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Research article

The predictive role of Systemic Inflammation Response Index (SIRI), Neutrophil-Lymphocyte Ratio (NLR), and Platelet-Lymphocyte Ratio (PLR) in the prognosis of acute coronary syndrome in a tertiary care hospital

Hamrish Kumar Rajakumar [a,*], Varsha Coimbatore Sathyabal [a], Mannar Vasanthan [b], Ramesh Dasarathan [b]

[a] Government Medical College, Omandurar Government Estate, Chennai, 02, Tamilnadu, India
[b] Department of General Medicine, Government Medical College, Omandurar Government Estate, Chennai, 02, Tamilnadu, India

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ABSTRACT

Background: & Objective: Acute coronary syndrome (ACS) is a major cause of mortality globally, with significant morbidity and economic impact. This study aimed to correlate the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic inflammatory response index (SIRI) values in ACS patients with their prognosis via the GRACE scoring criteria and to propose the SIRI as a superior inflammatory marker for predicting ACS prognosis.

Methods: Ethical approval was obtained for a retrospective cross-sectional study, which included patients from the outpatient department and Tamilnadu Accident Emergency Initiative Ward at Government Medical College, Omandurar Government Estate, who were diagnosed with ACS according to American College of Cardiology guidelines from January 2022 to December 2023. We excluded patients with familial hypercholesterolemia, platelet disorders, infections, inflammatory conditions, or incomplete health records. Data on demographics, clinical findings, blood counts, ECGs, cardiac enzymes, echocardiography, serum creatinine, and vital signs were collected and analyzed to calculate the NLR, PLR, SIRI, and GRACE scores. Statistical analyses included Kolmogorov–Smirnov and Anderson–Darling tests, Spearman correlation, Kruskal–Wallis one-way ANOVA, GLM modeling, k-fold cross-validation, and receiver operating characteristic (ROC) curve analysis.

Results: After applying the exclusion criteria, 247 ACS patients were included in the analysis. Significant associations were found between the NLR and the PLR, SIRI, and GRACE scores. The SIRI demonstrated the strongest association, whereas the PLR had the weakest association. All three variables significantly influenced prognostic risk, as determined by the GRACE score. GLM models highlighted the predictive significance of the NLR, PLR, and SIRI in estimating GRACE scores, with the SIRI showing potential superiority. K-fold cross-validation confirmed the superior predictive accuracy and ability of the SIRI to explain a larger proportion of variance in GRACE scores than the NLR and PLR.

Conclusions: The SIRI emerges as a promising prognostic marker for ACS, outperforming the NLR and PLR. Its ease of calculation from routine hemogram tests underscores its potential clinical

* Corresponding author. Government Medical College, Omandurar, India
E-mail addresses: hamrishkumar2003@gmail.com (H.K. Rajakumar), varshasathyabal@gmail.com (V. Coimbatore Sathyabal), dr.vasanthan89@gmail.com (M. Vasanthan), rameshdasarathan@gmail.com (R. Dasarathan).

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utility for risk stratification in ACS management. Further validation and integration into existing risk assessment models could enhance prognosis assessment in ACS patients.

1. Introduction

Acute coronary syndrome (ACS) includes a range of ischemic heart conditions, such as unstable angina (UA), non–ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI) [1]. Ischemic heart disease (IHD) is a leading cause of death globally, accounting for more than nine million deaths in 2016, with ACS responsible for half of all cardiovascular deaths and significant economic impacts [2,3]. India faces a high burden of IHD, with 1.54 million deaths and 36.99 million disability-adjusted life years recorded [4]. Patients typically present with chest discomfort worsened by activity or stress and relieved by rest or nitrates, whereas UA patients present with intense pain at rest radiating to areas such as the neck and left arm. Atypical symptoms include dyspnea, nausea, and syncope [5]. Diagnosis is confirmed by ECG, troponin levels, and medical history [6]. The ESC 2023 guidelines include medical therapy with antiplatelets, anticoagulants, beta-blockers, and statins, along with revascularization strategies such as PCI or CABG. Secondary prevention focuses on lifestyle changes, medication adherence, and cardiac rehabilitation to prevent recurrence [7].

Risk stratification is essential for optimizing the management of patients with ACS, as it helps identify those at high risk who would benefit from timely and aggressive interventions such as PCI within 24–48 h [8]. Accurate early risk assessment improves treatment decisions and clinical outcomes in high-risk patients where poor survival rates demand precise triage and care delivery [9]. Several scoring systems are available to assess the prognosis of ACS because of its high global burden. It plays a vital role in risk stratification and guiding treatment decisions.

The CRUSADE score predicts in-hospital mortality and bleeding risk for non-ST-segment elevation ACS patients [10]. The PAMI risk score is used for assessing prognosis in patients undergoing PCI for STEMI [11]. The PURSUIT risk score estimates the risk of death or myocardial infarction in ACS patients undergoing noninvasive treatment [12]. The Global Registry of Acute Coronary Events (GRACE) score predicts in-hospital and long-term mortality risk for patients with ACS on the basis of factors such as age, heart rate, blood pressure, creatinine levels, and history of heart failure [13]. Several studies have demonstrated that the GRACE score is a reliable tool for predicting adverse cardiovascular outcomes in patients with acute coronary syndrome [14–16]. The common limitation among these scoring systems is that they rely heavily on clinical variables available at the time of presentation and often require time-consuming investigations or data collection to assess a patient's risk accurately. This can include obtaining laboratory results, imaging studies, and detailed clinical information, which may delay the risk assessment process. Additionally, these methods are based on retrospective data and may not always accurately predict individual outcomes. Owing to these limitations, we aimed to identify alternative parameters for quick measurement in the Emergency Department.

ACS is closely linked to inflammation, with both innate and adaptive immune responses playing crucial roles in regulating atherosclerosis progression, plaque stability, and thrombus formation. Dysregulation of immune and inflammatory processes contributes to the pathogenesis of ACS, where an imbalance between proatherogenic and antiatherogenic immune networks can destabilize plaques and trigger acute coronary events [17]. Given this context, we chose to investigate the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR) because they are established markers of inflammation that are easily derived from routine investigations. Additionally, we examined the systemic inflammatory response index (SIRI), a newer marker offering a broader assessment of systemic inflammation.

Our primary objective was to evaluate the prognostic accuracy of the NLR, PLR, and SIRI in predicting the prognosis of ACS patients

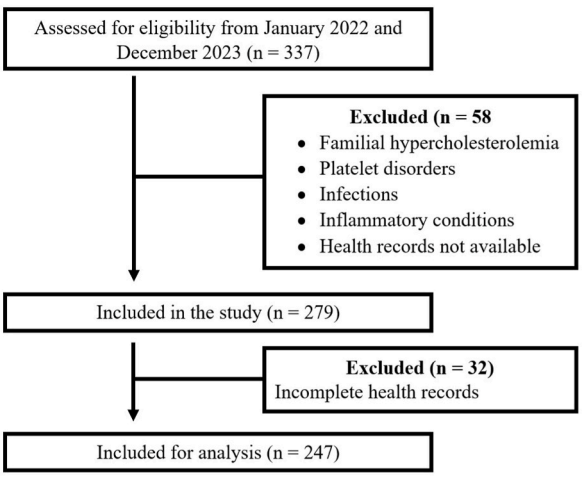

Fig. 1. STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) flow chart.

compared with the GRACE score. The secondary objectives of this study include comparing the predictive performance of these markers to propose the SIRI as a superior inflammatory marker compared with the NLR and PLR for predicting ACS prognosis and identifying optimal cutoff values for categorizing patients.

2. Patients and methods

2.1. Study population

The participants of this retrospective cross-sectional study were patients who reported to the outpatient department (OPD) and Tamilnadu Accident Emergency Initiative (TAEI) Ward of Government Medical College, Omandurar, Government Estate, from January 2022 to December 2023 and had received a diagnosis of ACS following the American College of Cardiology (ACC) guidelines. Patients presenting with chief complaints typical of ACS, such as persistent chest pain unrelieved by medication or rest, underwent a 12-lead ECG to identify ischemic changes. Cardiac enzyme levels (troponins) were measured, with an elevation exceeding 99 times the upper limit of normal considered indicative of significant myocardial injury. All individuals in our cohort were diagnosed on the basis of these criteria.

Patients with a medical history of familial hypercholesterolemia, platelet disorders, infections, or inflammatory conditions and whose health records were not available were excluded from the study. This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines, as shown in the flowchart in Fig. 1.

2.2. Data collection method

In our study, patient information was sourced from the department's nominal registers and the TAEI ward admission register. Using the unique hospital identification number assigned to each patient, their health records were located and obtained from the Medical Records Department (MRD) of our institution.

From these health records, we collected a dataset, including demographic details; medical history; clinical examination findings; parameters from the complete blood count (CBC), such as neutrophil, platelet, lymphocyte, and monocyte counts; electrocardiograms; cardiac enzyme profiles (including creatine kinase-MB and cardiac troponin levels); echocardiography reports; serum creatinine values from renal function tests; and vital signs at presentation (pulse rate and blood pressure).

All this information was documented in a study-specific proforma (available as supplementary material). Any patient data left incomplete in the process resulted in the exclusion of the respective patient from the statistical analysis. From this dataset, we calculated the NLR, PLR, SIRI, and GRACE scores.

2.3. Statistical analysis

All the data were collected in Microsoft Excel 2020 and later imported into Jamovi Software V.2.3.1 and R software for statistical analysis. Age, the NLR, the PLR, the SIRI, and GRACE scores were entered as continuous variables. The GRACE category was recorded as a categorical variable. The Kolmogorov–Smirnov test and Anderson–Darling test were used to check the normal distribution of the data (normality). Continuous variables are expressed as the mean ± standard deviation (SD) or median with a 25–75 % interquartile range (IQR). Categorical variables are expressed as percentages with 95 % confidence intervals. Group values with p values < 0.001 were deemed to be significant.

To obtain an overall view of the data collected, descriptive analysis was performed. Summary statistics such as the mean, median, standard deviation, and interquartile range were computed. The relationships between the NLR, PLR, and SIRI and the prognosis of ACS patients calculated via the GRACE score were established via Spearman rank correlation to determine whether there was any association between these parameters and the prognosis of ACS patients.

The patients were then categorized into low, intermediate, and high risk of in-hospital mortality groups on the basis of their GRACE scores. Low (1–108), intermediate (109–140), and high (141–372). To determine the impact of ACS prognosis on the NLR, PLR, and SIRI, a Kruskal–Wallis one–way analysis of variance (ANOVA) was used to evaluate whether the prognosis of ACS patients influenced the variations observed in these hematological parameters. The Dwass-Steel-Critchlow-Fligner (DSCF) post hoc test was subsequently performed to make pairwise comparisons between the various risk groups. This post hoc analysis revealed specific group distinctions between the categories.

We employed generalized linear models (GLMs) with a gamma distribution and log-link function to investigate the relationships between the predictor variables (NLR, PLR, and SIRI) and the target variable (GRACE scores). The rationale behind using GLMs with a gamma distribution and log-link function lies in the nature of the response variable, GRACE scores, which are continuous and potentially skewed. The gamma distribution is well suited for modeling positive-valued continuous data that may exhibit the right skewness, making it appropriate for modeling GRACE scores. Additionally, the log-link function is commonly used with a gamma distribution in GLMs to ensure that the predicted values remain positive.

We conducted k-fold cross-validation to assess the performance of linear regression models using predictor variables to predict GRACE scores in participants. The rationale lies in the need to evaluate the generalizability of the predictive models. By splitting the dataset into k subsets/folds, training the model on k-1 folds, and validating it on the remaining fold, we can obtain more reliable estimates of the model's performance than can a single train–test split. This approach helps mitigate the risk of overfitting and provides a more accurate assessment of how well the model performs on unseen data. To obtain the cutoff values of the NLR, PLR, and

SIRI for categorizing patients according to low-, intermediate-, and high-risk hospital mortality, we plotted ROC curves individually between i) low- and intermediate-risk patients and ii) intermediate- and high-risk patients. The cutoff values were chosen on the basis of the highest Youden index.

2.4. Ethical approval and informed consent

This study was approved by the Institutional Ethics Committee of Government Medical College, Omandurar, Government Estate (Registration Number – ECR/1492/Inst/TN/2021), with approval number 73/IEC/GOMC/2023 dated September 5, 2023.

All procedures performed in studies involving human patients followed the ethical standards of the 1964 Helsinki Declaration and its later amendments. The Institutional Ethics Committee waived the requirement for written informed consent from all individual participants involved in the study because of its retrospective nature. This article does not contain any studies with animals performed by any of the authors.

3. Results

Between January 2022 and December 2023, 337 individuals received a diagnosis of acute coronary syndrome (ACS) following the American College of Cardiology (ACC) guidelines from our institution. After applying the exclusion criteria, we identified a group of 279 individuals. However, after those with incomplete medical records were excluded, only 247 individuals were included in the analysis. Table 1 presents summary statistics and demographic details of the study participants.

The results of the Kolmogorov–Smirnov and Anderson–Darling tests revealed that the data did not follow a normal distribution. Spearman correlation analysis revealed a significant association between the GRACE score and hematological parameters (NLR, PLR, and SIRI), with p values less than 0.001. Among these variables, the SIRI demonstrated the strongest association, with a Spearman rho value of 0.943. In contrast, the PLR exhibited the weakest association, with a Spearman rho value of 0.488. The NLR displayed an intermediate level of association, with a Spearman rho value of 0.795.

We employed Kruskal–Wallis one-way analysis of variance to assess the influence of the NLR, PLR, and SIRI on the prognostic risk determined by GRACE. The results indicate significant differences for all three variables: NLR ($\chi^2 = 106.4$, df = 2, $p < 0.001$), PLR ($\chi^2 = 49.7$, df = 2, $p < 0.001$), and SIRI ($\chi^2 = 153.5$, df = 2, $p < 0.001$). The DSCF post hoc test was subsequently performed to make pairwise comparisons between the various risk groups. This post hoc analysis revealed specific group distinctions between pairwise prognostic risk comparisons. The results from this analysis are presented in Table 2.

GLMs with a gamma distribution and log-link function demonstrated significant associations between NLR, PLR, and SIRI levels and GRACE scores. The findings, summarized in Table 3, underscore the significance of all three variables in predicting GRACE scores. The models suggested that the SIRI could be marginally superior, as indicated by its comparatively smaller standard error. However, additional validation is necessary to confirm this observation.

The k-fold cross-validation results for predicting GRACE scores via the predictor variables are summarized in Table 4. The mean squared error (MSE), mean absolute error (MAE), and R-squared values were calculated for each predictor. Among the three predictors, the SIRI yields the lowest MSE and MAE values, indicating superior predictive accuracy compared with the NLR and PLR. Additionally, the SIRI has the highest R-squared value, suggesting that it explains a larger proportion of the variance in the GRACE scores.

We generated individual receiver operating characteristic (ROC) plots for the following pairwise prognostic risk groups: 'Low' vs. 'Intermediate' and 'Intermediate' vs. 'High.' On the basis of the highest Youden's index, cutoff points for the NLR, PLR, and SIRI to distinguish prognosis were identified and are tabulated in Table 5.

4. Discussion

We found significant associations between the NLR, PLR, SIRI, and GRACE score in ACS patients. The SIRI exhibited the strongest association, whereas the PLR had the weakest association. All three variables significantly influenced prognostic risk, as determined by the GRACE score. GLM models highlighted the predictive significance of the NLR, PLR, and SIRI in estimating GRACE scores, with the SIRI showing potential superiority. K-fold cross-validation confirmed the superior predictive accuracy and ability of the SIRI to explain a larger proportion of variance in GRACE scores than the NLR and PLR. Individual ROC analysis identified optimal cutoff points for distinguishing prognostic risk groups on the basis of these predictors.

Table 1
Summary statistics of age, NLR, PLR, SIRI, and GRACE score.

	Mean ± SD	Median (25–75)
Age	55.9 ± 10.8	55 (49.0–62.0)
NLR	5.35 ± 10.6	4.23 (2.34–6.31)
PLR	157 ± 117	137 (96.8–189)
SIRI	8498 ± 9956	5370 (2305–13,212)
GRACE Score	116 ± 35.9	112 (89.8–141)

Table 2
Pairwise comparisons of predictor variables across GRACE score categories.

Comparison	Variable	W	p-value
Low vs. Intermediate	NLR	11.87	<0.001
	PLR	6.92	<0.001
	SIRI	14.44	<0.001
Intermediate vs. High	NLR	2.70	0.136
	PLR	3.65	0.027
	SIRI	9.40	<0.001
Low vs. High	NLR	10.80	<0.001
	PLR	8.37	<0.001
	SIRI	12.10	<0.001

Table 3
GLM model summary for NLR, PLR, and SIRI.

Predictor	Estimate	t-value	Dispersion	Residual Deviance	AIC	Fisher Scoring Iterations
NLR	0.012	6.929	0.083	22.329	2441.7	14
PLR	0.001	4.963	0.085	23.556	2455.1	9
SIRI	0.00003	20.42	0.041	12.549	2297.7	11

Table 4
Performance metrics of predictors in K-fold cross-validation.

Predictor	Mean Squared Error	Mean Absolute Error	R-squared
NLR	1108.24	26.8088	0.1344467
PLR	1217.18	27.7391	0.0493634
SIRI	577.115	16.5506	0.5492625

Table 5
Prognostic risk group differentiation by predictor cut-off points and performance characteristics.

Risk Group Comparison	Predictor	Cut-off Point	AUC	Sensitivity (%)	Specificity (%)
Low vs. Intermediate	NLR	3.31579	0.870	98.33	63.64
	PLR	99.0625	0.715	95.00	40.91
	SIRI	5870.118	0.950	98.33	81.17
Intermediate vs. High	NLR	5.81818	0.620	84.85	43.33
	PLR	166.364	0.662	84.85	53.33
	SIRI	17873.85	0.918	90.91	98.33

Neutrophils are the earliest leukocytes to arrive at the site of infarction during ACS and release free radicals, which serve as a pathway for injuring cardiomyocytes. They also release enzymes that aid in the clearance of infarcted tissue and enhance immune cell recruitment (macrophages) [18–20]. In the subsequent phases, lymphocytes play critical roles in myocardial remodeling. T cells recruit proangiogenic macrophages and facilitate collateral artery formation [21,22]. B cells contribute to monocyte recruitment through the CCL7 pathway [23]. Monocytes are actively involved in triggering the inflammatory cascade in ACS. Activated monocytes promote the synthesis of proinflammatory molecules, such as IL-6 and TNF-α [24]. Additionally, damaged atherosclerotic plaques activate platelets, potentially leading to thrombus formation and subsequent obstruction of coronary blood flow, resulting in myocardial ischemia [25].

With respect to the importance of these pathways, studies have focused on investigating the utility of markers such as the NLR and PLR in assessing ACS prognosis. These investigations were prompted by the accessibility and affordability of hemogram tests routinely conducted in all admitted patients [26–34]. SIRI is a novel inflammatory marker that has been investigated in rheumatoid arthritis [35] and various tumors [36–38]. Few studies have investigated the role of the SIRI in ACS prognosis [39,40].

A study by Qiuxuan Li et al. investigated the prognostic value of lymphocyte-based inflammatory indices, including the NLR, PLR, and SIRI, for predicting major adverse cardiovascular events (MACEs) in ACS patients and concluded that the SIRI was a superior predictor of MACEs compared with other indices and that combining the SIRI with the GRACE risk score enhanced the accuracy of risk prediction [40]. Oncel RC et al. examined the relationship between the NLR and the GRACE risk score in STEMI patients and reported that the NLR was significantly associated with worse in-hospital outcomes independent of the GRACE score [28].

In a review by Budzianowski J et al., the role of various hematological indices in ACS highlighted the growing interest in these indices for their prognostic value in risk stratification and their utility in combination with other markers, such as troponin and GRACE scores [41]. De Liyis BG et al. explored the prognostic significance of the NLR and PLR in predicting high-risk mortality in ACS patients and emphasized the independent predictive value of troponin, the NLR, and the MLR for high-risk mortality [42]. Zhou D et al. focused

on the association between the PLR and the GRACE score and concluded that the PLR could enhance the predictive value of the GRACE score [43].

The findings of this study hold significant clinical implications for the management of ACS. The SIRI, as a potential prognostic marker, offers insights into risk assessment and treatment planning. Unlike traditional scoring systems that rely on complex and time-consuming assessments, the SIRI can be easily calculated from routine hemogram tests with differentials, making it a convenient and cost-effective tool for risk stratification in the emergency department where clinicians can swiftly identify patients at greater risk of adverse outcomes and tailor their management strategies accordingly.

This study's strengths include establishing cutoff values for risk stratification, using GLM with a gamma distribution and log-link function, and employing readily available routine investigations that allow for easier integration of these markers into existing health record systems. The limitations of this study include its retrospective design and the absence of a longitudinal assessment. The retrospective nature of this study restricts the establishment of causal relationships between the NLR, PLR, SIRI, and ACS prognosis. Additionally, we did not evaluate the SIRI throughout treatment or follow-up, which overlooks potential fluctuations in inflammatory markers.

Several avenues can enhance the impact of our research on the prognostic assessment of ACS. First, multicenter validation studies are needed to evaluate the generalizability and external validity of the observed associations between the SIRI and ACS prognosis across diverse patient populations and healthcare settings. Additionally, longitudinal studies are essential to assess the long-term prognostic value of the SIRI in ACS patients. Moreover, investigating the feasibility of integrating the SIRI into existing risk prediction models, such as the GRACE score, could enhance their predictive performance and clinical utility. Implementation studies are also warranted to evaluate the feasibility, acceptability, and cost-effectiveness of incorporating the SIRI into routine clinical practice for risk assessment and management of ACS patients in real-world healthcare settings.

5. Conclusions

Our study revealed significant associations between the NLR, PLR, SIRI, and GRACE score in ACS patients. The SIRI has emerged as a promising prognostic marker, outperforming the NLR and PLR in predicting ACS outcomes. Its ease of calculation from routine hemogram tests underscores its potential clinical utility for risk stratification in ACS management. Despite these limitations, further validation and the integration of the SIRI into existing risk assessment models hold promise for improving prognosis assessment and risk stratification in ACS patients.

CRediT authorship contribution statement

Hamrish Kumar Rajakumar: Writing – original draft, Visualization, Validation, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Varsha Coimbatore Sathyabal:** Writing – original draft, Validation, Methodology, Investigation, Data curation, Conceptualization. **Mannar Vasanthan:** Writing – review & editing, Validation, Supervision, Resources. **Ramesh Dasarathan:** Writing – review & editing, Supervision.

Consent for publication

Not Applicable.

Availability of data and materials

The data utilized in this research will be accessible upon request from H.K but will not be publicly accessible to safeguard the confidentiality and privacy of the patients who participated. Requests for data access must specify the purpose for which the data will be utilized. In cases of data reuse, a proposal outlining the purpose, the intended usage of the data, and a letter from the department head or the institution's leadership will be mandatory. Additionally, any subsequent data generation should be communicated to the H.K.

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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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e39029.

References

[1] T. Hedayati, N. Yadav, J. Khanagavi, Non–ST-segment acute coronary syndromes, Cardiol. Clin. 36 (1) (2018) 37–52, https://doi.org/10.1016/j.ccl.2017.08.003 [Internet].

[2] E. Nabovati, M. Farzandipour, M. Sadeghi, N. Sarrafzadegan, F. Noohi, M. Sadeqi Jabali, A global overview of acute coronary syndrome registries: a systematic review, Curr. Probl. Cardiol. 48 (4) (2023) 101049, https://doi.org/10.1016/j.cpcardiol.2021.101049 [Internet].

[3] A. Timmis, D. Kazakiewicz, N. Townsend, R. Huculeci, V. Aboyans, P. Vardas, Global epidemiology of acute coronary syndromes, Nat. Rev. Cardiol. 20 (11) (2023) 778–788 [Internet], https://pubmed.ncbi.nlm.nih.gov/37231077/. (Accessed 5 September 2024).

[4] K.S. Chandra, A.J. Swamy (Eds.), Acute Coronary Syndromes, first ed., CRC Press, Boca Raton, 2020. CRC Press; 2020.

[5] G. Cervellin, G. Rastelli, The clinics of acute coronary syndrome, Ann. Transl. Med. 4 (10) (2016), https://doi.org/10.21037/atm.2016.05.10, 191–191. (Accessed 5 September 2024).

[6] J.N. Smith, J.M. Negrelli, M.B. Manek, E.M. Hawes, A.J. Viera, Diagnosis and management of acute coronary syndrome: an evidence-based update, J. Am. Board Fam. Med. 28 (2) (2015) 283–293, https://doi.org/10.3122/jabfm.2015.02.140189 [Internet].

[7] R.A. Byrne, X. Rossello, J.J. Coughlan, E. Barbato, C. Berry, A. Chieffo, et al., 2023 ESC Guidelines for the management of acute coronary syndromes, Eur. Heart J. 44 (38) (2023) 3720–3826, https://doi.org/10.1093/eurheartj/ehad191 [Internet].

[8] R. Khalill, L. Han, C. Jing, H. Quan, The use of risk scores for stratification of non-ST elevation acute coronary syndrome patients, Exp. Clin. Cardiol. 14 (2) (2009) e25.

[9] P.D. Myers, B.M. Scirica, C.M. Stultz, Machine learning improves risk stratification after acute coronary syndrome, Sci. Rep. 7 (1) (2017) 1–12 [Internet], https://www.nature.com/articles/s41598-017-12951-x. (Accessed 5 September 2024).

[10] S. Subherwal, R.G. Bach, A.Y. Chen, B.F. Gage, S.V. Rao, L.K. Newby, et al., Baseline risk of major bleeding in non–ST-segment–elevation myocardial infarction: the CRUSADE (can rapid risk stratification of unstable angina patients suppress ADverse outcomes with early implementation of the ACC/AHA guidelines) bleeding score, Circulation 119 (14) (2009), https://doi.org/10.1161/circulationaha.108.828541, 1873–82. (Accessed 4 March 2024).

[11] S. Addala, C.L. Grines, S.R. Dixon, G.W. Stone, J.A. Boura, A.B. Ochoa, et al., Predicting mortality in patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention (PAMI risk score), Am. J. Cardiol. 93 (5) (2004) 629–632, https://doi.org/10.1016/j.amjcard.2003.11.036 [Internet].

[12] E. Boersma, K.S. Pieper, E.W. Steyerberg, R.G. Wilcox, W.-C. Chang, K.L. Lee, et al., Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation: results from an international trial of 9461 patients, Circulation 101 (22) (2000), 2557–67, https://pubmed.ncbi.nlm.nih.gov/10840005/. (Accessed 4 March 2024).

[13] K.A.A. Fox, O.H. Dabbous, R.J. Goldberg, K.S. Pieper, K.A. Eagle, F. Van de Werf, et al., Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE), BMJ 333 (7578) (2006) 1091, https://doi.org/10.1136/bmj.38985.646481.55 [Internet].

[14] S. Littnerova, P. Kala, J. Jarkovsky, L. Kubkova, K. Prymusova, P. Kubena, et al., GRACE score among six risk scoring systems (CADILLAC, PAMI, TIMI, dynamic TIMI, Zwolle) demonstrated the best predictive value for prediction of long-term mortality in patients with ST-elevation myocardial infarction, PLoS One 10 (4) (2015) e0123215, https://doi.org/10.1371/journal.pone.0123215 [Internet]. (Accessed 5 September 2024).

[15] J. Yan, C.-J. Deng, S.-F. Wang, T.-T. Wu, Y.-Y. Zheng, X. Xie, et al., Predictive value of the modified GRACE scoring system for all-cause mortality in patients with acute myocardial infarction, Rev. Cardiovasc. Med. 24 (6) (2023) 161, https://doi.org/10.31083/j.rcm2406161 [Internet]. (Accessed 5 September 2024).

[16] P. de Araújo Gonçalves, J. Ferreira, C. Aguiar, R. Seabra-Gomes, TIMI, PURSUIT, and GRACE risk scores: sustained prognostic value and interaction with revascularization in NSTE-ACS, Eur. Heart J. 26 (9) (2005) 865–872 [Internet], https://pubmed.ncbi.nlm.nih.gov/15764619/. (Accessed 5 September 2024).

[17] H. Wang, Z. Liu, J. Shao, L. Lin, M. Jiang, L. Wang, et al., Immune and inflammation in acute coronary syndrome: molecular mechanisms and therapeutic implications, J Immunol Res (2020) 1–11 [Internet]. 2020, https://pubmed.ncbi.nlm.nih.gov/32908939/. (Accessed 5 September 2024).

[18] V. Frodermann, M. Nahrendorf, Neutrophil–macrophage cross-talk in acute myocardial infarction, Eur. Heart J. 38 (3) (2016), https://doi.org/10.1093/eurheartj/ehw085 ehw085. (Accessed 5 March 2024).

[19] E. Kolaczkowska, P. Kubes, Neutrophil recruitment and function in health and inflammation, Nat. Rev. Immunol. 13 (3) (2013) 159–175 [Internet], https://pubmed.ncbi.nlm.nih.gov/23435331/. (Accessed 5 March 2024).

[20] M. Horckmans, L. Ring, J. Duchene, D. Santovito, M.J. Schloss, M. Drechsler, et al., Neutrophils orchestrate post-myocardial infarction healing by polarizing macrophages towards a reparative phenotype, Eur. Heart J. 38 (3) (2016) ehw002, https://pubmed.ncbi.nlm.nih.gov/28158426/. (Accessed 5 March 2024).

[21] E. Stephenson, K. Savvatis, S.A. Mohiddin, F.M. Marelli-Berg, T-cell immunity in myocardial inflammation: pathogenic role and therapeutic manipulation, Br. J. Pharmacol. 174 (22) (2017) 3914–3925, https://doi.org/10.1111/bph.13613 [Internet]. (Accessed 5 March 2024).

[22] T.-T. Tang, J. Yuan, Z.-F. Zhu, W.-C. Zhang, H. Xiao, N. Xia, et al., Regulatory T cells ameliorate cardiac remodeling after myocardial infarction, Basic Res. Cardiol. 107 (1) (2012) [Internet], https://pubmed.ncbi.nlm.nih.gov/22189560/. (Accessed 5 March 2024).

[23] A. Inaba, Z.K. Tuong, A.M. Riding, R.J. Mathews, J.L. Martin, K. Saeb-Parsy, et al., B lymphocyte–derived CCL7 augments neutrophil and monocyte recruitment, exacerbating Acute kidney injury, J. Immunol. 205 (5) (2020) 1376–1384 [Internet], https://pubmed.ncbi.nlm.nih.gov/32737150/. (Accessed 5 March 2024).

[24] M. Satoh, Y. Shimoda, T. Akatsu, Y. Ishikawa, Y. Minami, M. Nakamura, Elevated circulating levels of heat shock protein 70 are related to systemic inflammatory reaction through monocyte Toll signal in patients with heart failure after acute myocardial infarction, Eur. J. Heart Fail. 8 (8) (2006) 810–815 [Internet], https://pubmed.ncbi.nlm.nih.gov/16714144/. (Accessed 5 March 2024).

[25] E. Falk, M. Nakano, J.F. Bentzon, A.V. Finn, R. Virmani, Update on acute coronary syndromes: the pathologists' view, Eur. Heart J. 34 (10) (2013) 719–728, https://doi.org/10.1093/eurheartj/ehs411 [Internet].

[26] P. Maréchal, J. Tridetti, M.-L. Nguyen, O. Wéra, Z. Jiang, M. Gustin, et al., Neutrophil phenotypes in coronary artery disease, J. Clin. Med. 9 (5) (2020) 1602, https://doi.org/10.3390/jcm9051602 [Internet]. (Accessed 5 September 2024).

[27] Y. Arbel, Y. Shacham, T. Ziv-Baran, M. Laufer Perl, A. Finkelstein, A. Halkin, et al., Higher neutrophil/lymphocyte ratio is related to lower ejection fraction and higher long-term all-cause mortality in ST-elevation myocardial infarction patients, Can. J. Cardiol. 30 (10) (2014) 1177–1182 [Internet], https://pubmed.ncbi.nlm.nih.gov/25154806/. (Accessed 5 March 2024).

[28] R.C. Oncel, M. Ucar, M.S. Karakas, B. Akdemir, A. Yanikoglu, A.R. Gulcan, et al., Relation of neutrophil-to-lymphocyte ratio with GRACE risk score to in-hospital cardiac events in patients with ST-segment elevated myocardial infarction, Clin. Appl. Thromb. Hemost. 21 (4) (2015) 383–388 [Internet], https://pubmed.ncbi.nlm.nih.gov/24078555/. (Accessed 5 March 2024).

[29] E. Gazi, B. Bayram, S. Gazi, A. Temiz, B. Kirilmaz, B. Altun, et al., Prognostic value of the neutrophil–lymphocyte ratio in patients with ST-elevated acute myocardial infarction, Clin. Appl. Thromb. Hemost. 21 (2) (2015) 155–159 [Internet], https://pubmed.ncbi.nlm.nih.gov/23754837/. (Accessed 5 March 2024).

[30] P. Venkataswamy Reddy, A. Ahuja, B. Asthana, K. Singh, G. Sagoo, To evaluate platelet indices, platelet to lymphocyte ratio and neutrophil to lymphocyte ratio as prognostic and risk factors in patients with coronary artery disease, Indian J Hematol Blood Transfus 40 (1) (2024) 103–107 [Internet], https://pubmed.ncbi.nlm.nih.gov/38312187/. (Accessed 5 September 2024).

[31] M. Ertürk, F.N. Turhan Caglar, İ. Bıyık, Correlations between hematological indicators and other known markers in acute coronary syndromes, E-J Cardiovasc Med 5 (4) (2017) 67–74, https://doi.org/10.15511/ejcm.17.00467 [Internet].
[32] B. Azab, N. Shah, M. Akerman, J.T. McGinn Jr., Value of platelet/lymphocyte ratio as a predictor of all-cause mortality after non-ST-elevation myocardial infarction, J. Thromb. Thrombolysis 34 (3) (2012) 326–334 [Internet], https://pubmed.ncbi.nlm.nih.gov/22466812/. (Accessed 5 March 2024).
[33] M. Ugur, M. Gul, M. Bozbay, G. Cicek, H. Uyarel, B. Koroglu, et al., The relationship between platelet to lymphocyte ratio and the clinical outcomes in ST elevation myocardial infarction underwent primary coronary intervention, Blood Coagul. Fibrinolysis 25 (8) (2014) 806–811 [Internet], https://pubmed.ncbi.nlm.nih.gov/24911455/. (Accessed 5 March 2024).
[34] Cetin EH. Ozcan, M.S. Cetin, D. Aras, S. Topaloglu, A. Temizhan, H.L. Kisacik, et al., Platelet to lymphocyte ratio as a prognostic marker of in-hospital and long-term major adverse cardiovascular events in ST-segment elevation myocardial infarction, Angiology 67 (4) (2016) 336–345 [Internet], https://pubmed.ncbi.nlm.nih.gov/26101368/. (Accessed 5 March 2024).
[35] Y. Xu, H. He, Y. Zang, Z. Yu, H. Hu, J. Cui, et al., Systemic inflammation response index (SIRI) as a novel biomarker in patients with rheumatoid arthritis: a multi-center retrospective study, Clin. Rheumatol. 41 (7) (2022) 1989–2000 [Internet], https://pubmed.ncbi.nlm.nih.gov/35266094/. (Accessed 5 March 2024).
[36] H. Yazici, S.C. Yegen, Is systemic inflammatory response index (SIRI) a reliable tool for prognosis of gastric cancer patients without neoadjuvant therapy? Cureus 15 (3) (2023) [Internet], https://pubmed.ncbi.nlm.nih.gov/37095818/. (Accessed 5 March 2024).
[37] X. Hua, Z.-Q. Long, X. Huang, J.-P. Deng, W. Wen, Z.-Y. He, et al., The preoperative systemic inflammation response index (SIRI) independently predicts survival in postmenopausal women with breast cancer, Curr. Probl. Cancer 44 (4) (2020) 100560 [Internet], https://pubmed.ncbi.nlm.nih.gov/32122667/. (Accessed 5 March 2024).
[38] T. Wang, D. Zhang, D. Tang, Y. Heng, L.-M. Lu, L. Tao, The role of systemic inflammatory response index (SIRI) and tumor-infiltrating lymphocytes (TILs) in the prognosis of patients with laryngeal squamous cell carcinoma, J. Cancer Res. Clin. Oncol. 149 (9) (2023) 5627–5636 [Internet], https://pubmed.ncbi.nlm.nih.gov/36520215/. (Accessed 5 March 2024).
[39] K. Han, D. Shi, L. Yang, Z. Wang, Y. Li, F. Gao, et al., Prognostic value of systemic inflammatory response index in patients with acute coronary syndrome undergoing percutaneous coronary intervention, Ann. Med. 54 (1) (2022) 1667–1677, https://doi.org/10.1080/07853890.2022.2083671 [Internet]. (Accessed 5 March 2024).
[40] Q. Li, X. Ma, Q. Shao, Z. Yang, Y. Wang, F. Gao, et al., Prognostic impact of multiple lymphocyte-based inflammatory indices in acute coronary syndrome patients, Front Cardiovasc Med 9 (2022), https://doi.org/10.3389/fcvm.2022.811790 [Internet].
[41] J. Budzianowski, K. Pieszko, P. Burchardt, J. Rzeźniczak, J. Hiczkiewicz, The role of hematological indices in patients with acute coronary syndrome, Dis. Markers (2017) 1–9, 2017, https://pubmed.ncbi.nlm.nih.gov/29109595/. (Accessed 5 September 2024).
[42] BG de Liyis, A.F. Ciaves, M.H. Intizam, P.J. Jusuf, I.M.J.R. Artha, Hematological biomarkers of troponin, neutrophil-to-lymphocyte ratio, and monocyte-toLymphocyte ratio serve as effective predictive indicators of high-risk mortality in acute, Biomedicine 13 (4) (2023) 32–43 [Internet], https://pubmed.ncbi.nlm.nih.gov/38532835/. (Accessed 5 September 2024).
[43] D. Zhou, Y. Fan, Z. Wan, W. Wen, X. Wang, J. Zhou, et al., Platelet-to-lymphocyte ratio improves the predictive power of GRACE risk score for long-term cardiovascular events in patients with acute coronary syndrome, Cardiology 134 (1) (2016) 39–46 [Internet], https://pubmed.ncbi.nlm.nih.gov/26866504/. (Accessed 5 September 2024).