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Comparative Evaluation of Corrected QT Interval Correction Formulas Across Controlled Heart Rate Conditions for Electrocardiogram-based Diabetes Risk Stratification

OhSuk Yang[1*] and JongHwi Song[2]

[1]Department of Business Administration, Kangwon National University,
Gangwondaehakgil 1, Chuncheon, Gangwon State, Republic of Korea
[2]Institute of AI Convergence Science, Yonsei University,
Yonseidae-gil, Wonju, Gangwon State, Republic of Korea

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In this study, we evaluated the heart-rate-independent performance of major corrected QT (QTc) interval correction formulas—Bazett, Fridericia, and Sagie—using electrocardiogram (ECG) waveforms collected at controlled heart rates (HRs) of 40, 60, 80, and 120 bpm. After converting raw hexadecimal ECG data into standardized signals, QT and RR intervals were extracted and QTc was computed separately for each formula. Empirical analysis showed that Fridericia formula provides the most stable, HR-independent QTc values, whereas Bazett formula displays pronounced HR-dependent distortion. These findings indicate that Fridericia is the most reliable correction method for ECG-based diabetes risk prediction, offering improved sensitivity and specificity for machine learning models.

1. Introduction

The corrected QT (QTc) interval is a fundamental electrocardiographic parameter representing the duration of ventricular depolarization and repolarization. Prolonged QTc has been associated with an increased risk of ventricular arrhythmias, sudden cardiac death, and systemic metabolic dysregulation, including diabetes mellitus.[1–3] Chronic hyperglycemia and insulin resistance alter myocardial ion channel dynamics and autonomic balance, contributing to delayed repolarization and QTc prolongation.[4,5] Therefore, accurate heart rate (HR) correction of the QT interval is essential for both clinical risk assessment and data-driven disease prediction models.

Because the QT interval varies inversely with HR, researchers have proposed several mathematical correction formulas. The Bazett formula (1920), Fridericia formula (1920), and Sagie (Framingham) formula (1992) are among the most widely used.[6–8] However, each produces different QTc values depending on HR, potentially distorting diagnostic thresholds.

*Corresponding author: osyang30@kangwon.ac.kr
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Bazett's correction tends to overestimate QTc at low HR and underestimate it at high HR, whereas the Fridericia and Sagie (Framingham) formulas provide more stable results across a broad HR range.[9–11] Despite these insights, few comparative studies on these formulas using electrocardiograms (ECGs) collected in metabolic or diabetes-specific populations have been carried out.

Although QT correction has been validated in cardiology and oncology cohorts,[12,13] limited evidence exists regarding which formula provides the most reliable HR-independent QTc values for metabolic disease risk stratification. Given the emerging evidence linking QTc prolongation to the future onset of type 2 diabetes,[14,15] empirical comparison of these correction formulas under controlled HR conditions (40–120 bpm) can clarify which formula offers the optimal sensitivity and specificity for machine-learning-based diabetes prediction.

Accordingly, in this study, we aim to (1) compare Bazett, Fridericia, and Sagie correction formulas using ECG waveforms recorded at HRs of 40, 60, 80, and 120 bpm; (2) evaluate HR-dependent bias patterns among the formulas; and (3) identify the correction method best suited for integration into ECG-based diabetes risk prediction frameworks. By establishing a reproducible benchmark for QT interval correction, we contribute to the development of interpretable and clinically robust digital biomarkers for metabolic disease prevention.

In accordance with the above objectives, the structure of this paper is as follows. Following the problem statement in Sect. 1, in Sect 2, we briefly introduce the machine learning algorithms used for diabetes prognosis detection and describe the calculation methods of QTc using the Bazett, Fridericia, and Sagie correction formulas, along with a review of prior studies concerning these three approaches. In Sect. 3, we summarize the analytical results of comparing QTc prolongation ratios across HR conditions (40, 60, 80, and 120 bpm) using the collected ECG data. In Sect. 4, we present the theoretical and practical implications derived from the findings and discuss their relevance to diabetes risk prediction. Finally, in Sect. 5, we provide the conclusions, emphasizing the clinical importance of selecting an appropriate QTc correction formula for ECG-based predictive modeling, and suggest future research directions not covered in this study.

2. Theoretical Background

2.1 ECG-based diabetes detection algorithm

A variety of noninvasive optical techniques have been explored for diabetes detection and early metabolic risk assessment. NIR spectroscopy is used to estimate glucose concentration by analyzing absorption spectra in the 700–2500 nm range,[16] while Raman spectroscopy enables the identification of glucose-specific vibrational signatures from skin or bodily fluids with high chemical specificity.[17] Optical coherence tomography has been used to visualize microvascular and retinal structural alterations associated with early diabetic complications,[18] and photoplethysmography combined with machine learning shows promise in evaluating vascular dysfunction and autonomic imbalance associated with prediabetes and diabetes.[19]

Although these optical approaches provide valuable physiological insights, several factors—such as skin pigmentation, hydration, tissue composition, and sensor contact—can reduce their accuracy. Additionally, many optical systems require high-cost instrumentation or meticulous calibration processes, which can limit their suitability for large-scale screening applications. In contrast, ECG-based diabetes detection directly captures subtle myocardial electrical remodeling—including QT interval prolongation, RR variability changes, and repolarization abnormalities—that often precede overt metabolic dysfunction. Unlike optical signals that depend heavily on optical–tissue interactions, ECG signals reflect electrophysiological pathways influenced by chronic hyperglycemia, autonomic dysregulation, and insulin resistance.[20] Therefore, QT-centered ECG modeling offers a robust, inexpensive, and scalable biomarker for early diabetes risk stratification.

Electrophysiological markers derived from the ECG offer a unique advantage in detecting abnormalities that emerge even before metabolic dysfunction becomes clinically apparent. Among these markers, the QT interval—the time required for ventricular depolarization and repolarization—has received growing attention as an indicator of impaired autonomic regulation and early metabolic disturbance associated with diabetes.[21,22]

However, the QT interval is inherently dependent on HR: it shortens during tachycardia and lengthens during bradycardia. As a result, direct comparison of raw QT interval values across individuals or time points can be misleading, because HR differences may obscure or distort the underlying electrophysiological changes of metabolic origin.[22,23]

For these reasons, diabetes prediction studies rely not on the QT interval itself but on the QTc. The QT interval adjusted relative to the RR interval to remove HR-related noise and has been shown to have stronger associations with chronic hyperglycemia, insulin resistance, and autonomic neuropathy than the uncorrected QT interval.[23–26] By eliminating HR-driven variability, QTc more clearly reflects intrinsic abnormalities in myocardial repolarization and therefore serves as a more reliable biomarker for early-stage diabetes risk and machine-learning-based prediction models.[24,26]

Accordingly, in the present study, we incorporate the QT interval as a foundational physiological marker but place primary emphasis on QTc as the central biomarker for diabetes prognosis detection.

2.2 QTc formula

Given the clinical advantages of QTc over the raw QT interval, an important methodological question concerns how QTc should be computed. Several correction formulas have been proposed to eliminate HR dependence, with the Bazett, Fridericia, and Sagie (Framingham) formulas being the most widely used in both clinical and research settings.[27–29] Although all three formulas are aimed at normalizing the QT interval relative to the RR interval, their mathematical structures differ, producing systematically different QTc values across the HR spectrum.

The Bazett formula, introduced in 1920, remains the most commonly applied owing to its simplicity, but the Bazett formula exaggerates QTc at high HRs and underestimates it at low

HRs.[30,31] The Fridericia formula applies a cubic-root transformation that improves stability across varying HR conditions and has demonstrated stronger associations with cardiovascular and metabolic risk in observational cohorts.[32] The Sagie (Framingham) formula, derived from a large longitudinal population study, uses a linear correction model and often produces conservative QTc values within physiologic HR ranges.[29]

Because these correction formulas yield divergent QTc estimates from the same ECG waveform—particularly under bradycardic or tachycardic conditions—they function as competing correction strategies rather than interchangeable tools. For research areas such as diabetes risk prediction, where subtle repolarization abnormalities may carry prognostic significance, the choice of correction formula is critical. Accordingly, in this study, we directly compare Bazett, Fridericia, and Sagie QTc values calculated under controlled HR conditions (40, 60, 80, and 120 bpm) to determine which approach most reliably captures diabetes-related electrophysiological alterations.

2.3 Review of previous studies

There are several prior studies on systematically comparing QTc correction formulas in cardiology and general populations. Early work established the Bazett formula as a practical standard, largely owing to its simple square-root structure.[27] However, subsequent analyses demonstrated that Bazett's correction introduces substantial HR-dependent bias, overestimating QTc at high HRs and underestimating it at low HRs.[30,31] In response, alternative formulas such as those of Fridericia and Sagie (Framingham) were proposed to reduce this bias by adopting cubic-root and linear adjustment models, respectively.[28,29]

Comparative evaluations in nondiabetic cohorts have consistently revealed that Fridericia and Sagie yield more stable QTc values across physiological HR ranges and provide better calibration for risk stratification than the Bazett formula.[32–35]

From a clinical perspective, differences among formulas are not merely mathematical. Studies in oncology and internal medicine have shown that the choice of QTc formula can directly influence therapeutic decision-making, including drug dosing, treatment discontinuation, and classification of QTc prolongation events.[36–38] For example, applying the Bazett formula often results in more patients being classified as having prolonged QTc compared with Fridericia- or Sagie-based calculations.[37]

Regarding diabetes and prediabetes, growing evidence suggests that QTc—not the raw QT interval—is associated with autonomic neuropathy, increased cardiovascular mortality, and future diabetes onset.[4,12,13,22–26] Population-based ECG follow-up studies indicate that QTc prolongation precedes incident diabetes and reflects early myocardial electrical remodeling associated with chronic hyperglycemia and insulin resistance.[12,13,20]

Despite these findings, few studies have explicitly examined how the choice of QTc correction formula affects diabetes risk prediction itself. In most existing work, either (i) a single formula—often Bazett—was adoped without comparison,[4,22–24] or (ii) correction formulas were evaluated mainly in the context of arrhythmic or oncologic outcomes.[33–37] Also, HR was rarely experimentally controlled in prior studies, making it difficult to disentangle intrinsic repolarization abnormalities from HR-induced variation.

Against this backdrop, in this study, we treat Bazett, Fridericia, and Sagie formulas not as interchangeable tools but as competing correction strategies. By using ECG datasets collected at controlled HRs (40, 60, 80, and 120 bpm) and focusing on diabetes-related risk stratification, we expand on the existing literature by (1) quantifying the HR dependence of each formula under standardized conditions, (2) assessing how these differences translate into QTc prolongation rates, and (3) identifying which formula provides the most stable QTc values for machine-learning-based diabetes prognosis models.

3. Materials and Methods

3.1 QTc calculation methods

The QTc interval is calculated by adjusting the measured QT interval in accordance with the RR interval to remove the strong dependence of QT duration on HR. Multiple correction formulas have been proposed, among which the Bazett, Fridericia, and Sagie (Framingham) formulas remain the most widely used in clinical and research settings.[27–29] Although they share the same purpose, their mathematical structures differ, resulting in systematic differences in QTc estimation across HR conditions.

(1) Bazett Formula

The Bazett correction, introduced in 1920, applies a square-root transformation:

$$QTc_{Bazett} = \frac{QT}{\sqrt{RR}}, \tag{1}$$

where QT and RR are expressed in seconds. Bazett's simplicity explains its widespread use; however, the formula is known to overcorrect QTc at high HR and undercorrect at low HR, resulting in HR-dependent distortion.[30,31]

(2) Fridericia Formula

The Fridericia formula uses a cubic-root adjustment:

$$QTc_{Fridericia} = \frac{QT}{RR^{1/3}}. \tag{2}$$

This transformation reduces the nonlinear curvature seen in Bazett's correction and provides more stable QTc values across physiological HR ranges. Several cohort studies suggest that the Fridericia formula offers superior predictive accuracy for cardiovascular and metabolic risk.[32]

(3) Sagie (Framingham) Formula

The Sagie or Framingham correction applies a linear regression model derived from a large longitudinal population dataset:

$$QTc_{Sagie} = QT + 0.154\left(1 - RR\right). \tag{3}$$

This linear approach generally produces more conservative QTc values and avoids extreme correction behaviors at unusually low or high HRs.[29]

3.2 QTc calculation procedure

In this study, QTc values were derived from ECG signals collected under controlled HR conditions of 40, 60, 80, and 120 bpm. The raw hexadecimal ECG data were first converted into standard electrocardiographic waveforms, after which preprocessing—including noise filtering and baseline-drift correction—was applied. QT intervals were computed by identifying the onset of the Q wave and the end of the T wave, while RR intervals were obtained from the duration between successive R peaks. All QT and RR values were converted into seconds to ensure consistency across formulas.

Once QT and RR intervals were extracted, the three correction formulas—Bazett, Fridericia, and Sagie—were independently applied to calculate QTc. Because these formulas differ mathematically, they produce distinct QTc values even from the same ECG waveform. To evaluate the HR dependence and stability of each correction approach, we computed the mean, variance, and proportion of QTc values exceeding the 440 ms threshold across all HR conditions.

Prior to their use in machine learning prediction models, all QTc values were standardized to have a mean of zero and a standard deviation of one. The Fridericia-corrected QTc, known for its relative stability across HR, was used as the primary feature in the prediction analyses, whereas Bazett- and Sagie-corrected QTc values were included as part of sensitivity analyses. Through this structured procedure, we systematically compared the behavior of the three correction formulas and identified the most reliable QTc computation strategy for diabetes risk prediction.

3.3 Data description

To evaluate QTc correction performance for diabetes risk prediction, we utilized simulated ECG waveforms collected under four controlled HR conditions: 40, 60, 80, and 120 bpm. For each HR level, ten ECG recordings were acquired using the same ECG simulator and standardized measurement environment. All recordings were provided in a proprietary hexadecimal (16 bit) format, which was decoded into millivolt (mV) waveforms using a custom Python extraction algorithm.

Each ECG file consisted of a single-lead (Lead II) waveform with a duration of approximately 10–20 s and a sampling frequency of 500 Hz. After waveform reconstruction, R-peak detection was performed to obtain RR intervals, and QT intervals were extracted on a beat-by-beat basis using Q-onset and T-wave termination landmarks. The beat-wise QT and RR values were then converted into QTc using the three correction formulas: Bazett, Fridericia, and Sagie (Framingham).

The number of analyzable beats obtained from each HR group was as follows: 40 bpm at 255 beats; 60 bpm at 269 beats; 80 bpm at 257 beats; 120 bpm at 237 beats. Minor differences in beat counts resulted from the removal of noisy beats, ambiguous T-wave boundaries, or RR detection errors during preprocessing. Although the dataset does not reflect metabolic abnormalities or hyperglycemia directly—because the ECGs were collected under controlled simulator-based

conditions—it provides an ideal testbed for isolating and evaluating HR-dependent bias among QTc formulas, independent of confounding physiological variability.

3.4 Data quality assessment

Prior to conducting QT/QTc computation and comparative analysis, a comprehensive data quality assessment was performed to ensure the integrity and analytical suitability of the collected ECG dataset. First, raw ECG signal integrity was examined. Signal continuity, sampling frequency consistency (500 Hz), baseline wander, saturation or clipping, and the presence of electromagnetic interference (EMI) or powerline noise (50/60 Hz) were assessed. These checks follow established recommendations for high-quality ECG signal processing.[33,34]

Second, beat detection accuracy was validated. R-peak detection was performed using a Pan–Tompkins-based algorithm,[35] and each detected beat was reviewed for missed detections, false positives, and physiological plausibility of RR intervals.

Third, QT and T-wave boundary detection quality was evaluated. Because QT measurement critically depends on the accurate identification of T-wave termination,[36] beats exhibiting low-amplitude, inverted, or morphologically distorted T-waves were excluded. Beats with ambiguous waveform boundaries were also removed to ensure reliable QT estimation.

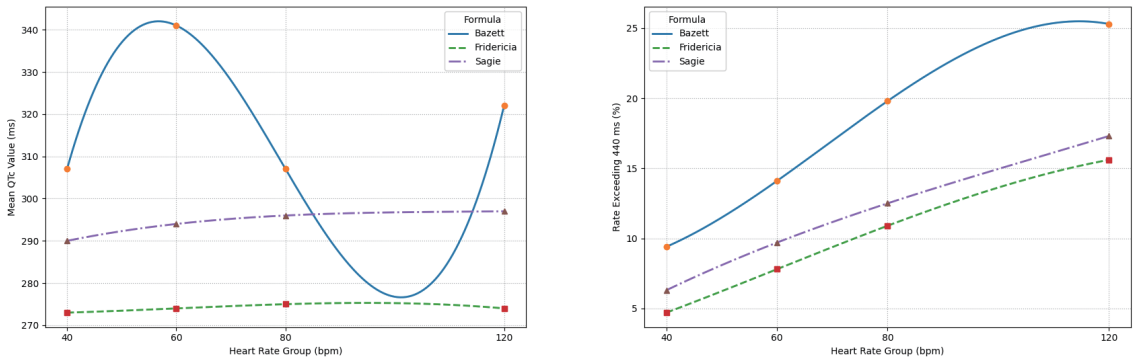
Fourth, a statistical consistency check was conducted. Covariance and correlation patterns between QT and RR intervals were examined to confirm consistency with known physiological behavior (i.e., QT shortens as RR decreases).[37] Distributions of QT, RR, and QTc values were reviewed to detect outliers, and beats with physiologically implausible QT (<200 or >600 ms) or excessive RR deviation (>±3 SD) were excluded.

Fifth, beat count validation confirmed that each HR group provided an adequate number of analyzable beats: 40 bpm, 255 beats; 60 bpm, 269 beats; 80 bpm, 257 beats; 120 bpm, 237 beats. This ensured a balanced dataset for HR-stratified comparison.

Sixth, formula-specific consistency checks were performed. As expected, the Bazett formula reproduced the characteristic HR-dependent slope documented in prior research,[27] whereas the Fridericia and Sagie formulas demonstrated minimal HR dependence and maintained stable QTc patterns across all HR conditions.[28,29] These observations confirm that the collected ECG dataset is well suited to evaluating HR-dependent bias among QTc correction methods.

4. Results

Figures 1(a) and 1(b) use spline interpolation to produce smooth curves that pass through the four original HR data points (40, 60, 80, and 120 bpm). Distinct markers (circles, squares, and triangles) indicate the exact locations of the measured data points. In Fig. 1(a), the mean QTc values computed using the Fridericia formula (green dashed line) remain nearly constant—approximately 274–275 ms—across the entire HR range from 40 to 120 bpm. This flat profile indicates excellent HR-independent correction performance.[28,38] In contrast, the Bazett formula (blue solid line) exhibits a characteristic U-shaped pattern: QTc is lowest around 80 bpm but increases substantially at both 40 and 120 bpm. This reflects the well-known tendency of the Bazett formula to overcorrect QTc at both low and high HRs, thereby introducing significant



(a) (b)

Fig. 1. (Color online) QTc value (ms) by formula and HR group: (a) mean QTc value (ms) by formula and HR group; (b) rate of $QTc > 440$ ms by formula and HR group.

HR-dependent bias.[27,30,31] The Sagie formula (purple dash-dot line) shows a moderate upward trend, with QTc increasing gradually as HR increases, but its variability is still far lower than that of the Bazett correction.[29,38]

Table 1 and Fig. 1(b) summarize the proportion of beats exceeding the conventional QTc threshold of 440 ms. Across all HR groups (40–120 bpm), the QTc prolongation rate increased in the order Fridericia < Sagie < Bazett.[31,33,34] As shown in Fig. 1(b), the Bazett formula yielded the highest QTc > 440 ms rates across all HR ranges, peaking at approximately 25% at 120 bpm. In contrast, the Fridericia and Sagie formulas produced substantially lower prolongation rates and exhibited a gradual increasing trend with rising HR, with notably smaller increases compared with the Bazett formula.[28,29,38]

Specifically, at 40 bpm, the QTc prolongation rates were 4.7% for Fridericia, 6.3% for Sagie, and 9.4% for Bazett calculations; and at 120 bpm, the rates increased to 15.6%, 17.3%, and 25.3%, respectively. This pattern shows that the Bazett formula exhibits the steepest HR-dependent increase, whereas the Fridericia formula remains the most stable.

Spline-smoothed trends further highlight that the Bazett case exhibits the steepest HR slope—overestimating QTc at low HR and underestimating it at high HR—thus confirming its structural HR-dependent distortion.[27,30,31] In contrast, Fridericia and Sagie cases maintained relatively flat profiles across HR levels, minimizing HR-related bias. These findings are fully consistent with previous comparative studies.[33–35,38]

Taken together, these results suggest that the Fridericia formula—and, to a similar extent, the Sagie formula—is more suitable than the Bazett formula for ECG-based diabetes risk stratification, particularly when ECG data are collected under variable HR conditions.

5. Discussion

The HR-dependent patterns observed in this study are consistent with prior comparative analyses of QTc correction formulas. Vandenberk *et al.*[1] demonstrated that the Fridericia and Sagie (Framingham) formulas provide the most accurate stratification for short-term mortality

Table 1
QTc prolongation (> 440 ms) rates across HR groups using three correction formulas (Fridericia, Sagie, and Bazett).

HR (bpm)	Fridericia	Sagie (Framingham)	Bazett
40	4.7% (12/255)	6.3% (16/255)	9.4% (24/255)
60	7.8% (21/269)	9.7% (26/269)	14.1% (38/269)
80	10.9% (28/257)	12.5% (32/257)	19.8% (51/257)
120	15.6% (37/237)	17.3% (41/237)	25.3% (60/237)

Notes: Values represent the percentage and count of beats exceeding the conventional upper QTc limit (440 ms); Fridericia: $QTc = QT/RR^{1/3}$; Sagie (Framingham): $QTc = QT + 0.154\ (1 - RR)$; Bazett: $QTc_{Bazett} = QT / \sqrt{RR}$; RR and QT are expressed in seconds. All QTc values were converted to milliseconds (ms). The dataset comprised ECG waveforms measured at 40, 60, 80, and 120 bpm, derived from a diabetes-risk ECG screening dataset.

risk, while subsequent studies published in *BMC Cardiovascular Disorders* and *JAMA Oncology* emphasized that the choice of QTc formula substantially alters the estimated prevalence of QTc prolongation and affects clinical decision thresholds.[37,38]

By replicating these tendencies within a diabetes-risk ECG dataset, we expand the scope of QT interval correction research into the field of metabolic disease. Chronic hyperglycemia and insulin resistance can alter ventricular repolarization and thereby contribute to QTc prolongation. These findings have important implications for the use of QTc metrics in predicting metabolic and cardiovascular risks among individuals with diabetes.[12] If the Bazett formula is applied, insufficient HR adjustment may cause QTc values to be over- or underestimated depending on instantaneous HR fluctuation, producing distorted risk stratification. In contrast, the Fridericia and Sagie formulas yield more stable HR-independent correction values, improving reliability in long-term ECG monitoring and in machine learning models for diabetes risk prediction.[36–38] Therefore, our findings indicate that adopting Fridericia as the primary correction method, while using Sagie as a secondary cross-validation approach, may enhance both sensitivity and specificity in ECG-based diabetes prediction algorithms.

From a machine learning perspective, QT interval correction can be interpreted as a feature engineering process that directly affects signal quality. An unstable correction formula, such as that of Bazett, introduces HR-dependent variability into the QTc feature, effectively injecting noise into the input space. This may lead machine learning models to misinterpret physiological HR fluctuations as pathological signals, thereby degrading predictive performance. In contrast, the Fridericia formula reduces HR-induced distortion and better preserves intrinsic electrophysiological characteristics associated with metabolic dysfunction. As a result, it enhances the signal-to-noise ratio of QTc-derived features, enabling more robust and interpretable model behavior. Therefore, the choice of QTc correction formula should not be regarded merely as a mathematical preference, but as a critical component of feature engineering in ECG-based machine learning pipelines. This perspective highlights the importance of preprocessing design in developing reliable digital biomarkers for precision medicine.

6. Conclusions

In this study, we compared three widely used QT correction formulas—Bazett, Fridericia, and Sagie (Framingham)—using ECG signals simulated under four controlled HR conditions (40, 60, 80, and 120 bpm) for diabetes risk prediction. The analysis showed that the Bazett formula introduces substantial HR-dependent variability, overestimating QTc at low HR and underestimating it at high HR. In contrast, the Fridericia and Sagie formulas demonstrated consistent correction performance across all HR ranges, showing minimal HR-related bias. A comparison of QTc values exceeding the clinical threshold of 440 ms further confirmed that the Bazett formula produced the highest exceedance rates, whereas the Fridericia formula produced the lowest, indicating that the Fridericia formula offers the most stable HR-adjusted correction.

Theoretically, the findings reaffirm that the choice of QT interval correction formula has a decisive impact on the interpretation of electrophysiological stability. Practically, the results suggest that ECG-based diabetes risk prediction models should adopt the Fridericia formula as the primary correction method, with the Sagie formula serving as a supplementary validation method. Such an approach can reduce false alarms caused by HR fluctuations and improve the accuracy of early risk stratification.

Nevertheless, we draw conclusions with limited generalizability owing to constraints in data scope and methodological boundaries. Above all, the ECG data were obtained from a simulator rather than real-world clinical populations. As a result, the dataset does not fully capture the complex pathophysiological and physiological variabilities inherent in human subjects, including autonomic fluctuations, comorbidities, and behavioral factors. However, this controlled experimental design was intentionally adopted to isolate the mathematical characteristics of QT interval correction formulas. By minimizing external confounding factors such as respiratory variability and physical activity, we provide a clear and reproducible benchmark for evaluating HR-dependent bias. From a methodological perspective, this controlled setting can be considered a “benchmark environment” for assessing formula-driven bias, which is a necessary prerequisite for developing robust ECG-based digital biomarkers. Future research should extend this work by validating the findings using large-scale, real-world ECG datasets, including diverse patient populations and longitudinal clinical data. In addition, future research should incorporate additional physiological markers—such as autonomic balance and glycemic variability—and validate the predictive model in long-term follow-up datasets and multi-ethnic cohorts to enhance robustness and external validity.

In this study, on the other hand, a unified QTc prolongation threshold of 440 ms was applied for analytical consistency. However, it is well established that normal QTc ranges differ by sex, with commonly accepted upper limits of approximately 450 ms for males and 460 ms for females. This implies that the use of a single threshold may introduce potential classification bias, particularly by overestimating QTc prolongation in female subjects. Nevertheless, the primary objective of this study was to compare the relative performance and HR dependence of different correction formulas rather than to establish clinical diagnostic thresholds. Therefore, while sex-specific differences may affect absolute prolongation rates, their impact on the comparative analysis across formulas is expected to be limited. Future studies incorporating sex-

stratified thresholds may further improve the clinical applicability and robustness of the findings.

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About the Authors

OhSuk Yang received his Ph.D. degree from Seoul National University, Republic of Korea, in 2011. His research interests range from statistics in business administration to software programming in relation to green and red bio-innovation and the application of the big data platform to digital healthcare. (osyang30@kangwon.ac.kr)

JongHwi Song received his Ph.D. degree from Yonsei University, Republic of Korea, in 2023. His research interests range from computer engineering to AI serving and AI modeling, encompassing the efficient deployment of deep learning models, real-time inference optimization, and large-scale AI system development. (jh_song@yonsei.ac.kr)