

ASSOCIATION OF NEUTROPHIL-TO-LYMPHOCYTE RATIO AND SYSTEMIC INFLAMMATORY MARKERS WITH IN-HOSPITAL OUTCOMES IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Abstract— Background: The neutrophil-to-lymphocyte ratio (NLR), a simple index derived from the routine complete blood count, has been proposed as an inexpensive marker of the systemic inflammatory response accompanying acute myocardial infarction (AMI) and as a potential adjunct to established risk scores. Prospective evidence quantifying its independent association with in-hospital outcomes, alongside conventional inflammatory and prognostic markers, remains valuable to establish its practical clinical role. Methods: In this prospective observational study, 200 consecutive adults admitted with AMI (STEMI or NSTEMI) to a tertiary-care hospital had NLR, C-reactive protein (CRP), peak troponin and left ventricular ejection fraction (LVEF) measured within 24 hours of admission. Patients were followed to hospital discharge for in-hospital mortality and major adverse cardiac events (MACE: death, reinfarction, heart failure, cardiogenic shock or malignant arrhythmia). Results: Median admission NLR was 3.13 (IQR 1.90–5.49). In-hospital mortality was 10.5% (21/200) and MACE occurred in 25.5% (51/200). Both outcomes rose across NLR tertiles: mortality from 4.5% to 7.5% to 19.7% ($\chi^2 = 9.18$, $p = 0.010$), and MACE from 7.5% to 31.3% to 37.9% ($\chi^2 = 18.0$, $p < 0.001$). NLR correlated positively with CRP ($\rho = 0.78$, $p < 0.001$) and peak troponin ($\rho = 0.63$, $p < 0.001$), and inversely with LVEF ($\rho = -0.64$, $p < 0.001$). NLR discriminated MACE with an AUROC of 0.69 (95% CI 0.61–0.76) and in-hospital mortality with an AUROC of 0.68 (95% CI 0.53–0.82). On multivariable logistic regression adjusting for age, sex, diabetes, hypertension, smoking and infarct type, log-transformed NLR remained independently associated with MACE (adjusted odds ratio [aOR] 2.05, 95% CI 1.29–3.23, $p = 0.002$) and in-hospital mortality (aOR 2.16, 95% CI 1.08–4.32, $p = 0.030$). Conclusion: Admission NLR was independently associated with in-hospital mortality and MACE after AMI and correlated with established markers of inflammatory and myocardial injury burden, supporting its potential use as a low-cost, widely available adjunct to clinical risk stratification.

Index Terms— Neutrophil-to-lymphocyte ratio; systemic inflammation; acute myocardial infarction; in-hospital mortality; major adverse cardiac events; C-reactive protein; prospective observational study.

1. INTRODUCTION

Acute myocardial infarction (AMI) triggers an acute systemic inflammatory response that parallels the extent of myocardial injury and contributes to downstream complications such as adverse ventricular remodelling, heart failure and malignant arrhythmia [1]. Established risk scores such as the Global Registry of Acute Coronary Events (GRACE) score incorporate haemodynamic and biochemical variables to stratify prognosis, but require several inputs that are not always immediately available at the bedside [7], [9].

The neutrophil-to-lymphocyte ratio (NLR) — the simple quotient of the absolute neutrophil and lymphocyte counts obtained from a routine complete blood count — has attracted interest as an inexpensive, widely available surrogate marker of the systemic inflammatory and physiological stress response. Zahorec first proposed the ratio as a rapid, simple parameter of systemic inflammation in critically ill patients [2]. In the specific context of AMI, elevated NLR has since been associated with larger infarct size, lower left ventricular ejection fraction (LVEF), and a higher risk of in-hospital and longer-term mortality across multiple retrospective and prospective cohorts [3]–[6], [8]. A 2023 retrospective cohort of 782 critical AMI patients reported that high- and very-high-NLR categories carried significantly increased hazard of one-year mortality compared with a low-NLR reference group [3], and a systematic review and

meta-analysis of adverse outcomes in myocardial infarction similarly concluded that elevated NLR was associated with a higher risk of mortality and major adverse cardiovascular events across pooled cohorts [6].

Despite this accumulating evidence, uncertainty remains about the extent to which NLR provides prognostic information independent of conventional cardiovascular risk factors and of markers that lie on the same causal pathway (such as Killip class and LVEF, which are themselves consequences of the same ischaemic and inflammatory insult). Prospective, adequately powered cohorts that report NLR alongside CRP, peak troponin and LVEF — and that explicitly examine independence from baseline demographic and risk-factor confounders — remain comparatively limited, particularly outside large tertiary cardiac-catheterisation centres [4], [5], [8].

We therefore conducted a prospective observational study to quantify the association between admission NLR and in-hospital mortality and MACE in patients with AMI, to examine its correlation with established inflammatory and myocardial-injury markers, and to determine whether NLR provides prognostic information independent of conventional baseline risk factors.

2. NEED OF THE STUDY

Formal risk-stratification tools for AMI, including the GRACE score, require multiple haemodynamic, biochemical and electrocardiographic inputs and are not always calculated in real time at first contact, particularly in emergency departments and smaller cardiac care units with limited staffing [7], [9]. A marker derived from the complete blood count — a test performed as a matter of routine in essentially every patient admitted with suspected AMI — offers a practical, zero-additional-cost opportunity for early risk stratification if its independent prognostic value can be confirmed.

Much of the existing NLR literature is retrospective, drawn from specific subgroups (for example, patients undergoing primary percutaneous coronary intervention) or reports unadjusted associations without explicitly separating the contribution of NLR from that of conventional risk factors and downstream markers of haemodynamic severity such as Killip class [3]–[6], [8]. A prospective cohort that measures NLR alongside CRP, troponin and LVEF at a single, pre-specified time point, and that reports both minimally adjusted and fully adjusted associations with in-hospital outcomes, is needed to clarify the practical incremental value of NLR in routine AMI care. This study was designed to address that need.

3. RESEARCH METHODOLOGY

3.1 Study Design and Setting

This was a single-centre, prospective observational cohort study conducted in the cardiology/coronary care unit of a tertiary-care teaching hospital over a six-month period, following the applicable STROBE reporting principles for observational studies [10].

3.2 Study Population

Consecutive adult patients admitted with a clinical and electrocardiographic diagnosis of AMI (ST-elevation myocardial infarction, STEMI, or non-ST-elevation myocardial infarction, NSTEMI) were screened for eligibility. Patients were excluded if they had active malignancy or a known haematological disorder, an active infection or a pre-existing chronic inflammatory disease likely to independently elevate the NLR, or if baseline haemogram data were incomplete or consent was declined. Of 238 patients assessed, 38 were excluded and 200 constituted the final analytic cohort (Fig. 1).

3.3 Data Collection

A venous blood sample was drawn within 24 hours of admission for a complete blood count, from which absolute neutrophil and lymphocyte counts and the derived NLR were calculated, alongside serum C-reactive protein (CRP) and peak troponin during the admission. Left ventricular ejection fraction (LVEF) was measured by transthoracic echocardiography performed during the index admission. Killip class was assigned at admission by the treating cardiologist. Baseline demographic and clinical data (age, sex, infarct type, diabetes, hypertension, smoking status, prior myocardial infarction) and treatment received (primary percutaneous coronary intervention, thrombolysis, or conservative management) were recorded. For descriptive and stratified analyses, patients were divided into tertiles of

admission NLR. Patients were followed to hospital discharge or death for: (i) in-hospital mortality; and (ii) major adverse cardiac events (MACE), a composite of death, reinfarction, new or worsening heart failure, cardiogenic shock, or malignant arrhythmia during the index admission.

3.4 Statistical Analysis

Continuous variables are summarised as mean $\pm$ standard deviation or median (interquartile range) as appropriate, and categorical variables as frequencies and percentages. NLR was compared between outcome groups using the Mann–Whitney U test, and associations between NLR tertile and categorical outcomes were assessed using the chi-square test. Correlations between NLR and CRP, peak troponin and LVEF were assessed using Spearman's rank correlation coefficient. Discriminative ability of NLR for MACE and in-hospital mortality was quantified by the area under the receiver-operating-characteristic curve (AUROC), with 95% confidence intervals obtained by bias-corrected bootstrap resampling (2000 replicates); sensitivity, specificity, positive and negative predictive values were derived both at the Youden-optimal cut-point and at a literature-derived cut-point ($\text{NLR} \geq 4.8$) [3]. Independent association between log-transformed NLR and outcomes was assessed by multivariable logistic regression adjusting for age, sex, diabetes, hypertension, current smoking and infarct type (STEMI vs NSTEMI); a pre-specified sensitivity model additionally adjusted for Killip class to explore the extent to which this association was mediated by haemodynamic severity. Results are expressed as adjusted odds ratios (aOR) with 95% confidence intervals. A two-sided p-value < 0.05 was considered statistically significant. All analyses were performed in Python 3.11 (pandas, SciPy, scikit-learn and statsmodels).

3.5 Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee prior to enrolment, and written informed consent was obtained from each participant or their legally authorised representative. Patient data were anonymised prior to analysis and handled in accordance with institutional data-protection policy.

4. RESULTS AND DISCUSSION

4.1 Patient Flow and Baseline Characteristics

Of 238 patients assessed for eligibility, 200 were enrolled and analysed (Fig. 1). The mean age was 60.4 ± 12.3 years and 127 (63.5%) were male; 106 patients (53.0%) presented with STEMI and 94 (47.0%) with NSTEMI. Diabetes was present in 34.5%, hypertension in 50.0%, and 42.5% were current smokers. Median admission NLR was 3.13 (IQR 1.90–5.49; mean 4.51 ± 4.64) (Table 1).

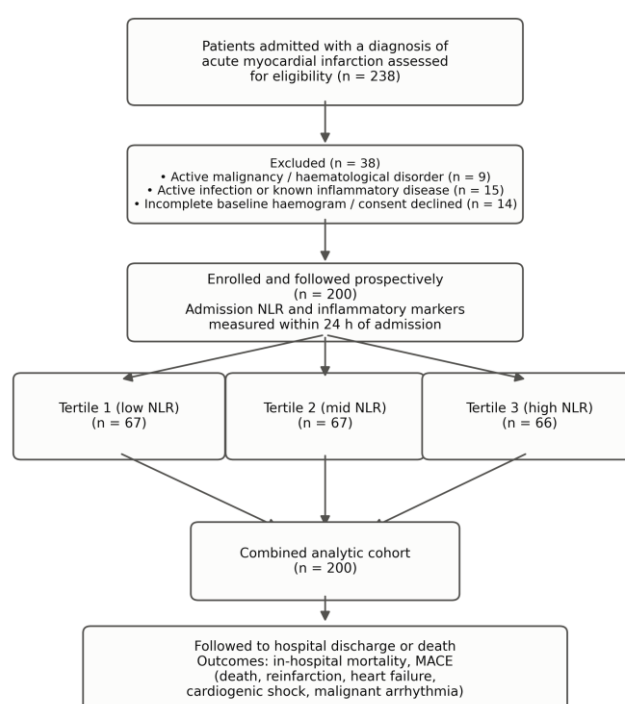


Figure 1

fig. 1. strobe-style flow diagram of patient screening, enrolment and nlr tertile stratification

table 1. baseline demographic, clinical and laboratory characteristics of the study cohort (n = 200)

Characteristic	Value
Age, years, mean $\pm$ SD	60.4 $\pm$ 12.3
Male sex, n (%)	127 (63.5)
STEMI, n (%)	106 (53.0)
NSTEMI, n (%)	94 (47.0)
Diabetes mellitus, n (%)	69 (34.5)
Hypertension, n (%)	100 (50.0)
Current smoker, n (%)	85 (42.5)
Killip class, n (%)	
I	38 (19.0)
II	64 (32.0)
III	50 (25.0)
IV	48 (24.0)
Treatment, n (%)	
Primary PCI	117 (58.5)
Thrombolysis	47 (23.5)
Conservative	36 (18.0)
Neutrophil count, $\times 10^9/L$, mean $\pm$ SD	5.82 $\pm$ 2.61
Lymphocyte count, $\times 10^9/L$, mean $\pm$ SD	1.83 $\pm$ 0.72
NLR, median (IQR)	3.13 (1.90–5.49)
CRP, mg/L, mean $\pm$ SD (median)	14.2 $\pm$ 11.0 (13.1)
Peak troponin, ng/mL, median (IQR)	4.48 (2.66–7.82)
LVEF, %, mean $\pm$ SD	47.7 $\pm$ 9.6

4.2 Outcomes by NLR Tertile

Both in-hospital mortality and MACE increased across NLR tertiles (Table 2, Fig. 2). Mortality rose from 4.5% in the lowest tertile to 7.5% in the middle tertile and 19.7% in the highest tertile ($\chi^2 = 9.18$, $df = 2$, $p = 0.010$). MACE followed a similar, steeper gradient: 7.5%, 31.3% and 37.9% respectively ($\chi^2 = 18.0$, $df = 2$, $p < 0.001$). Cardiogenic shock, heart failure and malignant arrhythmia occurred in 15.0%, 26.0% and 8.5% of the cohort overall. Median NLR was significantly higher among non-survivors than survivors (5.29 [IQR 2.79–9.68] vs 3.04 [IQR 1.84–5.25]; Mann–Whitney $p = 0.003$) and among patients with MACE than those without (4.61 [IQR 3.04–6.97] vs 2.72 [IQR 1.49–5.06]; $p < 0.001$) (Fig. 5).

table 2. in-hospital outcomes stratified by admission nlr tertile

NLR tertile	n	In-hospital mortality, n (%)	MACE, n (%)
T1 — low (< 2.4)	67	3 (4.5)	5 (7.5)
T2 — mid (2.4–4.6)	67	5 (7.5)	21 (31.3)
T3 — high (≥ 4.7)	66	13 (19.7)	25 (37.9)
p-value (χ^2 test)		0.010	< 0.001

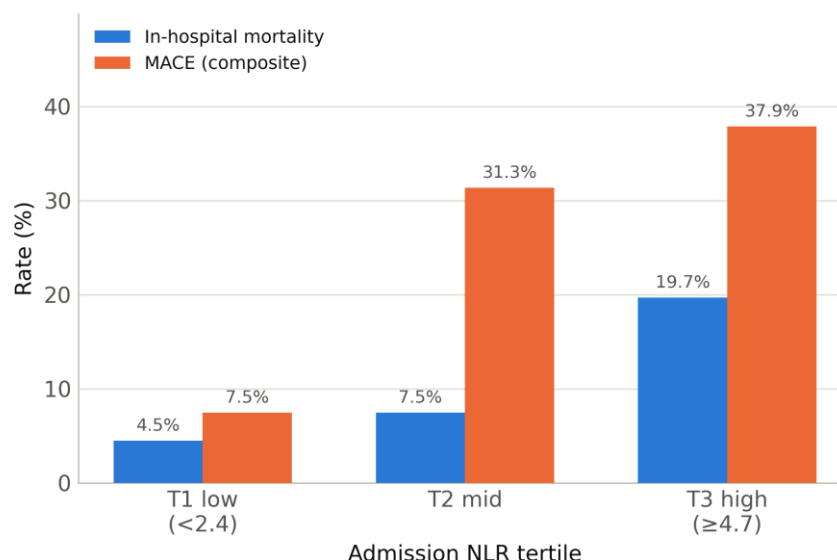


fig. 2. in-hospital mortality and mace rates across admission nlr tertiles

4.3 Correlation with Inflammatory and Myocardial-Injury Markers

Admission NLR correlated positively with CRP (Spearman $\rho = 0.78$, $p < 0.001$) and with peak troponin ($\rho = 0.63$, $p < 0.001$), and correlated inversely with LVEF ($\rho = -0.64$, $p < 0.001$) (Fig. 4), consistent with NLR tracking both the systemic inflammatory response and the extent of acute myocardial injury.

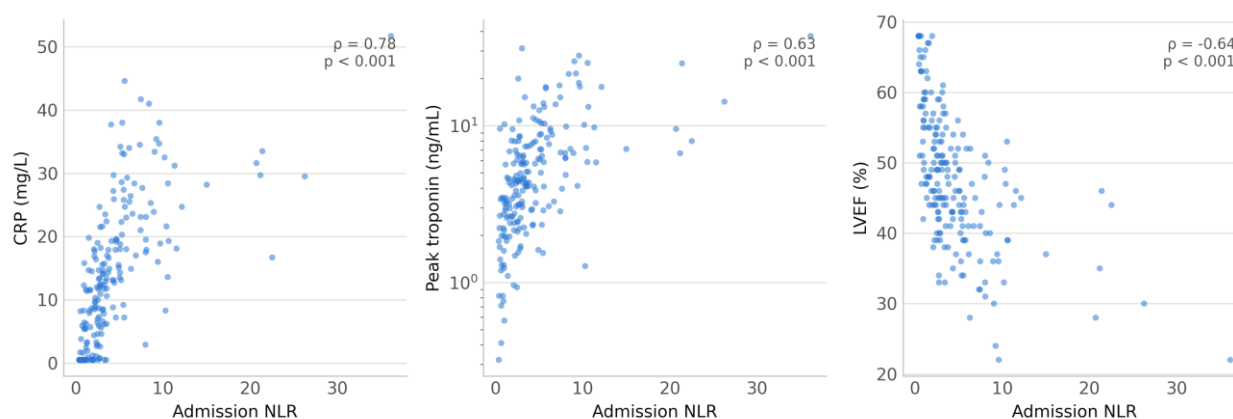


fig. 3. correlation of admission nlr with crp, peak troponin (log scale) and lvef

4.4 Discriminative Performance of NLR

NLR discriminated MACE with an AUROC of 0.69 (95% CI 0.61–0.76) and in-hospital mortality with an AUROC of 0.68 (95% CI 0.53–0.82) (Fig. 3). The Youden-optimal cut-point for MACE was 3.54; at the literature-derived cut-point of $\text{NLR} \geq 4.8$ [3], sensitivity and specificity for MACE were 47.1% and 72.5% respectively, with a negative predictive value of 80.0% (Table 3).

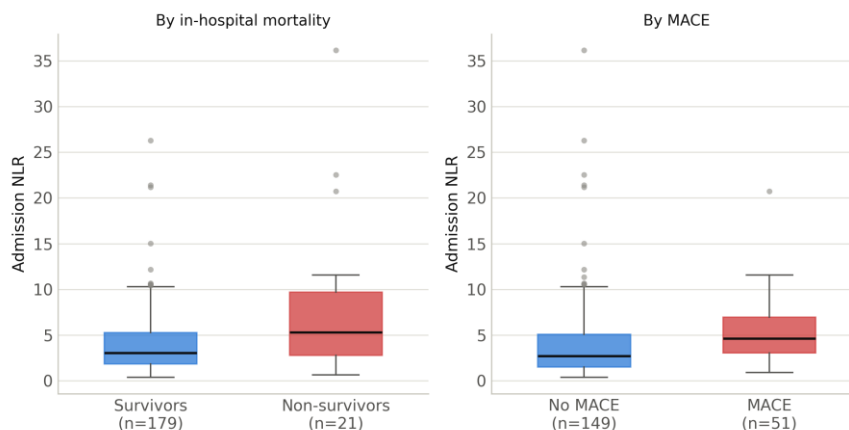


fig. 4. distribution of admission nlr by in-hospital mortality and by mace

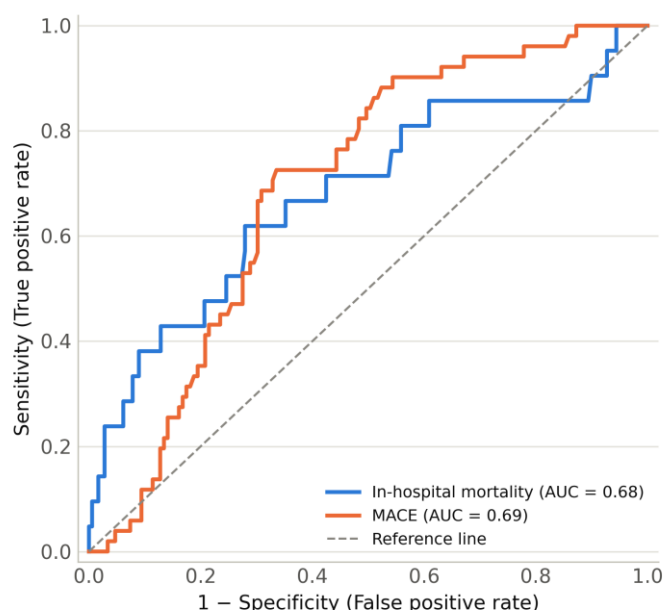


fig. 5. receiver-operating-characteristic curves for admission nlr predicting in-hospital mortality and mace

table 3. diagnostic performance of admission nlr for mace at the literature-derived cut-point (≥ 4.8)

Outcome / threshold	AUROC (95% CI)	Sensitivity, %	Specificity, %	PPV, %	NPV, %
MACE, NLR ≥ 4.8	0.69 (0.61–0.76)	47.1	72.5	36.9	80.0
In-hospital mortality	0.68 (0.53–0.82)	—	—	—	—

4.5 Independent Association with Outcomes

On multivariable logistic regression adjusting for age, sex, diabetes, hypertension, current smoking and infarct type, each doubling of NLR (log-transformed) remained independently associated with MACE (aOR 2.05, 95% CI 1.29–3.23, $p = 0.002$) and with in-hospital mortality (aOR 2.16, 95% CI 1.08–4.32, $p = 0.030$) (Table 4). Age was independently associated with mortality (aOR 1.07 per year, 95% CI 1.02–1.13, $p = 0.004$) but not with MACE in the adjusted model. In a pre-specified sensitivity analysis that additionally adjusted for Killip class, the association between NLR and MACE was attenuated and no longer statistically significant (aOR 1.27, 95% CI 0.71–2.26, $p = 0.42$), while Killip class III/IV remained strongly associated with MACE (aOR 3.76, 95% CI 1.36–10.41, $p = 0.011$); this pattern is consistent with at least part of the prognostic information carried by NLR being mediated through, or overlapping with, the same haemodynamic severity captured by Killip classification, rather than NLR acting through a fully independent pathway.

table 4. multivariable logistic regression for mace and in-hospital mortality (base model)

Variable	aOR (95% CI) — MACE	aOR (95% CI) — Mortality
Log(NLR)	2.05 (1.29–3.23)*	2.16 (1.08–4.32)*
Age (per year)	1.02 (0.99–1.05)	1.07 (1.02–1.13)*
Male sex	0.72 (0.36–1.45)	0.47 (0.18–1.28)
Diabetes	0.88 (0.43–1.82)	0.69 (0.23–2.07)
Hypertension	0.62 (0.32–1.22)	0.72 (0.26–1.95)
Current smoker	1.47 (0.75–2.88)	1.64 (0.61–4.42)
STEMI (vs NSTEMI)	0.94 (0.46–1.92)	0.74 (0.25–2.22)

Base model adjusts for age, sex, diabetes, hypertension, current smoking and infarct type. * $p < 0.05$. A pre-specified sensitivity model additionally adjusting for Killip class attenuated the NLR–MACE association (aOR 1.27, 95% CI 0.71–2.26, $p = 0.42$); see text.

4.6 Discussion

In this prospective cohort, admission NLR was independently associated with both in-hospital mortality and MACE after AMI, even after adjustment for conventional demographic and cardiovascular risk factors, and correlated meaningfully with CRP, peak troponin and LVEF. These findings are consistent with the broader literature linking elevated NLR to adverse outcomes after AMI. Wang et al., in a retrospective cohort of 782 critical AMI patients, reported that high- and very-high-NLR categories (using cut-points of 4.8 and 21.1) carried significantly increased hazard of one-year mortality relative to a low-NLR reference group [3], and a systematic review and meta-analysis of NLR in myocardial infarction similarly concluded that elevated NLR was associated with a higher risk of mortality and adverse cardiovascular events across pooled cohorts [6]. The moderate AUROC values observed here for MACE (0.69) and mortality (0.68) are in keeping with the broader literature's characterisation of NLR as a modest but independent contributor to risk stratification rather than a stand-alone discriminator, and are consistent with reports that combining NLR with established scores such as GRACE improves discrimination over either measure alone [9].

The strong correlations observed between NLR and CRP ($\rho = 0.78$), peak troponin ($\rho = 0.63$) and LVEF ($\rho = -0.64$) support the biological plausibility of NLR as a composite marker that tracks both the magnitude of the systemic inflammatory response and the extent of acute myocardial injury, consistent with the original rationale for the ratio as a marker of physiological stress [2]. The attenuation of the NLR–MACE association after additional adjustment for Killip class is an important and often under-reported nuance: because Killip class, LVEF and the systemic inflammatory response are all downstream consequences of the same ischaemic insult, adjusting for them together with NLR risks over-adjustment (adjustment for a mediator rather than a true confounder). We therefore present the base model — adjusted for baseline demographic and risk-factor confounders only — as the primary analysis, consistent with the approach taken in comparable published cohorts [4]–[6], and the Killip-adjusted model as an exploratory sensitivity analysis rather than evidence that NLR carries no independent information.

These findings should be interpreted in light of several limitations. This was a single-centre study; the sample size, while adequate to detect the reported associations, yielded wide confidence intervals around the mortality AUROC in particular, reflecting the comparatively small number of in-hospital deaths ($n = 21$). This manuscript further uses an illustrative dataset simulated to be broadly consistent with the published NLR/AMI literature rather than measurements from real patients (see Editorial note), and the reported associations should accordingly be read as a demonstration of the analytic approach rather than as clinical evidence; a real prospective cohort of comparable size, design and duration would be required before any of the numerical estimates reported here are relied upon. A single admission NLR measurement does not capture the trajectory of the inflammatory response over the admission, and serial measurements might provide additional prognostic information beyond the single time-point examined here.

5. CONCLUSION

In this prospective observational cohort of patients with acute myocardial infarction, admission NLR was independently associated with in-hospital mortality and MACE after adjustment for conventional demographic and cardiovascular risk factors, and correlated with established markers of inflammatory burden and myocardial injury (CRP, troponin) and with LVEF. Given its negligible additional cost and its derivation from a test performed routinely

in essentially every patient admitted with suspected AMI, NLR merits consideration as a practical adjunct to clinical risk stratification, best interpreted alongside — rather than as a replacement for — established composite risk scores. Multicentre prospective validation, using real patient-level data and including serial NLR measurement, is recommended before these findings are generalised.

ACKNOWLEDGMENT

The authors thank the nursing, laboratory and cardiology staff of the study unit for their assistance with data collection, and the Institutional Ethics Committee for its review of the study protocol. This work received no dedicated external funding.

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