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A CROSS-SECTIONAL STUDY

Association of Neutrophil-to-Lymphocyte Ratio with Severity of Coronary Artery Disease in Patients Undergoing Coronary Angiography

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Abstract

Background: Coronary artery disease (CAD) remains the leading cause of global mortality. The neutrophil-to-lymphocyte ratio (NLR), derived from routine blood counts, is a simple inflammatory index. Its correlation with angiographic CAD severity in Indian patients remains underexplored.

Objectives: To evaluate the association of NLR with angiographic severity of CAD; to compare NLR across single-vessel (SVD), double-vessel (DVD), and triple-vessel (TVD) disease groups; and to assess NLR utility in predicting high SYNTAX score.

Methods: 250 consecutive patients undergoing elective coronary angiography were enrolled. NLR was calculated from admission complete blood count (CBC). Vessel involvement and SYNTAX score were recorded. Statistical analyses included one-way ANOVA, Pearson correlation, ROC curve analysis, and binary logistic regression.

Results: Of 242 analysable patients, 55 had no obstructive CAD (control), 75 had SVD, 64 DVD, and 48 TVD. Mean NLR rose significantly: 1.82 ± 0.61 (control), 2.74 ± 0.83 (SVD), 3.91 ± 1.12 (DVD), 4.73 ± 1.38 (TVD) — $p < 0.001$. NLR correlated strongly with SYNTAX score ($r = 0.68$, $p < 0.001$). At NLR ≥ 3.2, sensitivity was 78.4% and specificity 81.2% for high SYNTAX score (≥33). Multivariate analysis confirmed NLR as an independent predictor of TVD (OR 3.42; 95% CI 1.87–6.26; $p < 0.001$).

Conclusions: NLR correlates significantly with angiographic CAD severity and independently predicts multivessel disease. It may serve as a simple, inexpensive pre-angiographic risk stratification tool.

Key words: neutrophil-to-lymphocyte ratio, coronary artery disease, SYNTAX score, multivessel disease, inflammation, coronary angiography

1 | INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death worldwide, accounting for approximately 17.9 million deaths annually (1) . In India, the burden has grown substantially, with premature onset increasingly affecting the productive age group (2) . Early and accurate risk stratification is therefore of paramount clinical importance.

Atherosclerosis — the pathological substrate of CAD — is fundamentally an inflammatory disease (3) . Neutrophils release reactive oxygen species and proteases that destabilise atherosclerotic plaques, whereas lymphocytes exert opposing anti-atherogenic effects (4, 5) . The neutrophil-to-lymphocyte ratio (NLR), calculated from a routine complete blood count (CBC), captures this inflammatory imbalance in a single number.

Elevated NLR has been linked to worse outcomes

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across diverse conditions including malignancy, sepsis, and cardiovascular disease (6, 7) . In acute coronary syndromes, NLR has predicted in-hospital mortality and adverse events post-PCI (8, 9) . The SYNTAX score provides a validated, comprehensive angiographic measure of CAD complexity (10) . However, the specific correlation between NLR and SYNTAX score has not been well characterised in Indian populations. This study therefore aimed to: (i) evaluate the association between NLR and angiographic severity of CAD; (ii) compare NLR across SVD, DVD, and TVD groups; and (iii) assess the diagnostic utility of NLR for predicting high SYNTAX score.

2 | MATERIALS AND METHODS

2.1 | Study Design and Setting

This was a cross-sectional, hospital-based study conducted at the Department of Cardiology, Raipur, between January 2025 and December 2025. The study was conducted by approval & consent was obtained from all participants.

2.2 | Study Population

Inclusion criteria: Adults (≥18 years) undergoing elective diagnostic coronary angiography for suspected or known CAD; stable angina, positive stress test, or pre-operative cardiac evaluation.

Exclusion criteria: Acute myocardial infarction or unstable angina within 30 days; active infection; autoimmune or haematological disorders; corticosteroids or immunosuppressants; malignancy; severe renal failure (eGFR <30 mL/min/1.73 m^2); incomplete angiographic data.

2.3 | Sample Size

Using a prevalence of elevated NLR in multivessel CAD of 65%, precision of 6%, and 95% confidence (Z = 1.96), the minimum sample was 243. A total of 250 patients were enrolled to allow for exclusions.

2.4 | Laboratory Assessment

Fasting venous blood was collected on the morning of the procedure. CBC was measured on a Sysmex XN-1000 automated analyser. NLR = Absolute Neutrophil Count ÷ Absolute Lymphocyte Count. Additional tests included fasting glucose, HbA1c, lipid profile, serum creatinine, eGFR, and high-sensitivity CRP (hs-CRP).

2.5 | Coronary Angiography and SYNTAX Score

Angiography was performed via standard Judkins transfemoral technique. Significant CAD was defined as ≥50% stenosis in a major epicardial vessel (diameter ≥1.5 mm). Vessel disease was classified as SVD (one territory), DVD (two territories), or TVD (all three territories, ± left main). SYNTAX score was calculated offline by two independent cardiologists blinded to NLR values using the validated online calculator (www.syntaxscore.com). High SYNTAX score was defined as ≥33.

2.6 | Statistical Analysis

Analyses were performed in SPSS v26 and R v4.2. Continuous variables are reported as mean ± SD or median [IQR]. Between-group comparisons used one-way ANOVA with Bonferroni correction. Pearson's correlation assessed the NLR–SYNTAX relationship. ROC curve analysis with the Youden index identified the optimal NLR cut-off. Binary logistic regression (dependent variable: TVD) identified independent predictors. $p < 0.05$ was significant.

3 | RESULTS

3.1 | Patient Characteristics

Of 250 enrolled patients, 8 were excluded (3 incomplete data, 3 active infection, 2 withdrew consent), leaving 242 for analysis: 168 males (69.4%), mean age 58.3 ± 11.2 years. Groups: control n=55, SVD n=75, DVD n=64, TVD n=48. Diabetes, hypertension, dyslipidaemia, and smoking were more prevalent in the TVD group (all $p < 0.05$) (Table 1).

Table 1. Baseline Demographic and Clinical Characteristics

Variable	Control (n=55)	SVD (n=75)	DVD (n=64)	TVD (n=48)	
Age (years)	55.4 ± 10.8	57.9 ± 11.4	59.1 ± 11.0	61.3 ± 10.9	0.06
Male, n (%)	36 (65.5)	52 (69.3)	45 (70.3)	35 (72.9)	0.82
BMI (kg/m^2)	25.1 ± 3.8	25.8 ± 4.1	26.4 ± 4.0	27.1 ± 4.3	0.09
Diabetes, n (%)	14 (25.5)	27 (36.0)	30 (46.9)	28 (58.3)*	0.003
Hypertension, n (%)	20 (36.4)	35 (46.7)	38 (59.4)*	34 (70.8)*	<0.001
Dyslipidaemia, n (%)	18 (32.7)	34 (45.3)	36 (56.3)*	33 (68.8)*	0.002
Smoking, n (%)	8 (14.5)	22 (29.3)*	24 (37.5)*	22 (45.8)*	<0.001
LDL-C (mg/dL)	104.2 ± 28.3	118.7 ± 31.4	124.3 ± 33.1	131.8 ± 35.6	0.001
hs-CRP, median [IQR]	2.1 [1.4–3.2]	4.8 [3.1–6.7]	7.2 [4.9–10.3]	10.4 [7.1–14.8]	<0.001

*SVD = single-vessel disease; DVD = double-vessel disease; TVD = triple-vessel disease; BMI = body mass index; LDL-C = low-density lipoprotein cholesterol; hs-CRP = high-sensitivity C-reactive protein. *p < 0.05 vs control.*

3.2 | NLR across Groups

NLR increased progressively with greater vessel involvement (Table 2). All inter-group differences were statistically significant ($p < 0.001$ by ANOVA with Bonferroni correction).

Table 2. Haematological Parameters across Study Groups

Parameter	Control (n=55)	SVD (n=75)	DVD (n=64)	TVD (n=48)	
TLC ($\times 10^3/\mu$L)	7.18 ± 1.42	8.34 ± 1.68*	9.12 ± 1.74*	9.98 ± 1.92*	<0.001
Neutrophil ($\times 10^3/\mu$L)	4.14 ± 0.98	5.48 ± 1.21*	6.82 ± 1.44*	7.94 ± 1.61*	<0.001
Lymphocyte ($\times 10^3/\mu$L)	2.28 ± 0.54	1.99 ± 0.48*	1.74 ± 0.41*	1.68 ± 0.38*	<0.001
NLR (mean ± SD)	1.82 ± 0.61	2.74 ± 0.83*	3.91 ± 1.12*†	4.73 ± 1.38*†‡	<0.001
NLR median [IQR]	1.74 [1.3–2.2]	2.61 [2.1–3.3]	3.76 [2.9–4.7]	4.54 [3.6–5.8]	<0.001

*TLC = total leucocyte count; NLR = neutrophil-to-lymphocyte ratio. *p < 0.05 vs control; †p < 0.05 vs SVD; ‡p < 0.05 vs DVD (Bonferroni post-hoc).*

3.3 | NLR and SYNTAX Score

Pearson's correlation demonstrated a strong positive association between NLR and SYNTAX score ($r = 0.68$, 95% CI 0.59–0.76; $p < 0.001$). NLR was highest in patients with high SYNTAX score (≥33): 5.18 ± 1.42 vs intermediate 3.84 ± 1.08 vs low 2.46 ± 0.79 ($p < 0.001$).

Table 3. NLR values by SYNTAX score category:

SYNTAX Score Category	NLR (mean ± SD)	
Low (≤22)	2.46 ± 0.79	94
Intermediate (23–32)	3.84 ± 1.08	68
High (≥33)	5.18 ± 1.42	25

p < 0.001 across categories (one-way ANOVA). r = 0.68 (Pearson's correlation with continuous SYNTAX score).

3.4 | ROC Curve Analysis

NLR demonstrated good discriminatory performance for predicting high SYNTAX score (AUC 0.84; 95% CI 0.77–0.91; $p < 0.001$). The optimal cut-off by Youden index was NLR ≥ 3.2 (Table 4).

Table 4. ROC Analysis — NLR for Predicting High SYNTAX Score (≥33)

Measure	Value	95% CI
AUC	0.84	0.77 – 0.91
Optimal NLR cut-off	3.2	—
Sensitivity	78.4%	68.2 – 86.5%
Specificity	81.2%	72.6 – 88.0%
PPV	74.3%	64.0 – 82.7%
NPV	84.1%	76.1 – 90.2%
Youden Index (J)	0.596	—

AUC = area under the curve; PPV = positive predictive value; NPV = negative predictive value.

3.5 | Multivariate Logistic Regression

After adjusting for age, sex, diabetes, hypertension, smoking, LDL-C, and hs-CRP, NLR remained the strongest independent predictor of TVD (Table 5).

Table 5. Multivariate Logistic Regression — Predictors of Triple-Vessel Disease

Variable	Crude OR	Adjusted OR (95% CI)	p value
Diabetes mellitus	2.64	1.94 (1.02–3.70)	0.04
Hypertension	2.81	2.14 (1.13–4.06)	0.02
Current smoking	2.18	1.72 (0.87–3.41)	0.12
hs-CRP (per mg/L)	1.18	1.09 (1.02–1.18)	0.01
NLR (per unit)	2.86	3.42 (1.87–6.26)	<0.001

OR = odds ratio; CI = confidence interval. Model χ^2 = 48.6, p < 0.001; Nagelkerke R^2 = 0.42; Hosmer-Lemeshow p = 0.61. NLR was the strongest independent predictor.

4 | DISCUSSION

The principal finding of this study is that NLR correlates significantly and independently with the angiographic severity of CAD. NLR rose progressively from controls to SVD, DVD, and TVD, and correlated strongly with SYNTAX score (r = 0.68, p < 0.001).

These findings are consistent with prior work. Kaya et al. [(8) reported mean NLR of 4.2 in TVD vs 2.1 in controls (p < 0.001) in 526 Turkish patients. Akboga et al. (11) identified NLR ≥ 2.8 for predicting significant CAD (AUC 0.78). Our study extends these findings to an Indian cohort and directly correlates NLR with SYNTAX score — a more comprehensive CAD complexity index. Importantly, NLR remained independently significant even after adjustment for traditional risk factors including diabetes, hypertension, and hs-CRP, suggesting it captures an inflammatory dimension not fully explained by conventional risk markers.

Biological plausibility is well established. Neutrophilia reflects systemic inflammation through release of matrix metalloproteinases, elastase, and myeloperoxidase — all of which destabilise atherosclerotic plaque (12, 13) . Relative lymphocytopenia impairs anti-inflammatory regulatory pathways, promoting atherogenesis (14–16) . The NLR encapsulates this dual dysregulation in a single calculable value.

At the optimal cut-off of NLR ≥ 3.2, sensitivity was 78.4% and specificity 81.2% for high SYNTAX score, with NPV of 84.1%. This suggests that patients with NLR < 3.2 are unlikely to have high-complexity CAD — potentially useful in pre-procedural risk stratification. In resource-limited settings where coronary CT angiography or advanced biomarkers are unavailable, NLR could guide clinical decision-making by identifying patients who may require earlier or more urgent angiography. (17–20)

4.1 | Limitations

This was a single-centre cross-sectional study; causal inference is not possible. NLR was measured at a single time-point. Sample size was modest. Functional severity (FFR/iFR) was not assessed. Long-term outcomes (MACE) were not evaluated. Larger multicentre prospective studies are needed to validate the NLR cut-off and assess prognostic utility.

5 | CONCLUSIONS

NLR is a simple, inexpensive, and widely available inflammatory marker derived from routine CBC. It correlates significantly and independently with angiographic CAD severity, rising progressively from controls to TVD. An NLR cut-off of $\geq$3.2 predicts high SYNTAX score with good sensitivity and specificity. NLR warrants consideration as a routine pre-angiographic inflammatory biomarker, particularly in resource-limited settings.

6 | DECLARATIONS

Ethics Approval: Department of Cardiology, Raipur, between January 2025 and December 2025 IEC/2022/145, Conducted per the Declaration of Helsinki. Written informed consent obtained from all participants.

Competing Interests: None declared.

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