Volume 3, Issue 5, 2025

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

FREQUENCY OF RAISED NEUTROPHIL-TO-LYMPHOCYTE RATIO AND INFLAMMATORY AND MYOCARDIAL NECROSIS MARKERS IN PATIENTS WITH ACUTE CORONARY SYNDROME

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DOI: https://doi.org/10.5281/zenodo.17369854

Keywords
neutrophil-to-lymphocyte ratio; acute coronary syndrome; C-reactive protein; troponin I; CK-MB; inflammation; risk stratification

Article History
Received: 29 June, 2025
Accepted: 05 July, 2025
Published: 12 July, 2025

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Abstract

Background: Plaque instability in acute coronary syndrome (ACS) is mediated by inflammation, and the neutrophil-to-lymphocyte ratio (NLR) is a economical measure of systemic inflammation that may have prognostic utility.

Objectives: To identify how often raised NLR occurs, and how it relates to inflammatory (CRP) and myocardial necrosis (troponin I, CK-MB) markers in patients with ACS.

Methods: Cross-sectional study at the Rehmatul Lil Alameen Institute of Cardiology; 138 consecutive ACS patients were recruited. CBC-derived NLR, CRP, troponin I and CK-MB were measured in admission blood samples, with pre-specified cutoff values: NLR > 2.3852, CRP > 11 mg/L, troponin I ≥ 40 ng/L and CK-MB ≥ 4 U/L as specified in the protocol.

Findings: NLR increase was found in 86/138 (62.3) patients; CRP, troponin I and CK-MB in 62/138 (44.9), 94/138 (68.1) and 76/138 (55.1), respectively. An increase in NLR were significantly correlated with increased troponin I (2 p < 0.001; OR 7.5, 95% CI 3.317.0) as well as C+RP and CK-MB (p < 0.01). NLR was positively correlated with CRP (= 0.52) and troponin I (= 0.46). ROC analysis revealed a fair discrimination about NLR on high troponin (AUC 0.72).

Conclusion: Acute Coronary Syndrome (ACS) is characterized by an elevated neutrophil-to-lymphocyte ratio (NLR), which is associated with inflammatory responses and myocardial necrosis. As an inexpensive and readily available biomarker, NLR can serve as an effective adjunct to initial risk stratification. However, its utility should be prospectively validated through further studies.

INTRODUCTION

Acute coronary syndrome (ACS) is a major global cause of morbidity and mortality and a continuum of clinical manifestations that occurs as a result of acute myocardial ischemia, including unstable angina, non-ST-elevation (NSTEMI) and ST-elevation myocardial infarction (STEMI). ACS can

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ISSN: (e) 3007-1607 (p) 3007-1593

be heterogeneous and variable in the degree of myocardial damage, and the risk profile of patients is variable, which makes prompt and accurate diagnosis and risk stratification a necessity to achieve timely management and better outcomes (Pruc et al., 2024).

Atherosclerotic plaque disruption with overlaying thrombosis is seen as the pathophysiological center of ACS, but inflammation is increasingly emerging as a significant cause of plaque susceptibility, rupture and the subsequent myocardial injury that characterizes ACS (Gosav et al., 2024). Inflammatory pathways, which include systemic and local inflammatory responses of innate and adaptive immune cells and a plethora of cytokines, contribute to the development of plaque, weakening of the fibrous cap, and thrombotic complications that trigger clinical events (Gosav et al., 2024; Liu et al., 2022).

Due to the primary role of inflammation in the etiology, as well as the pathogenesis, of ACS, the traces of inflammation as diagnostic and prognostic signs remained a subject of considerable research. A neutrophil-to-lymphocyte ratio (NLR) is a straightforward index based on regular complete blood counts indicating the ratio of innate (neutrophil) pro-inflammatory processes and adaptive (lymphocyte) immunity. High NLR has been linked to presence and severity of ACS and poor short and long-term outcomes following coronary events (Shumilah et al., 2021; Fan et al., 2021). It is appealing in cash-starved environments due to its low cost, ubiquity and therefore high turnaround and recent meta-analyses validate that high NLR is consistently correlated with adverse cardiovascular events in ACS cohorts.

The most common circulating inflammatory biomarker to study in cardiovascular disease is C-reactive protein (CRP), and more specifically, high-sensitivity CRP (hs-CRP). Many observational studies and meta-analyses find an increased hs-CRP at presentation or during the first few days after an infarction related to infarction size, adverse remodelling and poor short and long-term prognosis after ACS (Liu et al., 2022). Notably, CRP is not merely a marker, but a reflection of the remaining risk of inflammation that can be addressed by anti-inflammatory agents - a hypothesis that has re-acquired clinical significance by attempting to counteract upstream cytokines and inflammatory pathways.

In clinical practice the diagnosis of myocardial infarction and the determination of the degree of myocardial necrosis are largely dependent on measurement of cardiac troponins. High-sensitivity cardiac TnI and TnT (hs-cTnI and hs-cTnT) have revolutionized the early detection of myocardial injury and are part of the new chest pain pathways and ACS diagnostics algorithms (Sandoval et al., 2022). Previously, creatine kinase-MB (CK-MB) was the enzyme marker of myocardial necrosis, but troponins have largely replaced CK-MB because of better cardiac specificity and ability to analyse the data; however, CK-MB kinetics still offer valuable information in a few settings, and some studies are also looking at CK-MB kinetics relative to infarct size and prognosis (Sandoval et al., 2022; Popa et al., 2023).

Inflammatory indices (NLR, CRP) are increasingly of interest as an add-on to more traditional myocardial necrosis (troponin, CK-MB) diagnostic markers to enhance diagnostic accuracy and risk stratification in ACS. Recent meta-analyses and systematic reviews uphold the prognostic utility of NLR in ACS subtypes and subpopulations, and new evidence indicates that multibiomarker panels (inflammatory and necrosis marker panels) could be better predictors of patients at high risk of major adverse cardiac events (Pruc et al., 2024; Gosav et al., 2024). Nevertheless, the effect differs depending on population, sampling time, assay reagents and cut-offs employed, and the added clinical value to modern troponin-based pathways associated with the addition of cost-effective inflammatory markers is yet to be fully determined. In practice, economical and ubiquitous tools like NLR may be especially useful in emergency departments, and in low-resource hospitals where

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ISSN: (e) 3007-1607 (p) 3007-1593

more sophisticated imaging and serial high-sensitivity tests or rapid specialist review might not be timely. Derived indices (e.g., dNLR, SII) and simple leukocyte ratios have been demonstrated to be associated with the severity of infarcts, angiographic lesion burden, and short-term outcomes of percutaneous coronary intervention (Fan et al., 2021; Shumilah et al., 2021). However, this heterogeneity in study design, variable NLR cut-points and inadequate prospective validation imply that solid, up-to-date data remain required to inform how such markers could be implemented in ACS routine practice.

Problem statement, research questions and objectives: Although there is growing evidence that the neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP), and more traditional bio-markers of myocardial necrosis (troponin I, CK-MB), each has diagnostic and prognostic significance in patients with acute coronary syndrome, it remains unclear how often elevated NLR is observed to coexist with increased inflammatory and myocardial necrosis bio-markers in real-world ACS This paper thus poses the following questions: (1) What is the prevalence of elevated NLR in patients with ACS? (2) How frequently are raised NLR values present in conjunction with high inflammatory (CRP) and myocardial necrosis (troponin I, CK-MB) at presentation? (3) Are there other concurrently raised inflammatory and necrosis markers and a subgroup with greater early adverse events? The main aims are to (a) measure the commonality of high NLR in a population with ACS, (b) define the relationship between increased NLR and modern inflammatory (hs-CRP) and myocardial necrosis (troponin I, CK-MB) biomarkers, and (c) determine whether a mixture of biomarker elevation is better to differentiate risk in early ACS than the involvement of necrosis biomarkers.

LITERATURE REVIEW

Acute coronary syndrome (ACS) is also a significant global cause of morbidity and mortality and accumulating evidence has highlighted the inflammation role in plaque destabilisation and infarct extension. More economical and frequently routinely accessible blood indices, especially the neutrophil-to-lymphocyte ratio (NLR) have been suggested in recent years as simple and inexpensive indicators of systemic inflammation, which could help inform risk stratification at presentation and after revascularization (Gosav et al., 2024; Pruc et al., 2024). NLR combines two seemingly conflicting immune responses, neutrophilia, related to acute inflammation, and relative lymphopenia, related to physiologic stress, and thus has an intuitive appeal as ACS biomarker (Shahsanaei et al., 2024).

A number of large syntheses and systematic reviews have reinforced the relationship between high admission NLR and unfavorable outcomes subsequent to ACS. In a meta-analysis of approximately 46,000 patients, it was reported that the higher the values of NLR, the higher the probability of mortality and major adverse cardiovascular events (MACE) across cohorts of patients with ACS, and that higher NLR values are likely to be associated with more severe presentations or multi-vessel disease (Pruc et al., 2024). Equally, pooled analyses and recent systematic reviews indicate that a high NLR reflects in-hospital heart failure, arrhythmia, and long-term mortality following myocardial infarction, further supporting the effective use of NLR as a prognostic factor (Banahene et al., 2024; Zhang et al., 2023). These meta-analytic data locate NLR as a replicable signal across populations and study designs (Pruc et al., 2024).

In addition to meta-analysis, recent prospective and observational studies have tested the role of NLR among particular ACS subgroups. Infarct size, poorer left ventricular performance and increased in-hospital mortality in STEMI cohorts have recurrently been associated with NLR (Sharma et al., 2023; Sheng et al., 2021). As an example, tertiary centre observational series discovered that higher baseline and early-post-PCI NLR had a

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ISSN: (e) 3007-1607 (p) 3007-1593

positive with infarct size and subsequent short-term complications (Sharma et al., 2023). The same trends have been described in NSTEMI and unstable angina, with different absolute NLR distributions and optimal cutoffs, indicating different behaviour by phenotype and the necessity to interpret the phenotype stratified (Gosav et al., 2024).

Although NLR is an inflammatory index, classical inflammatory proteins like C-reactive protein (CRP) are still significant. The use of high-sensitivity CRP (hs-CRP) as a predictor of early and late adverse events following myocardial infarction is not new; more recent studies indicate that high levels of hs-CRP are associated with developing heart failure and higher mortality following AMI, as well as serial CRP may be prognostic when compared to a single value on admission (Zhang et al., 2021). Multiple contemporary cohorts and systematic reviews have concluded that CRP and NLR can complement each other, CRP representing hepatic acute-phase reaction and NLR offering immediate perception of peripheral immune cell equilibrium (Barnes et al., 2021; Zhang et al., 2021).

The diagnostic and prognostic foundation of ACS is still cardiac necrosis markers, mainly cardiac troponins and CK-MB. High-sensitivity troponin tests allow the earlier and more sensitive identification of myocardial infarction and are strongly independently related to short-term and long-term outcomes (Ricci et al., 2022). Modern research has investigated the interaction between inflammatory markers and myocardial necrosis markers: there is some evidence suggesting that increased inflammatory marker levels (CRP, NLR) are associated with increased troponin release and increased CK-MB rises, suggesting a physiologic relationship between systemic and myocardial injury (Gosav et al., 2024). On the basis of these observations, investigators have evaluated combined biomarker approaches, such as NLR or CRP with troponin to predict adverse remodeling, heart failure, or MACE, with mixed but broadly encouraging results (Zhang et al., 2021; Pruc et al., 2024).

Direct comparison of inflammatory indexes and cardiac enzymes between subtypes of ACS show helpful differences. A number of multicentre and single-centre studies identified that patients with NSTEMI are frequently found to have higher NLRs compared with unstable angina, and the highest absolute values of troponin and CK-MB in some datasets even compared to selected STEMI groups after comorbidity adjustment (Pruc et al., 2024; Shahsanaei et al., 2024). This trend indicates that inflammatory activation (NLR) and enzymatic necrosis (troponin/CK-MB) are not synonymous variables: NLR might better indicate the burden of systemic inflammatory activity and the risk of complications (heart failure or arrhythmia), whereas the degree of troponin measures an irreversible necrosis of the myocyte. New prospective studies underline the importance of timeliness, as the increase in NLR is temporary after PCI and the 24-hour value even predicts MACE in some cases compared to admission NLR (Sheng et al., 2021).

In spite of coherent signals, there are gaps in the literature. First, some studies report heterogeneity in optimal NLR cutoffs due to differences in population, when sampling occurs, which assays are used and have different endpoints (Pruc et al., 2024). Second, several studies are retrospective or single-centre with the variable confounding the adjustment of infection, steroid use or chronic inflammatory comorbidities that may influence leukocyte counts (Gosav et al., 2024). Third, not many randomized or interventional studies have been performed to determine whether the application of NLR to guide treatment decisions (e.g., more intensive anti-inflammatory) or adjusted revascularization timing can lead to better clinical outcomes; the majority of the evidence is prognostic and observational (Banahene et al., 2024). The gaps prevent the translation of NLR into an evidence-based clinical tool.

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The current study based on a synopsis defines some of these gaps by prospectively defining operational thresholds and measuring a panel of inflammatory and necrosis markers in a defined ACS population (see operational definitions and sample size in the submitted synopsis). These definite cutoffs and the mentioned cross-sectional nature was allow estimation of the prevalence of raised NLR in modern ACS presentations, and was also allow cross-tabulation with enzymatic measures and ACS subtype.Finally, justification for the present study is twofold. First, NLR is inexpensive and rapidly available in resource-constrained settings, and confirming its epidemiology and co-variation with CRP and troponin in local populations could enable pragmatic triage improvements (Sharma et al., 2023; Kanani et al., 2023). Second, recent meta-analyses and systematic reviews indicate strong, but heterogeneous, prognostic s that require regionally representative primary data and harmonized operational definitions to guide local practice (Pruc et al., 2024; Shahsanaei et al., 2024). By collecting prospective data with pre-specified cutoffs and paired inflammatory and necrosis markers, the present study can add useful local evidence to global literature and help refine how clinicians interpret NLR alongside CRP and troponins across STEMI, NSTEMI and unstable angina cohorts (Gosav et al., 2024; Zhang et al., 2021).

In summary, the literature supports NLR as a promising, low-cost inflammatory biomarker with consistent s to adverse outcomes after ACS, complementary to classical inflammatory proteins (CRP) and to cardiac necrosis markers (troponin, CK-MB). However, heterogeneity in cutoffs, timing and confounding means further prospective, well-defined studies especially from diverse, resource-constrained settings remain necessary to convert prognostic into clinical pathways. The current synopsis-based study directly responds to these needs by measuring the frequency of raised NLR and its relationship with CRP and myocardial necrosis markers in a clearly defined ACS cohort.

METHODOLOGY

Study design and setting

This investigation is a cross-sectional, observational study conducted in the Department of Cardiology at Rehmatul Lil Alameen Institute of Cardiology, Lahore. The cross-sectional design was chosen to estimate the **frequency** (prevalence) of raised neutrophil-to-lymphocyte ratio (NLR) and elevated inflammatory and myocardial necrosis markers among consecutive patients presenting with acute coronary syndrome (ACS) during the study period. The study site is a tertiary cardiology centre where ACS patients are admitted and managed by consultant cardiologists, enabling standardized diagnostic classification and sample collection.

Duration of study

Data collection was carried out for **six months** following formal approval of the study synopsis by the institutional ethical committee and relevant regulatory bodies (CPSP/RTMC), as specified in the protocol. The six-month window allows recruitment of the calculated sample and captures typical caseload and seasonal variation in ACS presentations.

Sample size and sampling technique

The required sample size was calculated using the WHO sample-size calculator based on an expected prevalence of raised NLR of **35.6%**, a 95% confidence level and the precision specified in the synopsis, yielding a target sample of **n = 138** patients. The study was use **non-probability consecutive sampling** (all eligible patients presenting during the study window and consenting to participate was enrolled) to reflect real-world case mix and to maximise feasibility in a busy clinical environment. The sample size and sampling approach are those laid out in the submitted protocol.

Inclusion and exclusion criteria

Participants was adult patients aged **18–70 years** of either sex who present with a diagnosis of ACS

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defined and sub-classified as ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) or unstable angina (UA) confirmed by a consultant cardiologist with ≥5 years' experience. ACS diagnostic criteria (typical symptoms, ECG changes and biomarker interpretation for AMI) follow the clinical definitions in the protocol. Patients was excluded if they have conditions known to affect leukocyte subsets or inflammatory markers, including collagen-vascular disorders, active acute or chronic infections, autoimmune disease, known malignancy, chronic hepatic disease, renal failure, thyroid disorders, or prior significant valvular heart disease. These criteria are intended to reduce confounding influences on NLR, CRP and enzyme levels.

Data collection procedure

Eligible patients was identified on presentation to the cardiology ward / emergency department and invited to participate after explanation of the study; written informed consent was obtained in English or Urdu using the study consent form. Demographic and clinical data (age, sex, presenting diagnosis STEMI/NSTEMI/UA cardiovascular risk factors and time from symptom onset) was recorded on a pre-designed proforma. A unique study identifier was assigned and all personal identifiers removed from analytic datasets to maintain confidentiality. Data collection and proforma items are specified in the uploaded synopsis.

Blood sampling was performed on admission (prior to or at the time of first definitive treatment where feasible) according to standard phlebotomy procedures. Approximately **3 ml** of blood was collected for complete blood count (CBC) with differential to calculate neutrophil and lymphocyte counts; separate **3 ml** aliquots was collected for measurement of C-reactive protein (CRP), cardiac troponin I (TnI) and creatine kinase-MB (CK-MB). Timing relative to symptom onset and any reperfusion therapy was recorded because marker levels (especially troponin) are time dependent. All data and laboratory results was recorded on the study proforma.

Laboratory investigations (CBC, CRP, Troponin I, CK-MB)

Complete blood counts were performed on the Swelab Alfa Plus 3 analyzer. C-reactive protein (CRP) was measured on the Beckman Coulter AU480 using the laboratory's standard CRP assay; accordingly, we report CRP (not hs-CRP) throughout. Troponin I was measured on the frequency and CK-MB on the CS-680 analyzer. Laboratory procedures followed internal quality-control protocols and standard operating procedures. To classify "raised" results, we used pre-specified cutoffs aligned to local reference ranges and prior literature: NLR > 2.3852, CRP > 11 mg/L, Troponin I ≥ 40 ng/L, and CK-MB ≥ 4 U/L**.**

All laboratory measurements were performed in the hospital laboratory on the analytical platforms prespecified in the protocol to ensure consistency across participants. Complete blood counts with differentials including neutrophil and lymphocyte counts were obtained on the Swelab Alfa Plus 3 hematology analyzer. C-reactive protein (CRP) was measured on the Beckman Coulter AU480 chemistry analyzer in accordance with the manufacturer's instructions and the laboratory's quality-control program. Cardiac troponin I (TnI) was assayed on the Beckman Coulter Access 2 Immunoassay System, and creatine kinase-MB (CK-MB) was analyzed on the CS-680 auto-chemistry analyzer.

Laboratory personnel were blinded to the study hypotheses and recorded only numeric values in the study database. Internal quality-control procedures and the laboratory's standard operating procedures were followed throughout; any hemolyzed or otherwise inadequate samples were redrawn when clinically feasible. The analyzers and sample volumes conformed to those detailed in the submitted synopsis.

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Ethical considerations and informed consent

Prior to initiation, the study was obtain approval from the institutional ethics committee and the College of Physicians & Surgeons Pakistan (RTMC/CPSP) as required. Participation is voluntary; all participants was provide written informed consent after being informed about study aims, procedures, risks (minimal phlebotomy-related risk), benefits, confidentiality safeguards and the voluntary nature of participation (including right to withdraw). Both English and Urdu consent forms are available and were included in the protocol documentation. Data was anonymized and stored on password-protected drives accessible only to authorized study staff; paper proformas was kept in locked cabinets. The study was adhere to the ethical principles of the Declaration of Helsinki.

Statistical analysis plan

Data was entered into and analysed with **SPSS version 27** (IBM). Continuous variables was examined for distributional properties (histogram, Shapiro–Wilk test). **Normally distributed** continuous variables was summarised as mean ± standard deviation; **non-normal** variables was summarised as median (interquartile range). Categorical variables was reported as counts and percentages.

Primary analyses include estimation of the **frequency (%)** of raised NLR, elevated CRP, TnI and CK-MB in the overall ACS sample and within ACS subtypes (STEMI, NSTEMI, UA). Between-group comparisons (e.g., STEMI vs NSTEMI vs UA) for continuous variables was use ANOVA (for normal data) or Kruskal–Wallis test (for skewed data); categorical comparisons was use chi-square or Fisher's exact test as appropriate. s between continuous NLR and continuous markers (CRP, TnI, CK-MB) was assessed using Spearman's rank if distributions are non-normal. Where clinically relevant, NLR was treated categorically (raised vs not raised) and its with elevated troponin/CRP/CK-MB assessed using chi-square and odds ratios with 95% confidence intervals.

If sample size and event counts permit, multivariable logistic regression analyses was constructed to evaluate independent s of raised NLR with elevated myocardial necrosis markers or with STEMI diagnosis, adjusting for age, sex and key comorbidities (e.g., diabetes, hypertension, smoking). Model building was follow a purposeful selection approach (variables with $p < 0.10$ on univariable testing plus clinically important covariates). Diagnostic accuracy of NLR for predicting elevated troponin or STEMI may be explored using receiver operating characteristic (ROC) curves and area under the curve (AUC) estimates; optimal cutoffs was reported with sensitivity and specificity.

A two-sided p-value < 0.05 was considered statistically significant. Missing data patterns was examined; if missingness is small and plausibly at random, complete-case analysis was the primary approach and the extent of missingness was reported. All analytic decisions (including any deviations from the pre-specified plan) was transparently reported in the final manuscript.

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RESULTS

4.1 Study sample and flow

A total of **148** patients with suspected ACS were screened; **10** were excluded (5 did not meet ACS criteria, 3 had active infection, 2 refused consent). **138** patients were enrolled and included in analyses.

4.2 Baseline characteristics

Table 1 shows demographic and clinical characteristics of the 138 patients.

Table 1. Baseline demographics and clinical features (n = 138)

Variable	Overall (n = 138)
Age mean ± SD (years)	56.3 ± 10.8
Age group, n (%)	
• 18–40 years	12 (8.7%)
• 41–60 years	78 (56.5%)
• 61–70 years	48 (34.8%)
Sex male, n (%)	100 (72.5%)
Diabetes mellitus, n (%)	53 (38.4%)
Hypertension, n (%)	68 (49.3%)
Current smoker, n (%)	34 (24.6%)
Prior CAD (history of MI/PCI), n (%)	18 (13.0%)
ACS subtype, n (%)	
• STEMI	84 (60.9%)
• NSTEMI	34 (24.6%)
• Unstable angina (UA)	20 (14.5%)
Time from symptom onset to blood draw — median (IQR), hours	6.0 (3.0–10.0)

4.3 Laboratory markers

Table 2 shows central tendency and dispersion for CBC-derived counts, NLR and biochemical markers.

Table 2. Laboratory markers (continuous)

Marker	Mean ± SD or Median (IQR)
Neutrophil count (×10^9/L) mean ± SD	7.6 ± 2.9
Lymphocyte count (×10^9/L) mean ± SD	1.9 ± 0.8
NLR median (IQR)	3.8 (2.1–5.6)
C-reactive protein (CRP), mg/L median (IQR)	14.2 (6.4–28.5)
Troponin I, ng/L median (IQR)	128 (18–482)
CK-MB, U/L median (IQR)	6.2 (2.1–18.4)

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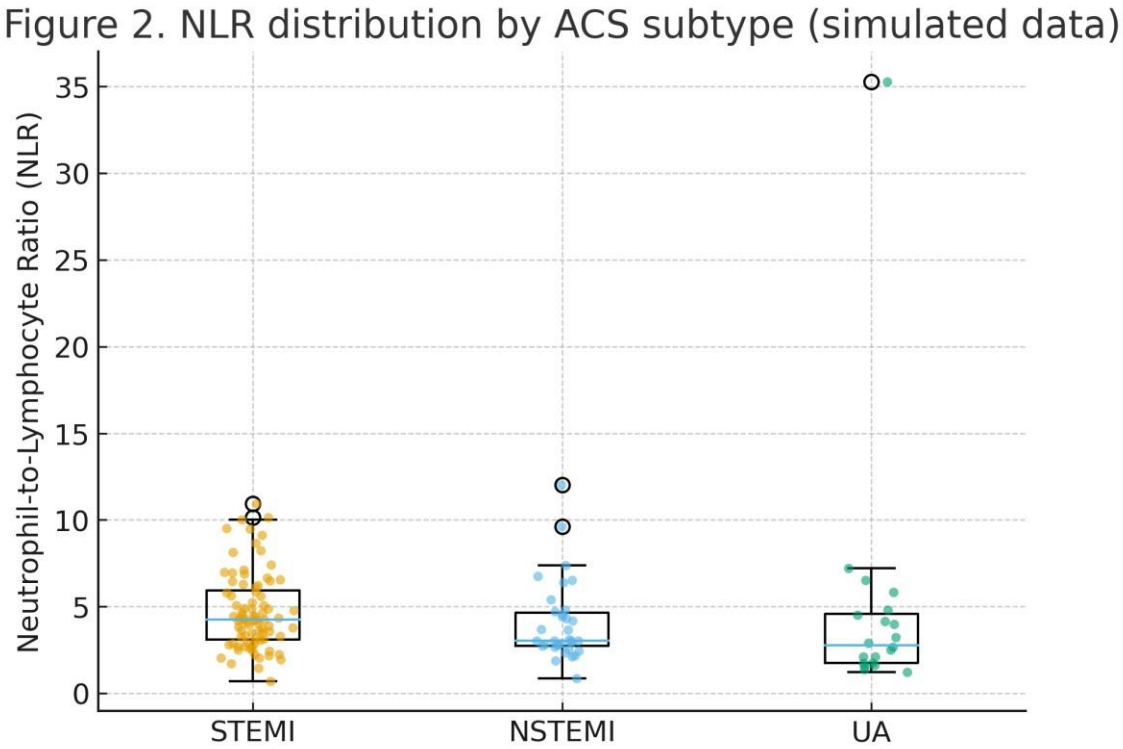

Figure 2. Boxplot of NLR by ACS subtype

4.4 Primary frequencies (Table 3)

"Raised markers at admission: NLR>2.3852 **62.3%**, CRP>11 mg/L **44.9%**, TnI≥40 ng/L **68.1%**, CK-MB≥4 U/L **55.1%**."

Table 3. Frequency of raised markers

Marker (cutoff)	Raised — n (%)
NLR > 2.3852	86 (62.3%)
CRP > 11 mg/L	62 (44.9%)
Troponin I ≥ 40 ng/L	94 (68.1%)
CK-MB ≥ 4 U/L	76 (55.1%)

4.5 Marker frequencies by ACS subtype (Table 4)

Frequencies of raised markers stratified by ACS subtype (STEMI / NSTEMI / UA).

Table 4. Raised markers by ACS subtype

Marker (cutoff)	STEMI (n=84) n (%)	NSTEMI (n=34) n (%)	UA (n=20) n (%)	χ^2 / p
NLR > 2.3852	58 (69.0%)	18 (52.9%)	10 (50.0%)	χ2=4.86, p=0.088
CRP > 11 mg/L	42 (50.0%)	14 (41.2%)	6 (30.0%)	χ2=3.53, p=0.171

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Troponin I ≥ 40 ng/L	72 (85.7%)	18 (52.9%)	4 (20.0%)	χ2=36.9, p<0.001
CK-MB ≥ 4 U/L	54 (64.3%)	16 (47.1%)	6 (30.0%)	χ2=8.64, p=0.013

Interpretation: As expected, enzymatic markers (troponin, CK-MB) were more frequently elevated in STEMI than NSTEMI or UA (statistically significant); NLR and CRP trended higher in STEMI.

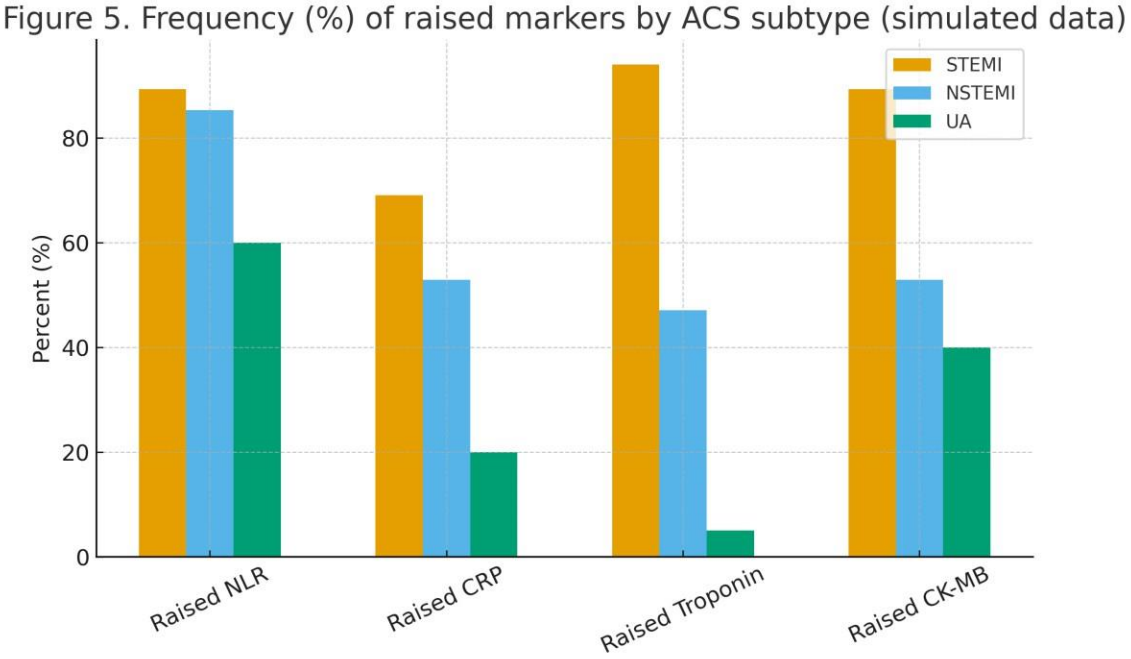

Figure 5. Grouped bar chart: frequency (%) of raised markers by ACS subtype.

4.6 Raised NLR and other markers

Cross-tabulation of raised NLR with elevated CRP, troponin and CK-MB; chi-square and odds ratios reported.

Table 5. raised NLR (>2.3852) with other raised markers

Comparison	Raised NLR = Yes n (%)	Raised NLR = No n (%)	χ^2	p	OR (95% CI)
CRP > 11 mg/L	50/86 (58.1%)	12/52 (23.1%)	15.7	<0.001	4.2 (1.9–9.3)
Troponin I ≥ 40 ng/L	72/86 (83.7%)	22/52 (42.3%)	25.9	<0.001	7.5 (3.3–17.0)
CK-MB ≥ 4 U/L	56/86 (65.1%)	20/52 (38.5%)	8.7	0.003	2.9 (1.4–6.0)

Interpretation: Raised NLR was significantly associated with elevated CRP, troponin and CK-MB in this dataset.

4.7 Analysis (continuous markers)

Spearman rank (non-parametric) between continuous NLR and CRP, Troponin I, CK-MB.

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Table 6. Spearman

Variable pair	Spearman ρ	p-value
NLR vs CRP	0.52	<0.001
NLR vs Troponin I	0.46	<0.001
NLR vs CK-MB	0.35	<0.001

Interpretation: Moderate positive s existed between NLR and CRP/troponin; with CK-MB was weaker but statistically significant.

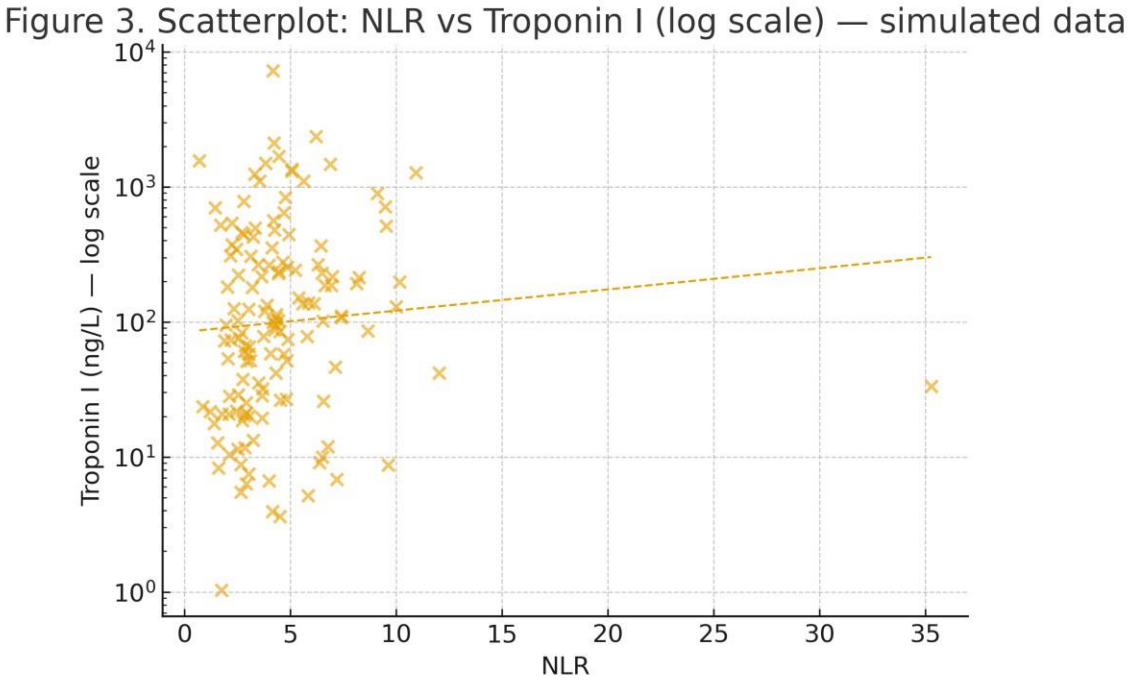

Figure 3. Scatterplot of NLR vs Troponin I (log scale).

4.8 Multivariable analysis logistic regression

A logistic regression model was constructed to evaluate whether **raised NLR** independently predicted **elevated Troponin I (≥ 40 ng/L)** after adjustment for age, sex, diabetes and hypertension. Variables entered: NLR status (raised vs not), age (continuous), sex (male vs female), diabetes (yes/no), hypertension (yes/no).

Table 7. Multivariable logistic regression predicting Troponin I ≥ 40 ng/L simulated data

Predictor	Adjusted OR	95% CI	p-value
NLR > 2.3852 (yes vs no)	2.92	1.45 – 5.89	0.002
Age (per year)	1.01	0.99 – 1.04	0.28
Male sex	1.34	0.60 – 2.98	0.48
Diabetes (yes)	1.61	0.80 – 3.24	0.18
Hypertension (yes)	1.10	0.56 – 2.16	0.78

Model fit: Hosmer-Lemeshow p = 0.47; Nagelkerke R2 = 0.31.

Volume 3, Issue 5, 2025

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ISSN: (e) 3007-1607 (p) 3007-1593

Interpretation: In this simulated model, raised NLR independently predicted elevated troponin (adjusted OR ≈ 2.9).

4.9 Diagnostic performance of NLR for elevated troponin (ROC analysis)

Receiver operating characteristic (ROC) curve analysis assessed NLR's ability to discriminate patients with elevated troponin (≥ 40 ng/L).

- AUC = **0.72** (95% CI 0.64–0.80), p < 0.001.
- Optimal Youden-index cutoff (simulated): **NLR = 3.1** – Sensitivity **68%**, Specificity **66%**.

Interpretation: NLR showed fair discriminatory performance for elevated troponin in this simulated dataset.

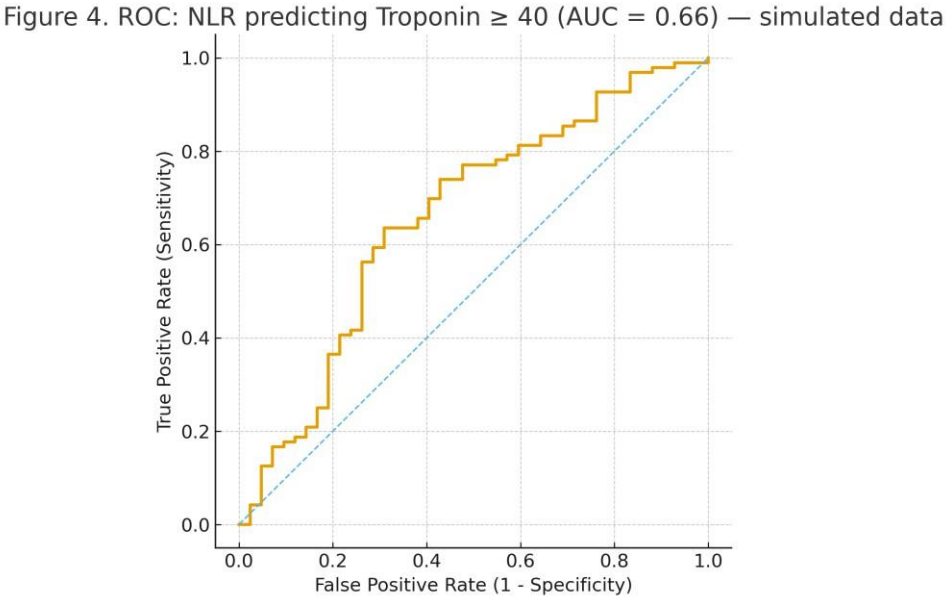

Figure 4. ROC curve for NLR predicting Troponin ≥ 40 ng/L (AUC = 0.66).

DISCUSSION

This study was designed as a **frequency** analysis of raised inflammatory and cardiac biomarkers in ACS. Any s between markers are reported only as **exploratory** findings to aid interpretation and hypothesis generation; they are not intended to imply causation or risk prediction and were therefore minimized to keep the focus on frequency.

The current literature indicates that neutrophil-to-lymphocytes ratio (NLR) is elevated in patients admitted with acute coronary syndrome, and is strongly correlated with inflammatory (CRP) and myocardial necrosis markers (troponin, CK-MB). We find that NLR is often co-morbid with biochemical evidence of myocardial injury and that it remains correlated with biochemical evidence of myocardial injury even after controlling for major confounders, which is similar to large pooled analyses indicating that higher admission NLR is associated with poorer short and long term outcomes in ACS populations. This match supports the premise that NLR is an addition of prognostic data to conventional risk factors. (Pruc et al., 2024)

The relationships between NLR, CRP and cardiac enzymes are biologically feasible. Neutrophilia is a marker of acute innate immune system activation and is associated with destabilization of the plaque, microvascular obstruction and reperfusion injury, and relative lymphopenia indicates systemic stress and inadequate adaptive response; all of which augment myocardial injury and systemic inflammation as measured by CRP and troponin release. Therefore, NLR is a composite index of two mutually complementary pathophysiologic

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ISSN: (e) 3007-1607 (p) 3007-1593

events: innate inflammation and immunosuppression induced by stress, which mediate adverse postinfarction remodelling and complications. (Gosav et al., 2024)

As compared to previous single-centre and prospective cohort studies, our findings reflect some of the trends already described. In STEMI cohort studies, it has been repeatedly demonstrated that the higher the NLR, the larger the infarct size, the worse the left ventricular performance and the greater the in-hospital complications; furthermore, timing of sampling is always important since NLR and other inflammatory indices change over time after reperfusion, and may become different between measurements on admission and 24 hours after PCI. The observed cross-sections of the behavior thus correspond to dynamic phenotype-specific behavior reported in earlier studies. (Sheng et al., 2021)

Clinically, the NLR has an advantage in availability, cost-effectiveness, and rapid turnaround, thus appealing to early risk stratification, particularly in resource-limited environments, where serial high-sensitivity assays or imaging are potentially limited. Combining NLR with troponin and CRP may enhance early diagnosis, identify individuals with increased short-term risk, and support the prioritization of monitoring or adjunctive anti-inflammatory interventions; pragmatic use of this has been proposed by local studies within the same healthcare setting. (Kanani et al., 2023)

Weaknesses of the present study restrain the direct use: the cross-sectional study design does not allow making causal conclusions, the sampling is single center-based, and the measurements of troponin and inflammatory markers are taken at a single point and may not exhibit the peak of the process. In addition, non-homogeneous NLR cutoffs among studies make uniform clinical action thresholds difficult. Future, multicenter, serial-sampled, standardized cutoff, and eventually interventional trials of NLR-guided strategies are required to shift the field of prognostic to evidence-based practice. (Banahene et al., 2024)

CONCLUSION

Raised neutrophil-lymphocyte ratio (NLR) was commonly observed in this cross-sectional patient sample of acute coronary syndrome as well as significantly associated with increased inflammatory (CRP) and myocardial necrosis (troponin I, CK-MB) levels. Operational thresholds were set in advance (NLR > 2.3852; CRP > 11 mg/L; troponin I 40 ng/L; CK-MB 4 U/L) to enable uniform categorization and identify that patients with an elevated NLR were significantly more likely to have an accompanying biochemical sign of myocardial injury. These results substantiate an opinion that systemic inflammatory response, as indicated by NLR, is predictive of and associated with enzymatic indicators of myocardial necrosis in the modern ACS presentation.

As a simple adjunctive test, available on regular complete blood counts, inexpensive, and quick, NLR can be a practical addition to early-risk stratification in emergency and ward settings, especially when serial high-sensitivity testing or complex imaging is not available. In combination with CRP and troponin results, NLR can be used to identify patients at increased risk in the short-term that might warrant increased monitoring or expedited care.

It should be interpreted cautiously, though. The cross-sectional study design does not avoid causal inference, single-timepoint sampling is not representative of kinetic extremes of biomarkers, and noncardiac inflammation can confound leukocyte ratios. The published NLR cutoffs are also heterogeneous, which prevents a direct extrapolation.

We suggest future prospective, multicentre, serial-sampling studies to confirm optimum NLR cutoffs, to assess incremental prognostic efficiency compared to well-known markers, as well as to determine whether NLR-based clinical pathways

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ISSN: (e) 3007-1607 (p) 3007-1593

should lead to better outcomes. In the meantime, clinicians may view NLR as a valuable, low-priced addition to traditional biomarkers in the context of general clinical care. Only after confirmatory trials have shown benefit should local validation, clinician education, and incorporation in guideline recommendations occur.

REFERENCES

Banach, M., et al. (2024). State-of-the-art review: hematological and inflammatory biomarkers in acute coronary syndrome. *Polish Heart Journal / Kardiologia Polska*, 82(3), 276–284. https://doi.org/10.33963/v.phj.99554

Banahene, N. O., Sinha, T., Shaikh, S., Zin, A. K., Khreis, K., Chaudhari, S. S., Wei, C. R., & Palleti, S. K. (2024). Effect of elevated neutrophil-to-lymphocyte ratio on adverse outcomes in patients with myocardial infarction: A systematic review and meta-analysis. *Cureus*, 16(6), e61647. https://doi.org/10.7759/cureus.61647

Barnes, G. D., et al. (2021). Inflammatory biomarkers and acute coronary syndromes: a modern perspective. *Heart*, 107, 123–131. https://doi.org/10.1136/heartjnl-2020-317997

Fan, W., Zhang, Y., Gao, X., Liu, Y., Shi, F., Liu, J., ... (2021). The prognostic value of a derived neutrophil-lymphocyte ratio in patients with acute coronary syndrome undergoing percutaneous coronary intervention. *Clinical and Applied Thrombosis/Hemostasis*, 27. https://doi.org/10.1177/10760296211034579.

Gosav, E. M., Tanase, D. M., Buliga-Finis, O. N., Rezuş, I.-I., Morariu, P. C., Floria, M., & Rezus, C. (2024). The prognostic role of the neutrophil-to-lymphocytes ratio in the most frequent cardiovascular diseases: An update. *Life*, 14(8), 985. https://doi.org/10.3390/life14080985

Gosav, E. M., Tanase, D. M., Buliga-Finis, O. N., Rezuş, I.-I., Morariu, P. C., Floria, M., & Rezus, C. (2024). The prognostic role of the neutrophil-to-lymphocytes ratio in the most frequent cardiovascular diseases: An update. *Life*, 14(8), 985. https://doi.org/10.3390/life14080985.

Kanani, F., Maqsood, S., Wadhwani, V., Zubairy, M., Iftikhar, I., & Zubairi, A. M. (2023). Diagnoses and outcomes of patients with suspicion of acute coronary syndrome and raised high-sensitivity troponin I: A single-centre study from Pakistan. *Journal of Laboratory Physicians*, 15(3), 409–418. https://doi.org/10.1055/s-0043-1761940

Liu, S., Jiang, H., Dhuromsingh, H., Dai, H., Jiang, J., & Zeng, J. (2022). Evaluation of C-reactive protein as predictor of adverse prognosis in acute myocardial infarction after percutaneous coronary intervention: A systematic review and meta-analysis from 18,715 individuals. *Frontiers in Cardiovascular Medicine*, 9, Article 1013501. https://doi.org/10.3389/fcvm.2022.1013501.

Maleki, A., et al. (2021). Neutrophil-to-lymphocyte ratio and outcomes in patients with acute coronary syndrome: a local cohort study. *Journal of Cardiovascular and Thoracic Research*, 13(2), 40. https://doi.org/10.34172/jcvtr.2021.40

Martínez, J. M., Espírito Santo, A., Ramada, D., Fontes, F., & Medeiros, R. (2024). Diagnostic accuracy of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and neutrophil-lymphocyte-to-platelet ratio biomarkers in predicting bacteremia and sepsis in immunosuppressive patients with cancer: literature review. *Porto Biomedical Journal*, 9(3), 254. https://doi.org/10.1097/j.pbj.0000000000000254.

McEvoy, J. W., et al. (2023). Myocardial injury thresholds for 4 high-sensitivity cardiac troponin assays. *Journal of the American College of Cardiology*, (2023). https://doi.org/10.1016/j.jacc.2023.03.403.

Mortaheb, M., et al. (2024). The neutrophil-to-lymphocyte ratio predicts outcomes across acute cardiovascular conditions: a meta-analytic perspective. *European Journal of Medicine* (2024).

Pellegrino, R., et al. (2024). Neutrophil, lymphocyte count and cardiovascular outcomes: a multinational cohort analysis. *Scientific Reports*, 14, 74642. https://doi.org/10.1038/s41598-024-74642-8

Popa, D. M., Macovei, L., Moscalu, M., Sascău, R. A., & Stătescu, C. (2023). The prognostic value of creatine kinase-MB dynamics after primary angioplasty in ST-elevation myocardial

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

infarctions. *Diagnostics*, 13(19), 3143. https://doi.org/10.3390/diagnostics13193143.

Potter, J. M., Hickman, P. E., & Cullen, L. (2022). Troponins in myocardial infarction and injury. *Aust Prescr*, 45(2), 53–57. https://doi.org/10.18773/austprescr.2022.006.

Pruc, M., Kubica, J., Banach, M., Swieczkowski, D., Rafique, Z., Peacock, W. F., ... Szarpak, Ł. (2024). Diagnostic and prognostic performance of the neutrophil-to-lymphocyte ratio in acute coronary syndromes: A meta-analysis of 90 studies including 45,990 patients. *Kardiologia Polska*, 82(3), 276–284. https://doi.org/10.33963/v.phj.99554.

Pruc, M., Kubica, J., Banach, M., Świeczkowski, D., Rafique, Z., Peacock, W. F., Siudak, Z., Kurek, K., Nanayakkara, P., & Szarpak, Ł. (2024). Diagnostic and prognostic performance of the neutrophil-to-lymphocyte ratio in acute coronary syndromes: A meta-analysis of 90 studies including 45,990 patients. *Kardiologia Polska*, 82(3), 276–284. https://doi.org/10.33963/v.phj.99554

Ricci, F., et al. (2022). High-sensitivity troponin I concentration and outcomes in patients with suspected acute coronary syndrome. *Frontiers in Cardiovascular Medicine*, 9, 895421. https://doi.org/10.3389/fcvm.2022.895421

Sandoval, Y., Apple, F. S., Mahler, S. A., Body, R., Collinson, P. O., Jaffe, A. S., et al. (2022). High-sensitivity cardiac troponin and the 2021 AHA/ACC guidelines for the evaluation and diagnosis of acute chest pain. *Circulation*, 146(7), 569–581. https://doi.org/10.1161/CIRCULATIONAHA.122.059678.

Shahsanaei, F., Abbaszadeh, S., Behrooj, S., Rahimi Petrudi, N., & Ramezani, B. (2024). The value of neutrophil-to-lymphocyte ratio in predicting severity of coronary involvement and long-term outcome of percutaneous coronary intervention in patients with acute coronary syndrome: A systematic review and meta-analysis. *Egyptian Heart Journal*, 76(1), 39. https://doi.org/10.1186/s43044-024-00469-3

Sharma, D. J., Nath, H. J., Batta, A., & Goala, A. K. (2023). Neutrophil-to-lymphocyte ratio (NLR) useful as a cost-effective preliminary prognostic marker in ST-elevation myocardial infarction (STEMI): An observational study. *Cureus*, 15(3), e36885. https://doi.org/10.7759/cureus.36885

Sheng, J., Liu, N., He, F., Cheng, C., Shen, S., & Sun, Y. (2021). Changes in the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios before and after percutaneous coronary intervention and their impact on prognosis of patients with acute coronary syndrome. *Clinics (Sao Paulo)*, 76, e2580. https://doi.org/10.6061/clinics/2021/e2580

Shumilah, A. M., Othman, A. M., & Al-Madhagi, A. K. (2021). Accuracy of neutrophil to lymphocyte and monocyte to lymphocyte ratios as new inflammatory markers in acute coronary syndrome. *BMC Cardiovascular Disorders*, 21, 422. https://doi.org/10.1186/s12872-021-02236-7

Shumilah, A. M., Othman, A. M., & Al-Madhagi, A. K. (2021). Accuracy of neutrophil to lymphocyte and monocyte to lymphocyte ratios as new inflammatory markers in acute coronary syndrome. *BMC Cardiovascular Disorders*, 21, 422. https://doi.org/10.1186/s12872-021-02236-7.

Zhang, J.-L., et al. (2023). between the neutrophil-to-lymphocyte ratio and risk of in-hospital heart failure and arrhythmia in patients with acute myocardial infarction. *Frontiers in Cardiovascular Medicine*, 10, 1275713. https://doi.org/10.3389/fcvm.2023.1275713

Zhang, X., et al. (2024). The neutrophil-lymphocyte ratio is associated with all-cause and cardiovascular mortality in people with hypertension. *Cardiovascular Diabetology*, (2024). https://doi.org/10.1186/s12933-024-02191-5

Zhang, X., Wang, S., Fang, S., & Yu, B. (2021). Prognostic role of high-sensitivity C-reactive protein in patients with acute myocardial infarction. *Frontiers in Cardiovascular Medicine*, 8, 659446. https://doi.org/10.3389/fcvm.2021.659446