Research Article

Neutrophil-to-lymphocyte ratio and corrected QT interval in acute coronary syndrome: a cross-sectional study from South India

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Credit authorship contribution statement
Mantri Srikar: Conceptualization, Investigation, Data curation, Formal analysis, Writing – original draft. Athulya G Asokan: Conceptualization, Methodology, Supervision, Writing – review & editing. Jacob Cyriac: Supervision, Validation, Writing – review & editing.

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Abstract

Background: Systemic inflammation may prolong ventricular repolarisation, but its relationship with the corrected QT interval (QTc) in acute coronary syndrome (ACS) is poorly defined. We examined the association between the neutrophil-to-lymphocyte ratio (NLR) and QTc across ACS subtypes.

Methods: In this cross-sectional study, 112 adults with ACS admitted to a tertiary care centre in South India between June 2023 and June 2024 had a complete blood count and 12-lead electrocardiogram before anticoagulation, thrombolysis or revascularisation. QTc was calculated with Bazett's formula. Associations were assessed with Pearson and partial correlation and multiple linear regression.

Results: Patients had ST-elevation myocardial infarction (STEMI, n=53), non-ST-elevation myocardial infarction (NSTEMI, n=37) or unstable angina (UA, n=22); mean age was 58.7±7.4 years and 77% were men. QTc correlated with NLR overall (r=0.51, 95% CI 0.36–0.64) and after accounting for ACS subtype (partial r=0.55, 95% CI 0.41–0.67; both p<0.001). After adjustment for age, sex and subtype, each unit increase in NLR was associated with a 13.2 ms (95% CI 9.3–17.1) longer QTc. The association was steepest in STEMI (21.0 ms per unit; interaction p<0.001). QTc prolongation occurred only in STEMI (21/53, 39.6%), and these patients had a higher NLR than STEMI patients with normal QTc (5.30 vs 4.47, p<0.001).

Conclusions: Admission NLR was independently associated with QTc in ACS, most strongly in STEMI. Prospective studies should test whether combining the two markers improves arrhythmic risk stratification.

Keywords: Acute coronary syndrome; Neutrophil-to-lymphocyte ratio; QT interval; Inflammation; Myocardial infarction; Electrocardiography

1. Introduction

Acute coronary syndrome (ACS) comprises ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA), all resulting from an abrupt reduction in coronary blood flow [1]. It remains a leading cause of death worldwide, and India carries a disproportionate share of this burden, with coronary disease presenting nearly a decade earlier than in Western populations [2]. Simple and inexpensive tools for early risk stratification are therefore of particular value in Indian practice.

Inflammation is central to every stage of coronary atherothrombosis, from plaque formation and rupture to the myocardial response to necrosis [3,4]. The neutrophil-to-lymphocyte ratio (NLR), derived from a routine complete blood count, integrates two opposing arms of the immune response: neutrophilia, reflecting acute inflammation and catecholamine release, and relative lymphopenia, reflecting physiological stress and cortisol excess. An elevated admission NLR has been associated with mortality, lesion complexity and major adverse cardiac events across the ACS spectrum [5–7].

The corrected QT interval (QTc) reflects the duration of ventricular depolarisation and repolarisation, and its prolongation increases susceptibility to polymorphic ventricular tachycardia and sudden cardiac death. In ACS, QTc prolongation is common and carries prognostic significance [8]. QTc lengthens early during transmural ischaemia and correlates with the severity of the underlying ischaemic burden [9,10].

A growing body of evidence suggests that inflammation itself prolongs ventricular repolarisation. Inflammatory cytokines such as interleukin-6, tumour necrosis factor-α and interleukin-1 modulate cardiomyocyte potassium and calcium currents, prolonging the action potential [11], and systemic inflammation has been identified as an independent QT-prolonging risk factor in patients with torsades de pointes [12]. If inflammation contributes to repolarisation abnormality in ACS, NLR and QTc may carry related rather than independent prognostic information.

Few studies have examined this relationship. A retrospective study of 649 Turkish patients with ACS reported a weak positive correlation between NLR and QTc [13], but did not examine whether the association held within individual ACS subtypes or was explained by differences between them. No comparable data are available from India.

We therefore assessed the association between admission NLR and QTc in patients with ACS, determined whether it persisted after accounting for ACS subtype, age and sex, and compared both parameters across STEMI, NSTEMI and UA.

2. Methods

2.1. Study design and setting

This hospital-based cross-sectional study was conducted in the Departments of General Medicine and Cardiology and the Coronary Care Unit of Government Medical College, Kottayam, Kerala, India, from June 2023 to June 2024. It is reported according to the STROBE statement for observational studies [14]. The study was approved by the Institutional Ethics Committee (approval no. 217/23, dated 27 June 2023), and written informed consent was obtained from all participants in English or Malayalam. The study was conducted in accordance with the Declaration of Helsinki.

2.2. Participants

Patients aged over 18 years admitted with ACS during the study period were enrolled. ACS was diagnosed according to the Fourth Universal Definition of Myocardial Infarction [15]; troponin I was considered positive when it exceeded the 99th percentile upper reference limit of the assay. STEMI was defined as ischaemic chest pain lasting more than 10 min with ST-segment elevation, reciprocal changes and a positive troponin I. NSTEMI was defined as ischaemic chest pain lasting more than 10 min with ST-segment depression or T-wave inversion and a positive troponin I. UA was defined as rest chest pain lasting more than 10 min with ST-segment depression or T-wave inversion and a negative troponin I.

Patients were excluded if they had conditions likely to alter leukocyte counts or the QT interval independently of ACS: chronic infection (tuberculosis, hepatitis B or C, human immunodeficiency virus, syphilis), sepsis, haematological malignancy or blood dyscrasia, autoimmune or rheumatological disease, and current use of corticosteroids, immunosuppressants or chemotherapy. Patients were also excluded if they had atrial fibrillation, bundle branch block, paced rhythm or complete atrioventricular block; advanced valvular heart disease, cardiomyopathy, congenital heart disease or an implantable cardioverter-defibrillator; current use of antidepressants, antipsychotics, antiarrhythmics or other QT-prolonging drugs; or abnormal serum potassium or calcium.

2.3. Sample size

The sample size was calculated with G*Power software [16]. Assuming a moderate correlation coefficient of 0.3 between QTc and NLR [17], chosen as the smallest association considered clinically meaningful, with a two-sided α of 0.05 and power of 90%, the required sample was 112 patients.

2.4. Data collection and measurements

Demographic details, comorbidities and cardiac troponin I were recorded on a structured proforma. A venous blood sample for complete blood count was drawn at admission, before heparin, thrombolysis or percutaneous coronary intervention, and analysed on an automated haematology analyser using the impedance principle (Sysmex Corporation, Kobe, Japan). NLR was calculated as the absolute neutrophil count divided by the absolute lymphocyte count.

A standard 12-lead electrocardiogram (ECG) was recorded at admission, before any intervention, at a paper speed of 25 mm/s. The QT interval was measured manually from the onset of the QRS complex to the end of the T wave in lead V2, and QTc was calculated using Bazett's formula ($QTc = QT/\sqrt{RR}$) [18]. QTc was considered prolonged when it exceeded 450 ms in men or 460 ms in women [19].

Patients with STEMI underwent two-dimensional transthoracic echocardiography by a cardiologist (Siemens Healthineers, Erlangen, Germany); echocardiography was also performed in one patient with NSTEMI and one with UA. Left ventricular ejection fraction (LVEF) was categorised as normal (50–70%), mildly reduced (40–49%), moderately reduced (30–39%) or severely reduced (<30%) [20]. All patients with STEMI and one patient with NSTEMI underwent percutaneous transluminal coronary angioplasty; the remaining patients were managed medically.

2.5. Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) and categorical variables as number (percentage). Normality was assessed with the Shapiro–Wilk test. Baseline characteristics were compared across subtypes with one-way analysis of variance (ANOVA) or the chi-square test. QTc and NLR were compared across subtypes with one-way ANOVA, with eta-squared (η^2) as the effect size, followed by the Tukey–Kramer test for pairwise comparisons.

The association between QTc and NLR was assessed with Pearson's correlation coefficient (r), with 95% confidence intervals (CI) from Fisher's z-transformation, and confirmed with Spearman's rank correlation (ρ) because QTc was not normally distributed in some subgroups. To determine whether the association was explained by differences between subtypes, we calculated the partial correlation between QTc and NLR controlling for ACS subtype. Multiple linear regression was performed with QTc as the dependent variable and NLR, age, sex and ACS subtype (UA as reference) as independent variables; collinearity was assessed with variance inflation factors (VIF) and residual normality with the Shapiro–Wilk test. Effect modification by subtype was tested by adding NLR × subtype interaction terms. NLR was compared between patients with and without prolonged QTc using the independent-samples t-test.

Analyses were performed with NCSS 2024 (NCSS LLC, Kaysville, UT, USA); confidence intervals, partial correlation, interaction and collinearity diagnostics were computed with SciPy in Python 3. A two-sided $p<0.05$ was considered statistically significant.

3. Results

3.1. Baseline characteristics

A total of 112 patients were included: 53 (47.3%) with STEMI, 37 (33.0%) with NSTEMI and 22 (19.6%) with UA. The mean age was 58.7 ± 7.4 years (range 40–75) and 86 (76.8%) were men. Dyslipidaemia (78.6%), type 2 diabetes mellitus (69.6%) and hypertension (67.0%) were the most frequent comorbidities. Patients with STEMI were younger than those with NSTEMI or UA, and were more often smokers and more often had chronic obstructive pulmonary disease (Table 1). Among patients with STEMI, LVEF was normal in 4 (7.5%) and mildly, moderately and severely reduced in 15 (28.3%), 15 (28.3%) and 19 (35.8%), respectively; NLR did not differ significantly across LVEF categories (ρ=0.10, p=0.45).

3.2. QTc and NLR across ACS subtypes

The mean QTc of the cohort was 419.4 ± 26.7 ms and the mean NLR was 4.58 ± 0.77. QTc differed markedly across subtypes (F=104.3, η^2=0.66, $p<0.001$): it was longer in STEMI (442.2 ± 21.2 ms) than in NSTEMI (400.5 ± 8.8 ms) or UA (396.6 ± 7.1 ms), which did not differ from each other (Table 2). QTc was prolonged in 21 patients (18.8%), all of whom had STEMI (21/53, 39.6%). NLR also differed across subtypes (F=22.2, η^2=0.29, $p<0.001$): it was similar in STEMI and NSTEMI (4.80 ± 0.68 vs 4.77 ± 0.56, p=0.95) and lower in UA (3.74 ± 0.76; $p<0.001$ vs both) (Table 2, Fig. 1).

3.3. Correlation between QTc and NLR

QTc correlated positively with NLR in the whole cohort (r=0.51, 95% CI 0.36–0.64, $p<0.001$) and in each subtype (Table 3, Fig. 2). The correlation was strongest in STEMI (r=0.67, 95% CI 0.49–0.80), followed by UA (r=0.58, 95% CI 0.21–0.81) and NSTEMI (r=0.34, 95% CI 0.01–0.59). Spearman coefficients were consistent. After controlling for ACS subtype, the partial correlation between QTc and NLR was 0.55 (95% CI 0.41–0.67, $p<0.001$).

Among patients with STEMI, those with prolonged QTc had a higher NLR than those with normal QTc (5.30 ± 0.69 vs 4.47 ± 0.43, $p<0.001$).

3.4. Multivariable analysis

On multiple linear regression, NLR remained independently associated with QTc after adjustment for age, sex and ACS subtype: each unit increase in NLR was associated with a 13.2 ms longer QTc (95% CI 9.3–17.1, $p<0.001$; standardised β=0.38) (Table 4). STEMI was also independently associated with longer QTc (β=31.7 ms vs UA, $p<0.001$), whereas age and sex were not. The model explained 76% of the variance in QTc (adjusted R^2=0.75). All VIFs were below 3 and residuals were normally distributed (Shapiro–Wilk p=0.53). The NLR × subtype interaction was significant ($p<0.001$): the slope of QTc on NLR was 21.0 ms per unit (95% CI 14.6–27.4) in STEMI, compared with 5.3 ms (95% CI 0.4–10.2) in NSTEMI and 5.4 ms (95% CI 2.1–8.7) in UA (Table 3).

4. Discussion

In this cross-sectional study of 112 patients with ACS, admission NLR was positively associated with QTc. The association was present in each ACS subtype, persisted after accounting for differences between subtypes and after adjustment for age and sex, and was steepest in STEMI. QTc prolongation occurred only in STEMI, and within that group it was accompanied by a higher NLR. These findings support the hypothesis that systemic inflammation and ventricular repolarisation abnormality are linked in ACS.

The demographic profile of our cohort, with a mean age of 58.7 years and 77% men, is comparable to that of other ACS series [13,21] and to an urban Indian cohort [22]. Dyslipidaemia, diabetes and hypertension were common, as in other ACS cohorts [21,22]. Smoking and chronic obstructive pulmonary disease were concentrated among patients with STEMI, consistent with the established role of smoking as a trigger of acute plaque rupture and thrombosis.

The mean NLR of 4.58 is comparable to the 4.11 reported by İnci and Erat [13]. NLR was similar in STEMI and NSTEMI and lower in UA. This pattern is biologically plausible, because myocardial necrosis, present in both forms of infarction but absent in UA, is a potent stimulus for neutrophil mobilisation and stress-related lymphopenia. Previous studies have associated higher admission NLR with greater infarct burden, lower LVEF and higher mortality [5,6,23]. In our STEMI subgroup, NLR did not differ across LVEF categories; this may reflect small numbers within each category and the timing of echocardiography relative to revascularisation.

QTc was substantially longer in STEMI than in NSTEMI or UA, which did not differ from each other. This agrees with reports that QTc lengthens uniformly during early transmural ischaemia [9] and that admission QTc reflects the extent of the underlying ischaemia [10]. Proposed mechanisms include heterogeneous changes in action potential duration between ischaemic and adjacent myocardium and increased sympathetic activation, although these were not examined in the present study. The shorter QTc in NSTEMI and UA is consistent with the smaller, subendocardial ischaemic territory in these conditions.

The central finding of this study is the association between NLR and QTc. İnci and Erat reported a similar positive association in a retrospective cohort of 649 patients, although the correlation was weak (r=0.10–0.20) [13]. Because both NLR and QTc differ between ACS subtypes, a pooled correlation could simply reflect case mix. Our partial correlation (0.55) and regression analyses show that this was not the case: the association persisted within subtypes and after adjustment. Our stronger association may also reflect the exclusion of patients with conditions that independently affect leukocyte counts or the QT interval, and sampling of both measurements before any intervention.

Several mechanisms may underlie this relationship. Pro-inflammatory cytokines, particularly interleukin-6, tumour necrosis factor-α and interleukin-1, inhibit delayed-rectifier potassium currents and enhance L-type calcium current in cardiomyocytes, both of which prolong the ventricular action potential [11]. Inflammation also increases sympathetic tone, and the catecholamine surge of ACS simultaneously raises neutrophil counts and alters repolarisation. Systemic inflammation has been identified as an independent risk factor for QT prolongation and torsades de pointes [12]; our data extend this observation to ACS.

The steeper slope in STEMI, where myocardial necrosis is greatest, suggests that the inflammatory response to transmural injury and its effect on repolarisation are most closely coupled in this setting. The association was nonetheless also present in UA, despite the absence of necrosis and the narrow range of QTc values in that group, suggesting that low-grade inflammation associated with an unstable plaque may itself influence repolarisation.

These findings have potential clinical relevance. Both markers are available at admission from routine, inexpensive tests. A patient with a high NLR and a prolonged QTc may represent a phenotype at higher arrhythmic risk, in whom closer rhythm monitoring and avoidance of QT-prolonging drugs would be prudent [19]. NLR has already been combined with established risk scores to improve prediction of in-hospital events [24]; whether adding QTc further improves risk stratification requires prospective evaluation against clinical outcomes.

4.1. Strengths and limitations

Strengths of this study include prospective enrolment with blood sampling and ECG recording before any intervention, broad exclusion of conditions and drugs that independently affect leukocyte counts or the QT interval, and analyses that separate the within-subtype association from differences between subtypes.

Several limitations should be acknowledged. This was a single-centre cross-sectional study, so causality cannot be inferred, and no clinical outcomes such as arrhythmia or mortality were assessed. The subgroups were unequal, with relatively few patients with UA. QTc was calculated with Bazett's formula, which overcorrects at high heart rates; because heart rate was not included in the analysis, residual confounding by heart rate, which may rise with both inflammation and infarct size, cannot be excluded. QTc values in NSTEMI and UA fell within a narrow range, which limits the precision of subtype-specific estimates. QT was measured manually and inter-observer variability was not assessed. Other inflammatory markers, such as high-sensitivity C-reactive protein, and infarct size were not measured. Finally, residual confounding by unmeasured factors, including prior medications and smoking intensity, cannot be excluded.

5. Conclusions

In patients with ACS, admission NLR was positively and independently associated with QTc, and the association persisted within subtypes. It was strongest in STEMI, where all cases of QTc prolongation occurred. These

findings link systemic inflammation with ventricular repolarisation abnormality in ACS. Because both markers come from routine admission tests, their combined value for predicting arrhythmia and mortality merits evaluation in prospective, multicentre studies.

Ethics statement

The study was approved by the Institutional Ethics Committee of Government Medical College, Kottayam (approval no. 217/23). Written informed consent was obtained from all participants.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The de-identified data that support the findings of this study are available from the corresponding author on reasonable request.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used Claude (Anthropic) to restructure the dissertation into manuscript format, edit the language and perform supplementary statistical calculations from the study data. No images were generated or altered by AI; the figures are direct plots of the study data. All study design, data collection and clinical interpretation were carried out by the authors. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Table 1 Baseline characteristics of the study population by acute coronary syndrome subtype

Characteristic	All (n=112)	STEMI (n=53)	NSTEMI (n=37)	UA (n=22)	p
Age (years)	58.7 ± 7.4	56.1 ± 5.9	61.6 ± 6.6	60.1 ± 9.9	0.001
Male sex	86 (76.8)	44 (83.0)	29 (78.4)	13 (59.1)	0.079
Weight (kg)	68.4 ± 9.4	70.5 ± 8.7	66.8 ± 10.6	66.1 ± 7.8	0.083
Dyslipidaemia	88 (78.6)	39 (73.6)	30 (81.1)	19 (86.4)	0.424
Type 2 diabetes mellitus	78 (69.6)	43 (81.1)	23 (62.2)	12 (54.5)	0.036
Hypertension	75 (67.0)	39 (73.6)	25 (67.6)	11 (50.0)	0.141
Current smoking	39 (34.8)	30 (56.6)	8 (21.6)	1 (4.5)	<0.001
COPD	37 (33.0)	29 (54.7)	7 (18.9)	1 (4.5)	<0.001
Hypothyroidism	28 (25.0)	18 (34.0)	4 (10.8)	6 (27.3)	0.043
Previous stroke	25 (22.3)	10 (18.9)	10 (27.0)	5 (22.7)	0.657

Values are mean ± SD or n (%). Continuous variables compared with one-way ANOVA and categorical variables with the chi-square test. COPD, chronic obstructive pulmonary disease; NSTEMI, non-ST-elevation myocardial infarction; SD, standard deviation; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

Table 2 Corrected QT interval and neutrophil-to-lymphocyte ratio across acute coronary syndrome subtypes

Variable	STEMI (n=53)	NSTEMI (n=37)	UA (n=22)	F (η^2)	p
QTc (ms)	442.2 ± 21.2	400.5 ± 8.8	396.6 ± 7.1	104.3 (0.66)	<0.001
NLR	4.80 ± 0.68	4.77 ± 0.56	3.74 ± 0.76	22.2 (0.29)	<0.001
Prolonged QTc, n (%)	21 (39.6)	0 (0)	0 (0)	–	–

Values are mean ± SD unless stated; F and p from one-way ANOVA. Tukey–Kramer pairwise p-values for QTc: STEMI vs NSTEMI <0.001, STEMI vs UA <0.001, NSTEMI vs UA 0.642; for NLR: STEMI vs NSTEMI 0.954, STEMI vs

UA <0.001, NSTEMI vs UA <0.001. Prolonged QTc was defined as >450 ms in men and >460 ms in women. NLR, neutrophil-to-lymphocyte ratio; QTc, corrected QT interval; η², eta-squared; other abbreviations as in Table 1.

Table 3 Correlation between corrected QT interval and neutrophil-to-lymphocyte ratio

Group	n	Pearson r (95% CI)	p	Spearman ρ	p	Slope, ms per unit NLR (95% CI)
All ACS	112	0.51 (0.36–0.64)	<0.001	0.48	<0.001	17.7 (12.1–23.3)
STEMI	53	0.67 (0.49–0.80)	<0.001	0.70	<0.001	21.0 (14.6–27.4)
NSTEMI	37	0.34 (0.01–0.59)	0.042	0.51	0.001	5.3 (0.4–10.2)
UA	22	0.58 (0.21–0.81)	0.005	0.54	0.010	5.4 (2.1–8.7)
All ACS, partial*	112	0.55 (0.41–0.67)	<0.001	–	–	–

*Partial correlation controlling for ACS subtype. Slopes are from unadjusted linear regression of QTc on NLR. NLR × subtype interaction p<0.001. CI, confidence interval; other abbreviations as in Tables 1 and 2.

Table 4 Multiple linear regression of corrected QT interval on neutrophil-to-lymphocyte ratio and covariates

Variable	β (ms)	95% CI	p	VIF
NLR (per unit)	13.21	9.34 to 17.08	<0.001	1.42
Age (per year)	−0.04	−0.40 to 0.32	0.844	1.14
Male sex	−1.23	−7.32 to 4.86	0.689	1.06
STEMI (vs UA)	31.73	23.53 to 39.93	<0.001	2.68
NSTEMI (vs UA)	−9.44	−17.74 to −1.14	0.026	2.44

Dependent variable: QTc (ms). $R^2 = 0.76$; adjusted $R^2 = 0.75$. Standardised β for NLR = 0.38. β, unstandardised regression coefficient; VIF, variance inflation factor; other abbreviations as in Tables 1–3.

Figure legends

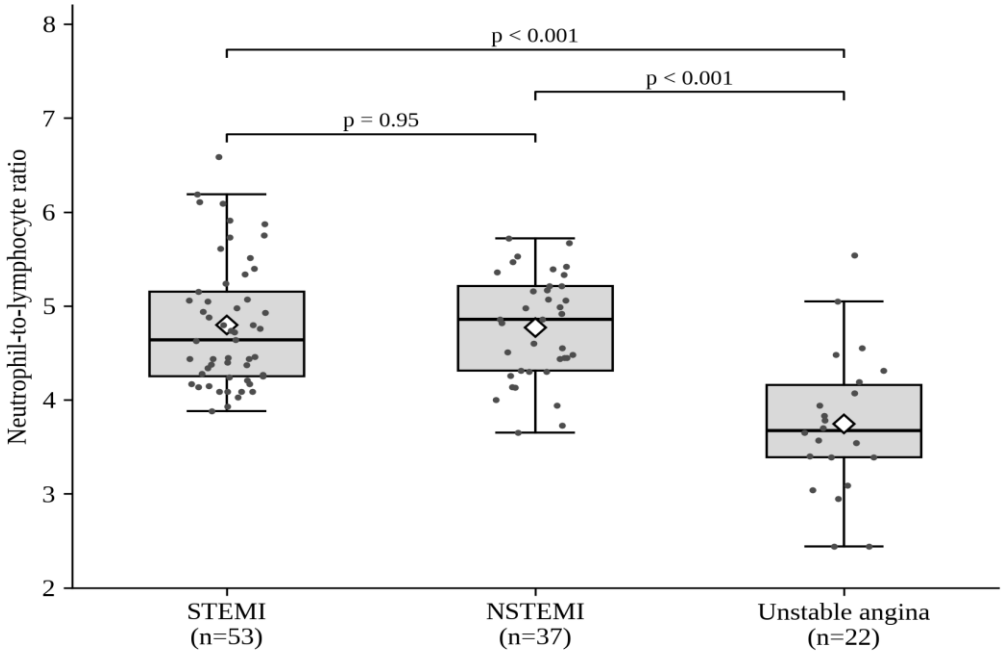


Fig. 1. Neutrophil-to-lymphocyte ratio (NLR) by acute coronary syndrome subtype. Boxes show the median and interquartile range, whiskers extend to 1.5 times the interquartile range, diamonds mark the mean and dots show individual patients. p-values are from the Tukey–Kramer post hoc test. STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction.

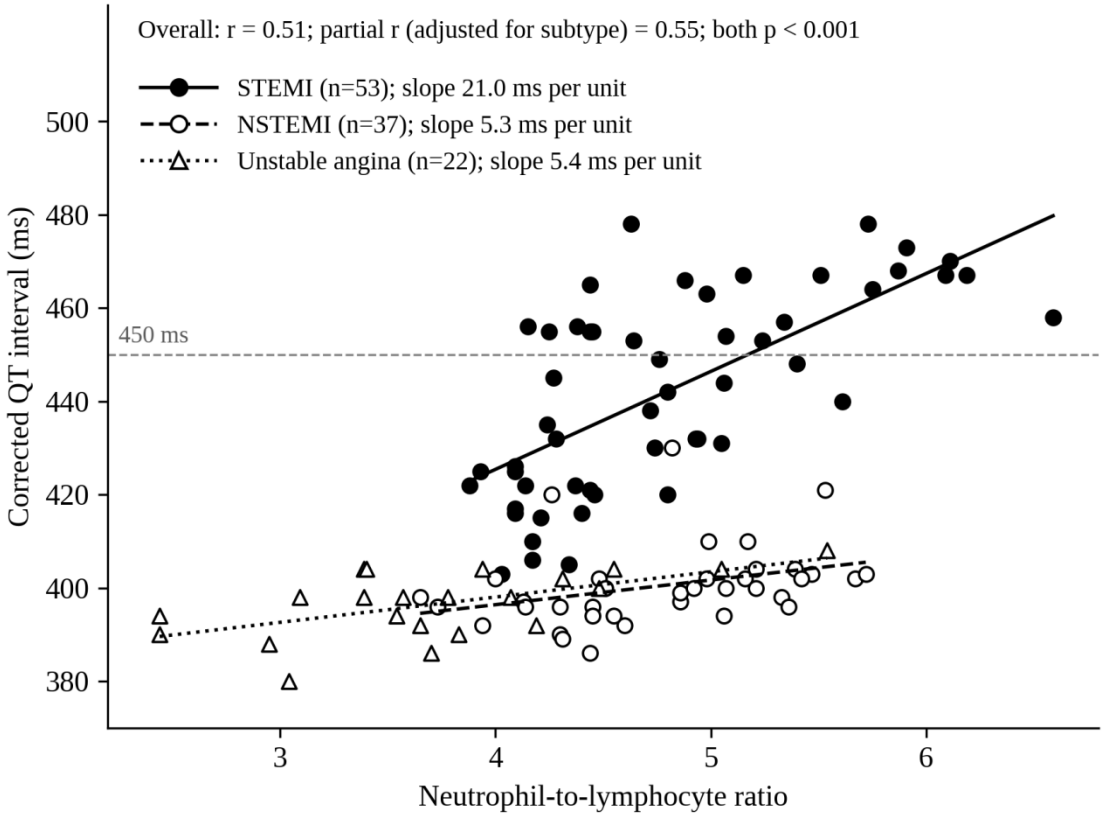


Fig. 2. Association between NLR and corrected QT interval (QTc) in 112 patients with acute coronary syndrome. Lines are least-squares regression lines for each subtype, with slopes in milliseconds per unit increase in NLR. The partial correlation is adjusted for subtype. The horizontal dashed line marks a QTc of 450 ms. Abbreviations as in Fig. 1.