assess by Bazett's formula (A), Fridericia formula (B) and Framingham linear formula (C)



A B C

Figure 3 Bland-Altman plot showed the agreement of QTc as assess by Bazett's formula (A), Fridericia formula (B) and Framingham linear formula (C) in AF and SR

Discussion

The present study is the retrospective study to evaluate the correlation of QT correction method in patients with AF compared with SR. Because of the irregularity of QT interval and RR interval, these patients have the uncertainty of QT interval. Until now, there are several QT correction methods such as Bazett's formula, Fridericia formula, Framingham linear formula, etc. Previous study by Musat et al showed Fridericia formula most closely approximated the QTc during AF to QTc during SR, but it had several limitations such as they used the dofetilide that could prolong QT and there was small sample size. The present study is larger than previous study to assess the correlation of QT correction method in AF patients. The author used the ECGs during AF and SR without the effect of QT prolonging drugs by selecting the ECGs from the patients with paroxysmal AF or persistent AF terminated with electrical cardioversion or class IC antiarrhythmic drugs. The present study analyzed the correlation between the corrected QT intervals in AF and SR by the Pearson's correlation and confirmed the agreement by Bland-Altman plot.

The present study showed the fair linear relationship between QTc during AF and SR as assess by Bazett's formula, Fridericia formula, and Framingham linear formula despite exclusion of the QT prolonging drugs, but QTc calculated by using Fridericia formula was less dependent on heart rate than Bazett's formula and Framingham linear formula. However, our study still had some limitations. First, the present study was the retrospective study and may be the missing data affecting the QT interval. Second, there was unclear in the end of T wave in patients with coarse AF, so the measurement of QT interval may be variable in each QT interval and in each AF patients. However, the author tried to measure the QT interval at the end of T wave in lead II compared with the another one in other leads at the same time as drawing the vertical line from the end of T wave in the another leads to lead II. However, the reliability of QT measurement was assessed by very strong correlation of 2 independent authors as well (r = 0.87). The present study showed the Fridericia formula may be moderately use to correct the QT interval in patients with AF compared with Bazett's formula and Framingham linear formula. However, the other QT correction methods are still needed to investigate for the better results in patients with AF in the future.

Conclusion

QTc calculated by using Bazett's formula, Fridericia formula and Framingham linear formula had the fair correlation in patients with AF compared with SR, but Fridericia formula was less dependent on heart rate than Bazett's formula and Framingham linear formula.

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