Optimal QT Interval Correction Method in Patients with Atrial Fibrillation

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Objective: *To determine the optimal QT interval correction method in patients with atrial fibrillation (AF).*

Material and Method: *This retrospective study included the AF patients treated at Central Chest Institute of Thailand. The corrected QT intervals (QTc) during AF and sinus rhythm (SR) were calculated by using the Fridericia formula, Van de Water formula, and Hodges formula. A paired Student's t-test was used to compare the average QTc in AF and SR in each formula.*

Results: *Eighty-eight patients were enrolled. Most patients were paroxysmal AF. Comparing with SR, Hodges formula overestimated the QTc during AF with rapid response, while Fridericia formula and Van de Water formula underestimated the QTc. The QTc calculated by using Fridericia formula was less dependent on heart rate ($r = 0.20$, $p = 0.07$) than Hodges formula ($r = -0.51$, $p<0.01$) and Van de Water formula ($r = 0.61$, $p<0.01$). The Hodges formula was less dependent on heart rate ($r = -0.24$, $p = 0.29$) in 21 patients with heart rate in AF or SR between 60 to 100 beats/minute. However, there was no significant difference between QTc in AF and SR calculated by using Hodges formula ($p = 0.86$).*

Conclusion: *Although the QTc during AF and SR, calculated by using Hodges formula, was nearly the same, but the Fridericia formula was the least dependent on heart rate. The Hodges formula is the optimal QT correction method in AF patients without tachycardia or bradycardia.*

Keywords: *Atrial fibrillation, Corrected QT interval, Fridericia formula, Van de Water formula, Hodges formula*

J Med Assoc Thai 2017; 100 (11): 1184-8
Website: http://www.jmatonline.com

Atrial fibrillation (AF) is a common cardiac arrhythmia in clinical practice. It can lead to 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. Therefore, the RR interval is used to correct the QT interval[2,3].

There are currently several QT correction methods such as Bazett's formula[4], Fridericia formula[5], and Framingham linear formula[6], etc. The measurement of the QT interval is problematic in AF patients because of its irregularity leading to the inaccuracy of this interval.

Musat et al studied QT interval correction methods in patients with persistent AF terminated with dofetilide[7]. However, that study had some limitations such as the dofetilide could prolong QT interval and There was a small sample size. Other QT correction methods have not been studied in the AF patients such as Van de Water formula[10], Hodges formula[11], or logarithmic methods[8].

A 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. The present study was conducted to determine the optimal QT correction method in patients with AF compared with sinus rhythm (SR).

Material and Method

This retrospective study included 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 author excluded the patients using QT prolonging drugs (e.g., amiodarone, quinolone, or macrolide, etc.) or QT shortening drugs (e.g., lidocaine) within one week, or for amiodarone within one month. The AF patients with recent acute coronary syndrome (ACS) within one month, abnormal electrolyte, or conditions affecting QT prolongation (e.g., hypocalcemia, hypokalemia, hypomagnesemia, overt hypothyroidism, or intracranial bleeding, etc.) or affecting QT shortening (e.g., hypercalcemia, or hyper-kalemia, etc.), intraventricular conduction disturbance with QRS duration in lead II

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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 QTc was calculated according to the three following formulas:

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

2. Van de Water formula = QT interval - [0.087 x (RR interval - 1)]

3. Hodges formula = QT interval + [0.105 x (RR^{-1} - 1)]

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 and 0.20 for type II error with 80% power. A sample size of 81 patients or more was calculated by the t-test for dependent means. A paired Student's t-test was used to compare the average QTc in AF and SR as calculated by the above three formulas. 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 RR interval. 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 of 0.05 or less was considered the statistical significance.

Results

Eighty-eight patients with AF were included. The average age was 64 years. A half of the patients were male and most patients were paroxysmal AF. Of the 88 patients, 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.

The QTc calculated by using Fridericia formula, Van de Water formula, and Hodges formula on the ECGs taken during AF were analyzed, and compared with SR. There was no significant difference between the QTc in AF and SR, calculated by using Hodges formula as shown in Table 2.

The QTc during AF were analyzed by using Pearson's correlation relative to concurrent RR interval. It showed the correlation coefficients using Fridericia formula, Van de Water formula, and Hodges formula were 0.20, 0.61, and -0.51, respectively (Fig. 1). During rapid heart rate, Hodges formula overestimated the QTc during AF ($p<0.01$), in contrast, Fridericia formula and Van de Water formula underestimated it ($p = 0.07$ and $p<0.01$, respectively). Fridericia formula was less dependent on heart rate ($r = 0.20$, $p = 0.07$) than Hodges formula ($r = -0.51$, $p<0.01$) and Van de Water formula ($r = 0.61$, $p<0.01$) (Fig. 1). When the QTc in 21 patients with their heart rate in AF or SR between 60 and 100 beats/minute were analyzed by using Pearson's correlation relative to concurrent RR interval,

Table 1. Baseline characteristics of the patients

Characteristics	Total n = 88 n (%) or mean ± SD
Age (years)	64.76±12.22
Male gender	44 (50.00)
Paroxysmal AF	85 (96.60)
Heart rate (beats/minute)	
During AF	112.78±29.03
During SR	68.67±16.84
Medical history	
Diabetes mellitus	19 (21.59)
Hypertension	56 (63.64)
Hypercholesterolemia	45 (51.14)
Coronary artery disease	28 (31.82)
Valvular heart disease	23 (26.14)
Chronic kidney disease	6 (6.82)
History of previous ischemic stroke or TIA	9 (10.23)
LVEF (%)	55.15±22.10
Medications	
Beta-blockers	61 (69.32)
Nondihydropyridine CCB	6 (6.82)
Digoxin	22 (25.00)
Warfarin	40 (45.45)
Aspirin	47 (53.41)
Clopidogrel	16 (18.18)

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

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	*p*-value
Fridericia formula	395±34	414±43	<0.01
Van de Water formula	363±34	405±45	<0.01
Hodges formula	416±32	415±44	0.86

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

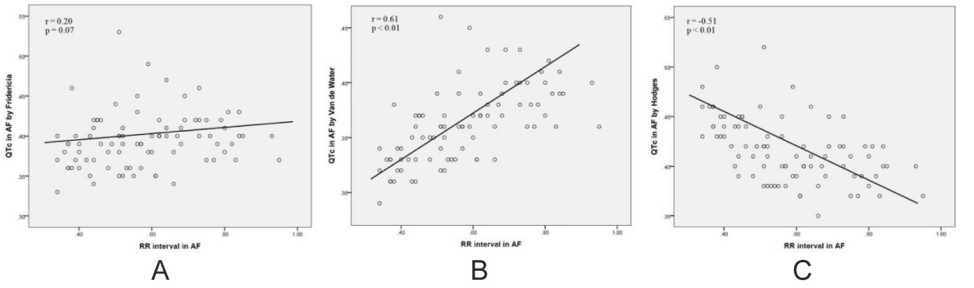

Fig. 1 Relationship between the QTc during AF and RR interval as assess by Fridericia formula (A), Van de Water formula (B), and Hodges formula (C).

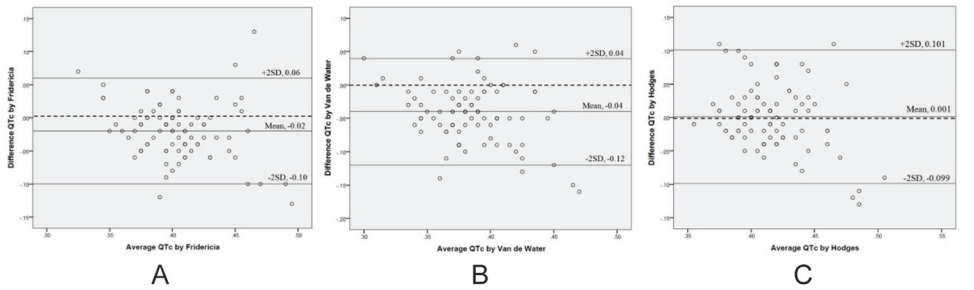

Fig. 2 Bland-Altman plot showed the agreement of the QTc as assess by Fridericia formula (A), Van de Water formula (B), and Hodges formula (C) in AF and SR.

the Hodges formula was less dependent on their heart rate (r = -0.24, p = 0.29).

The Bland-Altman plot was performed to confirm the agreement of QTc calculated by using Fridericia formula, Van de Water formula, and Hodges formula for individual patients in AF to SR (Fig. 2).

Discussion

The present study was the retrospective study to evaluate the optimal QT correction method in patients with AF compared with SR. Because of its irregularity of the QT interval and the RR interval, these patients had the uncertainty of the QT interval. There are currently several QT correction methods such as Bazett's formula, Fridericia formula, Framingham linear formula, etc. Previous study by Musat et al[7] showed QTc during AF and SR using Fridericia formula was nearly the same, but that study had several limitations such as they used dofetilide that could prolong QT interval and there was a small sample size. Moreover, there are the other QT correction methods used in the AF patients such as Van de Water formula, Hodges formula, or logarithmic methods. The present study is larger than the previous study to assess the optimal 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. The author selected Fridericia formula, Van de Water formula, and Hodges formula to assess the QTc in the present study, because of lack of data in the other QT correction methods compared with Fridericia formula.

The present study showed no significant difference between the QTc in AF and SR calculated by using Hodges formula. However, the previous study by Musat et al[7] showed no significant difference between the QTc in AF and SR calculated by using Fridericia formula, while the present study showed significant difference between the QTc in AF and SR calculated by the same formula. The reason for this difference was the present study was larger than the previous study.

The QTc calculated by using Fridericia formula was still less dependent on heart rate than Van de Water formula and Hodges formula. When the patients with tachycardia or bradycardia were excluded, the rest patients were reanalyzed. The present study showed the Hodges formula was less dependent on heart rate (r = -0.24, p = 0.29) in 21 patients with their heart rate in AF or SR between 60 to 100 beats/minute. However, the present study still has some limitations. First, the present study was the retrospective study so there may be some missing data affecting the QT interval. Second,

the end of the T wave was unclear in patients with coarse AF, so the measurement of the QT interval may be variable about the QT interval in each QRS complex, and between individual AF patients. However, the author tried to measure the QT interval at the end of T wave in lead II compared with the other leads at the same time as drawing the vertical line from the end of T wave in the other leads to lead II. The reliability of the QT measurement was assessed by two independent cardiologists. There was high reproducibility as reflected by a correlation coefficient of 0.87. The present study showed the Hodges formula may be moderately used to correct the QT interval in AF patients compared with Fridericia formula and Van de Water formula, especially in patients without tachycardia or bradycardia. However, another complicated QT correction methods such as logarithmic method is still needed to investigate for the better results in AF patients in the future.

Conclusion

Although the QTc calculated by using Hodges formula during AF and SR are the same, the Fridericia formula was the least dependent on heart rate. The Hodges formula is the optimal QT correction method in AF patients without tachycardia or bradycardia.

What is already known on this topic?

The QT interval is dependent on heart rate. Several QT correction methods are calculated in patients with SR.

What this study adds?

Hodges formula is the optimal QT correction method in AF patients without tachycardia or bradycardia, but Fridericia formula has the least dependence on heart rate.

Potential conflicts of interest

None.

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การศึกษาเพื่อหาวิธีวัดระยะ corrected QT ที่เหมาะสมในผู้ป่วยที่มีหัวใจห้องบนสั่นพลิ้ว

คมสิงห์ เมธาวีกุล, รติกร เมธาวีกุล

วัตถุประสงค์: *เพื่อศึกษาวิธีวัดระยะ corrected QT ที่เหมาะสมในผู้ป่วยที่มีหัวใจห้องบนสั่นพลิ้ว*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาแบบย้อนหลังในผู้ป่วยหัวใจห้องบนสั่นพลิ้วที่ได้รับการรักษาในสถาบันโรคทรวงอกใน พ.ศ. 2543 ถึง พ.ศ. 2558 โดยนำระยะ corrected QT ตอนเป็นหัวใจห้องบนสั่นพลิ้วและ sinus rhythm (SR) ที่คำนวณโดยใช้สูตร Fridericia formula, Van de Water formula และ Hodges formula มาเปรียบเทียบค่าเฉลี่ยของระยะ corrected QT ตอนเป็นหัวใจห้องบนสั่นพลิ้วกับตอนเป็น SR ในแต่ละสูตรโดยใช้ paired Student's t-test*

ผลการศึกษา: *ผู้ป่วยหัวใจห้องบนสั่นพลิ้วจำนวน 88 ราย ได้รับการคัดเลือกเข้ามาในการศึกษา ผู้ป่วยส่วนใหญ่เป็นหัวใจห้องบนสั่นพลิ้วเป็นครั้งคราว เมื่อหัวใจเต้นเร็วพบว่า ระยะ corrected QT ที่คำนวณโดย Hodges formula จะมากกว่าปกติตอนเป็นหัวใจห้องบนสั่นพลิ้วเทียบกับตอนเป็น SR ในขณะที่ระยะ corrected QT ที่คำนวณโดย Fridericia formula และ Van de Water formula จะน้อยกว่าปกติตอนเป็นหัวใจห้องบนสั่นพลิ้วเทียบกับตอนเป็น SR ระยะ corrected QT ที่คำนวณโดย Fridericia formula ขึ้นอยู่กับอัตราการเต้นของหัวใจ ($r = 0.20$, $p = 0.07$) น้อยกว่าที่คำนวณโดย Hodges formula ($r = -0.51$, $p<0.01$) และ Van de Water formula ($r = 0.61$, $p<0.01$) โดยที่ Hodges formula จะขึ้นอยู่กับอัตราการเต้นของหัวใจ ($r = -0.24$, $p = 0.29$) น้อยลงในผู้ป่วยจำนวน 21 ราย ที่มีอัตราการเต้นของหัวใจตอนเป็นหัวใจห้องบนสั่นพลิ้ว หรือ SR อยู่ระหว่าง 60 ถึง 100 ครั้งต่อนาที อย่างไรก็ตามไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างระยะ corrected QT ตอนเป็นหัวใจห้องบนสั่นพลิ้ว และ SR ที่คำนวณโดยใช้ Hodges formula ($p = 0.86$)*

สรุป: *แม้ว่าระยะ corrected QT ที่คำนวณโดยใช้ Hodges formula ตอนเป็นหัวใจห้องบนสั่นพลิ้วจะใกล้เคียงกับตอนเป็น SR แต่ Fridericia formula จะขึ้นอยู่กับอัตราการเต้นของหัวใจน้อยที่สุด ดังนั้น Hodges formula จึงเป็นวิธีวัดระยะ corrected QT ที่เหมาะสมในผู้ป่วยหัวใจห้องบนสั่นพลิ้วที่ไม่มีหัวใจเต้นเร็วหรือช้ากว่าปกติ*