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Relationship between preoperative neutrophil to high-density lipoprotein ratio and postoperative systemic inflammatory response syndrome in elderly patients: a retrospective cohort study

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Abstract

Background Systemic inflammatory response syndrome (SIRS) remains a serious health problem that consumes a large amount of medical resources. The objective of the study was to investigate whether older patients with a high neutrophil to high-density lipoprotein ratio (NHR) before surgery were more susceptible to postoperative SIRS.

Methods This retrospective cohort study was conducted on patients older than 65 years admitted to the two campuses of the Third Affiliated Hospital of Sun Yat-sen University between January 2015 and September 2020. Patient baseline characteristics such as demographic information, medical history, laboratory test results, and variables related to postoperative SIRS were obtained from the electronic health record system. The main outcome was the occurrence of postoperative SIRS during the initial three days after surgery. The main exposure was the NHR, divided into two groups according to the optimal receiver operating characteristic (ROC) cut-off value: NHR < 4.82 and NHR ≥ 4.82.

Results The study involved 5696 older patients, among whom 1419 (24.91%) developed SIRS. The ROC analysis showed that the NHR had the largest curve area for predicting postoperative SIRS. The NHR ≥ 4.82 was independently linked to a higher risk of postoperative SIRS (aOR = 1.29, 95% CI: 1.10–1.52, *P* = 0.002). This association remained robust in various sensitivity and subgroup analyses. The NHR ≥ 4.82 was correlated with an elevated risk of hospital mortality, prolonged postoperative hospital stays, and increased direct medical expenses.

Conclusions The study found that older patients undergoing general anesthesia with NHR ≥ 4.82 were associated with an increased risk of postoperative SIRS.

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Keywords Neutrophil to high-density lipoprotein ratio, SIRS, Elderly patients

Introduction

Systemic inflammatory response syndrome (SIRS), characterized by unregulated inflammatory responses, is a major cause of multi-organ dysfunction induced by sepsis. As the population ages, an increasing number of elderly individuals are undergoing anesthesia and surgical procedures. Surgery triggers a significant inflammatory response, which can lead to SIRS [1, 2]. Studies have shown that older patients have greater morbidity and mortality related to SIRS than younger patients [3]. SIRS and sepsis remain the leading causes of death in elderly surgical patients, contributing to an increased medical burden and significantly impacting quality of life [4, 5]. Therefore, the early and accurate detection of elderly patients at high risk of postoperative SIRS is crucial.

Previous studies have identified several biomarkers associated with SIRS, including high-sensitive C-reactive protein (hs-CRP), the neutrophil to lymphocyte ratio, and the hs-CRP to albumin ratio [6]. However, none of these biomarkers have demonstrated strong predictive value. Inflammatory mediators and lipid molecules are crucial in the development of inflammation [7]. The neutrophil/high-density lipoprotein (HDL) ratio (NHR) has recently attracted attention as a new biomarker. Neutrophils are essential in the inflammatory response. When infected or injured, neutrophils rapidly migrate to the injured site to engulf, kill, and digest invading pathogens. However, in the late stage or persistent inflammation, neutrophils may become dysfunctional or have insufficient apoptosis, leading to increased inflammation, further damage to the body and an increased risk of disease [8]. HDL is a crucial part of plasma lipoproteins, with antioxidant, anti-inflammatory, anti-apoptotic and antithrombotic characteristics [9]. Studies have shown that HDL possesses the capacity to impede the activation, attachment, diffusion, and migration of neutrophils [10, 11]. However, a substantial quantity of activated neutrophils can impact the function of HDL by changing the structure and content of several apolipoproteins [12, 13]. Although neutrophils and HDL have different functions in the human body, recent studies have shown that the NHR might be intricately linked to the initiation and progression of numerous diseases. In elderly patients with acute myocardial infarction, patients in the high NHR group showed higher rates of mortality and recurrent myocardial infarction [14]. In addition, studies have found that the NHR is associated with the severity of ischemic stroke, acute pancreatitis, Parkinson's disease, and coronary artery stenosis [15–18].

However, there is currently limited research on the impact of preoperative NHR on postoperative SIRS in older patients. Therefore, we aimed to investigate the correlation between preoperative NHR and postoperative SIRS in the older individuals.

Materials and methods

Study population

Patients aged 65 years and older who underwent surgery at either of the two campuses of the Third Affiliated Hospital of Sun Yat-sen University between January 2015 and September 2020 were included in the data analysis. The Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University granted approval for this study (No. [2019] 02-609-02). This was a retrospective cohort study in which patients' data were de-identified and anonymized prior to analysis; thus, patient informed consent was not required. The inclusion criteria for patients were those older than 65 years who received general anesthesia at our hospital during the specified period. The exclusion criteria included: (1) preoperative SIRS; (2) surgeries involving regional nerve block or non-intubated general anesthesia; (3) patients with missing preoperative HDL and neutrophil values; and (4) patients with missing anesthesia method.

Data collection

Based on previous studies, we gathered patient baseline characteristics from the electronic health record system. These data included demographic information, medical history, the last laboratory test before surgery, and variables related to post-surgery SIRS. Specifically, we gathered baseline clinical data such as age, gender, diabetes, hypertension, smoking history, fever and intubation before surgery, and preoperative levels of hemoglobin, white blood cell count (WBC), hs-CRP, neutrophil count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum albumin, creatinine, HDL, low-density lipoprotein (LDL), total cholesterol (TC), triglycerides (TG) and NHR. For intraoperative data collection, we documented amount of bleeding, total fluid loss, fluid transfusion, operative grade, operative time, and type of surgery. We also recorded the intensive care unit (ICU) occupancy rate and American Society of Anesthesiologists (ASA) classification. Postoperative outcome data included length of hospitalization, direct costs, and hospital mortality.

Definitions of outcomes and exposure

The main outcome was the occurrence of postoperative SIRS within the initial three days following surgery. According to the diagnostic criteria of the American College of Chest Physicians, at least two of the following criteria must be met to confirm the presence of SIRS: (1) temperature < 36 °C or > 38 °C; (2) heart rate exceeding 90 beats per minute; (3) respiratory rate ≥ 20 breaths per minute or $PaCO_2$ < 32 mmHg; (4) WBC count < 4×10^9/L, > 12×10^9/L, or more than 10% immature bands [6]. The main exposure, referred to as CHR, was calculated by dividing the neutrophil count by the HDL levels based on the test results closest to the date of surgery.

Statistical analysis

Histograms and normal distribution graphs were employed to evaluate the normality of the baseline data. The mean and standard deviation described normally distributed continuous variables, and statistical analysis was conducted by the Student's t-test. Non-normally distributed continuous variables were defined using the median (interquartile range), and the Mann-Whitney U test was employed for statistical analysis. Categorical variables were expressed as numbers (percentages) and compared using either the chi-squared test or Fisher's exact test.

The receiver operating characteristic (ROC) curve was employed to identify the optimal cutoff value and calculate the area under the curve (AUC) to assess the diagnostic value. The DeLong test was used to evaluate whether there were statistically significant differences between the ROC curves. Univariate logistic regression analysis was conducted first, and variables with P-values below 0.05 were included in multivariable logistic regression to further explore potential confounders affecting the correlation between NHR and postoperative SIRS in older patients. Subsequently, a hierarchical logistic regression model was employed for subgroup analysis to investigate the association between NHR and postoperative SIRS. Additionally, stratified logistic regression analysis were conducted to investigate the factors influencing the association between NHR and postoperative SIRS. We performed some sensitivity analyses to assess the robustness of the association between preoperative NHR and postoperative SIRS. Secondary outcomes were assessed using logistic regression models or Hodges–Lehmann estimator, depending on the type of outcome.

R software 3.6.2 (Vienna, Austria) was used for all data analysis and statistical procedures. A P-value lower than 0.05 was deemed statistically significant for all two-sided statistical tests. Given that the missing values in the dataset are below 5%, the mean, median, or mode were used to impute missing covariates for normal distribution continuous variables, skewed distribution continuous variables and categorical variables, respectively.

Results

Clinical characteristics

After excluding participants based on the exclusion criteria, the final cohort included 5696 patients, of whom 1419 cases developed SIRS, with an incidence rate of 24.91% (Fig. 1). Elderly patients were divided into two cohorts according to the occurrence of SIRS after surgery. As far as hypertension and triglycerides were concerned, there were no significant differences between the groups (all $P > 0.05$). However, the SIRS group had a significantly higher mean age, proportion of males, prevalence of diabetes, personal smoking rate, and proportion of ASA III or higher compared to the non-SIRS group (all $P < 0.001$). Furthermore, a statistically significant difference was observed between the median NHR of the SIRS and non-SIRS groups [4.43 (2.84–7.39) vs. 3.50 (2.45–5.09), $P < 0.001$]. In addition, older patients in the SIRS group exhibited increased rates of preoperative fever and intubation, higher baseline levels of hs-CRP, WBC, neutrophil counts, blood glucose, creatinine, ALT and AST, and lower baseline levels of albumin, hemoglobin, HDL, and LDL (all $P < 0.05$). Detailed demographic and laboratory data for all patients can be found in Table 1.

In comparison to patients who did not develop postoperative SIRS, those who developed postoperative SIRS were more prone to having a higher surgical grade, longer operative duration, greater blood loss, increased fluid administration, greater fluid loss and higher ICU admission rates. It is important to highlight that patients who developed postoperative SIRS exhibited higher hospital mortality rates (0.26% vs. 2.82%, $P < 0.001$) and longer postoperative hospital stays [7 (IQR, 4–10) vs. 11 (IQR, 8–18) days, $P < 0.001$] and higher direct medical costs [7086 (IQR, 3878 – 10108) vs. 12208 (IQR, 8258–18402) dollars, $P < 0.001$]. These results are shown in Table 2.

ROC curve analysis

In this study, elderly patients were categorized into two groups: SIRS and non-SIRS, according to whether they developed SIRS after surgery. The ROC curve analysis revealed that the NHR had the largest curve area for predicting postoperative SIRS, with a value of 0.609 (95% CI: 0.591–0.627, $P < 0.001$), a sensitivity of 46.1% and a specificity of 72.2%. The Delong test showed that the NHR was significantly superior to HDL ($P < 0.001$), hs-CRP/albumin ($P = 0.018$), hs-CRP ($P < 0.001$), and neutrophil count ($P < 0.001$). The optimal critical value for the NHR in predicting postoperative SIRS was 4.82. Detailed results of the ROC curve analysis can be found in Table 3; Fig. 2.

Primary outcome

To investigate the relationship between preoperative NHR and postoperative SIRS, we divided older patients into two groups (NHR < 4.82 and NHR ≥ 4.82) based on

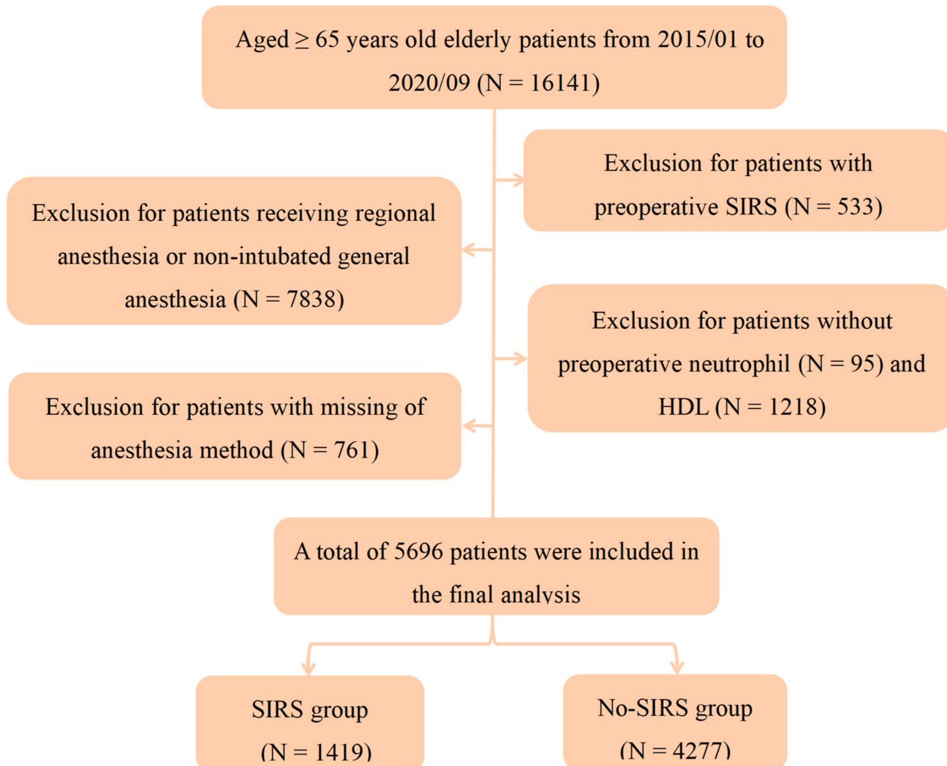

Fig. 1 Flow chart of the patient enrollment

the ROC curve values. The incidence rate of postoperative SIRS was 35.40% in the NHR ≥ 4.82 group and 19.90% in the NHR < 4.82 group. In univariate analysis, the risk of postoperative SIRS was found to be significantly higher in the NHR ≥ 4.82 group compared to the NHR < 4.82 group (OR = 2.21, 95% CI: 1.96–2.51, $P < 0.001$). This increased risk persisted even after adjusting for pre-specified confounders, with the NHR ≥ 4.82 group still showing a significantly elevated risk of SIRS when compared to the NHR < 4.82 group (aOR = 1.29, 95% CI: 1.10–1.52, $P = 0.002$, Table 4).

Secondary outcomes

The hospital mortality rate was 2.06% in the NHR ≥ 4.82 group and 0.34% in the NHR < 4.82 group. The NHR ≥ 4.82 group was associated with an increased risk of hospital mortality in both the univariate analysis (OR = 6.20; 95% CI, 3.39–12.13, $P < 0.001$) and the multivariable analysis (aOR = 2.76; 95% CI, 1.30–6.09, $P = 0.009$). The median postoperative hospitalization days were 9 days (IQR, 6–14) in the NHR ≥ 4.82 group and 8 days (IQR, 5–11) in the NHR < 4.82 group. The median direct hospitalization costs were 9090 dollars (IQR, 5913–13774) in the NHR ≥ 4.82 group and 7534 dollars (IQR, 4074–10827) in the NHR < 4.82 group. The NHR ≥ 4.82 group was associated with prolonged postoperative hospitalization days (MD = 1.04 days; 95% CI, 1.00–2.00, $P < 0.001$) and increased direct medical costs (MD = 1885 dollars; 95% CI, 1600–2175, $P < 0.001$) (Table 4).

Subgroup analyses

Subgroup analysis were conducted based on various factors such as age, gender, diabetes level, ASA classification, albumin level, preoperative fever, postoperative ICU admission, duration of surgery and surgical type. The results showed a consistent association between preoperative NHR and postoperative SIRS across all subgroups. Although different confidence intervals were observed among subgroups, the effect on the association was not statistically significant (all P for interaction > 0.05, Table 5). The findings indicated that the inclusion of different stratification factors did not alter the association between preoperative NHR and postoperative SIRS.

Sensitivity analyses

In sensitivity analysis, we further confirmed the association between preoperative NHR and postoperative SIRS. After excluding patients with preoperative fever or intubation, a higher risk of SIRS was observed in patients with NHR ≥ 4.82 compared with those with NHR < 4.82 (aOR = 1.28, 95% CI: 1.06–1.54, $P = 0.012$). Furthermore, even after removing instances without covariate information, the risk of postoperative SIRS remained higher in the NHR ≥ 4.82 group (aOR = 1.31, 95% CI: 1.08–1.58,

Table 1 Baselined characteristics of patients in SIRS group and non-SIRS group

Characteristics	All (*N* = 5696)	SIRS		*P* value
		No (*N* = 4277)	Yes (*N* = 1419)	
Demographics				
Age, years	70.0 [67.0, 75.0]	70.0 [67.0, 75.0]	71.0 [67.0, 76.0]	< 0.001
Gender				< 0.001
Female	2347 (41.20%)	1826 (42.69%)	521 (36.72%)	
Male	3349 (58.80%)	2451 (57.31%)	898 (63.28%)	
Hypertension				0.940
No	2213 (38.85%)	1660 (38.81%)	553 (38.97%)	
Yes	3483 (61.15%)	2617 (61.19%)	866 (61.03%)	
Diabetes mellitus				< 0.001
No	3842 (67.45%)	2981 (69.70%)	861 (60.68%)	
Yes	1854 (32.55%)	1296 (30.30%)	558 (39.32%)	
History of smoking				< 0.001
No	4963 (87.13%)	3770 (88.15%)	1193 (84.07%)	
Yes	733 (12.87%)	507 (11.85%)	226 (15.93%)	
ASA score				< 0.001
I/II	3647 (64.03%)	2989 (69.89%)	658 (46.37%)	
III/IV/V	2049 (35.97%)	1288 (30.11%)	761 (53.63%)	
Preoperative variables				
Intubation before surgery				< 0.001
No	5469 (96.01%)	4217 (98.60%)	1252 (88.23%)	
Yes	227 (3.99%)	60 (1.40%)	167 (11.77%)	
Fever before surgery				< 0.001
No	4928 (86.52%)	3855 (90.13%)	1073 (75.62%)	
Yes	768 (13.48%)	422 (9.87%)	346 (24.38%)	
hs-CRP, mg/L	6.48 [5.18,8.19]	6.36 [5.11,7.90]	6.98 [5.46,9.23]	< 0.001
Albumin, g/L	39.9 [36.9,42.9]	40.3 [37.3,43.1]	38.7 [35.2,41.9]	< 0.001
hs-CRP/albumin	0.16 [0.13,0.21]	0.16 [0.12,0.20]	0.18 [0.14,0.26]	< 0.001
ALT, U/L	18.0 [13.0,26.0]	17.0 [13.0,25.0]	19.0 [13.0,30.0]	< 0.001
AST, U/L	20.0 [17.0,27.0]	20.0 [17.0,26.0]	22.0 [17.0,31.0]	< 0.001
Creatinine, umol/L	75.0 [62.0,91.0]	74.0 [61.0,90.0]	78.0 [62.0,96.0]	< 0.001
Hemoglobin, g/L	128 [114,139]	128 [116,139]	125 [109,137]	< 0.001
WBC, 10^9/L	6.39 [5.19,8.09]	6.29 [5.13,7.81]	6.91 [5.45,9.01]	< 0.001
Blood glucose, mmol/L	5.41 [4.87,6.44]	5.39 [4.86,6.33]	5.49 [4.89,7.04]	< 0.001
HDL, mmol/L	1.07 [0.88,1.29]	1.09 [0.90,1.30]	1.01 [0.80,1.24]	< 0.001
hs_CRP/HDL	6.20 [4.43,8.56]	5.95 [4.31,7.94]	7.11 [4.83,10.9]	< 0.001
TG, mmol/L	1.12 [0.83,1.56]	1.12 [0.84,1.55]	1.11 [0.82,1.58]	0.465
TC, mmol/L	4.58 [3.98,5.09]	4.58 [4.05,5.14]	4.58 [3.71,4.92]	< 0.001
LDL, mmol/L	2.88 [2.22,3.57]	2.93 [2.29,3.59]	2.69 [2.02,3.44]	< 0.001
Neutrophil, 10^9/L	3.85 [2.93,5.33]	3.74 [2.87,5.04]	4.28 [3.20,6.26]	< 0.001
NHR	3.70 [2.53,5.53]	3.50 [2.45,5.09]	4.43 [2.84,7.39]	< 0.001

Abbreviation: ASA, American Society of Anesthesiologists; hs-CRP, high-sensitivity C-reaction protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cell count; HDL, high density lipoprotein; TG, triglyceride; *TC*, total cholesterol; LDL, low-density lipoprotein; NHR, neutrophil to high-density lipoprotein cholesterol ratio

$P = 0.006$). In addition, when the analysis was restricted to patients with normal TC levels, the NHR ≥ 4.82 group still showed an elevated susceptibility to SIRS (aOR = 1.42, 95% CI: 1.18–1.71, $P < 0.001$). Overall, the associations between preoperative NHR and postoperative SIRS remained robust across several sensitivity analyses (Table 6).

Discussion

In this retrospective cohort study, 1419 elderly patients developed SIRS postoperatively, with an incidence rate of 24.9%. Notably, a preoperative NHR threshold of 4.82 or higher was associated with an elevated risk of SIRS in elderly patients (aOR = 1.29, 95% CI: 1.10–1.52, $P = 0.002$). This association remained robust in various sensitivity and subgroup analyses. Furthermore, we found that preoperative NHR ≥ 4.82 was linked to higher

Table 2 Intraoperative variables and postoperative outcomes

Characteristics	All(N = 5696)	SIRS		P value
		No(N = 4277)	Yes(N = 1419)	
Intraoperative variables				
Operation grade				< 0.001
I/II	306 (5.37%)	259 (6.06%)	47 (3.31%)	
III	1712 (30.06%)	1440 (33.67%)	272 (19.17%)	
IV	3678 (64.57%)	2578 (60.27%)	1100 (77.52%)	
Type of surgery				< 0.001
Head and neck	456 (8.01%)	202 (4.72%)	254 (17.90%)	
Abdominal and pelvic	114 (2.00%)	81 (1.89%)	33 (2.33%)	
Liver	109 (1.91%)	90 (2.10%)	19 (1.34%)	
Cerebral	113 (1.98%)	105 (2.45%)	8 (0.56%)	
Urology	29 (0.51%)	7 (0.16%)	22 (1.55%)	
Skin, spine and joint	526 (9.23%)	342 (8.00%)	184 (12.97%)	
Cardiothoracic and vascular	4349 (76.35%)	3450 (80.66%)	899 (63.35%)	
Operative time, min	158 [91, 226]	140 [83, 202]	188 [132, 296]	< 0.001
Total fluid loss, ml	450 [200, 850]	400 [150, 750]	700 [350, 1200]	< 0.001
Fluid administration, ml	1700 [1100,2350]	1600 [1100,2200]	2200 [1600,3200]	< 0.001
Blood loss, mL	50 [20, 138]	50.0 [10, 100]	100 [50, 200]	< 0.001
Intensive care unit admission				< 0.001
No	5177 (90.89%)	4164 (97.36%)	1013 (71.39%)	
Yes	519 (9.11%)	113 (2.64%)	406 (28.61%)	
Postoperative outcomes				
Postoperative hospitalization, days	8 [5, 11]	7 [4, 10]	11 [8, 18]	< 0.001
Direct medical cost, dollars	8040 [34430, 85989]	7086 [3878, 10108]	12,208 [8258, 18402]	< 0.001
Hospital mortality.				< 0.001
No	5645 (99.10%)	4266 (99.74%)	1379 (97.18%)	
Yes	51 (0.90%)	11 (0.26%)	40 (2.82%)	

Table 3 The predictive value of NHR for SIRS in elderly patients

Variables	Best Predictive value	Sensitivity (%)	Specificity (%)	AUC (95%CI)	P value
NHR	4.82	46.1	72.2	0.609(0.591, 0.627)	< 0.001
hs-CRP/HDL	8.02	42.9	75.7	0.603(0.586, 0.621)	< 0.001
Albumin	38.35	47.6	67.1	0.591(0.573, 0.608)	< 0.001
HDL	0.87	32.6	79.1	0.577(0.559, 0.595)	< 0.001
hs-CRP/albumin	0.20	39.1	75.6	0.594(0.576, 0.612)	< 0.001
hs-CRP	8.13	35.0	77.6	0.575(0.557,0.593)	< 0.001
Neutrophil	4.97	40.2	74.0	0.587(0.570, 0.605)	< 0.001

hospital mortality, prolonged postoperative hospital stays and increased direct medical expenses.

In our study, we found that aged patients predisposed to postoperative SIRS had higher preoperative neutrophil counts and lower levels of HDL. In accordance with the present results, previous studies have demonstrated that patients with SIRS and sepsis had significantly higher neutrophil counts on admission compared with healthy controls [19, 20]. The acute phase response to sepsis is associated with notable changes in plasma lipoprotein lipid composition, particularly a decrease in HDL, which has been linked to adverse outcomes [21–23]. While there is limited research on the relationship between preoperative NHR and postoperative SIRS in elderly patients, comparable trends have emerged across other investigations. A retrospective observational study on acute myocardial infarction in elderly patients found that the NHR > 5.74 was associated with increased mortality and recurrent myocardial infarction [14]. In addition, a study in China reported that the NHR > 4.31 was linked to a higher risk of hemorrhagic transformation after acute ischemic stroke in elderly patients [15]. Our study showed that the preoperative NHR ≥ 4.82 in elderly patients was associated with an elevated risk for postoperative SIRS. Discrepancies in NHR cutoff values may be due to differences in the studied patient populations.

This study provides preliminary insights into the potential role of preoperative NHR in identifying elderly patients at risk of postoperative SIRS. The findings indicate that NHR in combination with inflammation

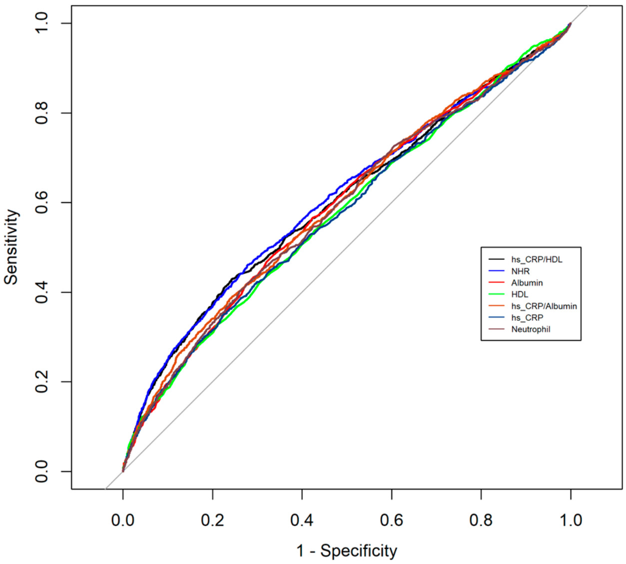

Fig. 2 ROC curves of NHR, hs-CRP/HDL, albumin, hs-CRP/albumin, hs-CRP and neutrophil predicting postoperative SIRS

markers and lipid metabolism indicators may provide better predictive performance than single neutrophil counts or HDL through ROC curve analysis. Additionally, we observed that preoperative NHR was independently associated with postoperative SIRS in elderly patients, suggesting NHR ≥ 4.82 as a potential risk factor. In the elderly population, NHR can be rapidly calculated upon admission through a simple blood test, which may serve as an effective tool for the early identification of high-risk patients. By monitoring preoperative NHR, clinicians may promptly recognize patients at elevated risk for postoperative SIRS, thereby facilitating early risk assessment and the implementation of preventive measures to reduce the incidence of SIRS. However, further prospective studies are required to validate the relationship between preoperative NHR and postoperative SIRS.

The specific mechanism underlying the association between the elevated NHR and the heightened risk of SIRS remains unclear. Studies have shown that neutrophils serve as the initial defense against infections and play a vital role in the innate immune system. Neutrophil activation is a critical step in the development of SIRS [24, 25]. Both patients and animal models have demonstrated that activated neutrophils within expanded capillary networks contribute to tissue injury and organ dysfunction [20, 26]. Additionally, impairment of neutrophil function is linked to adverse outcomes in sepsis [27]. HDL serves as a key regulator of lipid metabolism, and provides significant anti-inflammatory and antioxidant benefits that can protect against sepsis. Studies have shown that a decrease in HDL levels during sepsis is inversely related to the severity of the disease [28, 29]. Furthermore, animal research indicates that HDL and ApoA-I can modulate neutrophil behavior during inflammatory responses by suppressing their activation, adhesion, diffusion and migration [10]. Therefore, the NHR reflects the intricate interplay between neutrophils and HDL. The increased NHR may potentially correlate with perturbations in lipid metabolism and heightened inflammatory states.

Our study is subject to several notable constraints that warrant careful consideration. Firstly, the retrospective design inherently limits our ability to actively manage and gather data like prospective research. The exclusion of most elderly patients owing to incomplete data may have introduced a potential selection bias. Secondly, we only performed an initial assessment of preoperative NHR and did not evaluate the potential impact of time-dependent changes in NHR during follow-up on the occurrence of postoperative SIRS. Thirdly, although adjusted for various confounders in our analysis, we

Table 4 The relationship between preoperative NHR and outcomes in elderly patients

Outcomes	NHR < 4.82 (*n* = 3850)	NHR ≥ 4.82 (*n* = 1846)	Unadjusted OR/MD(95%CI)	*P*-value	Adjusted OR/MD(95%CI)[a]	*P*-value
Primary outcome						
SIRS#, n (%)	765(19.90)	654(35.40)	2.21(1.96, 2.51)	< 0.001	1.29(1.10, 1.52)	0.002
Secondary outcomes						
Hospital mortality#, n (%)	13(0.34)	38(2.06)	6.20(3.39, 12.13)	< 0.001	2.76(1.30, 6.09)	0.009
Postoperative hospitalization, days*, median (IQR)	8 [5, 11]	9 [6, 14]	1.04(1.00, 2.00)	< 0.001	/	
Direct medical cost*, dollars, median (IQR)	7534[4074,10827]	9090[5913,13774]	1885 (1600,2175)	< 0.001	/	

Abbreviations: CI, confidence interval; IQR, interquartile range; OR, odds ratio; MD, median difference

[a] Adjusted for age, gender, albumin, high-sensitivity C-reaction protein, alanine aminotransferase, aspartate aminotransferase, serum creatinine, triglyceride, total cholesterol, low-density lipoprotein, hemoglobin, hypertension, smoking history, diabetes, American Society of Anesthesiologists, preoperative fever

Age, gender, albumin, hypertension, smoking history, diabetes, American Society of Anesthesiologists, and preoperative fever were all classified according to Table 1

referred to logistic regression model

* referred to Hodges–Lehmann estimator

Table 5 Stratified logistic regression analysis to explore variables affecting the association between preoperative NHR and postoperative SIRS

Characteristics	Event (*N*, %)	Unadjusted model [a]	Full adjusted model [b]	
		OR (95%CI)	OR (95%CI)	*P*-interaction [c]
Age, years				0.404
65–75	985(23.86)	2.24 (1.93, 2.60)	1.29(1.06, 1.57)	
≥ 75	434(27.68)	2.07 (1.66, 2.60)	1.35 (1.00, 1.83)	
Gender				0.722
Female	521(22.20)	2.28(1.85, 2.79)	1.39(1.05, 1.82)	
Male	898(26.81)	2.13 (1.82, 2.49)	1.25(1.01, 1.53)	
Diabetes mellitus				0.194
No	861(22.41)	2.17(1.84, 2.55)	1.21 (0.98, 1.50)	
Yes	558(30.10)	2.03(1.66, 2.48)	1.41(1.08, 1.83)	
ASA score				0.196
I/II	658(18.04)	1.81(1.51, 2.16)	1.20 (0.95, 1.52)	
III/IV/V	761(37.14)	2.13 (1.82, 2.49)	1.38(1.10, 1.76)	
Albumin, g/L				0.766
> 35	1076(22.52)	2.04(1.76, 2.35)	1.35(1.12, 1.62)	
≤ 35	343(37.40)	1.82 (1.38, 2.43)	1.16(0.79, 1.69)	
Blood glucose, mmol/L				0.624
< 11.1	85(37.44)	2.62(1.44, 4.90)	1.50(0.67, 3.38)	
≥ 11.1	1334(24.39)	2.15(1.89, 2.44)	1.28(1.08, 1.51)	
Fever before surgery				0.486
No	1073(21.77)	2.03(1.76, 2.33)	1.28(1.06, 1.53)	
Yes	346(45.05)	1.90 (1.43, 2.54)	1.29 (0.88, 1.88)	
Intensive care unit admission				0.349
No	1013(19.57)	1.88 (1.63, 2.17)	1.29(1.04, 1.52)	
Yes	406(78.23)	2.30(1.50, 3.55)	1.44(0.81, 2.57)	
Operative time, min				0.322
< 120	298(14.33)	2.44(1.90, 3.13)	1.26 (0.90, 1.77)	
≥ 120	1121(30.99)	2.20 (1.90, 2.55)	1.38(1.14, 1.67)	
Blood loss, mL				0.782
< 100	578(16.98)	2.41(2.00, 2.89)	1.41 (1.11, 1.80)	
≥ 100	841(36.71)	1.98 (1.66, 2.36)	1.23 (0.97, 1.55)	
Type of surgery				
Head and neck	254(55.70)	2.25(1.54, 3.28)	0.81 (0.46, 1.42)	~
Abdominal and pelvic	33(28.95)	1.09(0.44, 2.47)	3.94(0.72, 24.58)	0.304
Liver	19(17.43)	2.72(0.94, 7.71)	3.11(0.54, 17.65)	0.299
Cerebral	8(7.08)	5.63(1.29, 29.06)	0.02 (0.00, 5.35)	0.716
Urology	22(75.86)	6.00 (0.83, 123.44)	~	~
Skin, spine and joint	184(34.98)	2.39(1.63, 3.51)	1.36 (0.84, 2.19)	0.097
Cardiothoracic and vascular	899(20.67)	1.98 (1.71, 2.31)	1.20(0.98, 1.47)	0.079

[a] a univariate Logistic model

[b] Adjusted for hemoglobin, age, albumin, high-sensitivity C-reaction protein, alanine aminotransferase, aspartate aminotransferase, serum creatinine, triglyceride, total cholesterol, low-density lipoprotein, gender, hypertension, history of smoking, diabetes mellitus, American Society of Anesthesiologists, fever before surgery. In each subgroup anylysis, the model was not adjusted for stratification variables

[c] Z-test was used to compare the OR values of stratified patients

Table 6 Sensitivity analysis by adjustment for some confounders

Condition	Population	No. of patients	aOR(95%CI)	*P* value
	Total	5696	1.29 (1.10, 1.52)	0.002
Condition 1	Excluded patients with fever or intubation before surgery	4779	1.28(1.06, 1.54)	0.012
Condition 2	patients with normal total cholesterol levels (3.1–5.7 mmol/L)	4519	1.42 (1.18, 1.71)	< 0.001
Condition 3	Excluded patients with missing covariates	4494	1.31(1.08, 1.58)	0.006

cannot completely eliminate the impact of residual and unmeasured confounders, such as weight, preoperative immunocompromise, preoperative infection status, and the use of lipid-lowering medications, on the study outcomes. Finally, our study concentrated on assessing preoperative NHR's effect on postoperative SIRS in older patients undergoing general anesthesia, potentially restricting the applicability of our findings to other populations or anesthetic modalities. Future investigations could endeavor to explore the intricate relationship between NHR and SIRS in diverse populations and under different anesthetic modalities.

Conclusion

In conclusion, the NHR ≥ 4.82 was associated with a higher risk of postoperative SIRS in elderly patients undergoing general anesthesia. This association was consistently observed across fully adjusted analyses, subgroup analyses, and sensitivity analyses. The NHR may be used as a potential biomarker to recognize elderly patients at an increased risk of postoperative SIRS. Further research is required to validate these results and assess the potential of using NHR ≥ 4.82 as a tool to identify high-risk patients and target therapy to prevent SIRS.

Author contributions

Jingjing Chen, M.M. Contribution: This author helped with the data analysis, data interpretation, and writing and final approval of the manuscript. Xiaorui Chen, M.M. Contribution: This author helped with the literature research, data interpretation, and writing and final approval of the manuscript. Hanbin Xie, M.M. Contribution: This author helped with patient recruitment, data collection, data interpretation, and final approval of the manuscript. Ziqing Hei, Ph.D. Contribution: This author helped with research design, data interpretation, writing, and final approval of the manuscript. Zifeng Liu, M.D. Contribution: This author helped with research conceptualization and design, data analysis, writing and final approval of the manuscript. Chaojin Chen, Ph.D. Contribution: This author helped with research conceptualization and design, patient recruitment, data collection, data interpretation, writing, and final approval of the manuscript. The authors declare that they have no conflicts of interest.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

This study was approved by the Institutional Ethics Committee from the two hospitals and was censored on 14 May 2021 (No. [2019]02-609-02). The requirement for informed consent and clinical trial registration were waived by the committee.

Competing interests

The authors declare no competing interests.

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