doi.org/10.36721/PJPS.2025.38.5.REG.14426.1

Assessment of pharmacist-driven QT interval prolongation in cardiac patients: Application of Framingham's heart rate corrected QT interval formula and the Tisdale risk score

Ahmad Ullah Humza[1]*, Sadia Ghousia Baig[1], Zafar Iqbal[2], Gul Sama[2], Imran Ahmed[2] and Amna Hamza[3]

[1]Department of Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi
[2]National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan
[3]Abdali Institute of Nursing and Health Sciences, Karachi, Pakistan

Abstract: QTc interval prolongation is a clinical concern in critically ill cardiac patients. Pharmacist-driven approaches that utilize accurate QTc interval measurements and risk stratification tools are essential for identifying high-risk patients and preventing arrhythmic events. This study evaluates the application of Framingham's heart rate corrected QT interval (QTc) formula and the Tisdale risk score for identifying QTc interval prolongation. This prospective observational study was conducted at the National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan. A total of 485 patients were analyzed. Of 485 patients, 71 (14.6%) exhibited QTc interval prolongation. Among them, 6 (1.2%) exhibited severe QTc interval prolongation, with values >500 ms. The Tisdale risk score classified 67.6% of the patients as high-risk before the intervention, and reduced to 36.6% post-intervention. Older patients (≥60 years) were significantly more likely to exhibit QTc interval prolongation, particularly in the >500 ms. Risk factors for QTc interval prolongation included female sex, hypokalemia, and the use of multiple QTc interval prolonging medications. This study underscores the importance of combining Framingham's formula and the Tisdale risk score, with pharmacist involvement, to accurately assess QTc interval prolongation and optimize patient management, enhancing safety and reducing arrhythmic risk in critically ill cardiac patients.

Keywords: QTc interval prolongation; torsade de pointes; Framingham's QTc interval correction formula; Tisdale; Pakistan

Submitted on 06-04-2025 – Revised on 26-06-2025– Accepted on 03-07-2025

INTRODUCTION

A prolonged heart rate corrected QT (QTc) interval is a pathological condition identified on an electrocardiogram (ECG) and is characterized by delayed ventricular repolarization. This abnormality increases the risk of developing Torsades de Pointes (TdP), a life-threatening ventricular arrhythmia that may lead to sudden cardiac arrest (Al-Azayzih, Al-Qerem *et al*., 2024). QTc prolongation and subsequent TdP can result from congenital or acquired conditions. The primary cause of acquired TdP is the use of medications that prolong the QTc interval, including antiarrhythmics, antiemetics, antibiotics, and neuroleptics. Additional risk factors include aging, female sex, thyroid disorders, diabetes, electrolyte imbalances (hypokalemia and hypomagnesemia), and cardiovascular conditions (Lima, Razmjouei *et al*., 2023).

Clinicians must accurately assess and interpret the causes and clinical implications of QTc interval prolongation in routine practice. To raise awareness of QTc interval, the American Heart Association and American College of Cardiology Foundation issued a statement recommending ECG monitoring and prevention of further QTc prolongation and TdP in hospitalized patients (Newell, Wirick *et al*., 2021).

Critically ill patients are more susceptible to QTc interval prolongation and TdP than other groups (Fernandes, Silva *et al*., 2018). Proarrhythmic complications in critically ill patients arise from multiple factors, including polypharmacy (use of five or more medications), renal and hepatic diseases, electrolyte imbalances, and other chronic comorbidities, all of which increase the risk of such events (Lima, Razmjouei *et al*., 2023, Tisdale, Jaynes *et al*., 2013). A study of critically ill ICU patients found that 69% met the American Heart Association (AHA) criteria for QTc interval monitoring, which include the use of QTc interval prolonging medications, bradyarrhythmia, and electrolyte disturbances, particularly hypokalemia and/or hypomagnesemia (Al-Azayzih, Al-Qerem *et al*., 2024). In other words, identifying high-risk patients and avoiding drugs that prolong the QTc interval or cause drug-drug interactions are quick and cost-effective strategies for reducing hospital mortality (Farzanegan, Hosseinpoor *et al*., 2020).

The University of Arizona's Center for Education and Research on Therapeutics (AzCERT) launched

**Corresponding author:* e-mail: ahmadullah.humza@gmail.com

CredibleMeds, an online tool that categorizes drugs based on their risk of causing QTc interval prolongation (www.crediblemeds.org). Drugs are classified into known risk, possible risk, and conditional risk of TdP. This classification is based on a thorough review of clinical trials, postmarketing surveillance, case reports, and in vitro studies (Skullbacka, Airaksinen *et al*., 2022).

Several formulas are available to calculate the QTc interval, each with varying accuracy based on the heart rate and patient factors. Bazett's formula, one of the most commonly used, often overestimates the QTc interval at high heart rates (Vandenberk, Vandael *et al*., 2016). Framingham's correction formula for QTc interval measurement has been noted for its utility across a wide range of heart rates (Andršová, Hnatkova *et al*., 2021). Framingham's correction formula for QTc interval measurement was used to reduce the influence of heart rate on QTc interval values. Studies show that, unlike Bazett's formula, which overcorrects at high heart rates, Framingham and Hodges provide more stable corrections across varying heart rates, making Framingham preferable, particularly in populations with diverse heart rates (Neto, De Oliveira *et al*., 2020).

The Tisdale risk score is a clinical tool for predicting QTc interval prolongation, a precursor of TdP, particularly in hospitalized patients. It is widely applied in cardiology, gastroenterology, and intensive care settings, where QTc interval-prolonging medications are commonly administered (Steinbrech, Amann *et al*., 2025). The score evaluates multiple risk factors such as age, sex, electrolyte disturbances, and concurrent use of QTc interval prolonging drugs to classify patients as low, moderate, or high risk. This risk stratification supports clinical decisions regarding monitoring and intervention. In ICU populations, the score demonstrates high sensitivity (97%) but low specificity (16%), effectively identifying at-risk patients, while limiting its utility in excluding low-risk cases (Su, McGloin *et al*., 2020, Tisdale, Jaynes *et al*., 2013).

The high prevalence of QTc interval prolongation in critically ill cardiac patients highlights the importance of precise risk management. Utilizing the most accurate QTc interval calculation methods and validated tools, such as the Tisdale score, can help prevent TdP and enhance patient outcomes (Skullbacka, Airaksinen *et al*., 2022). These tools enable the systematic identification of high-risk patients and support intervention strategies, including dose modification or substitution with safer medications (Rossi, Marzi *et al*., 2021).

Given the elevated risk of QTc interval prolongation in critically ill cardiac patients, particularly in the ICU, standardized evidence-based strategies are essential for effective risk management. Combining accurate correction methods, such as Framingham's formula, with risk assessment tools, such as the Tisdale score, enables early detection and intervention. This study evaluated a pharmacist-led approach to QTc interval monitoring, aiming to improve outcomes through targeted risk stratification and medication optimization.

MATERIALS AND METHODS

Study design, setting, and duration

This prospective, observational study was conducted in the Intensive Care Units (ICUs) of the National Institute of Cardiovascular Diseases (NICVD), a tertiary care cardiac hospital in Karachi, Pakistan. The study spanned nine months, from November 2022 to August 2023. The sample size was calculated using the WHO sample size calculator, assuming a 30% prevalence of QTc interval prolongation and 5% margin of error. After adjusting for potential random errors, a final sample size of 485 patients was included.

Participants

The study population comprised adult patients (aged ≥18 years) who were admitted to the NICVD ICUs. Exclusion criteria included pacemakers, atrial fibrillation, bundle branch block, congenital long QT syndrome (cLQTS), incomplete electrocardiographic (ECG) data, or ICU stay of less than 24 hours.

Data collection

Demographic, clinical, and pharmacological data were collected using a structured form based on patient medical records. Intravenous and oral medications were reviewed for their potential to prolong the QTc interval using the CredibleMeds online database's QT-Drug List from AzCERT (Skullbacka, Airaksinen et al., 2022;. Additionally, potential drug-drug interactions (pDDIs) associated with QTc interval prolongation were identified and categorized using Lexidrug® (Kheshti, Aalipour *et al*., 2016).

QTc interval measurement

The QTc intervals were manually measured using Framingham's correction formula (Vandenberk, Vandael *et al*., 2016) from ECG leads II and V5. QTc interval prolongation was defined as intervals ≥450ms in males and ≥460ms in females or an increase of ≥60ms from baseline. Two independent, trained investigators calculated the QTc interval, and a cardiologist reviewed any discrepancies.

Risk assessment

The risk of QTc interval prolongation was assessed using the Tisdale risk scoring system. The Tisdale Risk Score categorizes patients into three groups based on their total score: low-risk (≤6 points), moderate-risk (7-10 points), and high-risk (≥11 points) for QTc interval prolongation and TdP (Tisdale, Jaynes *et al*., 2013). The patients were followed up until discharge.

Ethical approval

Ethical approval for this study was obtained from the ethical review committee of the clinical research department, NICVD, Karachi (ERC-48/2022), as well as the institutional bioethics committee, University of Karachi (IBC KU-385/2023).

STATISTICAL ANALYSIS

Data were analyzed using SPSS (version 23) and Microsoft Excel 365. Continuous variables were reported as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Logistic regression analysis was used to identify predictors of QTc prolongation, reporting odds ratios (ORs) with 95% confidence intervals (CIs). Statistical significance was defined as a p-value of < 0.05.

RESULTS

QTc interval prolongation (QTc >450 ms in Males, >460 ms in Females)

Among the 485 patients, 71 (14.6%) exhibited QTc interval prolongation as defined by the criteria. The sex distribution was similar across groups (male: 73.9% vs. 70.4%, p=0.539), with no significant sex-related differences in QTc interval prolongation. However, the age distribution was significantly different ($p < 0.001$), with a greater proportion of patients aged 60 years or older (42.3% vs. 30.4%) showing a prolonged QTc interval. These findings highlight the increased risk of QTc interval prolongation with advancing age. table 1.

Hospitalization duration was significantly longer in patients with QTc interval prolongation (2.4 ± 1.1 days vs. 2.1 ± 1.0 days, p=0.044). Moreover, patients with prolonged QTc interval were more likely to have multiple comorbidities (54.9% vs. 51%, p=0.007), and a left ventricular ejection fraction (EF) <40% was more common in this group (32.4% vs. 21.7%, p=0.050). table 1.

Concerning medication use, patients with a prolonged QTc interval used fewer total medications (10.1 ± 2.4 vs. 11 ± 2.1, p=0.001), with a higher percentage receiving 5-10 drugs ($p < 0.001$). There was also a significant difference in the number of cardiovascular medications used (5.3±1.8 vs. 5.9±1.6, p=0.025) and a slightly lower use of non-cardiovascular drugs (4.7±1.7 vs. 5.1±1.3, p=0.049). In terms of the Tisdale risk score, high-risk patients with QTc interval prolongation were more prevalent pre-intervention (67.6% vs. 46.4%, p=0.003) and post-intervention (36.6% vs. 22%, p=0.029), indicating the utility of the Tisdale score in risk stratification. table 1.

QTc interval prolongation (QTc >500 ms)

In a subgroup of patients (n=6, 1.2%) with QTc >500 ms, these individuals were significantly older (62.7±16.8 years vs. 52.2±12.4 years, p=0.043), highlighting age as a significant factor in severe QTc interval prolongation. The use of medications was notably lower in this group (8.8 ± 2.9 vs. 10.9±2.2, p=0.022) and they had fewer non-cardiovascular medications (3.2±1.9 vs. 5.1±1.4, p=0.001). table 2.

The prevalence of Category D pDDIs by Lexidrug was significantly higher in the prolonged QTc interval group (8 cases vs. 274 in the normal QTc interval group, $p < 0.001$). Although the sample size for QTc >500 ms was small, these findings emphasize the heightened risk of drug interactions in this high-risk cohort.

Regarding the Tisdale risk score, patients in this group exhibited a high proportion of moderate-to high-risk scores (pre-intervention high-risk, 66.7%; post-intervention high-risk, 66.7%). This aligns with the findings in table 1, where a high Tisdale Risk Score was associated with QTc interval prolongation. table 2.

Tisdale risk score and QTc interval prolongation

The Tisdale Risk Score revealed several essential predictors of QTc interval prolongation. Female sex was significantly associated with prolonged QTc interval (OR, 1.94; 95% CI: 1.17-3.2, p=0.01), suggesting a higher risk for women. Hypokalemia, defined as serum potassium ≤3.5 mEq/L, also significantly predicted QTc interval prolongation (OR: 1.67, p=0.042), reinforcing the importance of electrolyte balance in QTc interval prolongation. The use of loop diuretics (such as furosemide) appeared to have an impact on QTc prolongation (OR: 0.44, p=0.031), which may be attributed to their role in managing fluid overload, although their potential to cause hypokalemia could also contribute to QTc interval prolongation risks. table 3.

Using ≥ 2 QTc interval prolongation medications was associated with QTc interval prolongation (OR: 0.23, p=0.017). This finding suggests that patients receiving multiple QTc interval prolonging drugs should be carefully monitored and managed, potentially reducing the prevalence of prolonged QTc intervals. Although conditions such as sepsis (OR: 3.45, p=0.06) and acute heart failure with an EF <40% (OR: 1.6, p=0.079) tended to be associated with QTc interval prolongation, they did not reach statistical significance. table 3.

This study found that older patients, particularly those aged ≥60 years, were significantly more likely to experience QTc interval prolongation, with a higher prevalence in those with QTc >500 ms. The Tisdale risk score is a valuable tool for predicting the risk of TdP concerning QTc interval prolongation, with a higher proportion of high-risk patients observed in the QTc interval prolongation group both pre-and post-intervention. Hypokalemia was identified as a significant risk factor for QTc interval prolongation. Female sex was also a significant predictor of QTc interval prolongation, underscoring the importance

of considering demographic and clinical factors in QTc interval risk assessment.

DISCUSSION

This study assessed the prevalence of QTc interval prolongation and its associated risk factors in critically ill cardiac patients using Framingham's correction formula for QTc interval measurement and the Tisdale risk score for risk stratification. Our findings align with those of previous research, which highlights the significance of age, electrolyte imbalances, and pharmacological factors in predicting QTc interval prolongation. Several key factors have been identified as contributing to risk in this cohort (Steinbrech, Amann *et al*., 2025).

Patients with QTc interval prolongation received fewer total medications (10.1±2.4 vs. 11±2.1, p=0.001), with a higher proportion taking 5-10 drugs ($p < 0.001$) (table 1). This suggests that the combination and type of medication, rather than the total number, were more influential in contributing to QTc interval prolongation. Similarly, in table 2, the QTc >500 ms group received fewer drugs (8.8±2.9 vs. 10.9±2.2, p=0.022), yet severe QTc interval prolongation indicates that drug interactions played a critical role. Comparable results were reported in a study by Humza *et al*., which highlighted the crucial role of clinical pharmacists in managing polypharmacy and mitigating the associated risks (Humza, 2024). Notably, 77.9% of these drugs were classified under the known risk of the TdP category.

Patients with QTc interval prolongation (table 1) had significantly higher exposures to Category B, C, D and X pDDIs (pDDI Category D: p=0.002, Category X: p=0.025), reflecting increased arrhythmic risk. Additionally, QT-specific pDDIs (QT-pDDIs) were more frequent in this group (Categories C, D, and X: $p < 0.01$), highlighting the importance of QTc interval prolongation of drugs and their interactions. As shown in table 2, Category D pDDIs were significantly more common in the QTc >500 ms subgroup ($p < 0.001$), emphasizing the compounded risk from high-risk drug interactions in severely prolonged QTc interval cases. A study conducted at a tertiary care cardiac institute in Pakistan by Humza *et al*. reported frequent pDDIs, emphasizing cardiovascular drugs as the major contributors (Humza, Akbar *et al*., 2024). Comparable results were observed in a Chinese tertiary care study by Wang *et al*., where cardiothoracic ICU patients exhibited a high incidence of pDDIs, including QTc interval prolonging pairs such as ciprofloxacin-domperidone and domperidone-propofol, also identified in this study (Wang, Shi *et al*., 2022). These correlations underscore the need for robust medication monitoring systems tailored to ICU settings to mitigate clinical risks associated with pDDIs and QT-pDDIs (Fernandes, da Silva Paulino *et al*., 2019, Humza, Siddiq *et al*., 2024).

In this study, we employed Framingham's formula for QTc interval correction, which has been demonstrated to provide more stable corrections across a range of heart rates compared to other methods, such as Bazett's formula. The Framingham correction is particularly useful in populations with diverse heart rates, as it mitigates the overcorrection observed with Bazett's formula at higher heart rates, thereby providing more accurate QTc interval measurements in patients with varying levels of tachycardia and bradycardia. The Framingham formula is utilized in clinical settings to adjust the QTc interval for heart rate variations, to provide a more accurate assessment of cardiac health. Its application is particularly relevant in monitoring conditions associated with QT prolongation, such as Long QT syndrome, and during drug therapy. However, this formula has limitations that can affect its clinical utility (Gervasi, Bianco *et al*., 2017).

Framingham's QTc interval correction formula provided accurate measurements, as reflected in the statistical findings in tables 1 and 2. table 1 allowed for precise differentiation between the QTc interval normal and QTc interval prolonged groups, with significant age-related differences ($p<0.001$) and medication use patterns ($p < 0.001$), which are crucial for risk assessment. Similarly, as shown in table 2, Framingham's formula ensured accurate QTc interval values, highlighting the older age of patients with QTc >500 ms (p=0.043) and lower medication use in this subgroup (p=0.022).

The formula's ability to correct heart rate variability helped avoid the overcorrection seen with Bazett's formula, thus supporting a more reliable risk stratification for QTc interval prolongation in hospitalized patients. Recent studies support these findings, showing that Framingham's formula offers more accurate QTc interval measurements than Bazett's formula, particularly in populations with heart rate fluctuations or critical conditions. Additionally, similar research has highlighted that precise correction of the QTc interval is essential for evaluating the effects of QTc interval prolonging drugs and predicting arrhythmic risk. These studies further confirmed the clinical relevance of Framingham's formula for improving patient safety and optimizing QTc interval monitoring in high-risk populations (Dogan, Tunc *et al*., 2005, Yazdanpanah, Naghizadeh *et al*., 2022).

Table 3 demonstrates the predictive value of the Tisdale risk score in identifying patients at high risk of QTc interval prolongation. This is consistent with the findings in table 1, where a significantly higher proportion of patients with QTc interval prolongation were classified as high-risk (67.6% vs. 46.4%, $p = 0.003$) using the Tisdale risk score at baseline, and a continued high-risk status was observed post-intervention (p=0.029). The score, which incorporates factors such as age, sex, and electrolyte disturbances, was strongly correlated with QTc interval prolongation in our study, particularly in female patients (OR: 1.94, $p = 0.01$) and those with hypokalemia (OR: 1.67, $p = 0.042$).

Table 1: QTc interval (Framingham)

	QTc Normal, M<450ms, F<460ms	QTc Prolonged, M>450ms, F>460ms	P-value
Total (N)	414	71	-
Gender			
Male	306 (73.9%)	50 (70.4%)	0.539
Female	108 (26.1%)	21 (29.6%)	
Age (years)	52.6 ± 12	51.3 ± 15.5	0.500
18-39	56 (13.5%)	19 (26.8%)	
40-59	232 (56%)	22 (31%)	<0.001
≥60	126 (30.4%)	30 (42.3%)	
Days in Ward	2.1 ± 1	2.4 ± 1.1	0.044
Comorbidities			
None	62 (15%)	19 (26.8%)	
Single	141 (34.1%)	13 (18.3%)	0.007
Multiple	211 (51%)	39 (54.9%)	
EF <40%	90 (21.7%)	23 (32.4%)	0.050
Total Drugs	11 ± 2.1	10.1 ± 2.4	0.001
0-4 Drugs	0 (0%)	2 (2.8%)	
5-10 Drugs	156 (37.7%)	38 (53.5%)	<0.001
≥11 Drugs	258 (62.3%)	31 (43.7%)	
QTc prolonging Drugs	3.4 ± 1.2	3.2 ± 1.1	0.076
0-4 Drugs	354 (85.5%)	62 (87.3%)	
5-8 Drugs	60 (14.5%)	9 (12.7%)	0.686
≥9 Drugs	0 (0%)	0 (0%)	
CV Drugs	5.9 ± 1.6	5.3 ± 1.8	0.025
0-5 Drugs	179 (43.2%)	41 (57.7%)	
6-12 Drugs	235 (56.8%)	30 (42.3%)	0.023
≥13 Drugs	0 (0%)	0 (0%)	
Non-CV Drugs	5.1 ± 1.3	4.7 ± 1.7	0.049
0-5 Drugs	264 (63.8%)	46 (64.8%)	
6-12 Drugs	150 (36.2%)	25 (35.2%)	0.869
≥13 Drugs	0 (0%)	0 (0%)	
No. of PDDs	4584	795	-
pDDI Category			
A	1 (0%)	1 (0%)	0.099
B	661 (0.1%)	150 (0.2%)	0.001
C	3415 (0.7%)	557 (0.7%)	0.002
D	225 (0%)	57 (0.1%)	0.002
X	282 (0.1%)	30 (0%)	0.025
No. of QT-PDDs	127	29	-
QT-pDDI Category			
A	0 (0%)	0 (0%)	0.160
B	88 (0.7%)	21 (0.7%)	0.001
C	5 (0%)	2 (0.1%)	0.009
D	24 (0.2%)	2 (0.1%)	0.008
X	10 (0.1%)	4 (0.1%)	0.008
Hypokalemia	123 (29.7%)	28 (39.4%)	0.102
Known risk (KR)	326 (78.7%)	51 (71.8%)	0.196
Possible risk (PR)	60 (14.5%)	11 (15.5%)	0.826
Conditional risk (CR)	389 (94%)	68 (95.8%)	0.545
Special risk (SR)	96 (23.2%)	11 (15.5%)	0.149
Tisdale Risk (pre)			
Low	6 (1.4%)	0 (0%)	
Moderate	216 (52.2%)	23 (32.4%)	0.003
High	192 (46.4%)	48 (67.6%)	
Tisdale Risk (post)			
Low	31 (7.5%)	4 (5.6%)	
Moderate	292 (70.5%)	41 (57.7%)	0.029
High	91 (22%)	26 (36.6%)	

Table 2: Comparison of QTc interval <500ms and >500ms

	QTc interval, <500ms	QTc interval, >500ms	P-value
Total (N)	479	6	-
Gender			
Male	352 (73.5%)	4 (66.7%)	0.707
Female	127 (26.5%)	2 (33.3%)	
Age (years)	52.2 ± 12.4	62.7 ± 16.8	0.043
18-39	74 (15.4%)	1 (16.7%)	
40-59	253 (52.8%)	1 (16.7%)	0.155
≥60	152 (31.7%)	4 (66.7%)	
Days in Ward	2.1 ± 1	2.3 ± 1	0.641
Comorbidities			
None	81 (16.9%)	0 (0%)	
Single	152 (31.7%)	2 (33.3%)	0.525
Multiple	246 (51.4%)	4 (66.7%)	
EF <40%	110 (23%)	3 (50%)	0.120
Total Drugs	10.9 ± 2.2	8.8 ± 2.9	0.022
0-4 Drugs	1 (0.2%)	1 (16.7%)	
5-10 Drugs	191 (39.9%)	3 (50%)	<0.001
≥11 Drugs	287 (59.9%)	2 (33.3%)	
QTc prolonging Drugs	3.4 ± 1.1	2.8 ± 1	0.219
0-4 Drugs	410 (85.6%)	6 (100%)	
5-8 Drugs	69 (14.4%)	0 (0%)	0.315
≥9 Drugs	0 (0%)	0 (0%)	
CV Drugs	5.8 ± 1.7	5.7 ± 1.6	0.871
0-5 Drugs	217 (45.3%)	3 (50%)	
6-12 Drugs	262 (54.7%)	3 (50%)	0.818
≥13 Drugs	0 (0%)	0 (0%)	
Non-CV Drugs	5.1 ± 1.4	3.2 ± 1.9	0.001
0-5 Drugs	305 (63.7%)	5 (83.3%)	
6-12 Drugs	174 (36.3%)	1 (16.7%)	0.319
≥13 Drugs	0 (0%)	0 (0%)	
No. of PDDs	5335	44	-
pDDI Category			
A	0 (0%)	0 (0%)	-
B	108 (0.7%)	1 (1%)	0.510
C	7 (0%)	0 (0%)	0.828
D	26 (0.2%)	0 (0%)	0.654
X	14 (0.1%)	0 (0%)	0.753
Hypokalemia	149 (31.1%)	2 (33.3%)	0.907
Known risk (KR)	373 (77.9%)	4 (66.7%)	0.512
Possible risk (PR)	71 (14.8%)	0 (0%)	0.307
Conditional risk (CR)	451 (94.2%)	6 (100%)	0.542
Special risk (SR)	105 (21.9%)	2 (33.3%)	0.503
Tisdale Risk (pre-intervention)			
Low	6 (1.3%)	0 (0%)	
Moderate	237 (49.5%)	2 (33.3%)	0.687
High	236 (49.3%)	4 (66.7%)	
Tisdale Risk (post-intervention)			
Low	35 (7.3%)	0 (0%)	
Moderate	331 (69.1%)	2 (33.3%)	0.047
High	113 (23.6%)	4 (66.7%)	

Table 3: Tisdale risk score with comparison of QTc interval Framingham's formulas (N=485)

Tisdale Risk Score	QTc interval ≥450 ms
Female Gender	1.94 [1.17-3.2], p = 0.01
Age ≥68 years	1.27 [0.56-2.88], p = 0.56
Loop Diuretics (Furosemide)	0.44 [0.21-0.93], p = 0.031
Serum potassium ≤3.5 mEq/L	1.67 [1.02-2.73], p = 0.042
Acute MI	0.76 [0.26-2.23], p = 0.611
≥2 QTc prolonging medications	0.23 [0.07-0.77], p = 0.017
Sepsis	3.45 [0.95-12.5], p = 0.06
Acute Heart Failure (<40% EF)	1.6 [0.95-2.72], p = 0.079

These results align with those of similar studies, highlighting the importance of Tisdale's score in risk stratification for QTc interval prolongation in hospitalized patients, especially those with electrolyte imbalances and polypharmacy. In table 2, where patients with QTc >500 ms were analyzed, the high-risk group was similarly more prevalent (66.7% vs. 49.3%, p <0.001), reinforcing the predictive utility of the Tisdale risk score in identifying patients at high risk of severe QTc interval prolongation. This is further corroborated by studies that have validated the Tisdale Risk Score in critical care settings, where patients often exhibit variable heart rates and complex medication regimens. The age-related risk observed in table 2 (p=0.043) also supports recent research showing that older age is a significant factor for QTc interval prolongation and arrhythmic risk. These findings align with the existing literature, which emphasizes electrolyte disturbances, comorbidities, and medication interactions as critical contributors to QTc interval variability in ICU settings (Simon, Lin *et al*., 2024).

Overall, the Tisdale risk score combined with Framingham's QTc interval correction formula provides a robust QTc interval risk stratification framework that integrates clinical and pharmacological factors to predict TdP risk more effectively. Recent studies have emphasized that combining these tools enhances the accuracy of QTc interval monitoring and risk management, particularly in critically ill and polypharmacy patients (Harb, Schwartz *et al*., 2024, Humza, Siddiq *et al*., 2024).

CONCLUSION

This study demonstrates the utility of Framingham's QTc interval correction formula and the Tisdale risk score in accurately identifying QTc interval prolongation and predicting outcomes in critically ill cardiac patients. The Tisdale risk score effectively stratified patients by risk, with female sex, hypokalemia, and polypharmacy emerging as significant predictors of QTc interval prolongation. These tools offer valuable support for QTc interval monitoring and medication optimization in hospitalized patients, particularly those at risk of arrhythmic events, thereby enhancing patient safety through targeted interventions.

Limitations

The observational nature of the study limits causal inferences, and the small sample size for QTc > 500 ms may affect the generalizability of the findings. Although Framingham's formula demonstrated reliability, further validation is required across diverse populations. The Tisdale risk score showed substantial predictive value but had low specificity, warranting cautious interpretation. Finally, the study was conducted in a single-center setting, limiting the broader applicability of the findings. Further multicenter studies are required to confirm these results.

Conflict of interest

The authors declare no conflicts of interest and confirm that the work was not supported or funded by any company.

REFERENCES

Al-Azayzih A, Al-Qerem W, Al-Azzam S, Muflih S, Al-Husein BA, Kharaba Z, Kanaan RJ and Rahhal D (2024). Prevalence of medication associated with QTc prolongation used among critically Ill patients. *Vasc. Health Risk Manag.,* **20**: 27-37.

Andršová I, Hnatkova K, Šišáková M, Toman O, Smetana P, Huster KM, Barthel P, Novotný T, Schmidt G and Malik M (2021). Influence of heart rate correction formulas on QTc interval stability. *Sci. Rep.,* **11**(1): 14269.

Dogan A, Tunc E, Varol E, Ozaydin M and Ozturk M (2005). Comparison of the four formulas of adjusting QT interval for the heart rate in the middle-aged healthy Turkish men. *Ann. Noninvas. Electrocardiol.,* **10**(2): 134-141.

Farzanegan B, Hosseinpoor Z, Baniasadi S, Seyyedi SR and Rajabi M (2020). An observational study of QTc prolongation in critically ill patients: Identification of incidence and predictors. *Indian J. Crit. Care Med.,* **24**(4): 270-275.

Fernandes FM, da Silva Paulino AM, Sedda BC, da Silva EP, Martins RR and Oliveira AG (2019). Assessment of the risk of QT-interval prolongation associated with potential drug-drug interactions in patients admitted to Intensive Care Units. *Saudi Pharm. J.,* **27**(2): 229-234.

Fernandes FM, Silva EP, Martins RR and Oliveira AG (2018). QTc interval prolongation in critically ill

patients: Prevalence, risk factors and associated medications. *PloS One.,* **13**(6): 1-12.

Gervasi SF, Bianco M, Palmieri V, Cuccaro F and Zeppilli P (2017). QTc interval in adolescents and young athletes: influence of correction formulas. *Int. J. Sports Med.,* **38**(10): 729-734.

Harb K, Schwartz S and Cooper J (2024). Pharmacist reported protocols for QTc monitoring of psychiatric medications. *J. Cureus.,* **16**(3): 1-8.

Humza AU, Akbar MA, Bilal Awan MA, Yousuf JB, Khan K and Ammar A (2024). Prevalence and comparative analysis of potential drug-drug interactions among hospitalized patients at a tertiary care cardiac institute in Pakistan: Findings from a single centre. *Pak. J. Pharm. Sci.,* **37**(5): 961-968.

Humza AU, Hameed A, Akbar MA, Ahmed I, Ali A and Yousuf JB (2024). Evaluation of medication use and polypharmacy in postoperative cardiac patients: The clinical pharmacist's imperative in a public institute of Pakistan. *Pak. J. Pharm. Sci.* **37**(1): 17-23.

Humza AU, Siddiq A, Baig SG, Ali A, Ahmed I and Yousuf JB (2024). Assessment of QTc-interval prolonging medication utilization and associated potential drug-drug interactions in hospitalized cardiac patients: A cross-sectional study in cardiology. *Jordan J. Pharm. Sci.,* **17**(3): 603-610.

Kheshti R, Aalipour M and Namazi S (2016). A comparison of five common drug-drug interaction software programs regarding accuracy and comprehensiveness. *J. Res. Pharm. Pract.,* **5**(4): 257-263.

Lima B, Razmjouei S, Bajwa MT, Shahzad Z, Shoewu OA, Ijaz O, Mange P, Khanal S and Gebregiorgis T (2023). Polypharmacy, gender disparities and ethnic and racial predispositions in long QT syndrome: An in-depth review. *Cureus.,* **15**(9): 1-22.

Neto NRDO, De Oliveira WS, Pinto GDC, De Oliveira ESR and Maria das Neves D (2020). A practical method for QTc interval measurement. *Cureus.* **12**(12): 1-7.

Newell B, Wirick N, Rigelsky F and Migal K (2021). Implementation of a Pharmacist Monitoring Process for Patients on QTc Prolonging Antibiotics: A Pilot Study. *Hosp. Pharm.,* **56**(6): 772-776.

Rossi M, Marzi F, Natale M, Porceddu A, Tuccori M, Lazzerini PE, Laghi-Pasini F and Capecchi PL (2021). Drug-associated QTc prolongation in geriatric hospitalized patients: A cross-sectional study in internal medicine. *Drugs-real world outcomes.,* **8**: 325-335.

Simon ST, Lin M, Trinkley KE, Aleong R, Rafaels N, Crooks KR, Reiter MJ, Gignoux CR and Rosenberg MA (2024). A polygenic risk score for the QT interval is an independent predictor of drug-induced QT prolongation. *PloS One.,* **19**(6): 1-15.

Skullbacka S, Airaksinen M, Puustinen J and Toivo T (2022). Risk assessment tools for QT prolonging pharmacotherapy in older adults: A systematic review. *Eur. J. Clin. Pharmacol.,* **78**(5): 765-779.

Steinbrech J, Amann U, Irlbeck M, Clauß S and Strobach D (2025). Risk stratification of QTc prolongations in hospitalized cardiology and gastroenterology patients using the tisdale score-a retrospective analysis. *J. Clin. Med.,* **14**(2): 339.

Su K, McGloin R and Gellatly RM (2020). Predictive validity of a QTc interval prolongation risk score in the intensive care unit. *Pharmacotherapy: J. Hum. Pharmacol. Drug Ther.,* **40**(6): 492-499.

Tisdale JE, Jaynes HA, Kingery JR, Mourad NA, Trujillo TN, Overholser BR, Kovacs RJ and Outcomes (2013). Development and validation of a risk score to predict QT interval prolongation in hospitalized patients. *Circ. Cardiovasc. Qual.,* **6**(4): 479-487.

Vandenberk B, Vandael E, Robyns T, Vandenberghe J, Garweg C, Foulon V, Ector J and Willems R (2016). Which QT correction formulae to use for QT monitoring? *J. Am. Heart Assoc.,* **5**(6): 1-10.

Wang H, Shi H, Wang N, Wang Y, Zhang L, Zhao Y and Xie J (2022). Prevalence of potential drug- drug interactions in the cardiothoracic intensive care unit patients in a Chinese tertiary care teaching hospital. *BMC Pharmacol. Toxicol.,* **23**(1): 39.

Woosley RG T, Woosley D and Romero KA (2023). QTdrugs list. 1457 E. Desert Garden Dr., Tucson, AZ 85718, AZCERT, Inc.

Yazdanpanah MH, Naghizadeh MM, Sayyadipoor S and Farjam M (2022). The best QT correction formula in a non-hospitalized population: The Fasa PERSIAN cohort study. *BMC Cardiovas. Disord.,* **22**(1): 1-12.