Journal of Inflammation Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Association and Comparison of Systemic Inflammation Indicators and Myocardial Injury After Noncardiac Surgery in Older Patients

Bingbing Meng[1,2,*], Kai Zhang[1,2,*], Chang Liu[2,3], Siyi Yao[1,2], Zhao Li[1,2], Jingsheng Lou[1,2], Qiang Fu[1,2], Yanhong Liu[1,2], Jiangbei Cao[1,2], Weidong Mi[1,2,4], Hao Li[1,2,4]

[1]Medical School of Chinese People's Liberation Army (PLA), Beijing, People's Republic of China; [2]Department of Anesthesiology, The First Medical Center, Chinese People's Liberation Army General Hospital (PLAGH), Beijing, People's Republic of China; [3]Nankai University, Tianjing, People's Republic of China; [4]National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing, People's Republic of China

*These authors contributed equally to this work

Correspondence: Weidong Mi; Hao Li, Department of Anesthesiology, The First Medical Center, Chinese People's Liberation Army General Hospital (PLAGH), 28th Fuxing Road, Haidian District, Beijing, 100853, People's Republic of China, Email wwdd1962@aliyun.com; lihao301@126.com

Objective: To identify the association between preoperative inflammatory state and myocardial injury after noncardiac surgery (MINS) in older patients using systemic inflammation indicators neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) and to compare their clinical predictive values.

Methods: This study included patients aged ≥65 years who underwent noncardiac surgery between January 2017 and August 2019. The relationship between preoperative inflammatory state and MINS was investigated using univariate and multivariate logistic regression analyses. The predictive values of NLR, PLR, and SII were determined by receiver operating characteristic (ROC) curve analysis. Based on the basic model we constructed, the predictive values were compared through separately adding NLR, PLR and SII.

Results: Among 12464 patients, 965 (7.74%) developed MINS. The optimal cut-off values of NLR, PLR, and SII were 597×10^9, 2.59, and 923. Univariate and multivariate analyses show that preoperative inflammatory state is associated with MINS. In the multivariate analysis, the OR values for NLR, PLR, and SII were (OR: 1.61, 95% CI: 1.36–1.89, p<0.001), (OR: 1.28, 95% CI: 1.07–1.52, p=0.006), and (OR: 1.43, 95% CI: 1.20–1.70, p<0.001). ROC curve analysis indicated that NLR was more predictive of MINS (area under the curve [AUC]: 0.671, 95% CI: 0.652–0.689) than PLR (AUC: 0.635, 95% CI: 0.616–0.655) and SII (AUC: 0.648, 95% CI: 0.628–0.667). The addition of the NLR to a basic prediction model improved its predictive ability to a greater extent than the addition of PLR and SII.

Conclusion: Higher preoperative inflammation levels are associated with an increased risk of MINS. The NLR, PLR, and SII are independent risk factors for MINS and NLR demonstrated better predictive value than that of PLR and SII.

Keywords: neutrophil-to-lymphocyte ratio, NLR, platelet-to-lymphocyte ratio, PLR, systemic, immune, inflammation index, SII, myocardial injury after noncardiac surgery, MINS

Introduction

Myocardial injury after noncardiac surgery (MINS) is a prevalent postoperative complication that frequently goes undetected owing to its asymptomatic manifestations.[1] Previous studies have reported MINS incidence rates of 13%–18%.[2,3] In addition, the VISION study found a correlation between MINS and an increased 30-day mortality risk, with MINS responsible for at least one-sixth of total deaths.[4,5] It has also been shown that patients with MINS have a 1.48 times higher risk of one-year mortality than that of those without MINS.[6] Older patients are at a higher risk of postoperative complications owing to a decrease in physiological reserve and pre-existing comorbidities; careful observation of these patients is therefore required.[7] Additionally, due to the increased fragility of the cardiovascular systems in older patients, there exists a significantly elevated

Received: 1 November 2024
Accepted: 22 February 2025
Published: 10 March 2025

perioperative cardiovascular risk in this population.[8] The identification of risk factors for MINS would allow older patients at high risk to be closely monitored and enable timely intervention.

Preoperative inflammatory state has been shown to be related to postoperative complications such as ischaemic stroke, delirium, and renal injury.[9–11] Furthermore, high levels of inflammation increase the risk of postoperative mortality.[12] In recent years, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) have become well-accepted biomarkers of inflammation.[13–15] Studies have shown the potential value of the NLR, PLR, and SII in predicting cardiovascular diseases such as major adverse cardiovascular events, vascular disease, and ST-segment elevation myocardial infarction.[16,17] In addition, the NLR has been found to be closely related to the development of MINS in patients aged over 45 years.[18,19] Older patients more frequently present with greater levels of inflammation because they are more likely to exhibit a higher inflammatory burden, hypertension, anaemia, and poor nutritional status;[20] however, relatively little attention has been given to the relationship between the preoperative inflammatory state and MINS in these patients. Moreover, few studies have compared the clinical predictive values of the NLR, PLR, and SII in MINS. Therefore, this study aimed to explore the relationship between the preoperative inflammatory state and MINS in older patients and to evaluate the clinical predictive values of these three indicators of inflammation.

Methods

Study Design and Population

This study included 12464 older patients (≥65 years old) who underwent noncardiac surgery at the First Medical Center of the Chinese People's Liberation Army General Hospital (PLAGH) between January 2017 and August 2019. The inclusion criteria were as follows: (1) undergoing noncardiac surgery and (2) aged ≥65 years. The exclusion criteria were as follows: (1) American Society of Anesthesiologists (ASA) classification V; (2) outpatient surgery, hysteroscopic surgery, or body surface surgery; (3) surgery duration ≤30 min; and (4) incomplete clinical data. This study was approved by the Research Ethics Committee of the Chinese People's Liberation Army General Hospital (approval number: S2024-107-01) and was carried out in compliance with the principles outlined in the Declaration of Helsinki. Given the retrospective observational nature of the study, the requirement for informed consent was waived. Patient confidentiality was assured by the protection of personal information in the medical record system.

Clinical Outcomes and Definition of Variables

MINS was diagnosed as a result of at least one postoperative high-sensitivity troponin T (hs-TnT) measurement of 20–65 ng/L with an absolute change of ≥5 ng/L or a hs-TnT concentration ≥65 ng/L due to a presumed ischaemic aetiology, regardless of the presence or absence of clinical symptoms or electrocardiographic changes. Elevated hs-TnT concentrations caused by nonischaemic mechanisms, such as pulmonary embolism, sepsis, and renal failure, were not considered MINS.[21] In our hospital, patients with high risks for cardiovascular events are asked to undergo TnT measurements using a Roche Elecsys hs-cTnT assay and a Cobas c 801 analyser (Roche Diagnostics, Mannheim, Germany). Patients who were not tested were considered negative for MINS.

The preoperative inflammatory state was determined by calculating the NLR, PLR, and SII. The SII was calculated as platelet × neutrophil/lymphocyte counts. The NLR was calculated as neutrophil/lymphocyte counts. The PLR was calculated as platelet/lymphocyte counts. The results were classified as high or low based on the optimal cut-off points, as determined from the receiver operating characteristic (ROC) curves: SII, low $\leq 597\times10^9$, high $>597\times10^9$; NLR, low ≤2.59, high >2.59; and PLR, low ≤923, high >923.

Data Collection

Data were obtained from the Chinese People's Liberation Army General Hospital perioperative data warehouse, built in collaboration with Shanghai Lejiu Healthcare Technology Co., Ltd. (Shanghai, China). The collected data included: (1) demographic variables (sex, age, body mass index, smoking status, and drinking status); (2) previous history (hypertension, cerebrovascular disease, diabetes needing interventions, coronary heart disease, cardiac intervention, arrhythmia, valvular

heart disease, heart failure, and peripheral vessel stenosis); (3) preoperative laboratory test results (white cell counts, levels of haemoglobin, serum creatinine, fibrinogen, NLR, PLR, and SII); and (4) surgery-related information (ASA classification, surgery situation, surgery type, surgery duration, crystalloid fluid, colloidal fluid, urine volume, blood loss, duration of intraoperative mean arterial pressure [MAP] <65 mmHg, and intraoperative blood transfusion).

Statistical Analysis

Normally distributed continuous variables are expressed as means and standard deviations, whereas non-normally distributed continuous variables are expressed as medians and interquartile ranges (IQRs). Categorical data are presented as frequencies and percentages. The variance test or Kruskal–Wallis rank-sum test was used to detect differences between continuous variables, and the chi-squared test or Fisher's exact test was used to compare categorical variables, as appropriate.

Univariate and multivariate logistic regression analyses were conducted to examine the relationship between the preoperative inflammatory state and MINS. Factors with a p-value <0.05 in the univariate logistic analysis and those that are clinically meaningful were selected for inclusion in the multivariate logistic regression model.

The predictive abilities of the NLR, PLR, and SII to predict MINS were assessed using the area under the ROC curve (AUC) and compared using the DeLong test. To verify the predictive value of the NLR, PLR, and SII for MINS, we constructed three predictive models. First, the data used in this study were randomly divided into two groups, a training set and a validation set, at a ratio of 7:3. Univariate logistic regression analysis was used to identify risk factors for MINS; those with *a p-value <0.05* and clinically meaningful factors were included in the multivariate logistic regression analysis. The NLR, PLR, and SII were then separately added to the base model, resulting in three predictive models. The AUC was used to quantify the predictive ability of the three models in the training and validation sets. The net reclassification index (NRI) and integrated discrimination improvement (IDI) were used to assess and compare the discriminatory capacities of the three models for predicting MINS.

We also performed subgroup analysis according to sex (female or male), ASA classification (I/II or III/IV), surgery duration (more than or less than 3 hours), blood loss (more than or less than 200mL), surgery situation (elective surgery and emergency surgery) and surgery type (head and neck surgery, thoracic and vascular surgery, abdominal surgery, limb and spinal surgery and other surgery), repeating the analysis and identifying the influence of systemic inflammation indicators on MINS.

A two-tailed *p*-value <0.05 was considered significantly different. Statistical analyses were performed using R software version 3.6.3 (The R Foundation for Statistical Computing, Vienna, Austria; www.rproject.org).

Results

Patient Characteristics

From January 2017 to August 2019, a total of 16521 patients who underwent noncardiac surgery at the Chinese People's Liberation Army General Hospital were included in the study, of whom 965 (7.74%) developed MINS (Figure 1). The baseline characteristics of these older patients with or without MINS are summarized in Table 1. Patients with MINS had significantly higher white blood cell counts (median [IQR]: 6.27×10^9 [5.05×10^9, 8.01×10^9] vs 5.87×10^9 [4.88×10^9, 7.06×10^9], $p<0.001$), serum creatinine levels (median [IQR]: 76.3 [61.4, 93.1] vs 71.4 [61.05, 83], $p<0.001$), and fibrinogen levels (median [IQR]: 3.73 [3.06, 4.55] vs 3.3 [2.83, 3.89], $p<0.001$), and significantly lower haemoglobin levels (median [IQR]: 122 [106, 136] vs 132 [120, 142], $p<0.001$) than patients without MINS. Patients with MINS also had significantly higher NLRs (median [IQR]: 2.74 [1.84, 4.29] vs 1.94 [1.46, 2.72], $p<0.001$), SIIs (median [IQR]: 573.16×10^9 [360.62×10^9, 983.8×10^9] vs 404.7×10^9 [280.77×10^9, 597.87×10^9], $p<0.001$), and PLRs (median [IQR]: 883.87 [626.47, 1375] vs 692.31 [526.01, 939.21], $p<0.001$) than patients without MINS (Table 1 and Figure 2).

Relationship Between Preoperative Inflammatory State and MINS

To detect any correlations between MINS and preoperative inflammation state, the SII, NLR, and PLR results were classified as high or low based on the optimal cut-off points calculated from the ROC curves. The association between preoperative inflammatory state and MINS in older patients was evaluated using univariate and multivariate logistic

 https://doi.org/10.2147/JIR.S500795

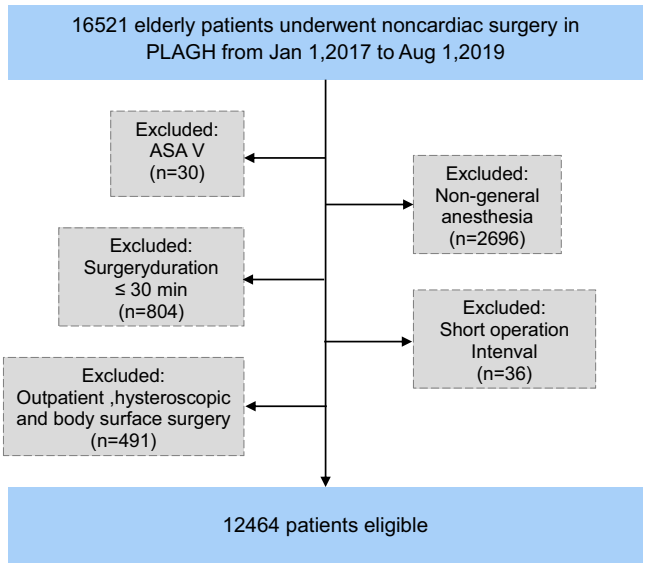

Figure 1 The flowchart of participants selection.

analyses. As shown in Table 2, univariate analysis revealed that in older patients, an NLR >2.59 (odds ratio [OR]: 3.08, 95% confidence interval [CI]: 2.70–3.52, $p<0.001$), a PLR >923 (OR: 2.56, 95% CI: 2.24–2.93, $p<0.001$), and an SII >597×10^9 (OR: 2.79, 95% CI: 2.44–3.19, $p<0.001$) were all associated with MINS. After adjusting for confounding factors in multivariate analysis, an NLR >2.59 (OR: 1.61, 95% CI: 1.36–1.89, $p<0.001$) demonstrated a higher OR value than PLR >923 (OR: 1.28, 95% CI: 1.07–1.52, $p=0.006$) or SII >597×10^9 (OR: 1.43, 95% CI: 1.20–1.70, *p<0.001*).

Table 1 Baseline Characteristics of Patients with or without MINS

Variable	Non-MINS (n=11499)	MINS (n=965)	Total (n=12464)	*P*
Demographic characteristics				
Male, n (%)	6222(54.1)	570(59.1)	6792(54.5)	0.003
Age (yr), median [IQR]	69(67,73)	72(68,77)	69(67,74)	<0.001
BMI (kg/m^2), median [IQR]	24.34(22.20,26.62)	23.82(21.39,26.4)	24.3(22.13,26.58)	<0.001
Smoking status, n (%)				0.693
Never smoker	8514(74)	721(74.7)	9235(74.1)	
Current smoker	1455(12.7)	113(11.7)	1568(12.6)	
Former smoker	1530(13.3)	131(13.6)	1661(13.3)	
Drinking status, n(%)				0.311
Never drinker	8728(75.9)	750(77.7)	9478(76)	
Current drinker	1885(16.4)	140(14.5)	2025(16.2)	
Former drinker	886(7.7)	75(7.8)	961(7.7)	
Previous history; n (%)				
Hypertension	5207(45.3)	518(53.7)	5725(45.9)	<0.001
Cerebrovascular diseases	834(7.3)	142(14.7)	976(7.8)	<0.001
Diabetes (need interventions)	2534(30)	288(29.8)	2822(22.6)	<0.001
Coronary heart disease	1319(11.5)	227(23.5)	1546(12.4)	<0.001
Cardiac interventions	355(3.1)	79(8.2)	434(3.5)	<0.001
Arrhythmia	1197(10.4)	180(18.7)	1377(11)	<0.001
Valvular heart disease	54(0.5)	7(0.7)	61(0.5)	0.393
Heart failure	14(0.1)	21(2.2)	35(0.3)	<0.001
Peripheral vessel stenosis	230(2)	35(3.6)	265(2.1)	0.001

(*Continued*)

Table 1 (Continued).

Variable	Non-MINS (n=11499)	MINS (n=965)	Total (n=12464)	*P*
Preoperative laboratory data				
White cell (10^9), median [IQR]	5.87(4.88,7.06)	6.27(5.05,8.01)	5.9(4.89,7.13)	<0.001
Hgb(g/L), median [IQR]	132(120,142)	122(106,136)	131(120,142)	<0.001
SCr (umol/L), median [IQR]	71.4(61.05,83)	76.3(61.4,93.1)	71.6(61.1,83.7)	<0.001
FB (g/L), median [IQR]	3.3(2.83,3.89)	3.73(3.06,4.55)	3.32(2.84,3.95)	<0.001
SII, Median (IQR)	404.7(280.77,597.87)	573.16(360.62,983.89)	413.35(285,621.38)	<0.001
NLR, Median (IQR)	1.94(1.46,2.72)	2.74(1.84,4.294)	2(1.47,2.82)	<0.001
PLR, Median (IQR)	692.31(526.01,939.21)	883.87(626.47,1375)	703.57(530.72,964.90)	<0.001
Surgery-related factors				
ASA classification, n (%)				<0.001
I	114(1)	8(0.8)	122(1)	
II	9346(81.3)	519(53.8)	9865(79.1)	
III	1994(17.3)	380(39.4)	2374(19)	
IV	45(0.4)	58(6)	103(0.8)	
Surgery situation, n (%)				<0.001
Elective surgery	11299(98.3)	882(91.4)	12,181(97.7)	
Emergency surgery	200(1.7)	83(8.6)	283(2.3)	
Surgery type, n (%)				<0.001
Head and neck	1893(16.5)	96(9.9)	1989(16)	
Thorax and vessel	1426(12.4)	91(9.4)	1517(12.2)	
Abdomen	4612(40.1)	513(53.2)	5125(41.1)	
Limbs and spine	2283(19.9)	216(22.4)	2499(20)	
Others	1285(11.2)	49(5.1)	1334(10.7)	
Surgery duration (min), median [IQR]	140(90,205)	195(127,273)	145(93,210)	<0.001
Crystalloid infusion (mL),median (IQR)	1600(1100,2100)	2100(1500,2600)	1600(1100,2100)	<0.001
Colloid infusion (mL),median (IQR)	500(0,500)	500(500,1000)	500(0,500)	<0.001
Urine volume (mL),median (IQR)	200(100,500)	400(200,700)	250(100,600)	<0.001
Blood loss(mL),median (IQR)	100(30,200)	200(70,400)	100(50,200)	<0.001
Duration of intraoperative MAP<65mmHg,median [IQR]	5.5(0.5,13.5)	8.5(1.5,29)	5.5(0.5,14.5)	<0.001
Intraoperative blood transfusion, n (%)	1005(8.7)	261(26)	1266(10.2)	<0.001

Abbreviations: IQR, interquartile ranges; BMI, body mass index; Hgb, hemoglobin; SCr, serum creatinine; FB, fibrinogen; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; RCRI, revised cardiac risk index; ASA, American Society of Anesthesiologists; MAP, mean arterial pressure.

Predictive Ability of Systemic Inflammation Indicators for MINS

To evaluate and compare the predictive values of the NLR, PLR, and SII for MINS, we performed ROC curve analysis. As shown in Figure 3, the NLR (AUC: 0.671, 95% CI: 0.652–0.689), PLR (AUC: 0.635, 95% CI: 0.616–0.655), and SII (AUC: 0.648, 95% CI: 0.628–0.667) all showed predictive ability for MINS (DeLong tests: all p=0.001). Further analysis of the ROC curves identified the optimal cut-off points for the NLR, PLR, and SII for the prediction of MINS as 2.59, 923, and 597×10^9, respectively. Full details of the optimal cut-off values and specificity and sensitivity are provided in Table 3.

Addition of Systemic Inflammation Indicators to a MINS Prediction Model

To enhance the practical predictive values of the NLR, PLR, and SII, a prediction model was established for MINS in older patients. The baseline patient characteristics of the training and validation sets are presented in Supplementary Table 1. After multivariate logistic regression analysis, eight clinically meaningful factors with p-values <0.05 were included in the prediction model: age, cerebrovascular diseases, coronary heart disease, arrhythmia, heart failure, surgery duration, duration of intraoperative MAP <65 mmHg, and intraoperative blood transfusion, were included in the prediction model (Supplementary Table 2). The AUC of the basic predictive model was 0.770 (0.752−0.789) in the

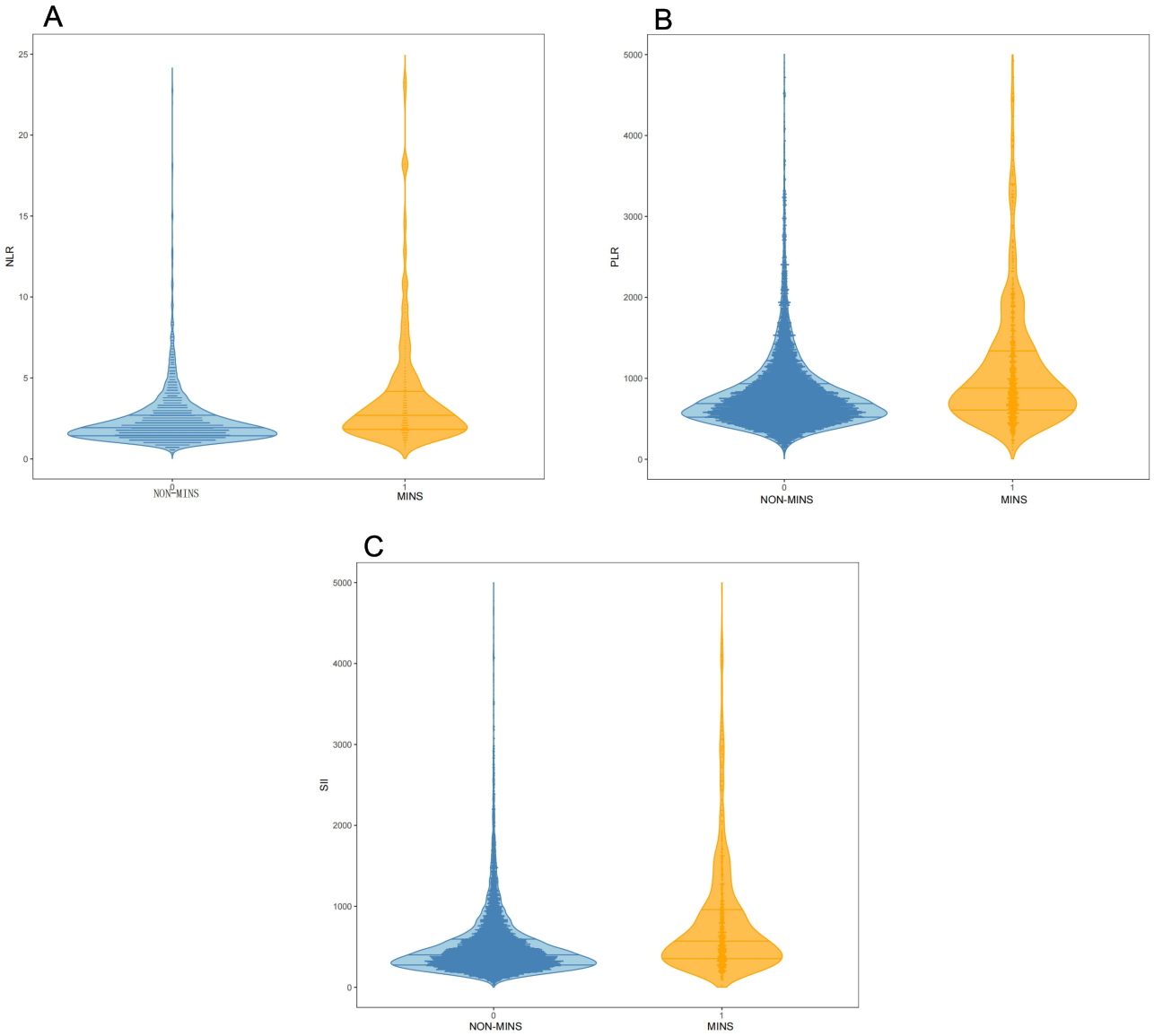

Figure 2 Violin plots of the NLR, PLR and SII showing the distribution in the non-MINS group and MINS group. (**A**) represents the violin plots of the NLR in the non-MINS group and MINS group. (**B**) represents the violin plots of the PLR in the non-MINS group and MINS group. (**C**) represents the violin plots of the SII in the non-MINS group and MINS group.

training set and 0.739 (0.710−0.767) in the validation set. The addition of the NLR to the predictive model increased the AUC to 0.797 (0.779−0.814) in the training set and 0.771 (0.744−0.798) in the validation set, improving the predictive ability. The addition of the PLR or SII to the predictive model also increased the AUC, to 0.790 (0.772−0.807) in the training set and 0.764 (0.736−0.791) in the validation set for the PLR, and 0.791 (0.774−0.809) in the training set and 0.765 (0.737−0.792) in the validation set for the SII. The addition of each of the three indices to the base model also resulted in significant increases in NRI and IDI. Comparing the three indices, we found that, when added to the base predictive model, the NLR had higher risk reclassification capabilities than the PLR and SII, as demonstrated by a higher NRI and IDI (Table 4).

Table 2 Univariate and Multivariate Logistic Analyses

Covariates	Univariate Analyses		Multivariable Analyses*	
	OR (95% CI)	P value	OR (95% CI)	P value
NLR	3.08(2.70–3.52)	<0.001	1.61(1.36–1.89)	<0.001
PLR	2.56(2.24–2.93)	<0.001	1.28(1.07–1.52)	0.006
SII	2.79(2.44–3.19)	<0.001	1.43(1.20–1.70)	<0.001

Notes: *Multivariable model was adjusted for variables including sex, age, BMI, smoking status, drinking status, hypertension, cerebrovascular diseases, diabetes (need interventions), coronary heart disease, cardiac interventions, arrhythmia, valvular heart disease, heart failure, peripheral vessel stenosis, white cell, hemoglobin, serum creatinine, fibrinogen, ASA classification, surgery situation, surgery type, surgery duration, crystalloid infusion, colloid infusion, urine volume, blood loss, duration of intraoperative MAP<65, intraoperative blood transfusion.

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

Subgroup Analysis

Supplementary Figure 1 shows the subgroup analysis according to sex, ASA classification, surgery duration, blood loss, surgery situation, and surgery type. The NLR was statistically significant in multiple subgroups. After dividing all patients according to surgery type, the odds ratio of NLR >2.59 was significant in head and neck surgery (OR=2.255, 95% CI: 1.078–4.707, p=0.03), thoracic or vascular surgery (OR=2.328 95% CI: 1.343–4.038, p=0.003), abdominal surgery (OR=1.932, 95% CI: 1.036–3.605, p=0.038), limb and spinal surgery (OR=1.450, 95% CI: 1.155–1.818, p=0.001), and other surgery (OR=1.598, 95% CI: 1.126–2.257, p=0.008). The NLR >2.59 was significant in elective surgery (OR=1.646, 95% CI: 1.393–1.944, p<0.001) but not in emergency surgery (OR=2.373, 95% CI: 0.486–14.825, p=0.311). The odds ratio of NLR >2.59 was also significant in sex, ASA classification, surgery duration, and blood loss. Additionally, the SII >597×10^9 was significant in surgery duration in sex, ASA classification, surgery duration and blood loss. The PLR >923 was not significant across all subgroups.

Discussion

In the present study, MINS developed in 7.74% of 12464 older patients undergoing noncardiac surgery. The NLR, PLR, and SII are independent risk factors for MINS through univariate and multivariate analyses and demonstrated that the preoperative inflammatory state is associated with MINS. ROC analysis also suggested that the predictive ability of the NLR was superior to that of the PLR and SII by comparing their AUC values. The NLR, PLR, and SII all enhanced the predictive ability of the basic model for MINS, with the NLR demonstrated a better predictive value than that of the PLR or SII. Subgroup analyses showed that the NLR was statistically significant in multiple subgroups.

Inflammation is an important contributor to organ injury and plays a major role in the development of postoperative complications. Kaufmann et al conducted a study of 96 patients who underwent lung surgery and were followed up for 30 days, with the results suggesting that inflammatory factors may be the origin of postoperative organ dysfunction; patients with higher inflammation levels were significantly more likely to develop postoperative complications.[10] Another study found that preoperative inflammation was a potential predictor of perioperative ischaemic stroke after noncardiac surgery in older patients.[9] However, to the best of our knowledge, few studies have explored inflammatory status and MINS in older patients. Our study explored this relationship and found that higher preoperative levels of inflammation were associated with an increased risk of MINS in older patients. A possible explanation for this is that inflammation damages endothelial cells and aggravates the formation and progression of atherosclerotic plaques, contributing to MINS.[22]

Recent studies have used inflammatory indicators, including the NLR, PLR, and SII, to predict the incidence of cardiovascular diseases. Xia et al revealed an association between higher preoperative inflammation levels and the risk of cardiovascular diseases; an SII of >655.56 increased the risk of cardiovascular mortality by more than 30%.[23] A meta-analysis found that a higher PLR was independently associated with an increased risk of in-hospital major adverse cardiovascular events.[24] In a recent study, Nilima et al observed that the NLR is a useful biomarker to predict in-hospital

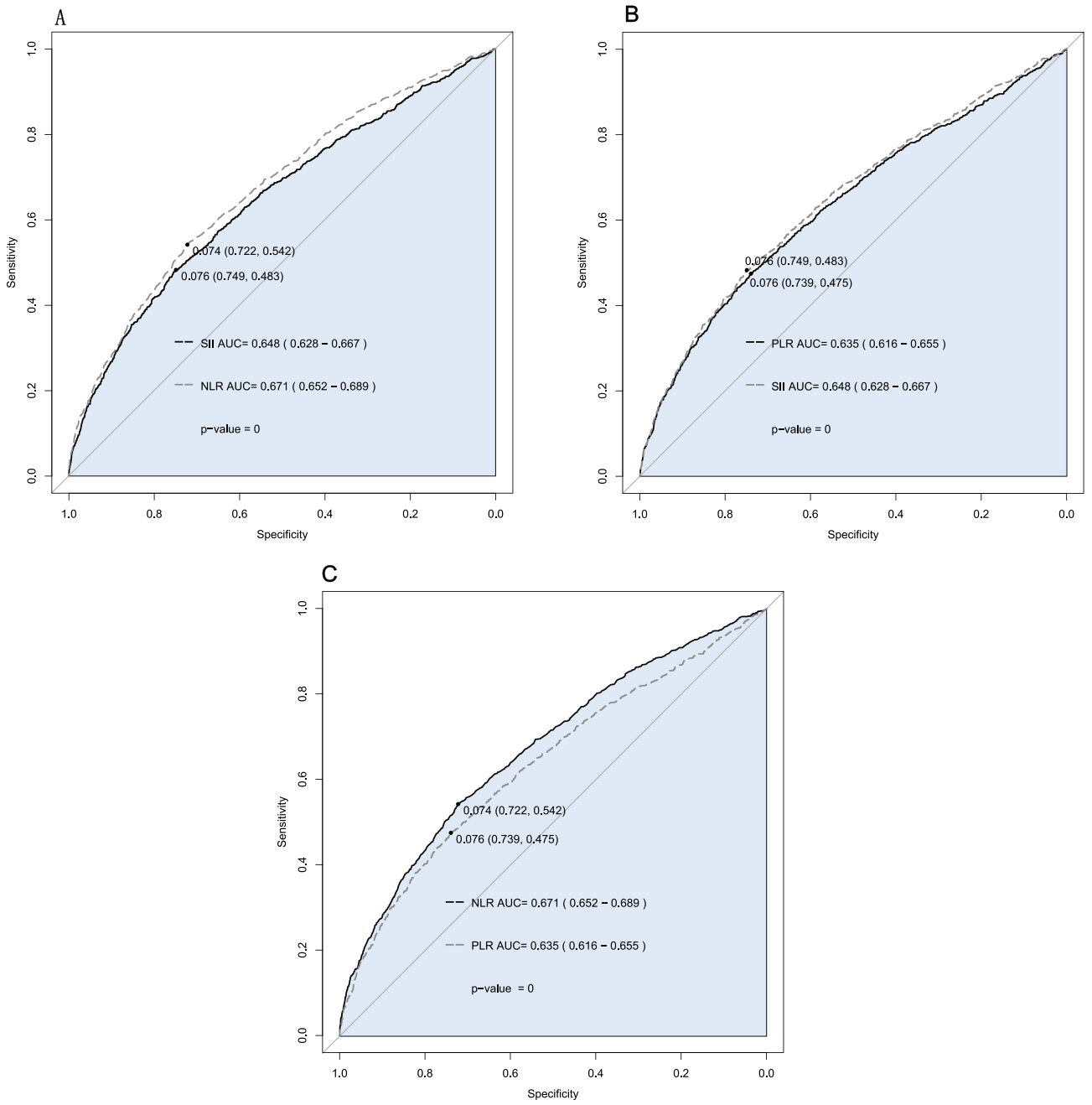

Figure 3 The DeLong test comparing differences between AUC curves. (**A**) represents the DeLong test between SII and NLR. (**B**) represents the DeLong test between SII and PLR.(**C**) represents the DeLong test between PLR and NLR.

mortality in patients with atrial fibrillation.[25] Previous studies have found a higher preoperative NLR was associated with an increased risk of MINS.[18,19] In contrast to previous studies, the present study compared the predictive value of all three of these inflammation indicators for MINS in older patients and identified the NLR was more predictive of MINS than the PLR or SII. The optimal cut-off value for the NLR was 2.59, which was lower than the cut-off values previously calculated by Durmuş et al and Ackland et al, which were 3.3 and 4.0, respectively.[18,19] The older age of the patients in our study may explain this difference in cut-off values. The probability of frailty increases with age, and associations between frailty and inflammatory markers have been described.[26,27] In addition, in order to enhance the practical predictive value, three prediction models including the NLR, PLR and SII were established. The results showed that

Table 3 The AUC Comparison Between NLR, PLR and SII

	AUC (95% CI)	Cutoff Value	Sensitivity	Specificity	PPV	NPV
NLR	0.671 (0.652, 0.689)	2.59	0.542	0.722	0.141	0.949
PLR	0.635 (0.616, 0.655)	923	0.475	0.739	0.133	0.944
SII	0.648 (0.628, 0.667)	597×10^9	0.483	0.749	0.139	0.945

Abbreviations: AUC, area under curve; PPV, positive predictive value; NPV, negative predictive value; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

Table 4 Performance of Models with Systematic Inflammation Factors to Predict MINS

	AUC		NRI	IDI
	Training Set	Validation Set		
Basic model	0.770(0.752–0.789)	0.739(0.710–0.767)		
+NRL	0.797(0.779–0.814)	0.771(0.744–0.798)	0.036(0.014–0.057)	0.026(0.017–0.034)
+PRL	0.790(0.772–0.807)	0.764(0.736–0.791)	0.031(0.010–0.052)	0.018(0.011–0.025)
+SII	0.791(0.774–0.809)	0.765(0.737–0.792)	0.034(0.013–0.055)	0.019(0.012–0.026)

Abbreviations: AUC, area under curve; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; NRI, net reclassification index; IDI, integrated discrimination improvement.

the addition of each of the three indices to the base model resulted in significant increases in AUC, NRI and IDI, indicating that all three systemic inflammation indicators can serve as predictors for MINS.

The results of the present study suggest that the NLR may offer clinicians greater value for assessing postoperative MINS risk than the PLR and SII and may be a useful tool to help guide perioperative management, potentially improving surgical outcomes in older patients. This result was also confirmed by the subgroup analyses, which showed that the NLR was significant in multiple subgroups, suggesting that it is a more robust predictor of MINS than the PLR or SII. A possible reason for the superiority of the NLR might be that high preoperative neutrophil levels injure vascular endothelial cells, resulting in vasospasm through the secretion of large amounts of cytotoxic substances and proinflammatory mediators.[28] Moreover, neutrophils adhere to endothelial cells and form microemboli.[29] MINS primarily occurs within two days of surgery,[30] with two-thirds to three-quarters of all cases likely caused by an imbalance between the supply and demand of coronary oxygen;[31,32] as early responders, neutrophils may play a role in this acute physiological process. Previous studies on systemic inflammatory indicators and cardiovascular diseases have focused on the predictive ability of the SII rather than the NLR.[33–36] This might be due to the fact that atherosclerosis is a chronic inflammatory disease in which platelets play an important role.

This cohort study has several strengths. First, our previous research found that the preoperative physical status of older patients was associated with the occurrence of postoperative cardiovascular complications.[37,38] Among the indicators identified, triglyceride-glucose index reflects the state of insulin resistance,[37] red blood cell distribution width indicates preoperative nutritional status,[38] and both also reflect inflammation and stress. However, little research has focused on the relationship between preoperative inflammatory status and MINS. The present study not only revealed the association between preoperative inflammatory status and MINS but also compared the clinical predictive values of these three inflammation indicators to provide a reference for clinical application. Second, the inflammatory indicators studied have the benefits of being easily available clinically and, as determined by the construction of predictive models, having moderate predictive power for MINS. Compared with single cell-type counts, the NLR is less affected by various physiological and pathological conditions. However, the study also has several limitations. First, a retrospective single-centre study cannot provide a high level of evidence and may be affected by selection bias. Prospective cohort studies and randomised controlled trials are required to verify our conclusions. Second, this study was a retrospective study and failed to collect data on coronary computed tomography angiography, coronary angiography, natriuretic peptide concentration, and other factors leading to coronary blockages, and therefore failed to perform a detailed analysis of these

factors. Third, although we carefully adjusted for a multitude of potential confounders, residual confounding and unmeasured factors cannot be entirely ruled out.

Conclusion

In conclusion, our study demonstrated that the preoperative inflammatory state, evaluated through the NLR, PLR, and SII, is independently associated with MINS. The NLR demonstrated a better predictive value for assessing MINS compared to the PLR and SII. Further prospective and interventional studies are needed to confirm its clinical utility and investigate the mechanisms underlying this association.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Acknowledgments

We thank Tongyan Sun, Longtao Wu, Wei Wei, Linlin Xu and Lei Mo of Shanghai Lejiu Healthcare Technology for their technical assistance in data extraction and statistical analyses.

Ethics Approval and Consent to Participate

The Research Ethics Committee of Chinese People's Liberation Army General Hospital approved this study (approval number: S2024-107-01).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research was supported by the National Key Research and Development Program of China (2018YFC2001900).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Lee SH, Park J, Lee JH. et al. Comparison of pre- and postoperative myocardial injuries on mortality after non-cardiac surgery: a retrospective analysis using an inverse probability weighting adjustment. *Sci Rep*. 2020;10(1):21050. doi:10.1038/s41598-020-78023-9 PMID: 33273559; PMCID: PMC7713127.
2. Prin M, Pattee J, Douin DJ, Scott BK, Ginde AA, Eckle T. Time-of-day dependent effects of midazolam administration on myocardial injury in non-cardiac surgery. *Front Cardiovasc Med*. 2022;9:982209. doi:10.3389/fcvm.2022.982209 PMID: 36386382; PMCID: PMC9650651.
3. Douville NJ, Surakka I, Leis A, et al. Use of a polygenic risk score improves prediction of myocardial injury after non-cardiac surgery. *Circ Genom Precis Med*. 2020;13(4):e002817. doi:10.1161/CIRCGEN.119.002817 PMID: 32517536; PMCID: PMC7442662.
4. Spence J, LeManach Y, Chan MTV, et al.; Vascular Events in Noncardiac Surgery Patients Cohort Evaluation(VISION) Study Investigators. Association between complications and death within 30 days after noncardiac surgery. *CMAJ*. 2019;191(30):E830–E837. PMID: 31358597; PMCID: PMC6663503. doi:10.1503/cmaj.190221
5. Park J, Kim J, Lee SH, et al. Postoperative statin treatment may be associated with improved mortality in patients with myocardial injury after noncardiac surgery. *Sci Rep*. 2020;10(1):11616. doi:10.1038/s41598-020-68511-3 PMID: 32669686; PMCID: PMC7363808.
6. Puelacher C, Lurati Buse G, Seeberger D, et al. BASEL-PMI Investigators. Perioperative myocardial injury after noncardiac surgery: incidence, mortality, and characterization. *Circulation*. 2018;137(12):1221–1232. doi:10.1161/CIRCULATIONAHA.117.030114 PMID: 29203498.
7. Sealy MJ, van der Lucht F, van Munster BC, et al. Frailty among older people during the first wave of the COVID-19 pandemic in The Netherlands. *Int J Environ Res Public Health*. 2022;19(6):3669. doi:10.3390/ijerph19063669 PMID: 35329352; PMCID: PMC8950938.

8. Zhang K, Liu C, Tan J, et al. Using preoperative N-terminal pro-B-type natriuretic peptide levels for predicting major adverse cardiovascular events and myocardial injury after noncardiac surgery in Chinese advanced-age patients. *J Geriatr Cardiol*. 2022;19(10):768–779. doi:10.11909/j.issn.1671-5411.2022.10.008 PMID: 36338282; PMCID: PMC9618846.
9. Zhang F, Niu M, Wang L, et al. Systemic immune-inflammation index as a promising biomarker for predicting perioperative ischaemic stroke in older patients who underwent non-cardiac surgery. *Front Aging Neurosci*. 2022;14:865244. doi:10.3389/fnagi.2022.865244 PMID: 35431888; PMCID: PMC9010030.
10. Kaufmann KB, Heinrich S, Staehle HF, Bogatyreva L, Buerkle H, Goebel U. Perioperative cytokine profile during lung surgery predicts patients at risk for postoperative complications-A prospective, clinical study. *PLoS One*. 2018;13(7):e0199807. doi:10.1371/journal.pone.0199807 PMID: 29969473; PMCID: PMC6029786.
11. Romagnoli S, Ricci Z. Postoperative acute kidney injury. *Minerva Anestesiol*. 2015, Jul 24;81(6):684–696. PMID: 25057935.
12. Keller MF, Reiner AP, Okada Y, et al. COGENT; biobank Japan Project (RIKEN) Working Groups. Trans-ethnic meta-analysis of white blood cell phenotypes. *Hum Mol Genet*. 2014;23(25):6944–6960. doi:10.1093/hmg/ddu401 PMID: 25096241; PMCID: PMC4245044.
13. Xiang X, Li N, Ding Z, Dai Z, Jin J. Peripheral lymphocyte counts and lymphocyte-related inflammation indicators during radiotherapy for pelvic malignancies: temporal characterization and dosimetric predictors. *Technol Cancer Res Treat*. 2022;21:15330338221116494. doi:10.1177/15330338221116494 PMID: 36114641; PMCID: PMC9486273.
14. Deng Y, Zhang J, Zou G, et al. Peripheral blood inflammatory markers can predict benign and malignant thyroid nodules. *Int J Endocrinol*. 2022;2022:2319660. doi:10.1155/2022/2319660 PMID: 35795844; PMCID: PMC9251144.
15. Bailey-Whyte M, Minas TZ, Dorsey TH, Smith CJ, Loffredo CA, Ambs S. Systemic inflammation indices and association with prostate cancer survival in a diverse patient cohort. *Cancers*. 2023;15(6):1869. doi:10.3390/cancers15061869 PMID: 36980755; PMCID: PMC10047449.
16. Saylik F, Akbulut T. Systemic immune-inflammation index predicts major cardiovascular adverse events in patients with ST-segment elevated myocardial infarction. *Arq Bras Cardiol*. 2022;119(1):14–22. doi:10.36660/abc.20210412 PMID: 35830117; PMCID: PMC9352114.
17. Zhao J, Lv H, Yin D, et al. Systemic immune-inflammation index predicts long-term outcomes in patients with three-vessel coronary disease after revascularization: results from a large cohort of 3561 patients. *J Inflamm Res*. 2022;15:5283–5292. doi:10.2147/JIR.S385990 PMID: 36120186; PMCID: PMC9480584.
18. Durmuş G, Belen E, Can MM. Increased neutrophil to lymphocyte ratio predicts myocardial injury in patients undergoing non-cardiac surgery. *Heart Lung*. 2018;47(3):243–247. doi:10.1016/j.hrtlng.2018.01.005 PMID: 29500104.
19. Ackland GL, Abbott TEF, Cain D, et al. Preoperative systemic inflammation and perioperative myocardial injury: prospective observational multicentre cohort study of patients undergoing non-cardiac surgery. *Br J Anaesth*. 2019;122(2):180–187. doi:10.1016/j.bja.2018.09.002 PMID: 30686303; PMCID: PMC6354048.
20. Ergelen M, Uyarel H, Altay S, et al. Predictive value of elevated neutrophil to lymphocyte ratio in patients undergoing primary angioplasty for ST-segment elevation myocardial infarction. *Clin Appl Thromb Hemost*. 2014;20(4):427–432. doi:10.1177/1076029612473516 Epub 2013 Jan 11. PMID: 23314674.
21. Taschner A, Kabon B, Graf A, et al. Perioperative supplemental oxygen and postoperative copeptin concentrations in cardiac-risk patients undergoing major abdominal surgery-A secondary analysis of a randomised clinical trial. *J Clin Med*. 2022;11(8):2085. doi:10.3390/jcm11082085 PMID: 35456178; PMCID: PMC9025821.
22. Libby P. Inflammation during the life cycle of the atherosclerotic plaque. *Cardiovasc Res*. 2021;117(13):2525–2536. doi:10.1093/cvr/cvab303 PMID: 34550337; PMCID: PMC8783385.
23. Xia Y, Xia C, Wu L, Li Z, Li H, Zhang J. Systemic immune inflammation index (SII), system inflammation response index (SIRI) and risk of all-cause mortality and cardiovascular mortality: a 20-year follow-up cohort study of 42,875 US adults. *J Clin Med*. 2023;12(3):1128. doi:10.3390/jcm12031128 PMID: 36769776; PMCID: PMC9918056.
24. Dong G, Huang A, Liu L. Platelet-to-lymphocyte ratio and prognosis in STEMI: a meta-analysis. *Eur J Clin Invest*. 2021;51(3):e13386. doi:10.1111/eci.13386 PMID: 32810283.
25. Kundnani NR, Sharma A, Lighezan DF, et al. Use of neutrophil-to-lymphocyte ratio to predict in-hospital mortality in patients admitted with acute decompensation of atrial fibrillation. *J Clin Med*. 2024;13(16):4719. doi:10.3390/jcm13164719 PMID: 39200861; PMCID: PMC11355835.
26. Aznar-Tortonda V, Palazón-Bru A, Gil-Guillén VF. Using the FRAIL scale to compare pre-existing demographic lifestyle and medical risk factors between non-frail, pre-frail and frail older adults accessing primary health care: a cross-sectional study. *PeerJ*. 2020;8:e10380. doi:10.7717/peerj.10380 PMID: 33240674; PMCID: PMC7666811.
27. Nishijima TF, Deal AM, Williams GR, Guerard EJ, Nyrop KA, Muss HB. Frailty and inflammatory markers in older adults with cancer. *Aging*. 2017;9(3):650–664. doi:10.18632/aging.101162 PMID: 28273043; PMCID: PMC5391224.
28. Zhou L, Xue C, Chen Z, Jiang W, He S, Zhang X. c-Fos is a mechanosensor that regulates inflammatory responses and lung barrier dysfunction during ventilator-induced acute lung injury. *BMC Pulm Med*. 2022;22(1):9. doi:10.1186/s12890-021-01801-2 PMID: 34986829; PMCID: PMC8734268.
29. Li Y, Xu J, Yu T, et al. A labeling strategy for the three-dimensional recognition and analysis of microvascular obstruction in ischemic stroke. *Theranostics*. 2023;13(1):403–416. doi:10.7150/thno.76879 PMID: 36593967; PMCID: PMC9800741.
30. Botto F, Alonso-Coello P, Chan MT, et al. Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. *Anesthesiology*. 2014;120(3):564–578. doi:10.1097/ALN.0000000000000113 PMID: 24534856.
31. Thygesen K, Alpert JS, Jaffe AS, et al.,;. Third universal definition of myocardial infarction. *Circulation*. 2012;126(16):2020–2035. PMID: 22923432. doi:10.1161/CIR.0b013e31826e1058
32. Lassale C, Curtis A, Abete I, et al. Elements of the complete blood count associated with cardiovascular disease incidence: findings from the EPIC-NL cohort study. *Sci Rep*. 2018;8(1):3290. doi:10.1038/s41598-018-21661-x PMID: 29459661; PMCID: PMC5818488.
33. Xiao S, Wang X, Zhang G, et al. Association of systemic immune inflammation index with estimated pulse wave velocity, atherogenic index of plasma, triglyceride glucose index, and cardiovascular disease: a large cross-sectional study. *Mediators Inflamm*. 2023;2023:1966680. doi:10.1155/2023/1966680 PMID: 36846196; PMCID: PMC9946741.

34. Jin Z, Wu Q, Chen S, et al. The associations of two novel inflammation indexes, SII and SIRI with the risks for cardiovascular diseases and all-cause mortality: a ten-year follow-up study in 85,154 individuals. *J Inflamm Res*. 2021;14:131–140. doi:10.2147/JIR.S283835 PMID: 33500649; PMCID: PMC7822090.
35. Ye Z, Hu T, Wang J, et al. Systemic immune-inflammation index as a potential biomarker of cardiovascular diseases: a systematic review and meta-analysis. *Front Cardiovasc Med*. 2022;9:933913. doi:10.3389/fcvm.2022.933913 PMID: 36003917; PMCID: PMC9393310.
36. Xu M, Chen R, Liu L, et al. Systemic immune-inflammation index and incident cardiovascular diseases among middle-aged and elderly Chinese adults: the Dongfeng-Tongji cohort study. *Atherosclerosis*. 2021;323:20–29. doi:10.1016/j.atherosclerosis.2021.02.012 PMID: 33773161.
37. Yao S, Zhang K, Yang Y, et al. Relationship between preoperative high triglyceride-glucose index and myocardial injury following non-cardiac surgery in advanced-age patients: a retrospective cohort study. *Diabetol Metab Syndr*. 2024;16(1):120. doi:10.1186/s13098-024-01348-2 PMID: 38812035; PMCID: PMC11138013.
38. Liu C, Zhang K, Zhang T, et al. Higher preoperative red blood cell distribution width increases the risk of myocardial injury after noncardiac surgery in advanced-age patients: a retrospective cohort study. *Clin Interv Aging*. 2023;18:169–179. doi:10.2147/CIA.S392778 PMID: 36818546; PMCID: PMC9930678.