

# World Journal of *Clinical Cases*

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## Retrospective Cohort Study

# Association between neutrophil-to-lymphocyte ratio and major postoperative complications after carotid endarterectomy: A retrospective cohort study

Yun Yu, Wei-Hua Cui, Chan Cheng, Yu Lu, Qing Zhang, Ru-Quan Han

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**statement:** This study was approved by the Ethics Committee of Beijing Tiantan Hospital (KY2017-024-01) and performed conforming to the 1964 Declaration of Helsinki and its later amendments.

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## Abstract

### BACKGROUND

Carotid artery cross-clamping during carotid endarterectomy (CEA) may damage local cerebral perfusion and induce cerebral ischemia-reperfusion injury to activate local inflammatory responses. Neutrophil-to-lymphocyte ratio (NLR) is an indicator that reflects systemic inflammation. However, the correlation between NLR and complications after CEA remains unclear.

### AIM

To investigate the association between NLR and major complications after surgery in patients undergoing CEA.

### METHODS

This retrospective cohort study included patients who received CEA between January 2016 and July 2018 at Beijing Tiantan Hospital. Neutrophil and lymphocyte counts in whole blood within 24 h after CEA were collected. The primary outcome was the composite of major postoperative complications including neurological, pulmonary, cardiovascular and acute kidney injuries. The secondary outcomes included infections, fever, deep venous thrombosis, length of hospitalization and cost of hospitalization. Statistical analyses were performed using EmpowerStats software and R software.

### RESULTS

A total of 224 patients who received CEA were screened for review and 206 were included in the statistical analyses; of whom, 40 (19.42%) developed major postoperative complications. NLR within 24 h after CEA was significantly correlated with major postoperative complications ( $P = 0.026$ ). After confounding factors were adjusted, the odds ratio was 1.15 (95%CI: 1.03-1.29,  $P = 0.014$ ). The incidence of major postoperative complications in the high NLR group was 8.47

authors declare no competing interests.

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times that in the low NLR group ( $P = 0.002$ ).

## CONCLUSION

NLR is associated with major postoperative complications in patients undergoing CEA.

**Key Words:** Carotid artery stenosis; Carotid endarterectomy; Neutrophil to lymphocyte ratio; Inflammation; Postoperative complication; Major organ dysfunction

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**Core tip:** We retrospectively evaluated the association between neutrophil-to-lymphocyte ratio (NLR) and major postoperative complications in patients undergoing carotid endarterectomy (CEA). Nearly 20% of patients developed major postoperative complications. NLR within 24 h after CEA was significantly correlated with major postoperative complications. The incidence of major postoperative complications in the high NLR group was 8.47 times that in the low NLR group after confounding factors were adjusted. Since early detection and early treatment help improve outcomes for CEA, inflammatory markers such as NLR may also become potential treatment targets.

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## INTRODUCTION

Carotid endarterectomy (CEA) is a classic surgical method for treating carotid artery stenosis. Occlusion and opening of the carotid artery during CEA may damage local cerebral perfusion and induce cerebral ischemia-reperfusion injury to activate local inflammatory responses[1]. Even after CEA, inflammatory responses in the whole body and carotid plaque tissue may still exist. Serum inflammatory and anti-inflammatory cytokines increase at 6 to 24 h after CEA. Compared with asymptomatic patients, patients with symptomatic carotid artery stenosis have higher concentrations of inflammatory markers in serum and tissues[2]. The elevation of perioperative inflammatory markers suggests an increase in the risk of early carotid artery restenosis after CEA[3]. Inflammatory markers can also become treatment targets[4].

Neutrophil-to-lymphocyte ratio (NLR) is an indicator that reflects systemic inflammation, which has been demonstrated to be an independent and convenient predictor of all-cause death or adverse events in many diseases[5-8]. Endothelial dysfunction is the early stage of atherosclerosis formation[9]. NLR is positively correlated with carotid intima-media thickness, and an increase in NLR may be associated with endothelial dysfunction[10]. NLR > 2.6 is an independent predictor of symptomatic carotid artery disease[11]. In patients receiving CEA for significant carotid artery stenosis, NLR is significantly correlated with the characteristics of vulnerable atherosclerotic carotid plaques on preoperative magnetic resonance angiography[12]. However, the correlation between NLR and complications after CEA remain unclear.

Therefore, we undertook this study to clarify whether NLR was significantly associated with major organ dysfunction after surgery in patients undergoing CEA.

## MATERIALS AND METHODS

### Study participants

This single-center retrospective cohort study was approved by the Ethics Committee of Beijing Tiantan Hospital (KY2017-024-01). Given the retrospective nature of the study, the Ethics Committee waived the need for written informed consent and no registration was required. Consecutive patients who underwent elective CEA between



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January 2016 and July 2018 at Beijing Tiantan Hospital were screened for eligibility. Characteristics of the patients at baseline, neuroimaging data, intraoperative anesthesia management, postoperative complications and length of hospitalization were acquired from the medical record system. Patients were excluded for the following reasons: incomplete data obtained from medical records; severe anemia (hemoglobin < 9 g/dL) before surgery; nongeneral anesthesia; and massive hemorrhage during surgery.

### **Anesthesia management**

The method for anesthesia involved intravenous-inhalation anesthesia or total intravenous anesthesia. Intraoperative fluid management involving crystalloids, colloids, blood loss and urine output was collected. Intraoperative blood pressure fluctuations were addressed as follows. The noninvasive blood pressure of the upper limbs was measured and recorded every 5 min during surgery. The mean systolic blood pressure ( $\text{mean}_{\text{SBP}}$ ), SD of systolic blood pressure ( $\text{SD}_{\text{SBP}}$ ), mean diastolic blood pressure ( $\text{mean}_{\text{DBP}}$ ), and SD of diastolic blood pressure ( $\text{SD}_{\text{DBP}}$ ) from entering to exiting the operating room were calculated to obtain the coefficient of variation in systolic blood pressure ( $\text{CV}_{\text{SBP}}$ ) and diastolic blood pressure ( $\text{CV}_{\text{DBP}}$ ). The coefficient of variation =  $\text{SD}/\text{mean value} \times 100\%$  [13]. Besides, intraoperative vasoactive drugs use including vasopressors and antihypertensive agents was also collected.

### **Laboratory and neuroimaging examination measures**

Complete blood count (CBC) was collected at admission and repeated after surgery. Neutrophil and lymphocyte counts in whole blood at admission and within 24 h after CEA were extracted from the medical record system. Preoperative basal NLR values and that within 24 h after CEA were calculated. By using the North American Symptomatic Carotid Endarterectomy Trial criteria, the degree of carotid artery stenosis was independently measured by two trained radiologists blinded to clinical data [14].

### **Outcome assessment**

The composite risk of major postoperative complications was adopted as the primary outcome, similar to those used in previous studies [15-17]. Major postoperative complications included neurological, pulmonary and cardiovascular complications and acute kidney injury (AKI). Neurological complications were defined by new focal neurological deficits confirmed by radiology. Pulmonary complications were defined by a new-onset requirement for oxygen or respiratory support [15]. Cardiovascular complications included new-onset myocardial infarction validated by cardiac enzymes, atrial or ventricular arrhythmias and heart failure. According to the Kidney Disease Improving Global Outcomes, AKI was defined as an increase in serum creatinine > 0.3 mg/dL within 48 h after surgery or serum creatinine value 1.5-fold the preoperative baseline value [18]. If the patient had one or more of the above complications, development of major postoperative complications was considered. No assumptions were made to process missing data, and statistical analyses were conducted for patients with complete data.

Secondary outcomes included fever, surgical site infections, urinary infections, deep venous thrombosis (DVT), length of stay in the intensive care unit (ICU), length of hospitalization and cost of hospitalization. A postoperative fever was considered if the axillary temperature was > 38°C. Surgical site infections were determined if wound cultures were positive. Urinary infections were defined as typical symptoms and signs confirmed by routine urine tests. DVT was diagnosed using the color Doppler ultrasound.

### **Statistical analysis**

Statistical analyses were performed using EmpowerStats software and R software (R version 3.4.3). Continuous variables were examined using the independent-samples *t*-test or Kruskal-Wallis test and expressed as mean  $\pm$  s or median (interquartile range). Analysis of categorical variables was performed using the  $\chi^2$  test and presented as a percentage. After adjusting the confounding factors, smooth curve fitting was used for analyzing the relationship between NLR and post-CEA major complications. By logistic regressions, odds ratios (ORs) and 95% CIs were calculated to assess the association of NLR within 24 h after surgery with postoperative major complications. Model I was adjusted for sex and age. Model II was adjusted for sex, age, body mass index (BMI), American Society of Anesthesiologists (ASA) grade, preoperative combined heart disease, anesthesia method, degree of stenosis on the surgical side,

degree of stenosis on the contralateral side, operating time, intraoperative intake and output, duration of carotid artery occlusion,  $CV_{SBP}$ , and  $CV_{DBP}$ .  $P < 0.05$  indicated that a difference had statistical significance.

## RESULTS

### Patient characteristics

This retrospective cohort study screened 224 patients. A total of 17 patients did not have CBC on postoperative day 1 and one patient underwent CEA with cervical plexus block. Therefore, 18 patients were excluded and the data for 206 patients were included in the statistical analyses (Figure 1).

Patients were divided into a group with major post-CEA complications (PC group) and a group without major post-CEA complications (WOPC group) according to whether major PC group were present. Baseline characteristics in the two groups are provided in Table 1. The percentage of patients with combined preoperative heart diseases in the PC group (40.0%) was significantly higher than that in the WOPC group (24.10%,  $P = 0.042$ ). The differences in age, sex, BMI, degree of carotid artery stenosis on the surgical side, degree of carotid artery stenosis on the contralateral side, anesthesia method, duration of carotid artery occlusion, intraoperative intake and output volume, intraoperative blood pressure fluctuation, and use of vasoactive drugs between the two groups were all nonsignificant.

### Postoperative outcomes

Outcome variables stratified by major postoperative complications are shown in Table 2. After CEA, 16 patients (7.77%) developed neurological complications, six (2.91%) developed cardiac complications, 14 (6.80%) developed respiratory complications, and nine (4.37%) developed renal complications. A total of 40 patients (19.42%) developed major postoperative complications. The incidence of fever, surgical site infections, urinary infections and DVT was 4.85%, 1.46%, 1.46% and 2.43%, respectively. The cost of hospitalization in the PC group was significantly higher than that in the WOPC group ( $P < 0.001$ ). More patients in the PC group suffered from fever and DVT ( $P < 0.001$ ). The differences in the length of stay in the ICU, the length of hospitalization, surgical site infections and urinary infections were not significant.

### Association between NLR and major post-CEA complications

The risk factors associated with post-CEA complications involving vital organs are presented in Table 3. Operating time was significantly correlated with major post-CEA complications ( $P = 0.038$ ). NLR within 24 h after CEA was also significantly correlated with post-CEA complications ( $P = 0.026$ ). Figure 2 showed the correlation between NLR within 24 h after CEA and major postoperative complications. NLR within 24 h after CEA and major postoperative complications showed a curvilinear relationship ( $P = 0.025$ , degree of freedom = 1.495). With the increase in NLR within 24 h after CEA, the incidence of major postoperative complications gradually increased.

Multiple logistic regression showed that NLR within 24 h after CEA and major postoperative complications were correlated (Table 4). After confounding factors were adjusted, the OR = 1.15 (95%CI: 1.03–1.29,  $P = 0.014$ ). The patients were divided into three groups according to their NLR tertiles within 24 h after CEA; namely, high NLR group (7.66–29.85), middle NLR (4.63–7.65), and low NLR (1.61–4.62). The incidence of post-CEA complications involving vital organs in the high NLR group was 8.47 times that in the low NLR group ( $P = 0.002$ ). The differences in major postoperative complications ( $P = 0.015$ ), fever ( $P = 0.040$ ) and cost of hospitalization ( $P = 0.032$ ) were significant among NLR tertile groups (Table 5).

## DISCUSSION

This study showed that 19.42% of patients developed major postoperative complications involving the neurological, cardiac and respiratory systems as well as AKI. NLR within 24 h after CEA was significantly correlated with major postoperative complications. The incidence of major postoperative complications in the high NLR group was much higher than that of in the low NLR group after confounding factors were adjusted.

**Table 1 Characteristics of the patients at baseline**

	Total	WOPC group	PC group	P
No. of cases	206	166	40	
Age (yr)	62.0 ± 7.2	61.6 ± 7.3	63.5 ± 6.8	0.151
Sex				0.616
Male	175 (84.95%)	140 (84.34%)	35 (87.50%)	
Female	31 (15.05%)	26 (15.66%)	5 (12.50%)	
BMI (kg/m <sup>2</sup> )	25.33 ± 2.89	25.25 ± 2.85	25.63 ± 3.04	0.461
Smoking history	118 (57.56%)	97 (58.79%)	21 (52.50%)	0.470
ASA grade				0.521
Grade II	157 (81.07%)	136 (81.93%)	31 (77.50%)	
Grade III	39 (18.93%)	30 (18.07%)	9 (22.50%)	
Preoperative combined diseases				
Hypertension	146 (70.87%)	114 (68.67%)	32 (80.0%)	0.157
Diabetes mellitus	74 (35.92%)	61 (36.75%)	13 (32.50%)	0.615
Heart disease	56 (27.18%)	40 (24.10%)	16 (40.0%)	0.042 <sup>a</sup>
Respiratory disease	11 (5.34%)	10 (6.02%)	1 (2.50%)	0.374
Neurological disease	96 (46.60%)	78 (46.99%)	18 (45.0%)	0.821
Kidney disease	4 (1.94%)	4 (2.41%)	0	0.321
Degree of carotid artery stenosis on the surgical side				0.449
Mild/moderate stenosis	3 (1.46%)	2 (1.20%)	1 (2.5%)	
Severe stenosis	201 (97.57%)	163 (98.19%)	38 (95.0%)	
Occlusion	2 (0.97%)	1 (0.60%)	1 (2.50%)	
Degree of carotid artery stenosis on the contralateral side				0.146
Mild/moderate stenosis	169 (85.35%)	132 (83.02%)	37 (94.87%)	
Severe stenosis	21 (10.61%)	19 (11.95%)	2 (5.13%)	
Occlusion	8 (4.04%)	8 (5.03%)	0	
Operating time (min)	141.33 ± 40.96	138.39 ± 38.78	153.57 ± 47.62	0.129
Duration of carotid artery occlusion (min)	22.00 (18.0–44.0)	22.00 (17.0–43.0)	27.0 (18.50–49.50)	0.328
Anesthesia method				
TIVA	163 (79.13%)	129 (77.71%)	34 (85.0%)	0.309
Combined intravenous-inhalation anesthesia	43 (20.87%)	37 (22.29%)	6 (15.0%)	
Intraoperative intake and output volume (mL)	897.57 ± 333.40	911.85 ± 331.01	839.75 ± 341.01	0.221
mean <sub>SBP</sub>	128.82 ± 12.92	128.37 ± 12.77	130.69 ± 13.54	0.309
SD <sub>SBP</sub>	20.26 ± 4.91	20.09 ± 5.01	20.93 ± 4.48	0.333
CV <sub>SBP</sub>	0.16 ± 0.04	0.16 ± 0.04	0.16 ± 0.03	0.550
mean <sub>DBP</sub>	69.61 ± 7.83	69.80 ± 7.77	68.82 ± 8.14	0.480
SD <sub>DBP</sub>	10.23 ± 2.70	10.18 ± 2.81	10.42 ± 2.26	0.612
CV <sub>DBP</sub>	0.15 ± 0.04	0.15 ± 0.04	0.15 ± 0.04	0.372
Intraoperative use of vasopressors	84 (40.78%)	65 (39.16%)	19 (47.50%)	0.335

Intraoperative use of antihypertensive agents	73 (35.44%)	63 (37.95%)	10 (25.0%)	0.124
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<sup>a</sup> $P < 0.05$ , statistically significant difference was observed between two groups.

ASA: American society of anesthesiologists; BMI: Body mass index; CEA: Carotid endarterectomy; CV<sub>DBP</sub>: Coefficient of variation in diastolic blood pressure; CV<sub>SBP</sub>: Coefficient of variation in systolic blood pressure; mean<sub>DBP</sub>: mean diastolic blood pressure; mean<sub>SBP</sub>: mean systolic blood pressure; PC: Post-CEA complications; SD<sub>DBP</sub>: Standard deviation of diastolic blood pressure; SD<sub>SBP</sub>: Standard deviation of systolic blood pressure; TIVA: Total intravenous anesthesia; WOPC: Without post-CEA complications.

**Table 2 Outcome variables, stratified by major postoperative complications**

	Total	WOPC group	PC group	P
No. of cases	206	166	40	
Major postoperative complications	40 (19.42%)	0	40 (100%)	
Neurological complications	16 (7.77%)	0	16 (40.0%)	< 0.001 <sup>a</sup>
Cardiac complications	6 (2.91%)	0	6 (15.0%)	< 0.001 <sup>a</sup>
Respiratory complications	14 (6.80%)	0	14 (35.0%)	< 0.001 <sup>a</sup>
AKI	9 (4.37%)	0	9 (22.50%)	< 0.001 <sup>a</sup>
Fever	10 (4.85%)	4 (2.41%)	6 (15.0%)	< 0.001 <sup>a</sup>
Surgical site infections	3 (1.46%)	1 (0.60%)	2 (5.0%)	0.097
Urinary infections	3 (1.46%)	1 (0.60%)	2 (5.0%)	0.097
DVT	5 (2.43%)	1 (0.60%)	4 (10.0%)	< 0.001 <sup>a</sup>
Length of stay in the ICU (d)	1.0 (0–1.0)	1.0 (0–1.0)	1.0 (1.0–1.0)	0.055
Hospitalization stay (d)	15.56 ± 4.30	15.16 ± 3.63	17.20 ± 6.17	0.105
Cost of hospitalization (CNY)	24085.15 (21694.72–28395.65)	23786.67 (21568.68–27139.36)	27127.94 (22326.75–31629.55)	< 0.001 <sup>a</sup>

<sup>a</sup> $P < 0.05$ , statistically significant difference was observed between two groups.

AKI: Acute kidney injury; CEA: Carotid endarterectomy; DVT: Deep venous thrombosis; ICU: Intensive care unit; PC: Post-CEA complications; WOPC: Without post-CEA complications.

For complications involving the neurological system, NLR can predict and affect clinical outcomes of stroke. Neutrophils are the first cells that invade injured tissues after focal cerebral ischemia. Their proinflammatory feature enhances tissue injury and may cause cerebral ischemia through the induction of thrombosis. Therefore, inflammatory markers may be potential targets for the treatment and prevention of stroke [19]. Within 48–72 h after acute ischemic stroke, patients with  $NLR \geq 4.58$  were 5.58 times more likely to have a poor outcome than patients with  $NLR < 4.58$  [20]. NLR independently predicted 3-month neurological outcomes and symptomatic intracranial hemorrhage in patients with acute stroke caused by large vessel occlusion of the anterior circulation [21]. Cerebral blood flow (CBF) autoregulation can maintain consistent CBF within a certain blood pressure range, and patients with sepsis usually have damaged CBF autoregulation [22]. Masse *et al* [23] showed that CBF in sedated septic patients was 62% higher than that in control subjects and did not change with mean arterial pressure. The relationship between inflammation and cerebral hyperperfusion needs to be further studied [23].

A considerable proportion of patients with carotid stenosis also have coronary heart disease. NLR is considered a potential indicator of cardiovascular events. Durmuş *et al* [24] studied the relationship between NLR and the development of myocardial injury after noncardiac surgery (MINS), which showed that NLR in the MINS group was significantly higher than that in the non-MINS group [24]. For coronary artery disease patients with low high-sensitivity C-reactive protein levels, the elevation of NLR levels could independently predict their long-term outcomes [25]. One *post hoc* analysis studied patients with coronary heart disease who underwent noncardiac surgery. The results showed that NLR was significantly correlated with major adverse cardiovascular and cerebrovascular events, which were defined as the composite endpoint of death, myocardial ischemia, myocardial infarction, MINS, or embolic or

**Table 3 Risk factors associated with major postoperative complications**

	Statistical value	Post-CEA major complications	P
Age (yr)	62.0 ± 7.2	1.04 (0.99, 1.09)	0.151
Sex			0.616
Male	175 (84.95%)	1.0	
Female	31 (15.05%)	0.77 (0.28, 2.15)	
BMI (kg/m <sup>2</sup> )	25.33 ± 2.89	1.05 (0.93, 1.17)	0.459
ASA grade			0.522
Grade II	167 (81.07%)	1.0	
Grade III	39 (18.93%)	1.32 (0.57, 3.05)	
Anesthesia methods			0.312
TIVA	163 (79.13%)	1.0	
Combined intravenous-inhalation anesthesia	43 (20.87%)	0.62 (0.24, 1.58)	
Degree of carotid artery stenosis on the surgical side			
Mild/moderate stenosis	3 (1.46%)	1.0	
Severe stenosis	201 (97.57%)	0.47 (0.04, 5.28)	0.538
Occlusion	2 (0.97%)	2.00 (0.05, 78.25)	0.711
Degree of carotid artery stenosis on the contralateral side			
Mild/moderate stenosis	169 (85.35%)	1.0	
Severe stenosis	21 (10.61%)	0.38 (0.08, 1.69)	0.201
Occlusion	8 (4.04%)	0 (0, Inf)	0.986
Operating time (min)	141.33 ± 40.96	1.01 (1.0, 1.02)	0.038 <sup>a</sup>
Intraoperative intake and output volume (mL)	897.57 ± 333.40	1.00 (1.0, 1.00)	0.221
Duration of carotid artery occlusion	22.0 (18.0–44.0)	1.01 (0.99, 1.03)	0.327
CV <sub>SBP</sub>	0.16 ± 0.04	16.36 (0.00, 150500.70)	0.548
CV <sub>DBP</sub>	0.15 ± 0.04	40.21 (0.01, 132798.95)	0.372
Preoperative NLR	2.08 ± 0.94	1.21 (0.87, 1.69)	0.264
NLR within 24 h after CEA	5.68 (3.93–8.91)	1.09 (1.01, 1.17)	0.026 <sup>a</sup>

<sup>a</sup>P < 0.05.ASA: American society of anesthesiologists; BMI: Body mass index; CEA: Carotid endarterectomy; CV<sub>DBP</sub>: Coefficient of variation in diastolic blood pressure; CV<sub>SBP</sub>: Coefficient of variation in systolic blood pressure; NLR: Neutrophil to lymphocyte ratio; TIVA: Total intravenous anesthesia.

thrombotic stroke within 30 d after surgery[5]. Systemic inflammation plays a critical role in the pathogenesis of cardiovascular diseases. Preoperative NLR > 4 was associated with perioperative myocardial injury (OR = 2.56), indicating that systemic inflammation might be associated with the development of perioperative myocardial injury[26].

Elevated NLR on postoperative day 2 was significantly correlated with higher in-hospital mortality, pneumonia, ICU readmission and prolonged ICU stay after cardiac surgery[27]. A study by Lee *et al*[28] showed that NLR in pneumonia patients in the ICU was significantly higher than that in pneumonia patients in a ward and healthy controls. Compared with the C-reaction protein level, NLR might be a better indicator for evaluating the severity of pneumonia[28]. Another study also proved that NLR was significantly correlated with the pneumonia severity index[29]. Nam *et al*[30] confirmed that a higher NLR could predict stroke-associated pneumonia in patients with acute ischemic stroke. Moreover, NLR was higher in patients with severe pneumonia[30]. Feng *et al*[31] studied patients on mechanical ventilation for > 72 h and showed that NLR levels could be used to assess risk factors for mortality caused by ventilator-associated pneumonia[31].



**Table 4 Correlation between neutrophil to lymphocyte ratio within 24 h after carotid endarterectomy and major postoperative complications**

Exposure factors	Unadjusted	P value	Model I	P value	Model II	P
NLR	1.09 (1.01, 1.17)	0.026 <sup>a</sup>	1.08 (1.00, 1.16)	0.041 <sup>a</sup>	1.15 (1.03, 1.29)	0.014 <sup>a</sup>
NLR tertile groups						
Low NLR group	1.0		1.0		1.0	
Middle NLR group	1.60 (0.63, 4.09)	0.322	1.52 (0.59, 3.92)	0.386	3.99 (1.03, 15.49)	0.046 <sup>a</sup>
High NLR group	2.92 (1.21, 7.02)	0.017 <sup>a</sup>	2.88 (1.17, 7.09)	0.022 <sup>a</sup>	8.47 (2.20, 32.63)	0.002 <sup>a</sup>

<sup>a</sup>P < 0.05.

Model I-adjusted variables: Sex and age; Model II-adjusted variables: Sex, age, BMI, ASA grade, preoperative combined heart disease, anesthesia method, degree of stenosis on the surgical side, degree of stenosis on the contralateral side, operating time, intraoperative intake and output volume, duration of carotid artery occlusion, CV<sub>SBP</sub>, and CV<sub>DBP</sub>. ASA: American society of anesthesiologists; BMI: Body mass index; CEA: Carotid endarterectomy; CV<sub>DBP</sub>: Coefficient of variation in diastolic blood pressure; CV<sub>SBP</sub>: Coefficient of variation in systolic blood pressure; NLR: Neutrophil to lymphocyte ratio.

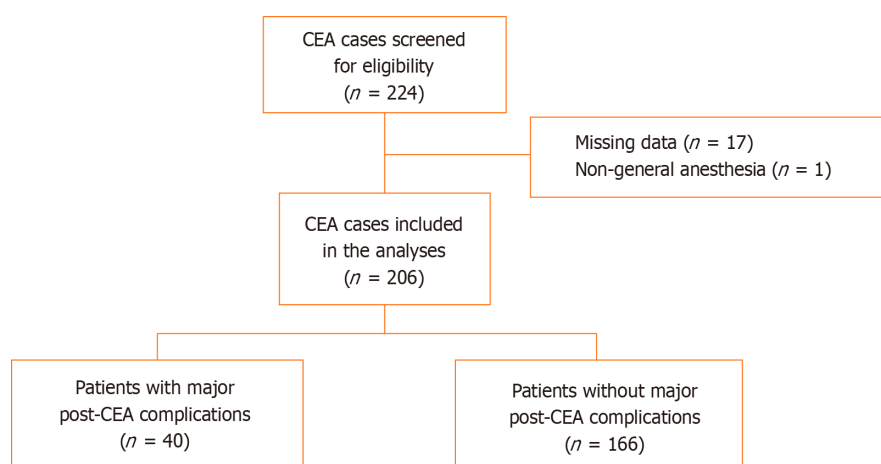
**Table 5 Outcome variables, stratified by NLR ratio tertile groups**

	Total	Low NLR group	Middle NLR group	High NLR group	P
No. of cases	206	68	69	69	
Major postoperative complications	40 (19.42%)	8 (11.76%)	11 (15.94%)	21 (30.43%)	0.015 <sup>a</sup>
Neurological complications	16 (7.77%)	4 (5.88%)	4 (5.80%)	8 (11.59%)	0.346
Cardiac complications	6 (2.91%)	0 (0.00%)	3 (4.35%)	3 (4.35%)	0.218
Respiratory complications	14 (6.80%)	2 (2.94%)	5 (7.25%)	7 (10.14%)	0.242
AKI	9 (4.37%)	2 (2.94%)	1 (1.45%)	6 (8.70%)	0.089
Fever	10 (4.85%)	1 (1.47%)	2 (2.90%)	7 (10.14%)	0.040 <sup>a</sup>
Surgical site infections	3 (1.46%)	1 (1.47%)	1 (1.45%)	1 (1.45%)	1.000
Urinary infections	3 (1.46%)	0 (0.00%)	1 (1.45%)	2 (2.90%)	0.367
DVT	5 (2.43%)	2 (2.94%)	1 (1.45%)	1 (1.45%)	0.766
Length of stay in the ICU (d)	1.0 (0–1.0)	1.0 (0–1.0)	1.0 (0–1.0)	1.0 (1.0–1.0)	0.079
Hospitalization stay (d)	15.56 ± 4.30	15.44 ± 4.40	15.28 ± 4.27	15.96 ± 4.26	0.627
Cost of hospitalization (CNY)	26886.26 ± 11277.49	24371.70 ± 5233.73	26837.07 ± 12681.34	29413.56 ± 13520.49	0.032 <sup>a</sup>

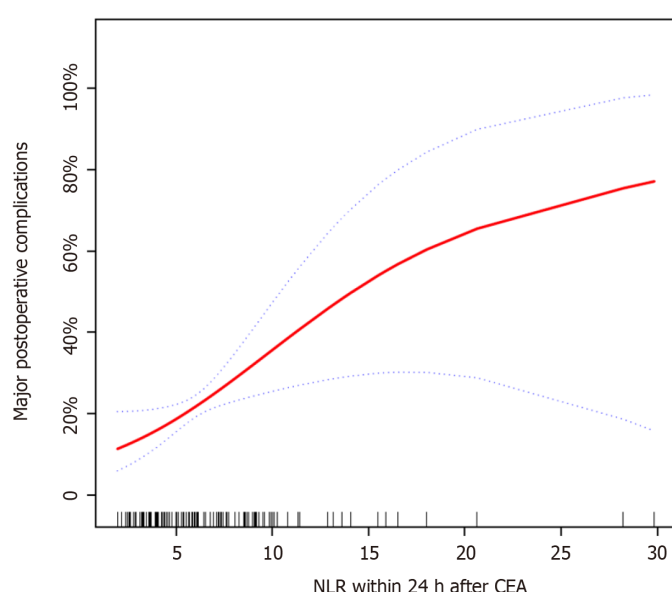
<sup>a</sup>Statistically significant difference was observed between the groups.

AKI: Acute kidney injury; CEA: Carotid endarterectomy; CNY: Chinese Yuan; DVT: Deep venous thrombosis; ICU: Intensive care unit; NLR: Neutrophil-to-lymphocyte ratio.

AKI results from a complex interaction between hemodynamic, toxic and inflammatory factors[32]. Long-term follow-up showed that NLR was an independent predictor of kidney function decline among individuals with diabetes and prediabetes [33,34]. The elevation of NLR immediately after cardiac surgery and on postoperative day 1 was associated with an increased risk of postoperative AKI and 1-year mortality; NLR could assist with the risk stratification of AKI and mortality in high-risk surgical patients[7,35,36]. High NLR levels were associated with increased risks of 30- and 90-day mortality in AKI patients; compared with the lower NLR group (NLR < 5.55), the hazard ratio in the higher NLR group (NLR > 12.14) was 1.37[37]. One recent systematic review and meta-analysis showed that when NLR was used to predict AKI, the sensitivity was 0.736, and the specificity was 0.686, indicating that NLR was a reliable biomarker for the early detection of AKI[38]. One prospective study evaluated the accuracy of a single emergency department measurement of NLR for the early diagnosis of AKI. The results showed that compared with normal controls, patients with AKI had a higher NLR. When the NLR cut-off value was 0.55, the sensitivity was 0.78, the specificity was 0.65, and the OR was 6.423[39].



**Figure 1 Patient flow chart.** CEA: Carotid endarterectomy.



**Figure 2 Smooth curve fitting for the relationships between NLR within 24 h after carotid endarterectomy and major postoperative complications.** CEA: Carotid endarterectomy; NLR: Neutrophil-to-lymphocyte ratio.

This study had several limitations. First, the small sample size and the low event rates might have increased the probability of committing a type II error and thus decrease the power of a hypothesis test. Second, this was a retrospective cohort study. The authenticity and completeness of medical records directly affected the reliability of the results.

## CONCLUSION

NLR within 24 h after CEA was associated with major postoperative complications. The incidence of major postoperative complications in the high NLR group was 8.47 times that in the low NLR group. Future prospective studies are needed for further evaluation.

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## ARTICLE HIGHLIGHTS

### Research background

Carotid artery cross-clamping during carotid endarterectomy (CEA) may induce cerebral ischemia-reperfusion injury to activate local inflammatory responses.

### Research motivation

There is no consensus on the correlation between neutrophil-to-lymphocyte ratio (NLR) and complications after CEA.

### Research objectives

This study aimed to evaluate the association between NLR and major complications after surgery in patients undergoing CEA.

### Research methods

The demographics, neutrophil and lymphocyte count in whole blood and postoperative outcomes of patients undergoing CEA were retrospectively analyzed.

### Research results

NLR within 24 h after CEA was significantly correlated with major postoperative complications. The incidence of major postoperative complications in the high NLR group was 8.47 times of that in the low NLR group.

### Research conclusions

NLR is associated with major postoperative complications in patients undergoing CEA.

### Research perspectives

Since early detection and early treatment help improve outcomes, inflammatory markers may become potential treatment targets for patients undergoing CEA.

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