Journal of Electrocardiology 56 (2019) 70–76

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

QT correction in atrial fibrillation – Measurement revisited

Aditee Dash, MBBS, Cyril Torado, MD, Nieman Paw, MD, Dali Fan, MD, Nayereh Pezeshkian, MD MPH, FHRS, Uma Srivatsa, MBBS, MAS, FHRS *

Division of Cardiovascular Medicine, University of California, Davis, United States of America

ARTICLE INFO

Keywords:
Atrial fibrillation
QT interval correction

ABSTRACT

Background: QT interval measured in the electrocardiogram (ECG) varies with RR interval challenging the calculation of corrected QT (QTc) in Atrial fibrillation (AF).
Objectives: To identify the ideal Lead, number of complexes and the formula to measure QTc that correlates best between AF and sinus rhythm (SR).
Procedure: We identified ECGs from patients with AF before and after conversion to SR. After excluding patients on drugs and clinical conditions that prolong QT interval, QTc was calculated from all the leads using the formulae: Bazett (BF), Fridericia (FF), Framingham(FrF), Hodges (HF), Saige (SF) and Rautaharju (RF) during AF and SR. After identifying the lead with best linear correlation, we calculated QTc following the longest RR, multiple QRS complexes and average automated RR interval during AF and compared to SR.
Findings: In 52 patients (male 69%, age 63 ± 9 yrs), QTc measured from Lead II correlated best with SR in majority of the formulae. QTc was consistently shorter with linear formulae. While BF overestimated QTc, FF was optimal comparing AF vs SR (416 ± 33 vs 411 ± 38 ms, ns) calculated from single, multiple or average automated RR interval. Bland Altman analysis of the average automated QTc versus the delta of individual automated QTcs shows the least variation in the QTc calculated by FF.
Conclusions: BF in commercial software is not ideal for measurement of QTc in AF, Fridericia Formula in lead II from the average RR from automated ECG measurement maybe utilized for the calculation of QTc.

Introduction

QT interval is the measurement of ventricular activity and includes ventricular depolarization and repolarization. It is measured form the beginning of QRS to the end of the T wave in the twelve lead electrocardiogram (ECG) [1]. Repolarization is a function of the underlying heart rate and decreases with progressive rise in ventricular rate. Moreover, it depends not only on the mean heart rate but also on the instantaneous preceding RR interval or the interval between beats. The significance of an accurate QT measurement is to assess risk of potentially lethal *torsades de pointes*, a condition which is exacerbated by electrolyte imbalance, QT-interval prolonging drugs and genetic abnormalities [2].

To account for the inconsistency in QT interval with heart rate, many correction formulae have been developed to calculate the corrected QT interval (QTc) normalized to a heart rate of 60 beats/min [1]. The most commonly used formula used in the automated algorithms is the Bazett (BF) but limitations on its usage include over-estimating QTc interval at high heart rates.

Atrial fibrillation (AF) is the most common sustained heart rhythm disorder worldwide and is associated with higher mortality, particularly when QT interval is prolonged [3]. AF is frequently associated with rapid heart rates, and requires the prescription of antiarrhythmic drugs, which often prolong the QT interval. The RR intervals in Atrial Fibrillation patients is irregular which makes QTc estimation highly variable due to the influence of instantaneous preceding RR interval as well as the average heart rate. Class III antiarrhythmic drugs are contraindicated in the presence of prolonged QTc interval [4].

During hemodynamic measurements in patients with AF, it is often a practice to average five beats to assess stroke volume and to measure

Abbreviations: AF, Atrial fibrillation; ECG, electrocardiogram; BF, Formulae: Bazett; FF, Fridericia; FrF, Framingham; HF, Hodges; SF, Saige; RF, Rautaharju; QTc, corrected QT interval; SR, sinus rhythm; ABL, Ablation; DM, Diabetes Mellitus; HTN, Hypertension.

* Corresponding author at: Division of Cardiovascular Medicine, Department of Internal Medicine, UC Davis School of Medicine, United States of America.
E-mail address: unsrivatsa@ucdavis.edu (U. Srivatsa).

https://doi.org/10.1016/j.jelectrocard.2019.06.009
0022-0736/

Table 1
Baseline characteristics.

Baseline characteristics	
Age	63 ± 8.6 yrs
Male	69.23%
Hypertension	61.54%
Diabetes	17.31%
Coronary artery disease	21.15%
Congestive heart failure	7.692%
Cerebrovascular disease	3.84%
Chronic obstructive pulmonary disease	3.8%
Obstructive sleep apnea	23.08%
CHA2DS2-VASc score	2.03 ± 1.4
Body mass index	31.21 ± 5.762 kg/m^2
Serum sodium	138.98 ± 2.82 mEq/L
Serum potassium	3.68 ± 0.14 mEq/L
Serum magnesium	1.966 ± 0.1959 mEq/L
Serum creatinine	1.0192 ± 0.4485 mg/dL
Smoking	32.69%
Alcohol use	51.92%
Prior ablation/cardioversion	19.23%
Spontaneous conversion	26.92%

gradient across the heart valves. However, there is no validity for such a practice for QT interval measurements. The aim of our study was to find the most accurate lead, formula and the optimal number of QRS complexes during AF that correlate best with QTc measured in the same patients during sinus rhythm (SR).

Methods

Patient selection and ECG recordings

After Institutional Review Board approval, we identified patients with established diagnosis of AF. Clinical characteristics and demographics, laboratory values, list of medications and procedures performed (Cardioversion and Endocardial Ablation) were obtained from the Electronic Medical Records (EMR). Patients <18 years of age, pregnant women, those on QT interval prolonging drugs, acute decompensated Heart Failure, known long QT Syndrome, acute coronary syndrome patients, acute medical illnesses, liver failure, acute stroke, renal failure, abnormal electrolytes were excluded from the study. All the ECGs at UC Davis were recorded using MAC 5500 devices (GE Healthcare, standard 12 lead resting ECGs, 25 mm/s paper speed, 10 mm/mV amplitude, and 250 Hz sampling rate). ECGs were selected from the MUSE software if SR and AF were available on the same day. SR ECG was selected for comparison if the heart rate was regular without any sinus arrhythmia. Ectopic and aberrantly conducted beats were excluded from further analysis.

QT measurement and selection of ideal lead

Digital and manual measurements of QT and RR intervals were made from single QRS complexes with best identifiable T wave all the leads. The recording for the ECGs was done at a paper speed of 25 mm/s and amplitude of 0.1 mV/mm. The QT interval was measured in all leads from the beginning of QRS complex to the point the T wave reached the baseline. Presence of U wave was excluded. The QT intervals were measured both manually and digitally. Digital QT interval was measured in the MUSE software. Manually, the QT interval was measured by drawing a tangent line to the steepest part of the descending portion of the T wave, taking its intercept with the isoelectric line as the end of the T wave.

QTc was calculated by the formulae [5]:

A: Non linear formulae:

BAZETT (BF): $QT/\sqrt{RR}$.
FRIDERICIA (FF): $QT/\sqrt[3]{RR}$

B: Linear formulae:

FRAMINGHAM (FrF): $QT + 0.154 \times (1 - RR)$
SAIGE (SF): $QT + 0.116 \times (1 - RR)$
HODGE (HF): $QT + 1.75 \times (HR - 60)$
RAUTAHARJU (RF): $QT - 0.185 \times (RR - 1) + k$ [k = +0.006 s for men and +0 s for women]

The above method was done for 25 patients in all the 12 leads. The ECG lead with the most linear correlation between AF and SR by majority of the formulae was recognized and selected for further observations.

Measurement of QTc from multiple QRS complexes during AF

After determining the lead for measurement, we set forth to determine how many QRS complexes are needed to calculate the QTc during AF that correlated best with SR. We included additional patients to calculate QT and RR intervals from multiple complexes.

From the rhythm strip of the ideal ECG lead identified as described above, we calculated QTc intervals from each QRS complex using all the formulae. To assess accuracy of manual vs digital measurement, the QTc in the best lead were measured utilizing manual and digital calipers as described above. RR interval used for the formula preceded the QT segment. The mean of QTc from single, three, five, ten complexes from the rhythm strip was calculated. We also used the average automated RR interval and median QT listed in the ECG software and the calculated QTc was termed as the "average" QTc. We compared these QTc to that during SR.

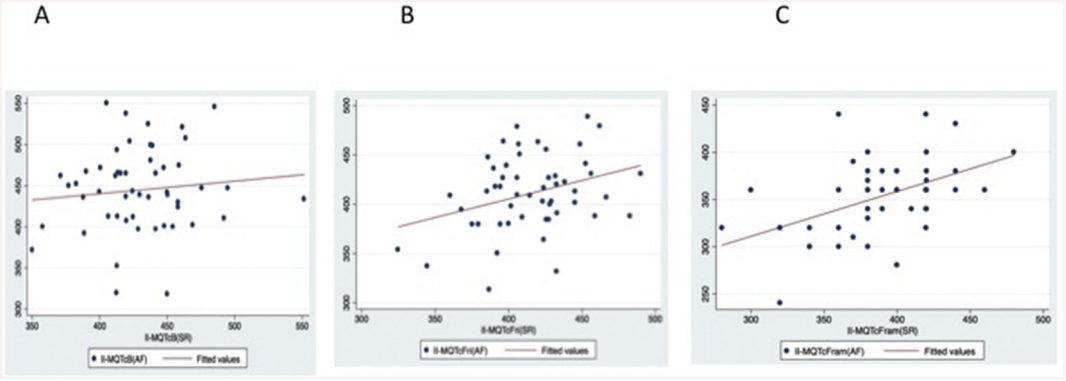

Fig. 1. Correlation between QTc calculated in sinus rhythm (X axis) and atrial fibrillation (Y axis) in Bazett (A), Friericia (B) and Framingham (C).

Statistics

Linear regression was used to correlate the QTc values in AF and SR; paired "*t*-test" was used to assess the difference between the QTc in AF and SR for the same patient. *P*-value ≤0.05 was taken as statistically significant for a correlation between SR and AF. A scatter plot was made to observe the relationship between preceding RR intervals and the QTc measured in AF. As QTc is standardized to the RR interval, it should not vary with preceding RR interval. The optimal result required would be the least slope, which would be non-significant.

A Bland-Altman Analysis was carried out to describe the agreement between two quantitative measurements, QTc during AF as described in methods section and delta difference from the group mean QTc calculated by BF, FF, FrF.

Results (Table 1)

From Electronic Medical Records (EMR), 155 patients were identified with ECG in AF and SR within 24 h span, and of these we selected 52 patients who fit the criteria of our study. About two thirds were male (males 69.23%) with mean age 63 ± 8.6 years, 61.54% had hypertension, 17.31% had Diabetes Mellitus. Mean RR interval was 831 ± 150 ms; QT interval in lead II during SR was 396 ± 38 ms and QTc calculated by BF during SR was 438 ± 38 ms. The mean ventricular rate during AF measured by automated algorithm was 641 ± 15 ms (SD). Mean duration of AF before cardioversion was 416 ± 125 days; 38% of the patients had long lasting AF (≥ 180 days). Duration between Afib and NSR ECG is 68 ± 25 h (SD). There were four patients with NSR ECG > 1 week after cardioversion.

Table 2
Lead selection:

Leads	Bazett (*P* value)	Fridericia (*P* value)	Framingham (*P* value)	Hodge (*P* value)	Saige (*P* value)	Rautaharju (*P* value)
I						
AF	427 ± 38	398 ± 32	349 ± 46	349 ± 46	349 ± 46	349 ± 46
SR	431 ± 32	416 ± 32	390 ± 42	390 ± 42	390 ± 42	390 ± 42
R^2	ns	0.45(0.02)*	ns	ns	ns	ns
II						
AF	430 ± 46	400 ± 35	350 ± 42	350 ± 42	350 ± 42	350 ± 42
SR	427 ± 36	413 ± 38	386 ± 47	386 ± 47	386 ± 47	386 ± 47
R^2		0.27(0.01)*	0.42(0.03)*	0.42(0.03)*	0.4(0.03)*	0.4(0.03)*
III						
AF	426 ± 57	394 ± 42	339 ± 39	339 ± 39	339 ± 39	339 ± 39
SR	430 ± 27	417 ± 27	391 ± 34	391 ± 34	391 ± 34	391 ± 34
R^2	ns	ns	0.3(0.04)*	0.3(0.04)*	0.3(0.04)*	0.3(0.04)*
aVR						
AF	429 ± 44	396 ± 31	340 ± 42	340 ± 42	340 ± 42	340 ± 42
SR	408 ± 34	396 ± 32	376 ± 44	376 ± 44	376 ± 44	376 ± 44
R^2	ns	ns	ns	ns	ns	ns
aVL						
AF	406 ± 46	378 ± 38	331 ± 45	331 ± 45	331 ± 45	331 ± 45
SR	415 ± 24	400 ± 29	374 ± 45	374 ± 45	374 ± 45	374 ± 45
R^2	ns	ns	ns	ns	ns	ns
aVF						
AF	435 ± 59	402 ± 44	345 ± 45	345 ± 45	345 ± 45	345 ± 45
SR	416 ± 22	401 ± 24	375 ± 36	375 ± 36	375 ± 36	375 ± 36
R^2	ns	ns	ns	ns	ns	ns
V1						
AF	450 ± 51	413 ± 39	352 ± 46	352 ± 46	352 ± 46	352 ± 46
SR	419 ± 42	408 ± 39	387 ± 47	387 ± 47	387 ± 47	387 ± 47
R^2	ns	ns	0.3(0.02)*	0.3(0.02)*	0.3(0.02)*	0.3(0.02)*
V2						
AF	446 ± 72	412 ± 54	357 ± 48	357 ± 48	357 ± 48	357 ± 48
SR	408 ± 30	397 ± 30	377 ± 41	377 ± 41	377 ± 41	377 ± 41
R^2	ns	ns	0.3(0.01)*	0.3(0.01)*	0.3(0.01)*	0.3(0.01)*
V3						
AF	448 ± 64	413 ± 42	356 ± 45	356 ± 45	356 ± 45	356 ± 45
SR	420 ± 32	409 ± 33	389 ± 45	389 ± 45	389 ± 45	389 ± 45
R^2	ns	ns	0.2(0.03)*	0.2(0.03)*	0.2(0.03)*	0.2(0.03)*
V4						
AF	450 ± 56	416 ± 38	357 ± 40	357 ± 40	357 ± 40	357 ± 40
SR	429 ± 32	418 ± 32	397 ± 41	397 ± 41	397 ± 41	397 ± 41
R^2	ns	ns	0.21(0.02)*	0.21(0.02)*	0.21(0.02)*	0.21(0.02)*
V5						
AF	448 ± 63	413 ± 43	355 ± 39	355 ± 39	355 ± 39	355 ± 39
SR	424 ± 34	412 ± 32	390 ± 39	390 ± 39	390 ± 39	390 ± 39
R^2	ns	ns	ns	ns	ns	ns
V6						
AF	451 ± 63	416 ± 44	357 ± 42	357 ± 42	357 ± 42	357 ± 42
SR	422 ± 34	410 ± 33	388 ± 41	388 ± 41	388 ± 41	388 ± 41
R^2	ns	ns	0.19(0.03)*	0.2(0.03)*	0.19(0.03)*	0.2(0.03)*

AF: atrial fibrillation; SR: sinus Rhythm; QTc intervals measured in AF and SR are displayed in each row in all the leads.
* $P < 0.05$.

Table 3
Comparison of manual and digital measurements.

	Manual QTc (ms)	*P*-value	R^2 (*P*-value)	Digital QTc (ms)	*P*-value	R^2 (*P*-value)
B-AF	445 + 51			448 + 49		
B-SR	430 + 36	ns	ns	438 + 38	ns	ns
Fri-AF	411 + 38			414 + 37		
Fri-SR	416 + 33	ns	0.1 (0.02)	423 + 33	ns	0.1(0.01)
Fram-AF	354 + 40			356 + 41		
Fram-SR	389 + 40	<0.0001	0.2(0.001)	396 + 38	<0.0001	0.2(0.003)
Hodge-AF	354 + 40			356 + 41		
Hodge-SR	389 + 40	<0.0001	0.2(0.002)	396 + 38	<0.0001	0.2(0.003)
Saige-AF	354 + 40			356 + 41		
Saige-SR	389 + 40	<0.0001	0.2(0.001)	396 + 38	<0.0001	0.2(0.003)
Rautaharju-AF	354 + 40			356 + 41		
Rautaharju-SR	389 + 40	<0.0001	0.2(0.001)	396 + 38	<0.0001	0.2(0.003)

Lead selection and assessment of formulae

Of all the formulae investigated, BF did not correlate with any leads both in SR and AF, it overestimated QTc during AF in the precordial leads (V1–V6). QTc during AF and SR calculated by FF correlated best in Lead II (400 ± 35 ms vs 413 ± 38 ms; R-squared value 0.27 ($P = 0.01$)). The linear formulas (Framingham, Hodges, Saige and Rautaharju) had good correlation in the precordial leads (V1–V6), however the QTc measured in AF was shorter than the QTc measured in SR by about 40 ms (<0.001) (Fig. 1) (Table 2).

Comparison of manual vs digital and multiple complexes in lead II

Manual and digital caliper measurements of QTc in lead II were found to be equivalent. (Table 3) Though there were differences between AF and SR, the manual vs digital measurements within the same formula was not different. BF was consistently longer, linear formulae were consistently shorter in AF; FF had the least difference between AF and SR in both manual and digital measurements.

Number of complexes during AF to calculate QTc: (Table 4)

With BF, the mean QTc were longer in AF (expressed as percent difference) when single (3.5%), three (3.3%), five (3.3%), ten complexes (4.1%) and the automated average (6.3%) were compared to SR; QTc following the longest RR had the most difference compared to SR (−11%). The QTc calculation for all the linear formulae was shorter than SR in all measurements by about 9% which was statistically significant. FF had the least difference between AF and SR with single (1.2%), three (1.9%), five (1.9%), ten (1.2%) complexes and the average (1.4%) QTc. following longest RR calculated by FF, similar to other formulae was significantly different (−10.3%).

QTc and RR relationship

Scatter plots were constructed to observe the relationship between preceding RR intervals and the QTc measured in AF. As QTc is standardized for RR interval, it should not vary with preceding RR interval. The optimal result would show the least slope which and non significant.

The plots of QTc for single complex Lead II (Fig. 2), FF showed the least slope with non-significant variation as opposed to QTc calculated by BF or FrF. BF shows a large decreasing slope for QTc with lengthening cycles, both following longest RR and with average RR (A & B, Fig. 3); FrF shows a large increasing slope for QTc in both longest RR and average RR; QTc calculated from in automated average RR by FF has the least slope (1.44%; ns), signifying stability with RR interval variations.

Table 4
Comparison of multiple complexes to sinus rhythm.

Formula	Sinus rhythm	1 complex	3 complexes	5 complexes	10 complexes	Longest RR	Average QTc
Bazett	430 + 36	445 + 51 (ns)	444 + 47 (0.04)	444 + 43	448 + 43	383 + 53	457 + 39
(*P*-value)		ns		(0.03)	(0.001)	(<0.0001)	(0.001)
R^2			0.2 (0.004)	0.1 (0.04)	0.1 (0.03)	ns	ns
(*P*-value)							
Fridericia	416 + 33	411 + 38 (ns)	408 + 39	408 + 35	411 + 35	373 + 44	422 + 33
(*P*-value)		0.1 (0.02)	(ns)	(ns)	(ns)	(<0.0001)	(ns)
R^2			0.3 (0.0001)	0.2 (0.001)	0.2 (0.001)	ns	0.1 (0.04)
(*P*-value)							
Framingham	389 + 40	354 + 40 (<0.0001)	348 + 43	347 + 41	348 + 39	356 + 49	362 + 42
(*P*-value)			(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)
R^2		0.2 (0.001)	0.2 (0.003)	0.2(0.003)	0.2 (0.003)	0.2 (0.002)	0.1 (0.01)
(*P*-value)							
Hodge	389 + 40	354 + 40 (<0.0001)	348 + 43	347 + 41	350 + 39	356 + 49	362 + 42
(*P*-value)			(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(0.001)
R^2		0.2 (0.002)	0.2 (0.003)	0.2 (0.003)	0.2	0.2	0.1
(*P*-value)					(0.001)	(0.002)	(0.01)
Saige	389 + 40	354 + 40 (<0.0001)	348 + 43	347 + 41	350 + 39	356 + 49	362 + 42
(*P*-value)			(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(0.0001)
R^2		0.2 (0.001)	0.2	0.2	0.2	0.2	0.1
(*P*-value)			(0.003)	(0.003)	(0.001)	(0.002)	(0.01)
Rautaharju	389 + 40	354 + 40 (<0.0001)	348 + 43	347 + 41	350 + 39	356 + 49	362 + 42
(*P*-value)			(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(0.001)
R^2		0.2 (0.001)	0.2	0.2	0.2	0.2	0.1
(*P*-value)			(0.003)	(0.003)	(0.001)	(0.002)	(0.01)

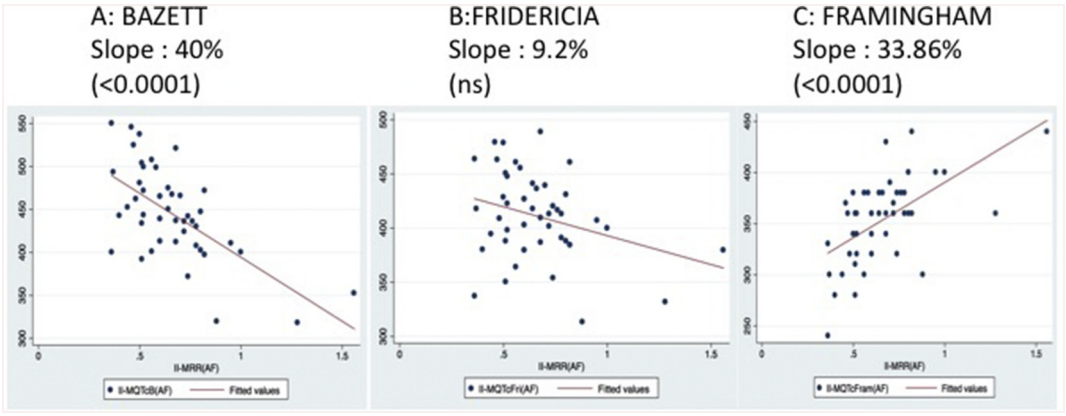

Fig. 2. Correlation between RR interval in seconds (X axis) and QTc from a single complex in Lead II in msec (Y axis); A: Bazett formula; B: Fridericia formula; C: Framingham formula.

We had 16 patients with average RR interval < 550 ms and 36 patients with RR interval > 550 ms. There was no difference in QTc calculated by FF between these groups: 421.4 ± 41 ms vs 421.9 ± 30 ms (ns) respectively.

Bland Altman analysis of the QTc

BA analysis of the random single complex from Lead II during SR is shown in Fig. 4(A–C) comparing the mean QTc during AF in the formulae (Bazett, Fridericia and Framingham) with the difference between individual QTc and the mean (Y axis). Lower and Upper limits of the 95% confidence interval of the mean difference were 70 to −85 ms respectively in the FF, which is the least among the three formulae. In Fig. 3(D–E) comparing the mean QTc calculated from the automated RR is compared with the delta of individual automated QTc, the plot shows that the lower and upper limits of the 95% confidence interval of the mean difference is 70 and –60 ms respectively in the FF. BF and FrF show wider variations.

The difference between male and female patients in our cohort is outlined in Table 5. There was no difference in age (63 ± 8 vs 63 ±

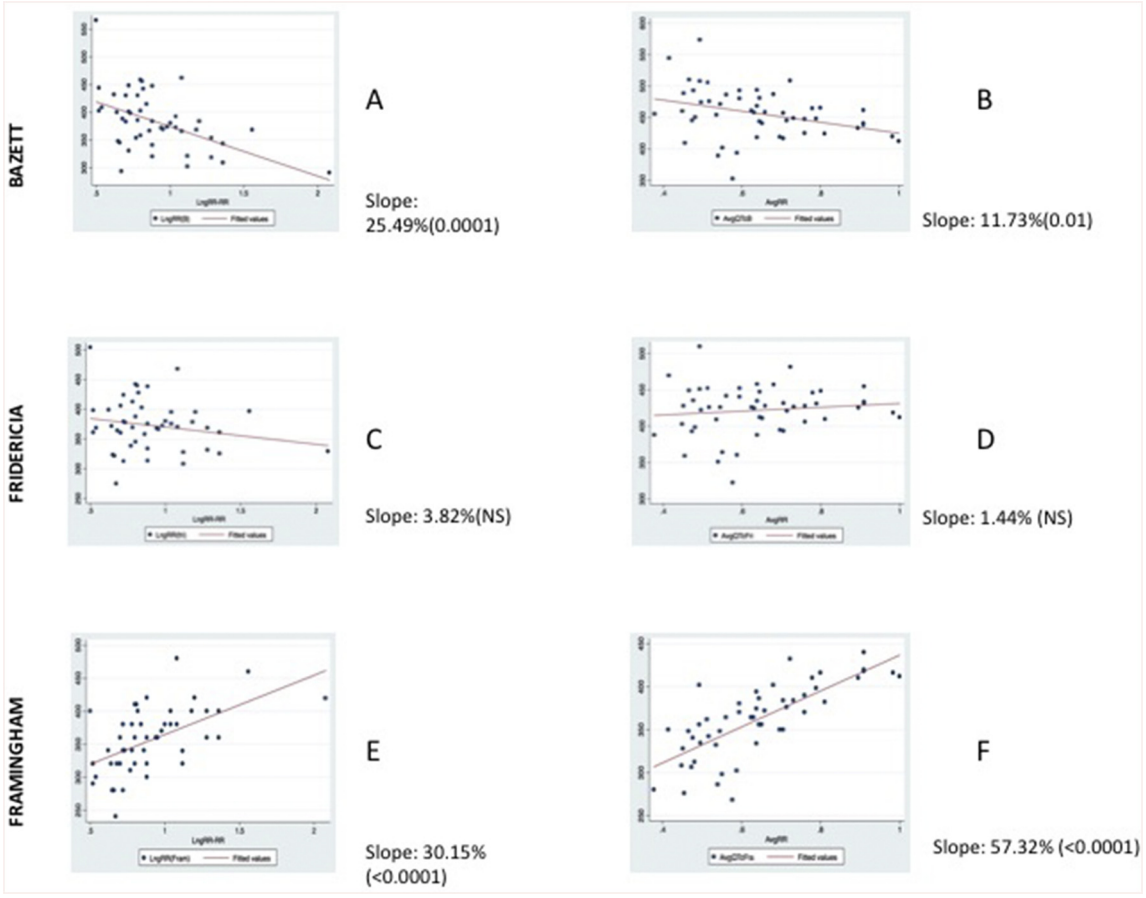

Fig. 3. Correlation between RR interval in seconds (X axis) and QTc from lead II in msec (Y axis) correlation; Top row: Bazett formula; middle row: Fridericia formula; Bottom row: Framingham Formula. QTc in A, C & E are from the longest RR interval; B, D and F are from the average RR interval. See text for details.

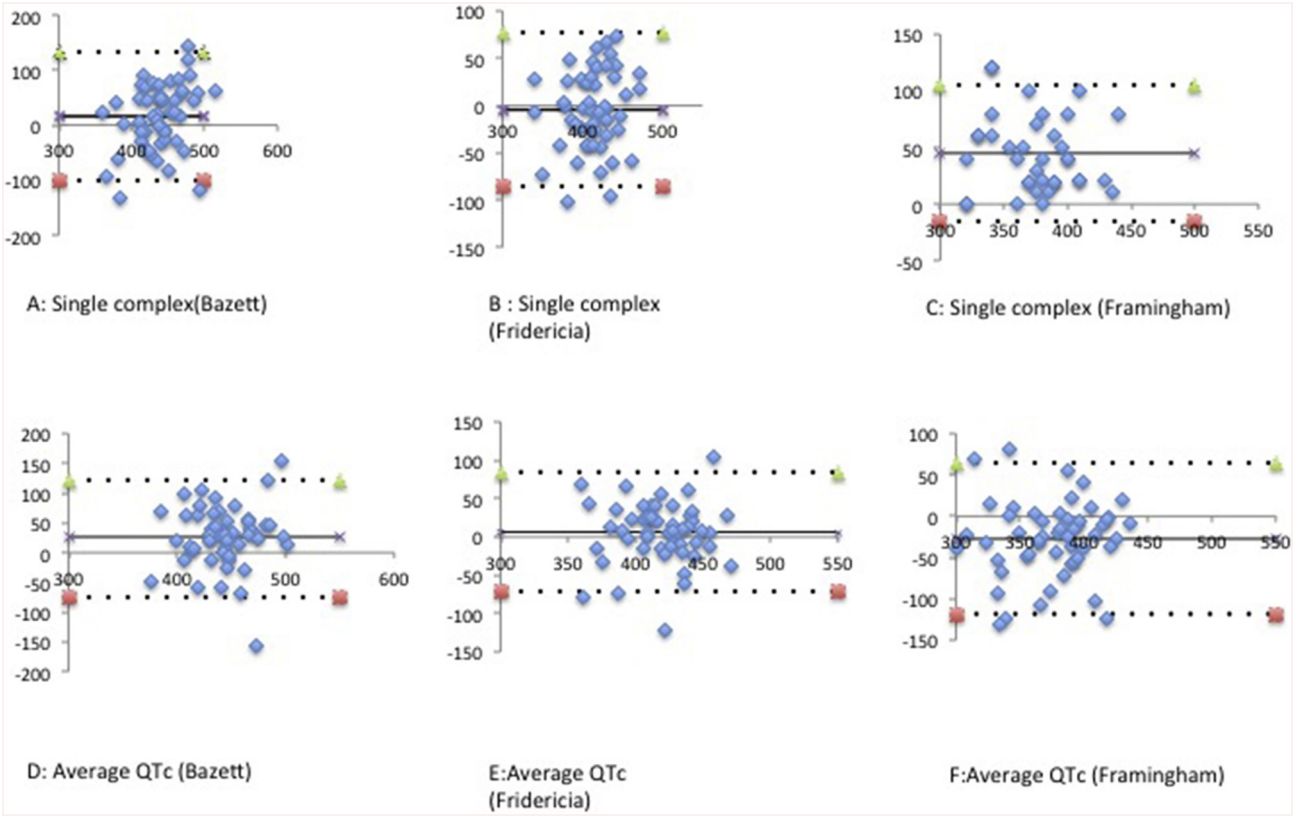

Fig. 4. Bland Altman analysis of Lead II single complex and Average QTc; X axis: QTc in msec; Y axis - delta difference between QTc in sinus rhythm and atrial fibrillation; A& D represent Bazett formula; B& E represent Fridericia formula; C & F represent Framingham formula; in the upper rows, QTc is derived from single complex, QTc in the lower is calculated from the average RR interval. Dotted line between green triangles: upper limit of agreement; Dotted line between red squares: lower limit of agreement; Black line represents bias. See text for details.

9 years, ns). Females have longer QTc when calculated by BF or FrF, QTc calculated by Framingham was shorter among females, but none of them were significant.

Discussion

The main finding of this study is that QTc during AF calculated from Fridericia formula from the automated average RR interval from the ECG reading in lead II best correlates with that during SR. BF consistently overestimates and linear formulae consistently underestimate the QTc.

Table 5
Sex differences in calculated QTc.

	Male (ms)	Female (ms)	P value
BF lead II SR	439 ± 42	435 ± 28	ns
BF lead II AF	442 ± 53	462 ± 35	ns
BF longest RR QTc	379 ± 55	390 ± 47	ns
BF average RR QTc	440 ± 40	471 ± 33	0.07
FF lead II SR	422 ± 36	425 ± 26	ns
FF lead II AF	411 ± 39	422 ± 30	ns
FF longest RR QTc	371 ± 45	376 ± 43	ns
FF average RR QTc	419 ± 36	427 ± 28	ns
FraF lead II SR	392 ± 41	405 ± 28	ns
FraF lead II AF	357 ± 41	354 ± 42	ns
FraF longest RR QTc	359 ± 49	351 ± 48	ns
FraF average RR QTc	366 ± 45	353 ± 35	ns

BF - Bazett formula.
FF - Fredericia formula.
FraF - Framingham formula.
R - sinus rhythm.
AF - atrial fibrillation.

In addition, measured QT following the longest RR interval underestimates the actual QTc during SR.

In a large study by Vandenberk et al., calculated QTc by different formulae were assessed for QTc/RR regression and relation to mortality. In patients with SR and without wide QRS, FF showed the best QT correction and improved mortality prediction [6]. In this study, the automated GE Marquette algorithm measuring the QT-interval in a median complex from the earliest detection of depolarization in any lead to the latest detection of repolarization in any lead was taken into account. Similarly, QTc by FF has also been shown to have excellent correlation in patients with atrial flutter [7]. Our study where we assessed QT intervals by multiple non-automated measurements validates this finding of QTc/RR regression. Our study also confirms the benefit of utilization of the automated QT and RR intervals. The slope of QTc/RR regression was the least when the automated measurements (Fig. 3D) were used to calculate FF as opposed to single lead (Fig. 2B) or that following the longest RR (Fig. 3C).

Since persistent fast heart rate can modulate IKr and IKs expression altering intrinsic repolarization in the myocardial cell, we evaluated the effect of fast heart rate. Most of our patients presented with well controlled heart rate. About a third of our patients had long standing AF; regardless of the duration of AF, or the heart rate, the findings remained similar.

Our findings are also similar to an investigation by Musat et al. where the investigators calculated QTc by BF, FF and FrF and studied the effects of dofetilide during AF. However in this report, the authors measured QT predominantly from lead II; if T wave was not discernible, then the lead with longest QT was utilized for calculation. Our evaluation included identification of the optimal lead, the best formula as well the most optimal complex or number of complexes needed for

QTc. Our findings suggest that the average automated QT and RR intervals may be utilized as they are consistent with SR without a need to specifically look for the most optimal lead or the complex with discernible T wave.

Women have longer QTc interval after puberty due to relatively reduced protective effect of testosterone that is noted in males [8]. However these studies were performed in SR and QTc calculated by BF. In our study, all the women were post-menopausal. Testosterone/estrogen ratio is higher among post-menopausal women and the difference in QTc among men and women is known to be lower with age [9,10]. Consistent with this mechanism, QTc did not differ among men and women in our study measured by any formulae (Table 5).

Our findings have clinical implications, as patients with prolonged QTc calculated by BF maybe denied antiarrhythmic drugs that can be useful. In addition, the conventional concept of QT following the longest RR interval may not be applicable in patients with AF who have variable RR intervals. Among these patients, the average RR interval correlates best with that measured during SR. Selection of patients for antiarrhythmic drugs based on QT measured following longest RR interval by underestimating may predispose patients to arrhythmias.

Our study limitations include single center analysis and lack of follow up to assess effect on clinical outcome including arrhythmias and mortality. The effect of cardio-version or ablation on QTc is unknown; we also have not validated FF with antiarrhythmic drug administration.

In conclusion, the automated QT and RR intervals may be utilized for QTc assessment in atrial fibrillation; Fridericia formula best correlates with that of sinus rhythm and has the least rate variation.

Declaration of Competing Interest
None.

References

[1] Goldenberg I, Moss AJ, Zareba W. QT interval: how to measure it and what is "normal". J Cardiovasc Electrophysiol 2006;17(3):333–6.
[2] Moss AJ. The QT interval and torsade de pointes. Drug Saf 1999;21(Suppl. 1):5–10 [discussion 81-17].
[3] Reusser A, Blum S, Aeschbacher S, Eggimann L, Ammann P, Erne P, et al. QTc interval, cardiovascular events and mortality in patients with atrial fibrillation. Int J Cardiol 2018;252:101–5.
[4] Li EC, Esterly JS, Pohl S, Scott SD, McBride BF. Drug-induced QT-interval prolongation: considerations for clinicians. Pharmacotherapy 2010;30(7):684–701.
[5] Molnar J, Weiss J, Zhang F, Rosenthal JE. Evaluation of five QT correction formulas using a software-assisted method of continuous QT measurement from 24-hour Holter recordings. Am J Cardiol 1996;78(8):920–6.
[6] Vandenberk B, Vandael E, Robyns T, Vandenberghe J, Garweg C, Foulon V, et al. QT correction across the heart rate spectrum, in atrial fibrillation and ventricular conduction defects. Pacing and clinical electrophysiology: PACE 2018;41(9):1101–8.
[7] Jacquemet V, Cassani Gonzalez R, Sturmer M, Dube B, Sharestan J, Vinet A, et al. QT interval measurement and correction in patients with atrial flutter: a pilot study. J Electrocardiol 2014;47(2):228–35.
[8] Jonsson MK, Vos MA, Duker G, Demolombe S, van Veen TA. Gender disparity in cardiac electrophysiology: implications for cardiac safety pharmacology. Pharmacol Ther 2010;127(1):9–18.
[9] Rabkin SW, Cheng XJ, Thompson DJ. Detailed analysis of the impact of age on the QT interval. J Geriatr Cardiol 2016;13(9):740–8.
[10] Zhao D, Guallar E, Ouyang P, Subramanya V, Vaidya D, Ndumele CE, et al. Endogenous sex hormones and incident cardiovascular disease in post-menopausal women. J Am Coll Cardiol 2018;71(22):2555–66.