An Improved QT Correction Method for use in Atrial Fibrillation and a Comparison with the Assessment of QT in Sinus Rhythm

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Abstract

Background: Conventional QT corrections may be inappropriate in atrial fibrillation (AF) due to RR variability and QT lag. Existing formulashave been modified by the formula RRmod to account for this lag. Wedeveloped a novel correction formula for use in AF (QTAF) based on the slope ΔQT/ΔRRmod and report its performance in AF. We also compare QTAF obtained in AF with rate-independent corrections in NSR.

Materials and Methods: A total of 3063 RR/QT pairs from 28 patients with AF were measured, 22 of whom also had measurements during sinus rhythm. QTc (the Bazett equation), QTLC (the Framingham linear correction), and QTAF were calculated utilizing RRmod, and the rate-independence of each formula in AF tested. Mean QTAF values in AF were compared to QT intervals corrected with QTLC in normal sinus rhythm.

Results: ΔQTc/ΔRRmod and ΔQTLC/ΔRRmod slopes were significantly non-zero whereas ΔQTAF/ΔRRmod was not. QTLC and QTc corrections were imperfect at extremes of RRmod while QTAF was constant. QTAF corrections in AF were shorter than QTc or QTLC corrections in NSR.

Conclusions: QTAF is a novel QT correction with a defined relationship to correction in NSR that performs better than existing strategies.

Introduction

Background

Atrial fibrillation (AF) is a common problem for which antiarhythmic drugs (AADs) are often prescribed. The most dangerous complication of AAD therapy is ventricular proarythmia, including torsades de pointes, the risk of which is largely predicted by a prolonged QT. The ability to accurately measure the QT interval before and during the AAD therapy of AF is therefore critical.

Since QT duration varies with heart rate, formulas that “correct” the QT based on the immediately preceding cycle (CL) are commonly used. While universally accepted in sinus rhythm (SR), this approach has been questioned in AF. Previous stud-
ies have shown that more remotely preceding CLs exert an additional, though smaller effect on the QT, a phenomenon known as QT lag. Under conditions of relative CL stability such as SR, this effect can be ignored. In AF, however, an incident QT may be preceded by CLs of variable durations whose lagging effect on the QT may be manifest, and thus must be accounted for in rate corrections to make them optimally meaningful.

Replacing the term “RR” (the R to R interval in seconds) in existing QT correction formulas with RRmod, a weighted average of the previous 5 RR intervals, has been shown to improve their ability to normalize QT intervals in AF, and has been suggested as a method for addressing QT lag. Recently, Larroude et al. described the relationship between QT and RRmod (ΔQT/ΔRRmod) in AF in patients with paroxysmal AF. ΔQT/ΔRR slopes have been successfully used in SR to construct correction formulas that improve on the inaccuracies in the commonly used Bazett formula. Specifically, the Framingham correction (QTLC) was designed using ΔQT/ΔRRas measured in SR, and has been shown in that rhythm to yield corrected QT values that are more stable than those obtained by Bazett’s formula over a widerange of cycle lengths. We hypothesized that ΔQT/ΔRRmod could be used to construct a linear QT correction formula (QTAF) that would similarly yield a rate-independent correction in AF. We chose to compare it to conventional formulas modified by RRmod; QTLC because of its utility in SR, and QTc given its ubiquity in QT correction (see Table 1 for list of QT correction formulas abbreviations).

Since AADs are often continued after conversion to SR, and previous studies have suggested intrinsic differences in repolarization between AF and SR, we additionally sought to define the relationship between QTAF measured during AF and commonly used correction formulas employed in SR. In this way, we hoped to define a rate-independent AF-specific formula that could be utilized not only to judge AAD risk in AF, but also to approximate AAD risk in SR.

### Population and data collection

Telemetry data was obtained from 28 randomly selected medical and surgical inpatients at New York-Presbyterian Hospital who had AF during their hospitalization. Approximately 60 seconds of telemetry data was retrieved for each patient. For patients with paroxysmal AF data collection started with the last five available sinus beats. Otherwise, the start time for data collection was random. Deidentified data, along with demographic, medication, and echocardiographic information, were provided to the investigators. The IRB of Columbia University approved the protocol. Because deidentified data was used, the requirement for informed consent was waived.

### QT and RR measurements

Telemetry was recorded using a five-lead wearable unit and wireless monitoring system (PatientNet Monitoring System, GE Healthcare, Piscataway, NJ) with a sampling rate of 200 Hz and a 10 mm/mV gain selection. Three-lead strips (I, II, and V1) were printed at a paper speed of 25 mm/sec. RR and QT intervals were manually measured with a resolution of 10 ms in the clearest of the three leads available. Measurements were performed by one of two readers (AS or JG). The RR interval was defined as the time elapsed between the initial deflections of adjacent QRS complexes. The QT interval was defined as the time elapsed from the initial inscription of the QRS to the point where the T-wave of the same beat intersected the isoelectric segment. In the casethat the T-wave did not return to baseline before the onset of the following P-QRS in SR or QRS in AF, the QT interval was taken to be the onset of the QRS to the extrapolated point at which the T wave would have intersected the isoelectric point had the following P-
QRS or QRS not occurred. VPCs during AF were excluded, as were the 4 subsequent RR/QT pairs.

**QRS and RRmod calculations, and analysis of ΔQTx/ΔRRmod in AF**

For each beat in AF, RRmod was calculated as $\text{RRmod} = (5\ast\text{RR}_1 + 2\ast\text{RR}_2 + \text{RR}_3 + \text{RR}_4 + \text{RR}_5)/10$. In order to account for QT lag, the original formulas for QTLC and QTc were modified from the original by substituting the term “RR” for RRmod as follows: $\text{QTc} = \text{QT}/(\text{RRmod})^{1/2}$, $\text{QTLC} = (1-\text{RRmod})^{0.154} + \text{QT}$. Since the value for $\Delta\text{QT}/\Delta\text{RRmod}$ in AF has been reported as 0.126 (8), QTAF was calculated as $\text{QTAF} = (1-\text{RRmod})^{0.126} + \text{QT}$. In order to allow for comparisons between patients, QTx data from each patient (where QTx represents QTc, QTAF, or QTLC) was normalized as deviation from that patient’s mean QTx. Normalized QTx vs. RRmod was then plotted for each formula. $\Delta\text{QTx}/\Delta\text{RRmod}$ for each correction formula was calculated, and deviation from a slope of 0 determined using linear regression. A perfect correction should be rate independent; that is, QTx should not vary with RRmod, and $\Delta\text{QT}/\Delta\text{RRmod}$ should have a slope of 0. The primary hypothesis was that QTAF would yield a rate-independent correction in AF, whereas QTLC and QTc corrections would not.

**QT corrections in Sinus Rhythm and comparison to atrial fibrillation**

Since the equation describing the relationship between QT and RRmod in AF has a nearly equal slope but a lower y-intercept than that in SR (8), our secondary hypothesis was that optimally corrected QT values in AF would be lower than optimally corrected values in SR, while comparisons made between AF and SR using a less ideal formula would fail to show a difference. We used QTAF as an example of an optimal correction in AF, QTLC as an optimal correction in SR, and QTc as a less ideal correction.

For subjects with paroxysmal AF, QTc and QTLC values were calculated for each of the last five sinus beats preceding the initiation of AF using their original formulas, and the minimum QTc and QTLC from each patient was recorded (QTc(min)) and QTLC(min)). Only AF initiations that did not include atrial ectopy during sinus rhythm were included for analysis. Minimum values were used in order to bias the results as much as possible towards the null hypothesis.

The mean SR QTc(min) in the population as a whole was compared to the mean QTc in AF calculated using RRmod. QTLC(min) was compared to the overall mean QTAF measured during AF. Since the slopes of the relationships describing QT and ΔRRmod in SR and AF are roughly equal even though their y-intercepts are not, QTAF was applied to the last five sinus beats, and the average QTAF calculated during SR was compared to the overall mean QTAF in AF.

**Subgroup Analysis**

Since some of the subjects were on drugs known to alter the QT interval at the time of data collection (digoxin, sotalol, amiodarone) and/or had baseline EKG abnormalities, we undertook a separate analysis of the subset of subjects with normal ejection fractions, normal baseline QRS morphologies, and who were not on the above drugs. Quality assurance was provided by a single nurse at a central coordinating centre. The first 30 patients chosen were reviewed by the coordinating centre nurse to ensure accurate patient selection. Data on selected patients was then entered into an electronic database. Although interrater reliability was not formally assessed, before a specific ED was included in the trial, data from the first 25 patients entered into the database from that centre was reviewed by the coordinating centre nurse to ensure consistency and accuracy of data abstraction throughout the various centres included in the study. The coordinating centre nurse was also regularly in contact with the individual research nurses through phone calls and emails to
clear up any ambiguities in patient data. Unclear elements were resolved by the coordinating centre nurse in conjunction with the principal investigator, and missing elements were clearly identified as such. Finally, some pertinent information was included from those patients who had a primary diagnosis of recent onset atrial fibrillation or flutter but met exclusion criteria.

Data Analysis

Patients were first stratified into whether or not they received warfarin upon discharge from the ED. CHADS² score was calculated for each patient. We then analyzed the compiled data with descriptive statistics with 95% confidence intervals. Univariate analyses were conducted using T-test or Chi-square to select factors, including CHADS² score, associated with anticoagulation initiation. Multiple logistic regression was employed to evaluate independent predictors of anticoagulation after adjustment for confounders. Only variables with p-values less than 0.05 were included in multivariate regression analysis. Data analyses were conducted with SAS statistical software. (version 9.2; SAS Institute, Inc.).

Results

The initial RAFF study identified a total of 2,464 RAFF patients at the 8 involved ED centers over the 12 month period. Of these, 1,068 met the initial inclusion criteria. After exclusion of patients already receiving warfarin prior to presentation to the ED, a cohort of 633 patients remained. Table 1 describes the characteristics of this cohort. There were no significant differences between patients that received warfarin and those that did not.

Univariate analysis results are listed in Table 2. Factors with the highest odds ratios were heparin administration in the ED (OR 10.14, 95% CI 5.77 – 17.83), cardiology follow-up organized in the ED (OR 5.66, 95% CI 2.91 – 11.00), having a new prescription of Metoprolol at discharge (OR 4.02, 95% CI 2.22 – 7.23), and having a new prescription of Diltiazem at discharge (OR 3.01, 95% CI 1.15 – 7.91). Notably, having a CHADS² score of 2 or higher, while doubling the odds of receiving warfarin at discharge (OR 2.01), was not significantly different from having a CHADS² score of 1 or higher (OR 2.07). Major factors associated with lack of warfarin administration included electrical (OR 0.37, 95% CI 0.21 – 0.65) and medical (OR 0.26, 95% CI 0.16 – 0.44) cardioversion, and having a history of AF (OR 0.50, 95% CI 0.30 – 0.83). Multivariate analysis demonstrated significant predictors of warfarin administration at discharge to again include heparin administration (OR 9.59, 95% CI 4.88 – 18.87), Metoprolol prescription (OR 9.59, 95% CI 4.88 – 18.87), cardiology follow-up (OR 5.61, 95% CI 2.62 – 12.02), and age by 10 year increments (OR 1.69, 95% CI 1.34 – 2.14). Odds ratios and confidence intervals are shown in Table 3. Interestingly, it was found that while patients with a CHADS² score of 1 or greater had double the likelihood of warfarin administration, it no longer became an independent predictor after regression analysis.

Validation

A total of 58 RR/QT pairs were overread by a second reader (JAR), and reread by the primary readers. Inter- and intraobserver variability was calculated using coefficients of variation (r²). Overall, interobserver variability was r²=0.998 for RR intervals and 0.856 for QT intervals, and intraobserver variability was r²=0.995 for RR intervals and 0.863 for QT intervals.

Statistical analysis

Comparisons of all continuous variables were performed using paired Student’s t-tests. Determinations of slopes and comparisons to a slope of 0 were performed using linear regression. Statistical significance was defined as p<.05. All tests were performed using a statistical software package (Prism 4.0c, GraphPad Software, San Diego, CA). Data is presented as mean ± SD. Since calculations involving QT and RR intervals were rounded to the nearest millisecond, rounding error may occur.

Results

Patient Characteristics and Data Collection

Patient characteristics are presented in Table 2. The population was 57% male. Twenty-two patients (79%) were surgical, and 6 (11%) were medici-
cal. The mean age was 72.4 ± 11.5. Five patients (18%) had an abnormal EF(< 50%), and 7 patients (25%) had conduction abnormalities on their surface EKG. Nine (22%) were on Class III antiarrhythmic drugs at the time of conversion to AF, and 5 (18%) were on digoxin.

A total of 3063 QT/RR pairs were counted in AF, a mean of 109 ± 25 pairs/patient (range 63-153). Due to the way RRmod iscalculated, the QT intervals associated with the first four RR intervals from each patient, or 112 total (3.6%), were excluded from QT/RRmod analysis. Thirty-eight intervals (1.2%) were excluded because of poor data quality. Exclusion of PVCs and the subsequent RR pairs removed an additional 116 beats (3.8%). There was no atrial ectopy noted. 2797 QT/RRmod pairs were therefore included in the final analysis. One hundred ten QT/RR pairs were counted in SR, all of which were included in analysis. In AF, the mean RR cycle length was 543ms±155 (range 270-1490), the mean RRmod cycle length was 538ms±124 (range 305-1211) and the mean QT was 348ms±48 (range 250-620). In SR, the mean RR interval was 757ms±115 (range 520-1010) and the mean QT was 408ms±51 (p<.0001 for comparison of both mean RR and QT intervals between AF and SR).

**QT Relationships and Correction slopes**

Slopes and p-values are presented in Table 3. The slopes obtained for ΔQT/ΔRR and ΔQTc/ΔRRmod agree closely with previously reported values.12, 20 The average of the individual ΔQTc/ΔRRmod and ΔQTLC/ΔRRmod slopes were both significantly non-zero, whereas the average ΔQTAF/ΔRRmod was not.

Normalized QTx vs. RRmod for the population as a whole is shown in Fig. 1. The overall ΔQTc/ΔRRmod slope was -0.081 ± 0.005 and the ΔQTLC/ΔRRmod slope was -0.014 ± 0.003. Both were significantly non-zero. The ΔQTAF/ΔRRmod slope was -0.003 ± 0.003, which did not significantly deviate from 0.

**Correction performance at the extremes of RRmod**

The three formulas were tested for performance at the extremes of RRmod (Fig. 2). QTc produced corrections on average 15ms ± 32 greater than the mean QTc in the first quartile of RRmod and 11ms ± 28 less than the mean QTc in the last quartile. Compared to QTAF, QTc corrections were on average 14ms ± 1 greater in the first quartile of RRmod and 11ms ± 1 shorter in the last quartile. QTLC generated corrections that were 3ms ± 19 greater than the mean QTLC in the first quartile of RRmod and 2ms ± 19 shorter in the last. Compared to QTAF, QTLC corrections were on average 1ms ± 0.1 greater in the first quartile of RRmod and 2ms ± 0.2 shorter in the last. QTAF corrections in the first quartile of RRmod were 1ms ± 18 greater than overall mean normalized QTAF. In the last quartile, they were 0.1ms ± 18 greater than the mean normalized QTAF. Neither difference was significantly nonzero.

**Subgroup analysis**

There were 11 patients with normal cardiac function, EKG, and not on AADs. The mean ΔQT/ΔRR slope was .086 ± .034 and the mean ΔQTc/ΔRRmod slope was .111 ± .060, similar to those in the group as a whole. The mean ΔQTLC/ΔRRmod slope was significantly non-zero (p<.0001), as was the average ΔQTAF/ΔRRmod slope (p<.005), whereas the average ΔQTAF/ΔRRmod was not (p>.05).

**Comparison to Sinus Rhythm**

Data for NSR was collected in 22 patients. The mean QTc(min) in SR was significantly less than the mean QTc in AF. Both QTLC(min) and QTAF in SR were greater than mean QTAF in AF (Fig. 3). QTAF in SR was on average 22ms ± 11 greater than QTAF in AF, while QTLC(min) in SR was on average 20ms ± 10 greater.

**Discussion**

We report the performance of a novel QT correction formula for use in AF, constructed by utilizing the linear relationship between the QT interval and RRmod, the RR interval adjusted to account for QT lag.8 QTAF yielded a more ideal correction overall and at the extremes of heart rate than either QTcor QTLC, despite modifying these formulas by RRmod. By studying a subset with paroxysmal AF at the onset of arrhythmia, we were further able to investigate the relationship between opti-
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mally corrected QTintervals in AF and those in SR.

**Linear QT corrections methods**

Linear approaches to QT correction are based on the assumption that a first order relationship exists between QT and RR with quantifiable slope ($\Delta QT/\Delta RR$). If, by convention, a patient’s “true” QT is taken to be equal to the QT measured at a “standard” heart rate of 60, an optimal correction would transform a raw QT measured at any CL into the “true” QT. If $\Delta QT/\Delta RR$ is known, this is achieved by calculating the difference between RR=1 sec and the measured RR (1-RR), multiplying that difference by $\Delta QT/\Delta RR$, and adding that product to the measured QT. In a perfect correction, there is no relationship between the corrected QT and RR, and the corrected QT vs. RR plot yields a line with a slope of 0 that intersects uncorrected QT vs. RR at RR=1 sec (Fig. 4). QTLC is an example of a linear equation, and has been shown to achieve a QT correction that is substantially more rate-independent.
Most studies, including a large series with over 10000 patients, have validated a linear relationship between QT and RR for SR, both on a population basis\(^{13,18}\) as well as individually\(^{19,20}\) and linear correction formulas perform at least equally well as non-linear models in SR.\(^{13}\) Although a linear relationship between QT and RR appears to be present in AF as well, \(\Delta QT/\Delta RR\) in SR is not equivalent to \(\Delta QT/\Delta RR\) in AF\(^{8,21}\) and does not account for QT lag. Corrections based on \(\Delta QT/\Delta RR\) relationships measured in SR will therefore be inaccurate in AF.

**QT lag and RR\(^{mod}\)**

RR\(^{mod}\) was proposed as a method of accounting for QT lag by Elhert, who showed that in AF, RRmod increased the goodness-of-fit of three different QT-RR relationship models by analysis of mean square residuals and Akaike information criteria.\(^{7}\) Larroude subsequently showed that it allows for the measurement of QT dynamics in AF, and renders previously divergent \(\Delta QT/\Delta RR\) relationships in AF and SR nearly parallel. In that study, \(\Delta QT/\Delta RR\) mod in AF was reported to be 0.126 (8). The use of the formula QTAF = (1-RRmod)*0.126+QT was based on this data and the above rationale. RRmod considers only the five most proximal RR cycles. Thus, contributions of more distant RR intervals to an incident QT will be ignored. The findings of pacing studies which have shown that an abrupt and sustained change in cycle length causes an initial rapid adaptation in QT followed by a new steady state that requires several minutes to achieve, while a brief interruption of the basic cycle length with a single premature stimulus causes a perturbation in steady state that requires up to 10 beats to regain\(^{4,22}\) suggest that while the majority of the QT adaptation is dominated by more proximal RR intervals, there is a substantial late component that would not be accounted for using RRmod. It is notable, however, that these studies were done under conditions in which a new steady state was allowed to develop. It is unclear what applicability these studies have in AF, where sufficient variability may exist to preclude the development of a longer-term steady state. Thus, although RRmod includes only the most proximal five RR intervals in correcting for QT lag, it likely subsumes the most influential cycles, and presents a reasonable balance between corrective accuracy and ease of calculation.

**QTA\(^{F}\)**

We confirmed that the relationship between QT and RR is adequately described by a first order equation, the slope of which (0.076) agrees well with the previously reported measurements of “7%” by Pai, et.al.\(^{21}\) and 0.068 by Larroude.\(^{8}\) We found that in distinction to the other correction tested, QTA\(^{F}\) values had no correlation to RRmod, an essential property of an ideal correction. This remained true at the extremes of RRmod.

The data on which QTA\(^{F}\) was based was derived in a cohort of medical subjects, including some with CHF, AAD use, and baseline conduction abnormalities. We studied a similar group of largely surgical subjects. Recognizing that it would be useful to determine the efficacy of QTA\(^{F}\) in a population of otherwise normal subjects, we tested our primary hypothesis in our subset of subjects with normal EFs, no AAD use, and with normal baseline EKGs and found them to be no different than the larger group. Since our institution has previously reported on alteration in repolarization duration due to IVCD,\(^{23}\) we also tested our primary hypothesis with these patients excluded.

### Table 3

Mean values of individually determined slopes. P-values indicate significance of difference from a slope of 0.

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Mean Slope</th>
<th>Range</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\Delta QT/\Delta RR)</td>
<td>0.076 ± 0.030</td>
<td>0.016 ~ 0.144</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(\Delta QTc/\Delta RR) mod</td>
<td>0.114 ± 0.045</td>
<td>0.025 ~ 0.256</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(\Delta QTc/\Delta RR) mod</td>
<td>-0.239 ± 0.126</td>
<td>-0.390 ~ 0.162</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(\Delta QTcL/\Delta RR) mod</td>
<td>-0.045 ± 0.069</td>
<td>-0.314 ~ 0.102</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>(\Delta QTAF/\Delta RR) mod</td>
<td>-0.011 ± 0.043</td>
<td>-0.101 ~ 0.130</td>
<td>NS</td>
</tr>
</tbody>
</table>
and found the same results. Although this study was not powered specifically to detect differences between subgroups and further studies are needed to determine optimal QT correction strategies in individual populations, these data suggest that QTAF may be applicable for a broad population of patients with AF.

Comparison to SR

Studies that have directly compared QT intervals in SR and AF using the Bazett correction have found the QT in SR to be either shorter or no different than that in AF. However, other observations are consistent with the interpretation that the QT may be shorter in AF compared to SR. For example, in the study of Larroude et al., although ΔQT/ΔRRmod in SR was nearly parallel to that for AF, the AF relationship had both a lower intercept and a lower QT at the “standard” heart rate of 60. The observations that a gain-of-function mutation in KCNQ1, which would be expected to shorten repolarization, can cause AF, and that excessive QT prolongation and torsades de pointes can both be seen during infusion of IKr blockers for the

\[
QT_{\text{ideal}} = (1-RR) \times \frac{\Delta QT}{\Delta RR} + QT_{\text{raw}}
\]
pharmacologic cardioversion of AF, but generally only after conversion to SR, are similarly intriguing in this regard. QT hysteresis, the observation that the time constant for QT rate adaptation during periods of heart rate acceleration is shorter than that for deceleration, has been suggested as one potential mechanism for this difference. Such a disparity in adaptation might favor an overall shortening of the QT in an irregular rhythm such as AF.

Our data showed that while QTc was shorter in SR than in AF, optimally corrected QT intervals in AF (using QTAF) were shorter than those in SR (using QTLC). One explanation for this discrepancy may be the Bazett equation’s overcorrection of the QT at the faster heart rates often seen in AF. Since ΔQT/ΔRRmod in AF has been reported to be approximately equal to that of SR, QTAF was applied to the last five sinus beats before the initiation of AF and compared to QTAF in AF, and the same results were obtained (Fig. 3). Given that we collected limited data in SR, and heart rates were significantly higher in AF than in SR, we were unable to directly compare QT intervals in SR and AF at similar values of RRmod.

**Clinical Implications**

These data imply that the use of QTc and, to a lesser degree, QTlc fail to achieve rate-independent corrections in AF, even after correction for QT lag. Clinicians using QTc in AF should account for an overcorrection of nearly 15 ms compared with QTlc. Fin the fastest quartile of RRmod, rates likely to be encountered in AF. Similarly, QT values should be considered underestimations of the duration of repolarization to be expected after conversion to SR. These observations will aid risk stratification of AAD therapy both during AF and after SR is obtained.

**Limitations**

The use of population-derived indices to construct common QT correction has the inherent limitation of discounting individual variability in ΔQT/ΔRR, producing skewed corrections in those individuals who differ substantially from the mean. Several studies have found substantial variability in ΔQT/ΔRR, and some investigators have argued for an emphasis on individualized approaches to QT correction in key circumstances. Individualizing QT corrections, however, may not be practical in most circumstances. For example, in our data set, the ΔQT/ΔRR slope of the first 10 data interval pairs differed from the ultimately derived slope by an average of 55%, suggesting that relying on the limited number of QT/RR measurements that, without automation, would be realistically made in daily clinical use, could yield substantially inaccurate corrections. Additionally, despite the individual variability seen, there is a very high degree of correlation in the population-averaged slopes measured in this and previous studies, suggesting that at least in AF, while individual variability may exist, the relationship is reasonably constant across populations. Future work should concentrate on identifying the factors that drive this variability and assessing their clinical impact in terms of the ability of a correction formula to predict hard endpoints, such as propensity for polymorphic ventricular arrhythmia. Similarly, although QTAF performed as well in patients with cardiac comorbidities as well as those without, further work should be done to prove its efficacy in populations that might be expected to have variability in repolarization dynamics.

In the comparison of SR with AF, we studied patients at the time of conversion from in order to minimize the confounding effects of differential autonomic tone between the two rhythms. It is possible, however, that the autonomic milieu present at the point of conversion from SR to AF may not be generalizable. It is also possible that the degree of RR variability seen in a population of patients with newly incident AF may not be the same as that seen in a more chronic population. Similarly, while our population was diverse in terms of EF, diagnosis, use of antiarrhythmic drugs, and age, all the patients in this subset had cardiac surgery. Whether these findings are generalizable to a larger population remains to be seen.

**Conclusions**

QTAF is a novel QT correction formula designed for use in AF, which exhibits correcting characteristics superior to the current strategy. Average QTAF values are shorter than QTlc values.
measured in SR, suggesting that the optimally corrected QT in AF is shorter than that in SR.

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**References**