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Ventricular repolarization heterogeneity on the admission electrocardiogram in acute coronary syndrome: relationship of the Tpeak–Tend interval and Tp-e/QTc ratio to angiographic complexity, clinical risk and six-month outcome

Santoshi Shamad

sshamad76@gmail.com

Srirama Chandra Bhanja (SCB) Medical College and Hospital

Sura Kishore Mishra

Srirama Chandra Bhanja (SCB) Medical College and Hospital

Pankaj Kumar Maravi

Ashwini hospital, CDA sector 1

Siddharth Pradhan

Srirama Chandra Bhanja (SCB) Medical College and Hospital

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Abstract

Background: Repolarization heterogeneity underlies malignant arrhythmia in acute coronary syndrome (ACS). We examined whether the admission Tpeak–Tend (Tp-e) interval and Tp-e/QTc ratio track angiographic complexity, clinical risk and six-month outcome.

Methods: We prospectively enrolled 250 consecutive patients with ACS at a single tertiary centre. Hodges-corrected QT, Tp-e and Tp-e/QTc were measured in leads V4–V6 on the admission electrocardiogram, with echocardiography, angiography and SYNTAX/GRACE scoring. The composite outcome comprised ventricular arrhythmia, heart failure, cardiogenic shock and death.

Results: Interobserver agreement was excellent (ICC 0.99–1.00). All three indices rose incrementally across SYNTAX and GRACE categories ($P < 0.001$). Tp-e correlated with SYNTAX ($r = 0.786$) and GRACE ($r = 0.645$), and both scores were independently associated with Tp-e/QTc ($\beta = 0.616$, $P < 0.001$ and $\beta = 0.167$, $P = 0.008$). Tp-e ≥ 125 ms identified a high SYNTAX (AUC 0.945) and a high GRACE (AUC 0.924) score. The composite outcome occurred in 48 patients (19.2%). Event-free survival was lower with QTc prolongation and an abnormal Tp-e/QTc (log-rank χ^2 25.86 and 15.61; $P < 0.001$). On Cox regression, Tp-e/QTc (HR 1.111, 95% CI 1.017–1.213) and ejection fraction (HR 0.948, 95% CI 0.922–0.976) remained independent predictors ($P = 0.019$ and $P < 0.001$). Adding Tp-e to GRACE improved prediction (IDI 0.044, $P = 0.027$; continuous NRI 0.235, $P = 0.020$).

Conclusions: In ACS, Tp-e and Tp-e/QTc increase with anatomical and clinical severity, and Tp-e/QTc independently predicts six-month events. By refining GRACE-derived prognostic information, these indices merit consideration in early risk stratification.

Introduction

Arrhythmic complications of acute coronary syndrome (ACS) range from isolated ventricular ectopy to sustained ventricular tachycardia and ventricular fibrillation. Some form of rhythm disturbance is documented in the majority of patients within the first 24 hours of infarction, and the risk of a malignant event is concentrated among those with severe left ventricular systolic impairment and multivessel involvement.[1, 2] Early identification of this subgroup remains a persistent clinical challenge.

Two instruments dominate contemporary risk assessment. The SYNTAX score quantifies anatomical disease burden angiographically, informs the selection of percutaneous rather than surgical revascularization,[3] and predicts recurrent infarction, repeat revascularization and death within its upper categories.[4, 5] The score developed from the Global Registry of Acute Coronary Events (GRACE) derives an estimate of in-hospital and six-month mortality from a limited set of admission variables[6, 7] and is recommended for early risk stratification in current guidelines.[8] Severity defined by either instrument has been associated with ventricular electrical instability and with arrhythmic death.[9, 10]

Repolarization proceeds non-uniformly across the ventricular wall. The interval between the apex of the T wave and its termination (Tp-e) provides a surface estimate of this transmural gradient, and its prolongation constitutes an established non-invasive marker of arrhythmic susceptibility.[11, 12] Because Tp-e is itself sensitive to cycle length and to the overall duration of repolarization, normalization to the corrected QT interval has been proposed as the more stable index,[13] and a prolonged Tp-e predicts sudden cardiac death in populations without known infarction.[14]

Evidence relating these indices simultaneously to an anatomical and to a clinical risk score remains limited, a single previous cohort having examined both together,[15] and sparser still in South Asian populations, in whom coronary disease manifests earlier and more diffusely.[16, 17] Whether either index contributes prognostic information beyond established scores has seldom been formally tested. The present study therefore evaluated Tp-e and Tp-e/QTc in relation to the SYNTAX score, the GRACE score and six-month clinical outcome in ACS.

Methods

Study design and population

This prospective observational cohort study was conducted in the cardiology department of a tertiary-care teaching hospital across the twelve months commencing April 2025, of which the first three months were given to enrolment, the ensuing six to follow-up and the last three to analysis, so that every participant completed six months of follow-up within the study period. Two hundred and fifty consecutive patients aged 18 years or older were enrolled, each presenting with one of three diagnoses — unstable angina, infarction without ST-segment elevation (NSTEMI) or infarction with ST-segment elevation (STEMI) — and each proceeding to coronary angiography.

Patients were ineligible where the coronary circulation had previously been revascularized, whether by percutaneous intervention or by bypass grafting, and where myocardial infarction had occurred on an earlier occasion. Additional exclusion criteria comprised active infection; inflammatory and haematological disorders; chronic hepatic, renal or obstructive pulmonary disease; malignancy; recent major trauma or surgery; and pregnancy. Because reliable timing of the T wave is precluded under certain circumstances, patients in atrial fibrillation, those whose QRS complex was widened by bundle branch block and those with ventricular pacing were likewise excluded, together with patients exhibiting significant electrolyte disturbance and those receiving QT-prolonging antiarrhythmic therapy at a dose that had not remained stable for at least one month. Incomplete electrocardiographic or angiographic records precluded inclusion of the remainder.

Patients of either sex were eligible. Sex as documented at admission was recorded for every participant and, in keeping with the Sex and Gender Equity in Research (SAGER) guidelines, baseline characteristics, repolarization indices and six-month outcomes are reported separately for male and for female patients.

Approval was obtained from the Institutional Ethics Committee of Srirama Chandra Bhanja (S.C.B.) Medical College and Hospital, Cuttack 753007, Odisha, India (approval number 2118/IEC/2025). The investigation was conducted in accordance with the Declaration of Helsinki; each participant provided written informed consent once the protocol had been explained; and this report follows the STROBE checklist for observational studies.

Electrocardiographic measurements

A 12-lead electrocardiogram was acquired on admission with the recorder set to 25 mm/s and 10 mm/mV. Measurements were performed manually in leads V4, V5 and V6 and averaged across three consecutive cardiac cycles. The QT interval was taken from the onset of the QRS complex to the point at which the descending limb of the T wave returned to the isoelectric baseline, and was corrected for heart rate by the linear formula of Hodges (QTc = QT + 1.75 × [heart rate − 60]);[18] this Hodges-corrected value served as the denominator of the Tp-e/QTc ratio. Tp-e was defined as the interval extending from the apex of the T wave to that same terminal point, with the nadir substituting for the apex where the T wave was biphasic or inverted.

Thresholds for the survival analysis were specified a priori, before any inspection of the dataset, as a Hodges-corrected QT above 440 ms in men and above 460 ms in women, and a Tp-e/QTc ratio above 0.25. All tracings were analysed by one observer blinded to the angiographic findings and to clinical outcome; a second observer, blinded to the same information, repeated the measurements in a randomly selected subset of 50 patients so that interobserver agreement could be quantified (Additional file 1: Methods S1).

Angiography, risk scores and follow-up

Vascular access was radial or femoral at the discretion of the operator. Stenosis was regarded as significant at 70% luminal narrowing, or at 50% for the left main stem. SYNTAX scores were derived using the online calculator and assigned to one of three categories: low at 22 or below, intermediate from 23 to 32, and high at 33 or above.[3] GRACE scores were calculated and stratified at 109 and at 140.[6] Left ventricular ejection fraction (LVEF) was determined by echocardiography within 24 hours using the biplane Simpson method. Surveillance encompassed the index admission together with review at one and at six months, drawing upon case records, outpatient attendance and telephone contact; the composite outcome comprised sustained ventricular tachycardia or fibrillation, heart failure, cardiogenic shock and sudden cardiac death (Additional file 1: Methods S2).

Statistical analysis

Analyses were performed in SPSS version 31.0. The Kolmogorov–Smirnov test was applied to assess distributional normality. Symmetrically distributed continuous variables are presented as mean ± SD and skewed variables as median with interquartile range; categorical variables are presented as frequency with percentage. Comparisons across groups relied upon the independent-samples t-test for normally distributed continuous variables, the Kruskal–Wallis test for skewed variables and the χ^2 test for proportions. Pearson coefficients quantified the association of Tp-e and Tp-e/QTc with each risk score, and Spearman coefficients are reported alongside them as a sensitivity analysis (Additional file 1: Table S4). The multivariable linear regression model, with Tp-e/QTc as the dependent variable, included eight prespecified covariates: the SYNTAX score, the GRACE score, haemoglobin, neutrophil percentage, LVEF, serum creatinine, random glucose and triglycerides. Discriminative performance of both indices for a high SYNTAX and a high GRACE score was assessed by receiver-operating-characteristic analysis; the threshold at which the Youden index reached its maximum is reported, together with the area under the curve (AUC) and its 95% confidence interval (CI).

Cumulative event-free survival was estimated by the Kaplan–Meier method, calculated once with patients dichotomized by QTc and again with patients dichotomized by Tp-e/QTc at the thresholds specified above, and the resulting strata were compared by log-rank test. Independent predictors of the composite outcome were sought by multivariable Cox proportional hazards regression, in which Tp-e/QTc was entered alongside hypertension, the SYNTAX score, LVEF, serum creatinine and haemoglobin; results are expressed as hazard ratios (HR) with 95% CI. Proportionality of hazards was verified in two ways, by inspection of log-minus-log survival plots and by examination of scaled Schoenfeld residuals.

Interobserver agreement for ECG parameters within the 50-patient subset was quantified as the intraclass correlation coefficient (ICC), computed on a two-way random-effects model with absolute agreement and reported with its 95% CI,[19] and was additionally assessed graphically for systematic bias and limits of agreement according to Bland and Altman.[20] The prognostic increment attributable to Tp-e beyond the GRACE score was quantified by the integrated discrimination improvement (IDI) and by the continuous net reclassification improvement (NRI), each reported with a 95% CI.[21] Further methodological detail, including the derivation of the reclassification indices, is provided in Additional file 1: Methods S3. Statistical significance was accepted at a two-sided P value below 0.05.

Results

Baseline characteristics

The cohort of 250 patients had a median age of 59 years (interquartile range 51–65) and comprised 194 men (77.6%). STEMI was the predominant presentation at 77.6%, ahead of NSTEMI at 21.2% and unstable angina at 1.2%. Hypertension was documented in 48.0% of patients, smoking in 41.2%, diabetes mellitus in 40.4% and dyslipidaemia in 33.2%. Median LVEF was 54% (41–61). Disease was confined to a single vessel in 52.8% of patients, involved two vessels in 37.6% and three vessels in 9.6%, with left main stem involvement in 8%. The SYNTAX score averaged 16.2 ± 10.7 and the median GRACE

score was 121 (110–132). These data are summarized in Table 1, and the laboratory variables by SYNTAX category in Additional file 1: Table S1.

Tp-e (120 ms [70–120] vs 120 ms [80–120], P = 0.33), Tp-e/QTc (0.26 [0.16–0.28] vs 0.26 [0.19–0.27], P = 0.80), SYNTAX (16.2 ± 10.9 vs 16.3 ± 10.0, P = 0.92) and GRACE (121 [110–133] vs 119 [108–131], P = 0.42) did not differ between men (n = 194) and women (n = 56), although QTc was longer in women (443 ms [434–470] vs 435 ms [418–462], P = 0.001). Six-month adverse events occurred in 35/194 men (18.0%) and 13/56 women (23.2%) (P = 0.44). These comparisons are set out in full in Additional file 1: Table S2.

Interobserver reproducibility

Agreement between the two observers was near-perfect for QTc (ICC 1.00, 95% CI 0.99–1.00) and excellent for Tp-e (0.99, 0.99–1.00) and for Tp-e/QTc (0.99, 0.98–0.99), each coefficient attaining P < 0.001. On Bland–Altman analysis the mean difference between observers was negligible, almost all paired measurements lay within the limits of agreement, and there was no indication that disagreement varied with the magnitude of the measurement (Additional file 1: Table S3 and Figure S4).

Repolarization indices across SYNTAX and GRACE categories

QTc, Tp-e and Tp-e/QTc all rose incrementally across the three SYNTAX categories, every comparison attaining P < 0.001 (Table 2). Median Tp-e measured 80 ms (66–120) in the low category, 120 ms (120–130) in the intermediate category and 150 ms (140–160) in the high category, with Tp-e/QTc rising in parallel from 0.19 to 0.27 and to 0.30 (Additional file 1: Figure S1). As angiographic complexity increased, LVEF declined from 56% to 38% and the GRACE score rose from 111 to 149, while ventricular arrhythmia (3.5% to 17.5%), heart failure (5.9 % to 20.0%), cardiogenic shock (2.9% to 15.0%) and death (1.79% to 15.0%) each became more frequent (P < 0.05 throughout).

Stratification by GRACE risk produced an equivalent gradient: median Tp-e measured 74 ms (64–110), 120 ms (72–120) and 150 ms (140–160) across the low, intermediate and high categories, with Tp-e/QTc at 0.17, 0.26 and 0.30 respectively (P < 0.001; Table 3; Additional file 1: Figure S2).

Correlation analysis and independent predictors of Tp-e/QTc

Tp-e correlated strongly with both risk scores (SYNTAX r = 0.786; GRACE r = 0.645), and Tp-e/QTc only marginally less so (0.716 and 0.595); the two scores were themselves correlated (r = 0.707), with P < 0.001 throughout (Additional file 1: Table S4 and Figure S3). On linear regression, Tp-e accounted for 62%

of the variance in the SYNTAX score ($R^2 = 0.617$) and for 42% of the variance in the GRACE score ($R^2 = 0.416$).

In the multivariable model ($F = 35.0$; $P < 0.001$; $R^2 = 0.541$), the SYNTAX score ($\beta = 0.616$; $P < 0.001$) and the GRACE score ($\beta = 0.167$; $P = 0.008$) were independently associated with Tp-e/QTc, with no material collinearity (Additional file 1: Table S5).

Discriminative performance for high SYNTAX and GRACE scores

Both indices discriminated high anatomical from high clinical risk effectively (Figure 1; Additional file 1: Table S6). For a high SYNTAX score, Tp-e attained an AUC of 0.945 (95% CI 0.909–0.981), marginally exceeding that of Tp-e/QTc at 0.893 (0.835–0.952); for a high GRACE score the corresponding values were 0.924 (0.881–0.968) and 0.906 (0.855–0.957). The Youden index reached its maximum at a Tp-e of 125 ms, which yielded sensitivities of 85.0% and 78.9% with specificities of 88.1% and 90.6% for the SYNTAX and GRACE scores respectively, whereas a Tp-e/QTc of 0.285 achieved greater specificity (93.8% and 93.4%) at the expense of sensitivity.

Kaplan–Meier event-free survival

Over six months, 48 of the 250 patients (19.2%) reached the composite outcome, and cumulative event-free survival diverged markedly by repolarization status (Additional file 1: Table S7). Among patients with QTc prolongation, 33 of 92 (35.9%) sustained an event, compared with 15 of 158 (9.5%) whose QTc was normal, and mean event-free survival fell from 5.61 to 4.85 months (log-rank $\chi^2 = 25.9$; $P < 0.001$; Figure 2A). An equivalent separation was evident for Tp-e/QTc, an event occurring in 37 of 128 patients (28.9%) with an abnormal ratio against 11 of 122 (9.0%) with a normal ratio, mean event-free survival falling from 5.65 to 5.02 months (log-rank $\chi^2 = 15.6$; $P < 0.001$; Figure 2B) — a greater than three-fold difference in event rate. In both analyses the curves had already separated within the first month and continued to diverge thereafter.

Multivariable Cox regression for adverse clinical events

With hypertension, the SYNTAX score, LVEF, serum creatinine and haemoglobin all retained in the model, Tp-e/QTc remained independently associated with the composite outcome (HR 1.111, 95% CI 1.017–1.213; $P = 0.019$), and a higher LVEF remained independently protective (HR 0.948, 95% CI 0.922–0.976; $P < 0.001$). Neither the SYNTAX score nor hypertension, serum creatinine or haemoglobin was independently associated with outcome. The model was highly significant overall (omnibus $\chi^2 = 56.2$; $P < 0.001$) and the proportional hazards assumption was satisfied (Figure 3; Additional file 1: Table S8).

Incremental value over the GRACE score

Incorporation of Tp-e into the GRACE score significantly improved prediction of six-month events, the IDI reaching 0.044 (95% CI 0.008–0.099; P = 0.027) and the continuous NRI 0.235 (95% CI 0.061–0.412; P = 0.020) (Additional file 1: Table S9).

Discussion

In this prospective cohort of 250 patients with ACS, Tp-e and Tp-e/QTc increased in graded fashion alongside both the angiographic complexity of coronary disease and clinical risk, discriminated high-risk from lower-risk categories with considerable accuracy and — in the case of Tp-e/QTc — predicted six-month adverse events after adjustment. The observation of greatest relevance to acute care is that Tp-e conveyed prognostic information beyond the GRACE score, an instrument already embedded within routine early management of ACS.[8] Considered together, these findings identify heterogeneity of ventricular repolarization as a shared electrophysiological correlate of anatomical and of clinical severity, one that may be read directly from the admission electrocardiogram.

A plausible mechanism is well characterized. Because ischaemia is not distributed equally among epicardial, mid-myocardial and endocardial layers, the transmural gradient of repolarization widens, and this widening is closely reflected at the body surface by lengthening of Tp-e.[11, 12] More extensive and more complex atherosclerotic disease enlarges the territory at risk, slows conduction and augments dispersion of recovery, manifesting as a longer Tp-e and a higher Tp-e/QTc — consistent with the concurrent movement of these indices, of LVEF and of event rates across the categories observed here. Relative to QT dispersion, constrained as it is by lead dependence and by limited reproducibility,[22] indices based upon Tp-e represent a more direct and more stable surrogate for transmural dispersion.

These results extend earlier work. Kahraman et al. and Erdoğan et al. reported correlations of Tp-e and Tp-e/QTc with the SYNTAX score that were positive but weaker than those observed here,[23, 24] while Şaylık et al. and Karadeniz et al. documented progressive prolongation of Tp-e as angiographic burden increased.[25, 26] The stronger correlations in the present cohort (r = 0.786 for Tp-e against the SYNTAX score) plausibly reflect a case mix in which STEMI accounted for 77.6% of admissions and in which multivessel and left main involvement were more prevalent, both of which amplify transmural ischaemia. That repolarization abnormality tracked clinical risk and arrhythmic events closely is consistent with the observations of Masuda et al. and of Gayretli Yayla et al., whose cohort of 421 patients likewise related both scores to repolarization indices, though less strongly than here (r = 0.489 and 0.274).[10, 15]

Diagnostic performance exceeded that of most earlier series, in which AUC values for Tp-e-based indices against angiographic severity have generally ranged between 0.72 and 0.84.[24, 26] A Tp-e of 125 ms combined acceptable sensitivity with acceptable specificity for a high score on either instrument, whereas a Tp-e/QTc of 0.285 favoured specificity over sensitivity. The two indices may therefore fulfil complementary roles at the bedside, Tp-e serving to screen and Tp-e/QTc to confirm high risk with fewer

false-positive classifications. Since these estimates derive from a single centre carrying an unusually high STEMI burden, external validation is required before any threshold is adopted in clinical practice.

The prognostic signal carries clinical relevance. Prolonged Tp-e has been linked to sudden cardiac death in the general population,[14] and an elevated Tp-e/QTc to malignant arrhythmia across both ischaemic and inherited syndromes.[12, 13] In the present cohort the Kaplan–Meier curves separated early and remained separated: QTc prolongation was associated with the loss of approximately three-quarters of a month of mean event-free survival across the six-month period, and an abnormal Tp-e/QTc identified patients whose event rate exceeded three times that of their counterparts (28.9% versus 9.0%). Because separation occurred within the first month, the greater part of the excess hazard accrued while monitoring intensity and the timing of revascularization remained modifiable. The association survived multivariable adjustment, Tp-e/QTc and LVEF alone predicting the composite outcome independently. That the SYNTAX score forfeited significance once these two variables entered the model suggests anatomical complexity operates largely through the electrical and mechanical consequences of ischaemia rather than independently of them, echoing reports that Tp-e-based indices identify residual risk once reperfusion has been achieved.[27–30]

The incremental contribution of any candidate marker to established scoring constitutes the practical test of its value. Incorporation of Tp-e into the GRACE score produced a significant IDI (0.044) and continuous NRI (0.235), implying that repolarization indices register an arrhythmic substrate not fully captured by the clinical variables within the GRACE model, and that their proper role is to refine rather than to displace established scores. Both indices are obtained at no additional cost from an electrocardiogram recorded as a matter of routine, which recommends them particularly in resource-limited settings where coronary disease presents early and diffusely.[16, 17]

Reproducibility represents the customary objection to manually measured repolarization indices, the terminal portion of the T wave being difficult to define with precision. In this study agreement between two independent observers was near-perfect for QTc and excellent for both Tp-e-based indices, with all coefficients ≥ 0.99 and negligible mean bias on Bland–Altman analysis. The absence of systematic error renders measurement error an improbable explanation for these associations and supports dependable bedside acquisition, provided that recording speed, lead selection and averaging across consecutive cycles are standardized.

Limitations

A single-centre observational design and follow-up restricted to six months limit generalizability and preclude assessment of longer-term outcome; the cohort was additionally weighted towards STEMI. The composite outcome combined arrhythmic with haemodynamic events, and the modest number of events (n = 48) constrained the number of covariates that the Cox model could accommodate, so that residual confounding cannot be excluded. The IDI and NRI were derived and tested within the same cohort, without external validation. Manual measurement of Tp-e remains operator-dependent whatever

level of agreement is achieved, standardized thresholds are not yet established, and repolarization was assessed at a single time point, without serial recordings or imaging correlates such as cardiac magnetic resonance.

Conclusion

In patients with acute coronary syndrome, the Tp-e interval and the Tp-e/QTc ratio increase in parallel with both the angiographic complexity of coronary disease and clinical risk, and both discriminate high SYNTAX and high GRACE scores with excellent accuracy. Six-month event-free survival was significantly lower in the presence of QTc prolongation or of an abnormal Tp-e/QTc ratio, and multivariable Cox regression confirmed Tp-e/QTc as an independent predictor of adverse events alongside LVEF. Measurements proved highly reproducible between independent observers (all ICC ≥ 0.99), and Tp-e conferred significant incremental prognostic value over the GRACE score. As inexpensive and universally available indices derived from a routine admission electrocardiogram, both may serve as adjuncts to established risk scores during early risk stratification. Prospective multicentre studies employing standardized measurement and longer follow-up are warranted.

Declarations

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Consent for publication. Each participant provided written informed consent both to participation and to publication of de-identified data. No individual participant is identifiable within this report.

Availability of data and materials. The data underlying this article will be shared on reasonable request to the corresponding author.

Authors' contributions

Santoshi Shamad: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing – original draft. Sura Kishore Mishra: Conceptualization, Methodology, Supervision, Writing – review and editing. Pankaj Kumar Maravi: Investigation, Resources, Writing – review and editing. Siddharth Pradhan: Investigation, Data curation, Writing – review and editing. All authors approved the final version and agree to be accountable for all aspects of the work.

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Tables

Table 1. Baseline characteristics of the study population (n = 250)

Variable	Value
Age, years	59 (51–65)
Male sex	194 (77.6)
Hypertension	120 (48.0)
Diabetes mellitus	101 (40.4)
Smoking	103 (41.2)
Dyslipidaemia	83 (33.2)
Haemoglobin, g/dL	12.2 (11.1–13.7)
Serum creatinine, mg/dL	0.80 (0.60–0.90)
LDL cholesterol, mg/dL	118 (88–138.5)
STEMI / NSTEMI / unstable angina, %	77.6 / 21.2 / 1.2
QTc, ms	438 (420–464)
Tp-e, ms	120 (72–120)
Tp-e/QTc	0.26 (0.17–0.27)
LVEF, %	54 (41–61)
GRACE score	121 (110–132)
SYNTAX score, mean ± SD	16.2 ± 10.7
Single / double / triple-vessel disease, %	52.8 / 37.6 / 9.6
Left main disease	20 (8.0)
Ventricular arrhythmia	17 (6.8)
Heart failure	23 (9.2)
Cardiogenic shock	14 (5.6)
Sudden cardiac death	13 (5.2)

Continuous variables are median (interquartile range) unless otherwise indicated; categorical variables are n (%). LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; NSTEMI, non–ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction. Abbreviations apply to all subsequent tables.

Table 2. Repolarization, echocardiographic, angiographic and outcome variables by SYNTAX category

Variable	Low (≤ 22) n = 167	Intermediate (23–32) n = 43	High (≥ 33) n = 40	P
Age, years	56 (50–64)	61 (55–67)	60 (54–71)	0.007
QTc, ms	424 (416–440)	456 (438–470)	495 (480–500)	<0.001
Tp-e, ms	80 (66–120)	120 (120–130)	150 (140–160)	<0.001
Tp-e/QTc	0.19 (0.16–0.26)	0.27 (0.27–0.27)	0.30 (0.28–0.31)	<0.001
LVEF, %	56 (44–63)	54 (40–60)	38 (34–54)	<0.001
GRACE score	111 (106–122)	133 (130–138)	149 (129–151)	<0.05
Diseased vessels, n	1.32 ± 0.49	1.82 ± 0.68	2.30 ± 0.60	<0.001
Left main disease, %	8(4.8%)	4(9.3%)	8(20.0%)	<0.05
Ventricular arrhythmia, %	6(3.5%)	4(9.3%)	7(17.5%)	<0.05
Heart failure, %	10(5.9%)	5(11.62%)	8(20.0%)	<0.05
Cardiogenic shock, %	5(2.9)	3(6.9%)	6(15.0%)	<0.05
Death, %	3(1.79%)	4(9.3%)	6(15.0%)	<0.05

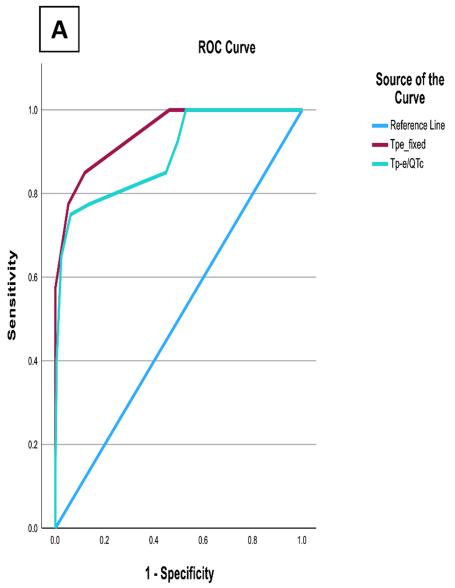
Values are median (interquartile range), mean ± SD or percentage.

Table 3. Ventricular repolarization indices by GRACE risk category

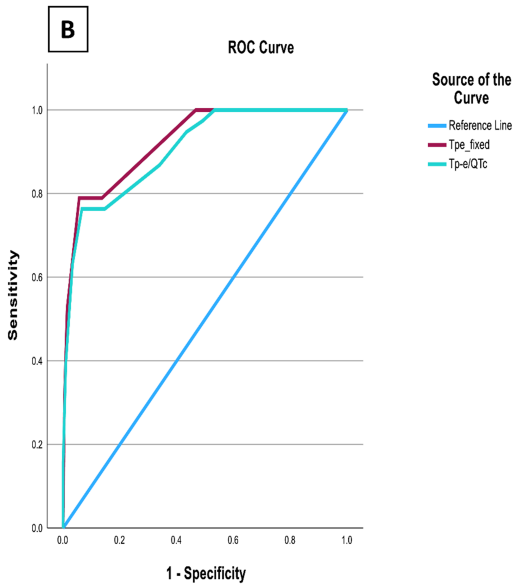
Variable	Low (< 109)	Intermediate (109–140)	High (> 140)	P
Tp-e, ms	74 (64–110)	120 (72–120)	150 (140–160)	<0.001
Tp-e/QTc	0.17 (0.15–0.24)	0.26 (0.17–0.27)	0.30 (0.28–0.31)	<0.001

Values are median (interquartile range); Kruskal–Wallis test.

Figures



ROC Curve for prediction of high SYNTAX score



ROC Curve for prediction of high GRACE score

Figure 1

Receiver-operating-characteristic curves for the Tp-e interval and Tp-e/QTc ratio. (A) Identification of a high SYNTAX score (≥ 33): AUC 0.945 (95% CI 0.909–0.981) for Tp-e and 0.893 (0.835–0.952) for Tp-e/QTc. (B) Identification of a high GRACE score (> 140): AUC 0.924 (0.881–0.968) and 0.906 (0.855–0.957) respectively. The diagonal reference line denotes absence of discrimination. The Youden index reached its maximum at 125 ms and at 0.285; P < 0.001 throughout.

Alt text: Two plots of sensitivity against one minus specificity. In both panels the curves for the interval and the ratio bend steeply towards the top left corner, well clear of the diagonal, the curve for the interval lying a little above the other.

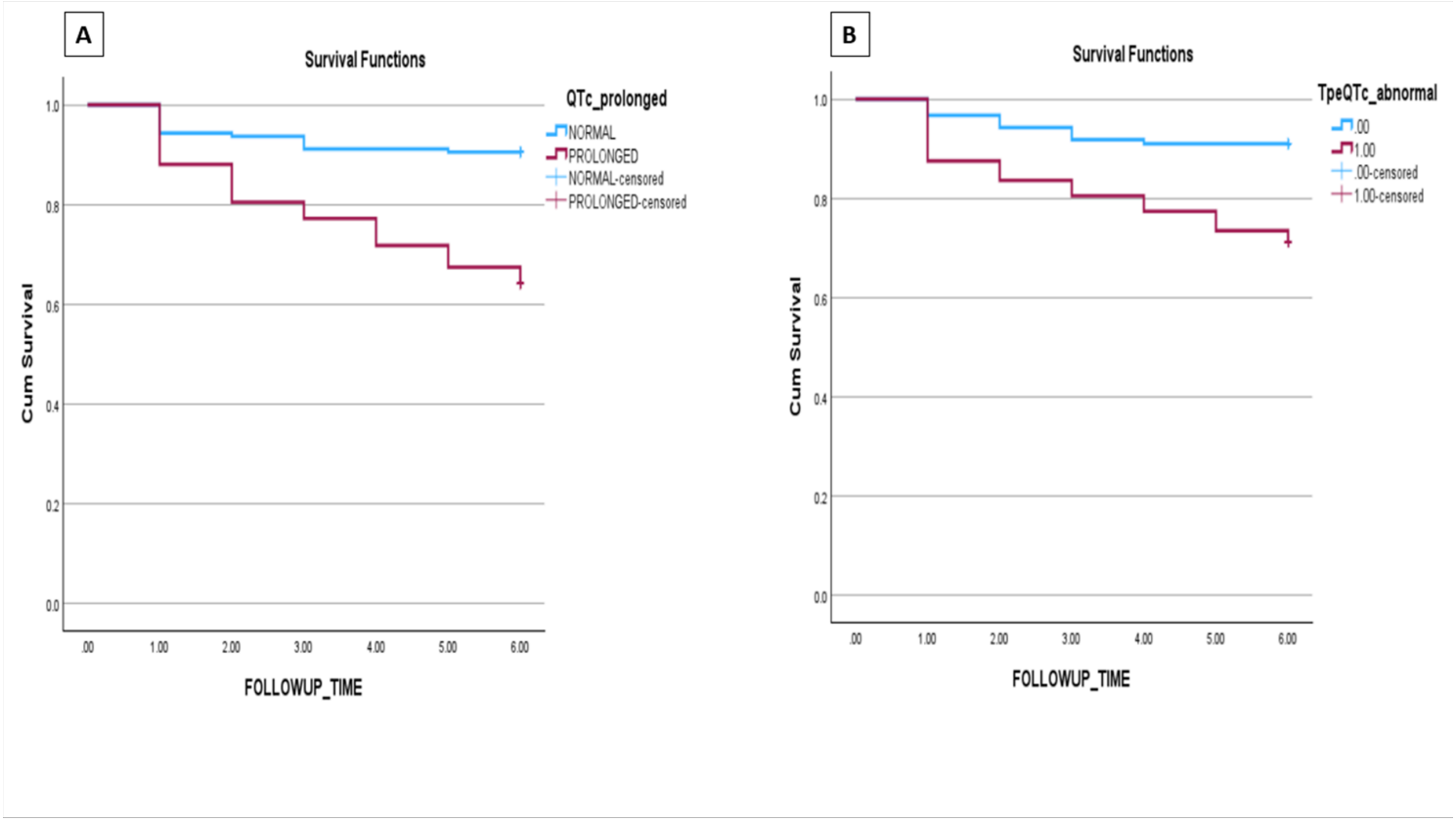


Figure 2

Kaplan–Meier curves for freedom from the six-month composite outcome defined in the Methods. (A) Patients dichotomized by QTc prolongation (prolonged, n = 92; normal, n = 158): log-rank $\chi^2 = 25.9$, $P < 0.001$. (B) Patients dichotomized by Tp-e/QTc abnormality (abnormal, n = 128; normal, n = 122): log-rank $\chi^2 = 15.6$, $P < 0.001$. Crosses denote censored observations; follow-up in months is plotted on the abscissa and cumulative event-free survival on the ordinate.

Alt text: Two Kaplan–Meier plots spanning six months. In each panel the curve for patients with a prolonged QTc interval (panel A) or an abnormal ratio (panel B) descends more steeply and pulls away from the curve for patients with normal values within the first month, the gap widening until follow-up ends.

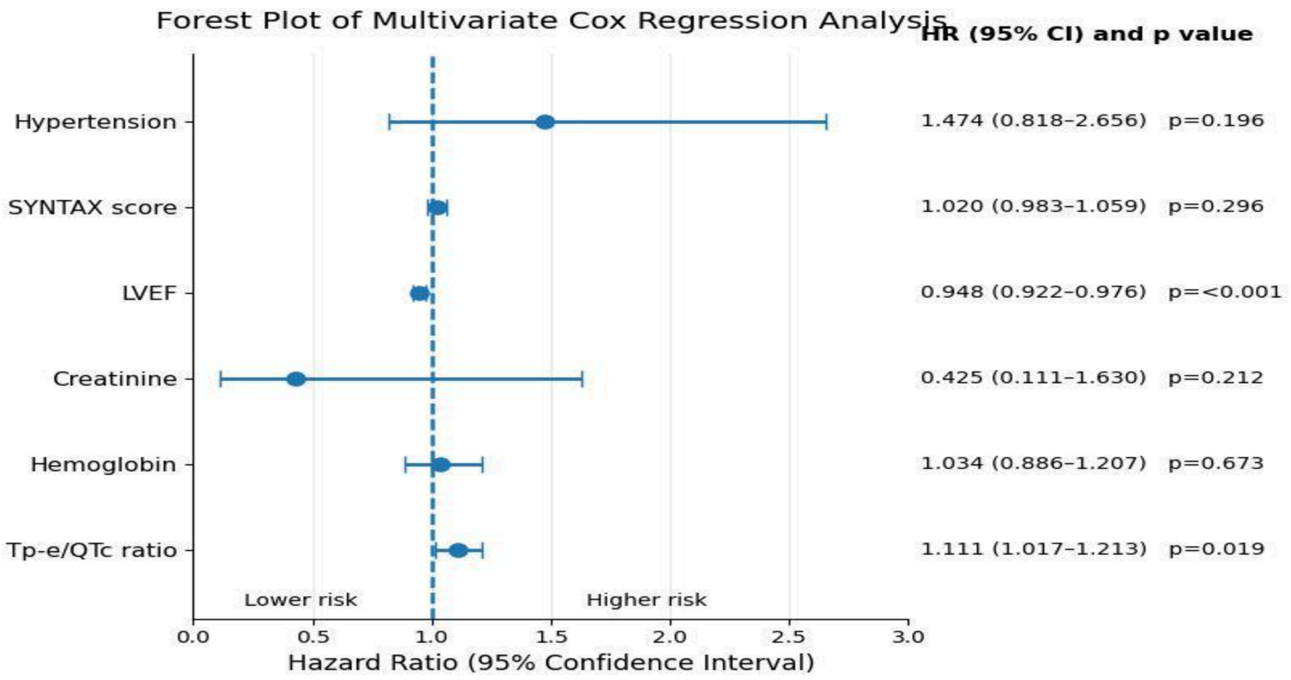


Figure 3

Forest plot of the multivariable Cox proportional hazards model for predictors of six-month adverse clinical events. Squares denote the hazard ratio and horizontal bars the 95% CI for each covariate; the vertical dashed line marks unity, values to its right indicating higher risk. Tp-e/QTc (HR 1.111, 95% CI 1.017–1.213; P = 0.019) and LVEF (HR 0.948, 95% CI 0.922–0.976; P < 0.001) were the only independent predictors. Omnibus χ^2 for the model = 56.2, P < 0.001.

Alt text: Forest plot listing hypertension, SYNTAX score, ejection fraction, creatinine, haemoglobin and Tp-e/QTc, each with a hazard ratio marker and interval bars. The interval for Tp-e/QTc lies wholly to the right of the line of no effect and that for ejection fraction wholly to its left; every other interval crosses it.

Supplementary Files

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- SupplementaryFigureS4.tiff