Journal of Geriatric Cardiology | JGC
RESEARCH ARTICLE
J Geriatr Cardiol 2026; 23(9): 576–589

Sleep-inflammation-coronary plaque phenotype axis: clinical validation and inflammation-mediated mechanisms based on optical coherence tomography

Yang LIU, Xun-Xun FENG, Qian-Yun GUO✉, Yu-Jie ZHOU✉

Beijing Key Laboratory of Precision Medicine of Coronary Atherosclerotic Disease, Beijing Institute of Heart Lung and Blood Vessel Disease, Clinical Center for Coronary Heart Disease, Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, Beijing, China

✉ Correspondence to: gqydyx3000@163.com (GUO QY); azzyj12@163.com (ZHOU YJ)

https://doi.org/10.26599/1671-5411.2026.09.002

ABSTRACT

Background The influence of sleep duration on vulnerable coronary plaques, as evaluated via optical coherence tomography (OCT), has not been clearly defined in coronary artery disease (CAD). Here, the relationships between habitual sleep duration and thin-cap fibroatheroma (TCFA) detected by OCT were investigated in individuals with CAD. We further investigated whether systemic inflammation, represented by the neutrophil-to-lymphocyte ratio (NLR), represents a mediator of this association.

Methods Overall, 1,178 patients with angiographically confirmed CAD who underwent OCT imaging and completed standardized sleep questionnaires were enrolled. Participants were categorized according to reported sleep duration. Multivariable logistic regression modeling was employed to assess the link between sleep duration and TCFA. Linear regression analyses assessed the association between sleep duration and NLR. Restricted cubic spline (RCS) modeling was applied as a means of detecting possible nonlinear associations between NLR and TCFA. Mediation analyses were then conducted to determine whether NLR functioned as an intermediate variable linking sleep duration and plaque vulnerability.

Results These results offer the first clinical evidence of the link between sleep duration and TCFA presence in individuals with CAD, with the TCFA risk in the abnormal sleep duration group being 2.16 times that of the normal group (95% CI: 1.63-2.88, $P < 0.001$). Sleep duration was also independently correlated with NLR, and RCS analysis highlighted a nonlinear relationship between NLR levels and TCFA risk ($P < 0.001$). Importantly, mediation analysis demonstrated that NLR partially mediated the effect of sleep duration on TCFA, supporting the existence of a sleep-inflammation-plaque vulnerability axis.

Conclusion The sleep duration has been shown to be significantly associated with the risk of developing TCFA. In addition, a partial mediating effect of NLR on this relationship has been found.

Short sleep duration has emerged as a major global public health issue. Between 1985 and 2012, the average sleep duration of American adults declined steadily, while the proportion of individuals sleeping six hours or less per night increased by 31%.[1] This trend reflects the combined effects of accelerated lifestyles, growing occupational stress, and widespread use of electronic devices, all of which contribute to chronic sleep insufficiency in modern society. At the same time, cardiovascular disease (CVD) remains driver of global morbidity and mortality.[2] Projections indicate that the global crude prevalence of CVD will rise from approximately 598 million cases in 2025 to more than 1.14 billion by 2050, with coronary artery disease (CAD) becoming the most prevalent subtype, affecting nearly 471 million individuals by that time.[3]

Given this dual public health burden, clarifying the relationship between sleep duration and cardiovascular health, particularly CAD, is of critical importance. Previous studies have demonstrated significant associations between short or disrupted sleep and increased CVD risk, together with a higher likelihood of adverse cardiovascular events.[4,5] In recognition of its clinical relevance, the American Heart Association incorporated sleep

© 2026 JGC All rights reserved; www.jgc301.com

as one of the eight core metrics of cardiovascular health in 2022.[6] Experimental and epidemiologic studies further suggest that sleep disturbances promote a sustained pro-inflammatory state, characterized by elevated circulating inflammatory mediators. [7] The neutrophil-to-lymphocyte ratio (NLR) is considered an accessible and robust biomarker of systemic inflammation. Neutrophils reflect nonspecific inflammatory activation, whereas lymphocyte counts are influenced by stress and immune suppression. Elevated NLR has been associated with unfavorable outcomes in patients with acute coronary syndromes (ACS)[8] and has been shown to predict adverse cardiovascular events.[9,10] Thin-cap fibroatheroma (TCFA), characterized by a large lipid-rich necrotic core covered by a thin fibrous cap, represents a highly vulnerable plaque phenotype.[8,11] Accumulating evidence indicates that overall plaque burden, rather than the degree of luminal stenosis, is the primary determinant of future cardiovascular events and mortality.[12] As such, the identification of modifiable factors that contribute to the development of vulnerable plaques is essential for preventing major adverse cardiovascular events.

Despite growing interest in sleep and inflammation, it remains unclear whether inflammatory markers such as NLR mediate the relationship between sleep duration and CAD. Moreover, the biological mechanisms linking sleep behavior to coronary plaque vulnerability have not been fully elucidated. By integrating OCT imaging with inflammatory profiling, the present study aims to visually and mechanistically characterize the link between sleep length and coronary plaque phenotypes. This work seeks to provide novel insights into the pathophysiological links between sleep, inflammation, and cardiovascular disease, thereby offering a theoretical basis for improved prevention and management strategies.

METHODS

Study Populations

This observational clinical cohort analysis was undertaken in accordance with the Declaration of Helsinki with approval from the Ethics Review Committee of Beijing Anzhen Hospital, Capital Medical University. From March 2023 to August 2025, a total of 1,178 individuals who received percutaneous coronary intervention (PCI) with concurrent OCT imaging at Beijing Anzhen Hospital were consecutively enrolled. All participants were screened using predefined inclusion and exclusion criteria. Patients were excluded if they had malignant tumors, active inflammatory or autoimmune diseases (including rheumatoid arthritis), recent acute infections, or severe hepatic or renal dysfunction (eGFR < 30 mL/min per 1.73 m^2). Additional exclusion criteria included long-term use of anti-inflammatory medications, severe psychiatric illness or cognitive impairment preventing questionnaire completion, chronic total occlusions, extreme vessel tortuosity, or severe calcification that precluded OCT imaging, as well as refusal to complete the sleep questionnaires (Figure 1).

Data Collection

Clinical and laboratory information was obtained from the electronic medical records of the hospital. Demographic variables included age and sex. Vital signs comprised heart rate, systolic and diastolic blood pressure, and BMI. Patients were classified as having stable angina or acute coronary syndrome (ACS), with further subdivision of ACS into ST-segment elevation myocardial infarction (STEMI), unstable angina, and non-STEMI (NSTEMI).[13] Comorbidities and medical history were recorded, including hypertension, type 2 diabetes, hyperlipidemia, previous PCI, in-stent restenosis, and prior coronary artery bypass grafting (CABG).

Following an overnight fast, venous blood samples were obtained at the time of admission. Complete blood counts were performed at the Beijing Anzhen Hospital Laboratory Center. Serum total cholesterol (TC), triglycerides (TG), and low- and high-density lipoprotein cholesterol (LDL, HDL) were measured using standard colorimetric assays. Creatinine was determined by the Jaffe method, and fasting blood glucose (FBG) was assessed using the hexokinase method. Left ventricular ejection fraction was measured by echocardiography, with all examinations independently interpreted by two experienced sonographers. The NLR was determined as the ratio of absolute neutrophil count to absolute lymphocyte count, representing an integrated means of gauging inflammation and the extent of immunosuppression.

Optical Coherence Tomography Imaging and Analysis

All intravascular imaging was performed using the Dragonfly OPTIS imaging catheter in combination with the OPTIS™ MOBILE System (Abbott Vascular, Shanghai, China). OCT examinations of the target coronary

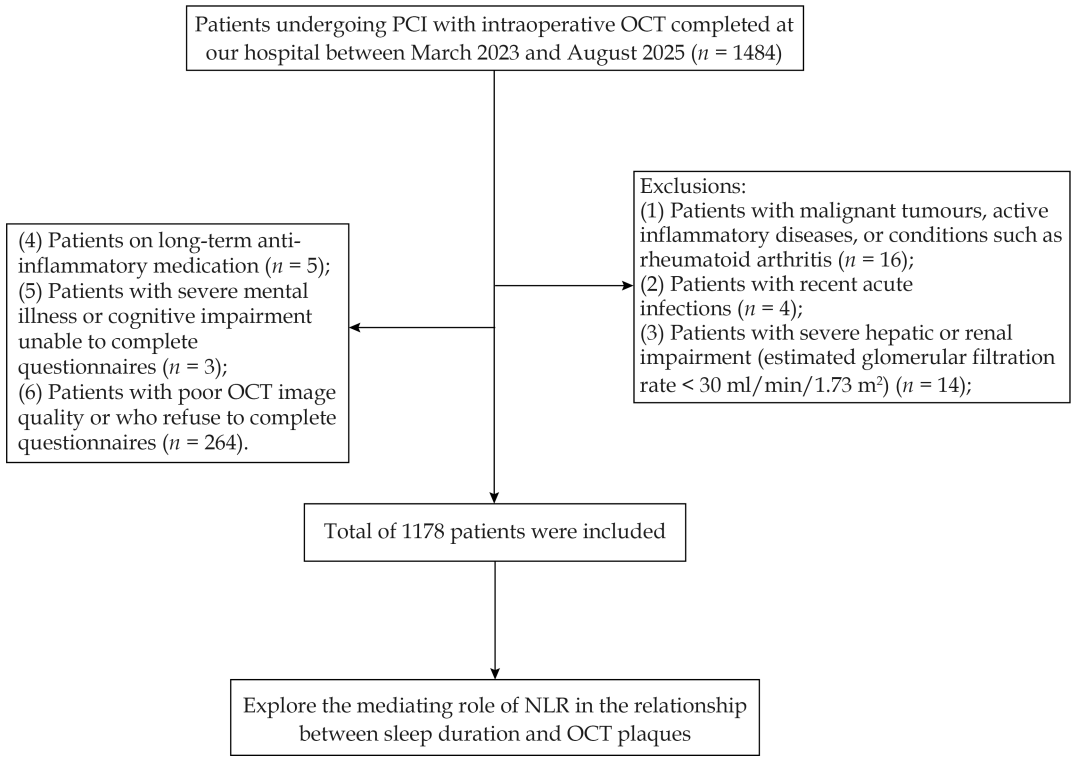


Figure 1 Flowchart. NLR: neutrophil-to-lymphocyte ratio; OCT: optical coherence tomography; PCI: percutaneous coronary intervention.

segments were independently conducted by two experienced interventional cardiologists. Image interpretation was subsequently carried out by two trained analysts who were blinded to all clinical and laboratory data. In cases of disagreement, a third investigator performed an independent review to reach consensus. The following OCT-derived parameters were systematically assessed: plaque phenotype, maximal lipid arc, minimal fibrous cap thickness, presence of TCFA, lipid plaque length, macrophage accumulation, healed plaques, cholesterol crystal deposition, microchannel formation, calcified nodules, mean reference lumen area, percent area stenosis, and minimum lumen area The thickness of the thinnest part of fibrous cap was determined three times, and the average value was recorded as the minimum thickness. The lipid arc was assessed at 1-mm points within the lesion, with the largest measurement being the maximal lipid arc. TCFA was represented by lipid-rich plaques with maximal lipid arcs ≥ 90° and minimum fibrous cap thicknesses ≤65 μm, in accordance with established criteria (Figure 2).[14]

Sleep Data Collection

All eligible participants completed a structured sleep questionnaire on the day following their OCT procedure. Prior to administration, a trained investigator provided standardized instructions to ensure comprehension. Sleep duration was determined by self-report, with patients estimating their average nightly sleep time over a typical period.

Statistical Analysis

Continuous variables are summarized as means and standard deviations if normally distributed, or as medians with interquartile ranges if non-normally distributed. Categorical variables are shown as frequencies and proportions. Between-group comparisons for continuous variables were conducted using *t*-tests or Mann-Whitney *U* tests, as appropriate, while chi-square tests were applied to categorical data.

Participants were stratified into two categories based on reported sleep duration: a normal sleep group (7-8 h/night) and an abnormal sleep group (< 7 h or > 8 h/night). Baseline clinical characteristics were compared between groups. Multivariable logistic regression was applied to evaluate the link between sleep duration and OCT-derived plaque features, shown with odds ratios (ORs) and 95% confidence intervals (CIs). Linear regres-

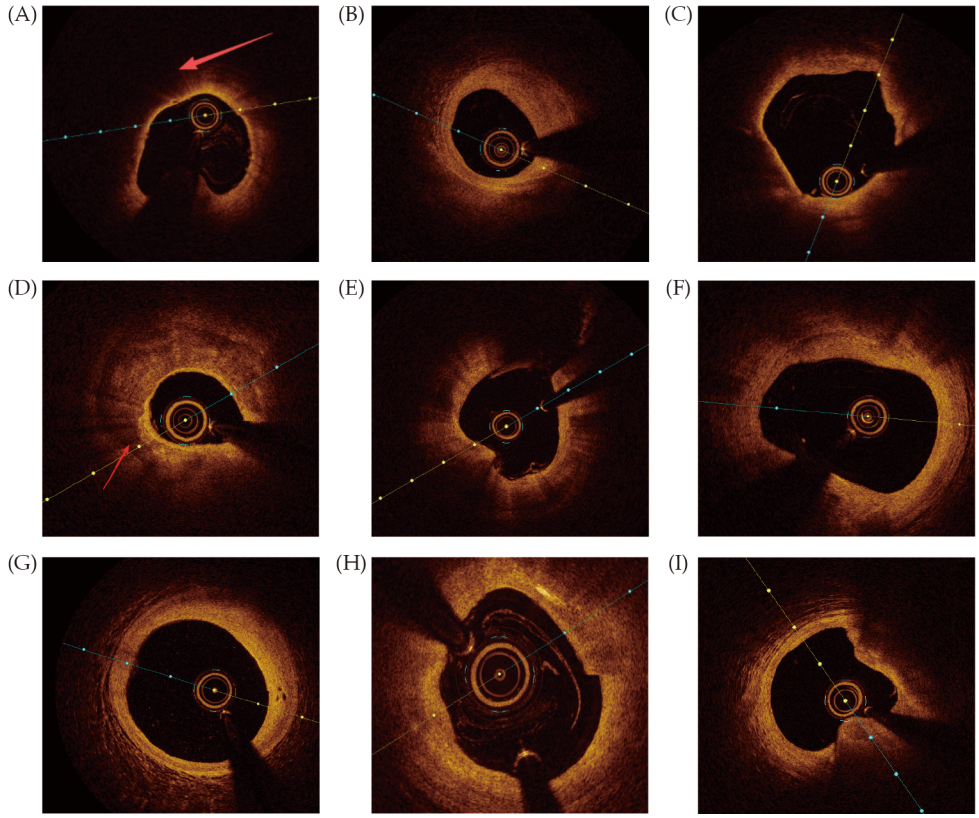


Figure 2 Plaque-related features in OCT images. (A): Lipid plaque; (B): fibrous plaque; (C): thin fibrous cap plaque; (D): calcification; (E): macrophage infiltration; (F): healed plaque; (G): microchannel; (H): cholesterol crystal; (I): calcified nodule. OCT: optical coherence tomography.

sion, with adjustments for potential confounders, was applied to estimate the association between sleep duration and NLR, with results expressed as unstandardized regression coefficients (B) and corresponding 95% CIs. To explore possible non-linear associations between NLR and TCFA, restricted cubic spline (RCS) models with multivariable adjustment were applied. A formal mediation framework was subsequently used to test whether NLR mediated the relationship between sleep duration and TCFA. First, the total effect of sleep duration on TCFA was estimated (path c). Next, a mediator model was fitted with NLR as the outcome and sleep duration as the predictor to obtain path a. An outcome model was then constructed with TCFA as the dependent variable and sleep duration and NLR as independent variables, allowing estimation of the direct effect of sleep duration (c′) and the link between NLR and TCFA (path b). The indirect effect was defined as a × b. Bootstrap resampling (5,000 iterations) was used to calculate 95% CIs for indirect effects. Significant mediation was recognized if the CI did not cross zero. The fraction of the total effect explained by the mediator was computed as ab/c, reflecting the relative contribution of NLR to the sleep-TCFA association. A mediation pathway diagram was generated to illustrate these relationships.

All regression models were adjusted for relevant covariates to minimize confounding. Statistical analyses were conducted using R (v 4.5.2). All tests were two-tailed, and $P < 0.05$ was considered significant.

RESULTS

Demographic and Clinical Characteristics

Overall, 1,130 patients undergoing PCI were retained for the final analysis, of whom 36.5% reported abnormal sleep duration (Table 1). When stratified by plaque phenotype, 23.8% of patients exhibited TCFA (Table 2). Within the sleep duration groups, significant differences were observed for age, WBC, neutrophil (NE), lymphocyte LYM), and monocyte (MON) counts, creatinine, eGFR, urinary albumin (UA), β-blocker use, and

ACEI/ARB use (all $P < 0.05$). NLR differed significantly across all sleep categories ($P < 0.05$). Among patients with TCFA, significant differences were noted for age, DBP, alcohol consumption, prevalence of UA, STEMI, and NSTEMI, as well as β-blocker use. Furthermore, significant differences were observed in laboratory parameters such as WBC, red blood cell (RBC) count, NE, LYM, MON, triglycerides (TG), HDL, LDL, C-reactive protein (CRP) among patients with TCFA (Table S2). The NLR was also markedly higher in the TCFA group ($P < 0.01$).

Sleep Duration and OCT Plaque Results

Marked differences in TCFA prevalence were observed across sleep duration categories (P < 0.001; Table S1). In univariate analyses, abnormal sleep duration was found to be linked to a markedly elevated TCFA risk (OR: 2.14; 95% CI: 1.63-2.81; Table 3). This relationship remained robust after adjustment for confounders (OR: 2.16; 95% CI: 1.63-2.88). Significant differences were also identified for lipid plaques (P < 0.001), macrophage infiltration (P < 0.001), and cholesterol crystals (P = 0.005). After multivariable adjustment, abnormal sleep duration remained independently associated with lipid plaques (OR: 1.74; 95% CI: 1.34-2.26), macrophage infiltration (OR: 1.55; 95% CI: 1.19-2.01), and cholesterol crystals (OR: 1.42; 95% CI: 1.11-1.82).

Sleep Duration and Inflammation Marker Results

Linear regression analyses demonstrated that both short and long sleep duration were associated with a 1.31-fold elevation in NLR ($P < 0.001$). This association remained significant after adjustment (B = 1.38, $P < 0.001$), indicating that abnormal sleep duration is linked to heightened systemic inflammatory activity.

NLR and OCT Plaque Findings

Following the grouping of NLR into three categories

Table 1 Baseline characteristics of sleep duration subgroups.

Characteristics	Total (n = 1178)	Normal Sleep Duration (n = 748)	Abnormal Sleep Duration (n = 430)	P-value
Demographics				
Age, yrs	61.0 [53.0, 68.0]	61.0 [53.0, 68.0]	62.0 [55.0, 70.0]	0.001
Male	904 (76.74%)	562 (75.1%)	342 (79.5%)	0.099
BMI, kg/m^2	25.4 [23.7, 27.7]	25.6 [23.7, 27.8]	25.4 [23.6, 27.4]	0.127
SBP, mmHg	130.0 [120.0, 140.0]	130.0 [120.0, 139.3]	130.0 [120.0, 143.0]	0.326
DBP, mmHg	78.0 [70.0, 85.0]	78.0 [70.0, 84.0]	77.5 [70.0, 85.0]	0.486
Previous smoking	637 (54.07%)	399 (53.34%)	238 (55.35%)	0.545
Previous drinking	323 (27.42%)	205 (27.41%)	118 (27.44%)	0.998
Medical histories				
Hypertension	748 (63.50%)	460 (61.50%)	288 (66.98%)	0.069
Diabetes mellitus	424 (35.99%)	272 (36.36%)	152 (35.35%)	0.775
Previous PCI	455 (38.62%)	288 (38.50%)	167 (38.84%)	0.959
Previous CABG	14 (1.19%)	7 (0.94%)	7 (1.63%)	0.438
Laboratory results				
WBC, 10^9/L	6.35 [5.35, 7.54]	6.23 [5.22, 7.36]	6.59 [5.58, 7.95]	< 0.001
RBC, 10^{12}/L	4.63 [4.31, 4.96]	4.64 [4.33, 4.98]	4.60 [4.26, 4.92]	0.068
PLT, 10^9/L	214.5 [179.0, 246.0]	215.0 [179.0, 250.3]	214.0 [180.0, 240.8]	0.174
Neutrophils, 10^9/L	4.14 [3.37, 5.12]	3.88 [3.22, 4.76]	4.60 [3.69, 5.56]	< 0.001
Lymphocyte, 10^9/L	1.58 [1.27, 1.97]	1.69 [1.40, 2.04]	1.40 [1.09, 1.75]	< 0.001
Monocyte, 10^9/L	0.37 [0.30, 0.46]	0.36 [0.29, 0.44]	0.39 [0.30, 0.49]	< 0.001
TG, mmol/L	1.57 [1.14, 2.14]	1.58 [1.16, 2.17]	1.54 [1.11, 2.05]	0.198
TC, mmol/L	3.71 [3.14, 4.41]	3.74 [3.17, 4.44]	3.67 [3.07, 4.35]	0.207
HDL-C, mmol/L	1.08 [0.91, 1.25]	1.08 [0.91, 1.25]	1.08 [0.90, 1.24]	0.518

Continued

Characteristics	Total (n = 1178)	Normal Sleep Duration (n = 748)	Abnormal Sleep Duration (n = 430)	P-value
LDL-C, mmol/L	1.98 [1.47, 2.56]	2.00 [1.48, 2.58]	1.94 [1.46, 2.55]	0.314
Creatinine, mmol/L	76.15 [66.30, 87.00]	75.80 [64.78, 86.60]	76.95 [67.80, 87.65]	0.026
NLR	2.53 [1.94, 3.49]	2.25 [1.84, 2.87]	3.33 [2.54, 4.35]	< 0.001
eGFR, mL/min per 1.73 m^2	88.68 [82.61, 98.50]	89.80 [84.67, 99.18]	88.67 [80.25, 96.78]	0.002
Uric acid, μmol/L	325.80 [272.13, 388.65]	327.65 [271.83, 390.60]	323.15 [273.40, 385.25]	0.786
CRP, mg/L	1.46 [0.62, 2.68]	1.49 [0.60, 2.68]	1.40 [0.66, 2.68]	0.355
FBG, mmol/L	6.19 [5.21, 8.17]	6.17 [5.22, 8.10]	6.32 [5.21, 8.24]	0.471
HbA1c, %	6.41 [5.90, 6.41]	6.41 [5.90, 6.41]	6.41 [6.00, 6.41]	0.375
LVEF, %	62.40 [62.00, 65.00]	62.40 [62.01 65.00]	62.40 [62.00, 65.00]	0.572
Diagnosis				
SAP	104 (8.83%)	62 (8.29%)	42 (9.77%)	0.451
UA	924 (78.44%)	602 (80.48%)	322 (74.88%)	0.030
STEMI	46 (3.90%)	26 (3.48%)	20 (4.65%)	0.397
NSTEMI	94 (7.98%)	51 (6.82%)	43 (10.00%)	0.068
ISR	152 (12.90%)	92 (12.30%)	60 (13.95%)	0.468
Medications				
DAPT	1035 (87.86%)	655 (87.57%)	380 (88.37%)	0.753
Statin	1114 (94.57%)	706 (94.39%)	408 (94.88%)	0.818
β-Blocker	508 (43.12%)	304 (40.64%)	204 (47.44%)	0.027
ACEI/ARB	472 (40.07%)	278 (37.17%)	194 (45.12%)	0.009
PCSK9i	295 (25.04%)	195 (26.07%)	100 (23.26%)	0.316
OCT characteristics				
Fibrous plaque	1132 (96.10%)	717 (95.86%)	415 (96.51%)	0.687
Lipid plaque	740 (62.82%)	440 (58.82%)	300 (69.77%)	<0.001
Plaque length, mm	4.60 [2.50, 8.30]	4.60 [2.60, 7.93]	4.80 [2.30, 8.83]	0.969
Fibrous cap thickness, um	80.0 [60.0, 120.0]	80.0 [60.0, 120.0]	80.0 [60.0, 120.0]	0.704
Lipid arc, deg	157.20 [112.70, 222.70]	153.40 [106.78, 223.18]	160.60 [118.90, 221.40]	0.204
TCFA	282 (23.94%)	140 (18.72%)	142 (33.02%)	<0.001
Calcification	668 (56.71%)	421 (56.28%)	247 (57.44%)	0.745
Macrophage infiltration	340 (28.86%)	190 (25.40%)	150 (34.88%)	< 0.001
Healed plaque	113 (9.59%)	73 (9.76%)	40 (9.30%)	0.878
Microchannel	220 (18.68%)	144 (19.25%)	76 (17.67%)	0.555
Cholesterol crystal	662 (56.20%)	397 (53.07%)	265 (61.63%)	0.005
Calcified nodule	154 (13.07%)	96 (12.83%)	58 (13.49%)	0.817
MLA, mm^2	1.87 [1.28, 2.61]	1.93 [1.31, 2.67]	1.76 [1.23, 2.47]	0.022
RLA, mm^2	6.39 [4.83, 8.45]	6.46 [4.92, 8.61]	6.22 [4.70, 8.24]	0.160
AS%	70.35 [60.40, 78.00]	70.35 [59.80, 77.90]	70.35 [61.43, 78.48]	0.289

Data are presented as n (%) or median (interquartile range). ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; AS: percent lumen area; BMI: body mass index; CABG: coronary artery bypass grafting; CRP: C-reactive protein; DAPT: dual antiplatelet therapy; DBP: diastolic blood pressure; FBG: fasting blood glucose; HDL-C: high-density lipoprotein cholesterol; ISR: in-stent restenosis; LDL-C: low-density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; MLA: minimal lumen area; NLR: neutrophil-to-lymphocyte ratio; NSTEMI: non-ST-segment elevation myocardial infarction; PCI: percutaneous coronary intervention; PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor; PLT: platelet count; RBC: red blood cell count; RLA: reference lumen area; SAP: stable angina pectoris; SBP: systolic blood pressure; STEMI: ST-segment elevation myocardial infarction; TC: total cholesterol; TCFA: thin-cap fibroatheroma; UA: unstable angina; WBC: white blood cell count.

Table 2 Basic demographics of the TCFA.

Characteristics	No-TCFA (*n* = 896)	TCFA (*n* = 282)	*P*-value
Demographics			
Age, yrs	62.0 [54.0, 69.0]	60.0 [50.3, 67.0]	0.003
Male	677 (75.56%)	227 (80.50%)	0.103
BMI, kg/m^2	25.39 [23.66, 27.57]	25.83 [23.56, 27.68]	0.207
SBP, mmHg	130.0 [120.0, 140.0]	130.0 [121.0, 143.0]	0.215
DBP, mmHg	77.0 [70.0, 84.0]	80.0 [72.0, 86.0]	0.005
Previous smoking	484 (54.02%)	153 (54.26%)	0.999
Previous drinking	259 (28.91%)	64 (22.70%)	0.050
Medical histories			
Hypertension	568 (63.39%)	180 (63.83%)	0.951
Diabetes mellitus	329 (36.72%)	95 (33.69%)	0.393
Previous PCI	359 (40.07%)	96 (34.04%)	0.082
Previous CABG	8 (0.89%)	6 (2.13%)	0.176
Laboratory results			
WBC, 10^9/L	6.22 [5.24, 7.36]	6.76 [5.63, 8.02]	< 0.001
RBC, 10^{12}/L	4.62 [4.30, 4.94]	4.66 [4.35, 5.06]	0.049
PLT, 10^9/L	213.0 [177.0, 244.3]	219.5 [182.0, 254.8]	0.074
Neutrophils, 10^9/L	3.94 [3.29, 4.86]	4.68 [3.75, 5.69]	< 0.001
Lymphocyte, 10^9/L	1.62 [1.33, 1.98]	1.46 [1.11, 1.85]	< 0.001
Monocyte, 10^9/L	0.37 [0.29, 0.45]	0.39 [0.30, 0.48]	0.019
TG, mmol/L	1.51 [1.11, 2.11]	1.69 [1.27, 2.18]	0.005
TC, mmol/L	3.68 [3.09, 4.39]	3.80 [3.26, 4.50]	0.112
HDL-C, mmol/L	1.12 [0.92, 1.26]	1.02 [0.87, 1.20]	< 0.001
LDL-C, mmol/L	1.96 [1.45, 2.51]	2.06 [1.58, 2.66]	0.047
Creatinine, mmol/L	75.80 [65.40, 86.60]	77.55 [68.40, 88.58]	0.008
NLR	2.41 [1.87, 3.24]	3.14 [2.31, 4.55]	< 0.001
eGFR, mL/min/1.73 m2	88.80 [82.66, 97.922]	88.67 [82.65, 99.21]	0.936
Uric acid,μmol/L	324.50 [270.20, 384.10]	328.55 [279.48, 398.88]	0.060
CRP, mg/L	1.32 [0.57, 2.68]	2.03 [0.81, 2.92]	< 0.001
FBG, mmol/L	6.18 [5.21, 7.99]	6.24 [5.30, 8.74]	0.348
HbA1c, %	6.41 [5.90, 6.41]	6.41 [5.90, 6.42]	0.253
LVEF, %	62.40 [62.00, 65.00]	62.40 [62.00, 65.01]	0.089
Diagnosis			
SAP	80 (8.93%)	24 (8.51%)	0.924
UA	719 (80.25%)	205 (72.70%)	0.009
STEMI	28 (3.12%)	18 (6.38%)	0.022
NSTEMI	62 (6.92%)	32 (11.35%)	0.023
ISR	122 (13.62%)	30 (10.64%)	0.231
Medications			
DAPT	779 (86.94%)	256 (90.78%)	0.106
Statin	844 (94.20%)	270 (95.74%)	0.400
β-Blocker	365 (40.74%)	143 (50.71%)	0.004
ACEI/ARB	350 (39.06%)	122 (43.26%)	0.236
PCSK9i	223 (24.89%)	72 (25.53%)	0.890

Data are presented as *n* (%) or median (interquartile range). ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; BMI: body mass index; CABG: coronary artery bypass grafting; CRP: C-reactive protein; DAPT: dual antiplatelet therapy; DBP: diastolic blood pressure; FBG: fasting blood glucose; HDL-C: high-density lipoprotein cholesterol; ISR: in-stent restenosis; LDL-C: low-density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; NLR: neutrophil-to-lymphocyte ratio; NSTEMI: non-ST-segment elevation myocardial infarction; PCI: percutaneous coronary intervention; PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor; PLT: platelet count; RBC: red blood cell count; SAP: stable angina pectoris; SBP: systolic blood pressure; STEMI: ST-segment elevation myocardial infarction; TC: total cholesterol; TCFA: thin-cap fibroatheroma; UA: unstable angina; WBC: white blood cell count.

Table 3 Logistic regression analysis of sleep duration and different types of plaques.

Variables	Univariate		Multivariable	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
TCFA	2.14 (1.63–2.81)	< 0.001	2.16 (1.63–2.88)	< 0.001
Lipid plaque	1.62 (1.26–2.08)	< 0.001	1.74 (1.34–2.26)	< 0.001
Fibrous plaque	1.20 (0.65–2.30)	0.576	1.21 (0.66–2.34)	0.548
Calcification	1.05 (0.83–1.33)	0.699	1.01 (0.79–1.28)	0.966
Macrophage infiltration	1.57 (1.22–2.04)	0.001	1.55 (1.19–2.01)	0.001
Healed plaque	0.95 (0.63–1.41)	0.798	0.99 (0.65–1.47)	0.946
Microchannel	0.90 (0.66–1.22)	0.504	0.91 (0.66–1.24)	0.558
Cholesterol crystal	1.42 (1.12–1.81)	0.004	1.42 (1.11–1.82)	0.005
Calcified nodule	1.06 (0.74–1.50)	0.749	0.96 (0.67–1.37)	0.834

TCFA: thin-cap fibroatheroma.

(NLR ≤ 2.15, 2.15 < NLR ≤ 3.12 and NLR > 3.12), the rates of TCFA occurrence in the low, medium and high NLR groups were 14.76%, 20.92% and 36.13% respectively (Table 4). As NLR levels increased, the proportion of TCFA cases increased progressively. A marked non-linear association between NLR and TCFA was found by RCS analysis after multivariable adjustment (non-linear P < 0.001; Figure 3). TCFA risk increased sharply at higher NLR values, suggesting a threshold effect. In adjusted logistic regression models, an increase in every standard deviation of NLR is associated with a 1.45-fold rise in the probability of TCFA occurrence(OR: 1.44; 95% CI: 1.31-1.58). A similar trend was observed across the NLR groups, with TCFA risk showing a progressive increase in Q2 and Q3 compared to Q1(Q2: OR 1.54; 95%CI: 1.06-2.25, Q3: OR 3.50; 95%CI: 2.46-5.04; Figure 4).

Mediating Role of NLR in the Sleep-TCFA Association

Mediation analysis (Figure 5) indicated substantial mediation of the slee- duration-TCFA association by NLR, with an indirect effect of 0.075 (95% CI: 0.032-0.116), representing 50.1% of the overall effect. Partial mediation by NLR was also observed for the link between sleep duration and lipid plaques (indirect effect: 0.027; 95% CI: 0.001-0.070), accounting for 22.5% of the overall effect. These findings indicate that systemic inflammation, as reflected by NLR, plays a substantial intermediary role in linking abnormal sleep duration to vulnerable coronary plaque phenotypes.

Table 4 Characteristics of OCT plaques in NLR groups within the general population.

Variables	Q1 (*n* = 393)	Q2 (*n* = 392)	Q3 (*n* = 393)	*P*-value
TCFA	58 (14.76%)	82 (20.92%)	142 (36.13%)	< 0.001
Lipid plaque	229 (58.27%)	238 (60.71%)	273 (69.47%)	0.003
Fibrous plaque	375 (95.42%)	375 (95.66%)	382 (97.20%)	0.377
Calcification	258 (65.65%)	258 (65.82%)	152 (38.68%)	< 0.001
Macrophage infiltration	85 (21.63%)	107 (27.30%)	148 (37.66%)	< 0.001
Healed plaque	36 (9.16%)	33 (8.42%)	44 (11.20%)	0.392
Microchannel	69 (17.56%)	71 (18.11%)	80 (20.36%)	0.567
Cholesterol crystal	192 (48.85%)	208 (53.06%)	262 (66.67%)	< 0.001
Calcified nodule	59 (15.01%)	55 (14.03%)	40 (10.18%)	0.105

Data are presented as *n* (%). NLR: neutrophil-to-lymphocyte ratio; OCT: optical coherence tomography; TCFA: thin-cap fibroatheroma.

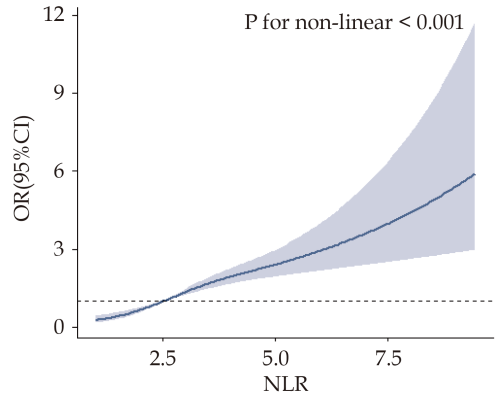


Figure 3 Restricted cubic spline plot of NLR and TCFA. Adjusted: age, DBP, previous drinking, HDL-C, LDL-C, UA, STEMI, NSTEMI, β-blocker. DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; STEMI: ST-segment elevation myocardial infarction; TCFA: thin-cap fibroatheroma; NLR: neutrophil-to-lymphocyte ratio; NSTEMI: non-ST-segment elevation myocardial infarction.

DISCUSSION

This investigation is the first to apply OCT to examine the potential mediation of the association between sleep duration and coronary plaque vulnerability by inflammatory biomarkers. A robust link between sleep duration and the presence of TCFA was found. Even after comprehensive adjustment for potential confounders, abnormal sleep duration was linked to significantly elevated NLR levels, and NLR in turn partially mediated the increased risk of TCFA. These findings suggest that inflammation represents a key biological pathway through which disturbed sleep may promote plaque instability in patients with CVD. Collectively, our results indicate that both short and long sleep durations may accelerate the development of vulnerable plaques by amplifying systemic inflammatory responses.

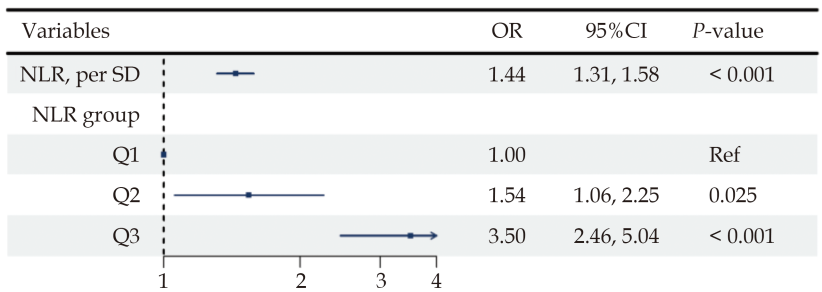


Figure 4 Total population NLR and OCT plaque forest plot. NLR: neutrophil-to-lymphocyte ratio; OCT: optical coherence tomography.

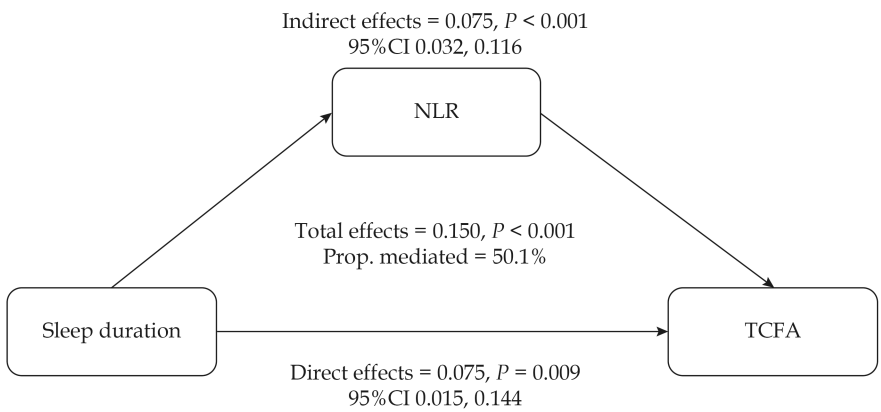


Figure 5 Mediation pathways between sleep duration and TCFA. Adjusted: sex, age, DBP, previous smoking, previous drinking, hypertension, diabetes mellitus, HDL-C, LDL-C, UA, STEMI, NSTEMI, DAPT, stain, β-blocker, ACEI/ARB, PCSK9i. ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; DAPT: dual antiplatelet therapy; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; NSTEMI: non-ST-segment elevation myocardial infarction; PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor; STEMI: ST-segment elevation myocardial infarction; TCFA: thin-cap fibroatheroma.

A growing body of epidemiologic evidence supports 7-8 hours of nightly sleep as the optimal range for cardiovascular health. Numerous studies have reported that sleeping fewer than six hours per night is associated with a substantially higher incidence of CVD.[15-17] Similarly, cross-sectional and longitudinal investigations consistently demonstrate that habitual sleep durations exceeding nine hours are also linked to greater cardiovascular risk when compared with 7-8 hours of sleep.[18,19] A large prospective cohort study with a median follow-up of 14.3 years further identified a U-shaped relationship between sleep duration and cardiovascular mortality. [20] In that study, both very short (≤ 4 h) and very long (≥ 10 h) sleep durations were linked to markedly higher mortality than sleeping 7 h per night. Consistent with these findings, a meta-analysis by Cappuccio et al. reported markedly increased CVD mortality in individuals with both short and long sleep durations.[21]

Several biological mechanisms have been suggested to explain the elevated cardiovascular risk associated with insufficient sleep. Experimental studies have shown that sleep deprivation impairs insulin sensitivity and promotes insulin resistance.[22] In addition, short sleep alters the regulation of leptin and ghrelin, thereby increasing appetite and food intake and contributing to weight gain.[23] In contrast, the physiological pathways through which excessive sleep increases morbidity and mortality remain less clearly defined.

Our results further reinforce the hypothesis that inflammation is closely involved in the association between sleep duration and cardiovascular disease.[24] In a controlled human study, participants were restricted to only 4 hours of sleep per night for five consecutive nights, followed by two nights of 8-hour recovery sleep.[25] Blood samples collected before sleep restriction, after restriction, and after recovery showed that sleep loss significantly increased circulating levels of CRP (145% of baseline), IL-1β (137%), IL-6 (163%), and IL-17 (138%) (all $P < 0.05$). Notably, IL-17 remained elevated even after two nights of recovery sleep (119% above baseline, $P < 0.05$), indicating that inflammatory responses persist beyond the immediate period of sleep deprivation. Although these effects are reversible, normalization requires prolonged recovery sleep or daytime naps.[26] Comparable findings have been reported in animal models, in which sleep-deprived rats exhibited marked increases in IL-1, IL-1β, IL-6, IL-17A, and TNF-α, followed by gradual normalization after restorative sleep.[27] These cytokines are not merely markers of inflammation but actively contribute to atherosclerotic disease progression. IL-6 stimulates hepatic CRP synthesis,[28] and CRP directly damages the coronary endothelium by activating complement pathways, promoting monocyte adhesion, and inducing endothelial apoptosis. TNF-α enhances monocyte migration across the endothelium by upregulating VCAM-1 and ICAM-1,[29] thereby exacerbating vascular wall inflammation. Moreover, cholesterol crystals within atherosclerotic plaques activate the NLRP3 inflammasome, which regulates IL-1β maturation and release.[30] This pathway is central to plaque instability and rupture, ultimately precipitating acute myocardial infarction.

Sleep loss also alters the cellular composition of peripheral blood. Hurtado et al. reported that acute sleep deprivation increases circulating leukocytes, particularly neutrophils and monocytes.[31] Conversely, prolonged sleep is likewise associated with heightened systemic inflammation. In one cohort study, individuals who slept longer than the population mean of approximately 7.6 hours exhibited 8% and 7% increases in CRP and IL-6, respectively, for each additional hour of sleep after adjustment for confounders.[32] These findings were confirmed in a large prospective study showing that women who slept ≥9 hours had CRP levels 44% higher than those sleeping 8 hours.[33] Another study involving 2,502 participants observed elevated levels of neutrophils and white blood cells in individuals who slept for long periods (≥ 9 h). This provides evidence at a cellular level that prolonged sleep may influence the number of inflammatory cells in the body.[34] The study also reported that there is a correlation between prolonged sleep and elevated levels of IL-6 and TNF-α.[35,36] These inflammatory markers are typically strongly linked to the risk of cardiovascular disease. Together, these data support the link between excessive sleep and chronic low-grade inflammation. It has been hypothesised by some researchers that this phenomenon may be associated with prolonged sleep and sleep fragmentation.[37] Sleep fragmentation are believed to increase activity in the sympathetic nervous system, thereby raising levels of inflammation in the body. Alternatively, the alteration of inflammation levels may be achieved by influencing the expression of cytokines (components found within and on immune system cells).[38]

Here, sleep duration was positively associated with both NLR and vulnerable plaque features, highlighting a

mechanistic link between sleep, inflammation, and plaque instability. Mediation analysis demonstrated that NLR partially or fully accounted for this relationship, indicating that improved sleep duration may lower TCFA risk by reducing systemic inflammatory activity. Immune cells such as neutrophils, lymphocytes, and monocytes are recognized as key contributors to cardiovascular pathology.[39,40] NLR, derived from neutrophil and lymphocyte counts, has been consistently associated with coronary artery disease and acute coronary syndromes.[41-43] Furthermore, an independent dose-response relationship has been reported between NLR and adverse cardiovascular outcomes,[44] including mortality and recurrent events.[45-47] Previous studies have identified a non-linear relationship between the NLR and sleep duration.[34] In a related finding, another study has indicated that, in patients who develop in-stent restenosis following PCI, an elevated NLR is closely associated with in-stent thrombosis and TCFA. After adjusting for confounding factors, the HR remained 2.673 (1.257–5.684; P = 0.038) and 4.272 (1.740–10.488; P = 0.004).[48] This evidence base supports the biological plausibility of our findings. Nevertheless, there remains a paucity of research exploring the potential role of NLR in the relationship between sleep duration and TCFA. This study is the first to reveal that NLR significantly mediates the association between the two. However, it should be noted that certain potential confounding factors in the study (such as psychological stress, economic status, physical activity and diet) not have been measured or adjusted for, which could introduce a degree of bias into the mediating effect. The present findings are consistent with extant evidence that the sleep-immune-cardiovascular axis is a key pathway linking behavioural factors to chronic diseases. NLR is a promising blood marker that may facilitate the identification of individuals at high risk. Future studies could incorporate genetic tools to further test the robustness of this mediating pathway.

Limitation

Several limitations warrant acknowledgment. First, sleep duration was estimated based on self-reported bedtimes and wake times, which may not accurately reflect true sleep duration. This reliance on time in bed may introduce misclassification bias. However, objective measures such as polysomnography are often impractical in large cohort studies, and this limitation is common in sleep research. Misclassification could attenuate observed associations, suggesting that the true effects of sleep disturbance may be even stronger than reported here. Second, despite the model having been adjusted for various socio-demographic and clinical confounding factors, variables such as psychological factors and individual stress were not included. Consequently, these factors may exert a simultaneous influence on sleep patterns, elevate levels of inflammation in the body, and increase the risk of TCFA, thereby partially confounding the observed mediating effect. Future studies using standardized psychological assessments may better clarify the independent associations among these three factors. Finally， the lack of longitudinal monitoring of sleep patterns, inflammatory biomarkers, and OCT plaque features limits our ability to infer causality. Future studies incorporating repeated assessments of these variables over time are needed to clarify their dynamic associations and their impact on cardiovascular outcomes.

Conclusion

The findings provide direct clinical evidence for the involvement of sleep duration in the development of atherosclerotic disease. Both insufficient and excessive sleep were associated with a greater likelihood of vulnerable plaque formation. Importantly, the inflammatory biomarker NLR was shown to mediate this association, suggesting that sleep disturbances may promote atherosclerosis through inflammatory pathways. These findings reveal a novel mechanistic link between sleep behavior and fundamental processes underlying cardiovascular disease. Improving sleep habits and reducing systemic inflammation may represent a practical approach for lowering cardiovascular risk in individuals with coronary artery disease.

DISCLOSURE

Acknowledgements

We thank all our colleagues at the department of Cardiology, Beijing Anzhen Hospital, Capital Medical University.

Authors' contributions

YL was responsible for composing the primary text of the manuscript and preparing all the figures, thereby ensuring that the visual representation of the research find-

ings was clear and informative. XXF contributed to the processing and analysis of the data, offering insights that informed the methodology and results sections. QYG made a significant contribution to the refinement of the manuscript's language and structure, thereby enhancing its clarity and coherence. YJZ provided revisions to the manuscript, offering expert feedback that enhanced the overall quality and robustness of the research. All authors participated in the review process and contributed to the final version of the manuscript.

Fundings

XXF was supported by the grant from China Scholarship Council (CSC) (Grant No. 202308110233). QYG was supported by the grant from Beijing Hospitals Authority Youth Programme (Grant No. QML20210601) and National Natural Science Foundation of China (Grant No. 82300368). YJZ was supported by National Key Research and Development Program of China (Grant No. 2022YFC3602500), Beijing Municipal Administration of Hospitals' Mission plan (Grant No. SML20180601), Capital's Funds for Health Improvement and Research (Grant No. CFH 2020-2-2063), National Natural Science Foundation of China (Grant No. 82070293) and Beijing Municipal Natural Science Foundation (Grant No. 7202041).

Availability of Data and Materials

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

Ethics approval and consent to participate

This study adhered to the tenants of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Anzhen Hospital.

Competing interests

None.

REFERENCES

[1] Ford ES, Cunningham TJ, Croft JB. Trends in Self-Reported Sleep Duration among US Adults from 1985 to 2012. *Sleep* 2015; 38: 829–832.

[2] Global Burden of Cardiovascular Diseases and Risks 2023 Collaborators. Global, Regional, and National Burden of Cardiovascular Diseases and Risk Factors in 204 Countries and Territories, 1990-2023. *J Am Coll Cardiol* 2025; 86: 2167–2243.

[3] Chong B, Jayabaskaran J, Jauhari SM, *et al*. Global burden of cardiovascular diseases: projections from 2025 to 2050. *Eur J Prev Cardiol* 2025; 32: 1001–1015.

[4] Nambiema A, Lisan Q, Vaucher J, *et al*. Healthy sleep score changes and incident cardiovascular disease in European prospective community-based cohorts. *Eur Heart J* 2023; 44: 4968–4978.

[5] Wang Z, Yang W, Li X, *et al*. Association of sleep duration, napping, and sleep patterns with risk of cardiovascular diseases: a nationwide twin study. *J Am Heart Assoc* 2022; 11: e025969.

[6] Lloyd-Jones DM, Allen NB, Anderson CAM, *et al*. Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health: A Presidential Advisory From the American Heart Association. *Circulation* 2022; 146: e18–e43.

[7] Veler H. Sleep and inflammation: bidirectional relationship. *Sleep Med Clin* 2023; 18: 213–218.

[8] Vergallo R, Park SJ, Stone GW, *et al*. Vulnerable or high-risk plaque: a JACC: cardiovascular imaging position statement. *JACC Cardiovasc Imaging* 2025; 18: 709–740.

[9] Li Y, Chen D, Fan Y, *et al*. Association between neutrophil to lymphocyte ratio and all-cause mortality in critical patients with coronary artery disease - a study based on the MIMIC-IV database. *Front Cardiovasc Med* 2025; 12: 1502964.

[10] Yang Y, Xu Y, Wang J, *et al*. Predictive efficacy of neutrophil-to-lymphocyte ratio for long-term prognosis in new onset acute coronary syndrome: a retrospective cohort study. *BMC Cardiovasc Disord* 2020; 20: 500.

[11] Tian J, Ren X, Vergallo R, *et al*. Distinct morphological features of ruptured culprit plaque for acute coronary events compared to those with silent rupture and thin-cap fibroatheroma: a combined optical coherence tomography and intravascular ultrasound study. *J Am Coll Cardiol* 2014; 63: 2209–2216.

[12] Mortensen MB, Dzaye O, Steffensen FH, *et al*. Impact of plaque burden versus stenosis on ischemic events in patients with coronary atherosclerosis. *J Am Coll Cardiol* 2020; 76: 2803–2813.

[13] Rao SV, O'Donoghue ML, Ruel M, *et al*. 2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2025; 151: e771–e862.

[14] Kume T, Okura H, Yamada R, *et al*. Frequency and spatial distribution of thin-cap fibroatheroma assessed by 3-vessel intravascular ultrasound and optical coherence tomography: an ex vivo validation and an initial in vivo feasibility study. *Circ J* 2009; 73: 1086–1091.

[15] Garde AH, Hansen ÅM, Holtermann A, *et al*. Sleep duration and ischemic heart disease and all-cause mortality: prospective cohort study on effects of tranquilizers/hypnotics and perceived stress. *Scand J Work Environ Health* 2013; 39: 550–558.

[16] Strand LB, Tsai MK, Gunnell D, *et al*. Self-reported sleep duration and coronary heart disease mortality: A large cohort study of 400, 000 Taiwanese adults. *Int J Cardiol* 2016; 207: 246–251.
[17] Westerlund A, Bellocco R, Sundström J, *et al*. Sleep characteristics and cardiovascular events in a large Swedish cohort. *Eur J Epidemiol* 2013; 28: 463–473.
[18] Consensus Conference Panel; Watson NF, Badr MS, Belenky G, *et al*. Joint Consensus Statement of the American Academy of Sleep Medicine and Sleep Research Society on the Recommended Amount of Sleep for a Healthy Adult: Methodology and Discussion. *J Clin Sleep Med*. 2015; 11: 931–952.
[19] Wang C, Bangdiwala SI, Rangarajan S, *et al*. Association of estimated sleep duration and naps with mortality and cardiovascular events: a study of 116 632 people from 21 countries. *Eur Heart J* 2019; 40: 1620–1629.
[20] Ikehara S, Iso H, Date C, *et al*. Association of sleep duration with mortality from cardiovascular disease and other causes for Japanese men and women: the JACC study. *Sleep* 2009; 32: 295–301.
[21] Cappuccio FP, Cooper D, D'Elia L, *et al*. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *Eur Heart J* 2011; 32: 1484–1492.
[22] Van Cauter E, Knutson KL. Sleep and the epidemic of obesity in children and adults. *Eur J Endocrinol* 2008; 159(Suppl 1): S59–S66.
[23] Spiegel K, Tasali E, Penev P, Van Cauter E. Brief communication: Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. *Ann Intern Med* 2004; 141: 846–850.
[24] Irwin MR. Sleep and inflammation: partners in sickness and in health. *Nat Rev Immunol* 2019; 19: 702–715.
[25] van Leeuwen WM, Lehto M, Karisola P, *et al*. Sleep restriction increases the risk of developing cardiovascular diseases by augmenting proinflammatory responses through IL-17 and CRP. *PLoS One* 2009; 4: e4589.
[26] Faraut B, Boudjeltia KZ, Dyzma M, *et al*. Benefits of napping and an extended duration of recovery sleep on alertness and immune cells after acute sleep restriction. *Brain Behav Immun* 2011; 25: 16–24.
[27] Yehuda S, Sredni B, Carasso RL, Kenigsbuch-Sredni D. REM sleep deprivation in rats results in inflammation and interleukin-17 elevation. *J Interferon Cytokine Res* 2009; 29: 393–398.
[28] Calabró P, Willerson JT, Yeh ET. Inflammatory cytokines stimulated C-reactive protein production by human coronary artery smooth muscle cells. *Circulation* 2003; 108: 1930–1932.
[29] Yan S, Zhang X, Zheng H, *et al*. Clematichinenoside inhibits VCAM-1 and ICAM-1 expression in TNF-α-treated endothelial cells via NADPH oxidase-dependent IκB kinase/NF-κB pathway. *Free Radic Biol Med* 2015; 78: 190–201.
[30] Duewell P, Kono H, Rayner KJ, *et al*. NLRP3 inflammasomes are required for atherogenesis and activated by cholesterol crystals. *Nature* 2010; 464: 1357–1361.
[31] Hurtado-Alvarado G, Pavón L, Castillo-García SA, *et al*. Sleep loss as a factor to induce cellular and molecular inflammatory variations. *Clin Dev Immunol* 2013; 2013: 801341.
[32] Patel SR, Zhu X, Storfer-Isser A, *et al*. Sleep duration and biomarkers of inflammation. *Sleep* 2009; 32: 200–4.
[33] Williams CJ, Hu FB, Patel SR, Mantzoros CS. Sleep duration and snoring in relation to biomarkers of cardiovascular disease risk among women with type 2 diabetes. *Diabetes Care* 2007; 30: 1233–1240.
[34] Wang M, Zeng X, Liu Q, *et al*. The association between sleep duration and cognitive function in the U. S. elderly from NHANES 2011-2014: A mediation analysis for inflammatory biomarkers. *J Affect Disord* 2025; 375: 465–471.
[35] Prather AA, Vogelzangs N, Penninx BW. Sleep duration, insomnia, and markers of systemic inflammation: results from the Netherlands Study of Depression and Anxiety (NESDA). *J Psychiatr Res* 2015; 60: 95–102.
[36] Grandner MA, Sands-Lincoln MR, Pak VM, Garland SN. Sleep duration, cardiovascular disease, and proinflammatory biomarkers. *Nat Sci Sleep* 2013; 5: 93–107.
[37] Matsubayashi H, Nagai M, Dote K, *et al*. Long sleep duration and cardiovascular disease: Associations with arterial stiffness and blood pressure variability. *J Clin Hypertens (Greenwich)* 2021; 23: 496–503.
[38] Grandner MA, Drummond SP. Who are the long sleepers? Towards an understanding of the mortality relationship. *Sleep Med Rev* 2007; 11: 341–360.
[39] Shah AD, Denaxas S, Nicholas O, *et al*. Neutrophil Counts and Initial Presentation of 12 Cardiovascular Diseases: A CALIBER Cohort Study. *J Am Coll Cardiol* 2017; 69: 1160–1169.
[40] Fernández-Velasco M, González-Ramos S, Boscá L. Involvement of monocytes/macrophages as key factors in the development and progression of cardiovascular diseases. *Biochem J* 2014; 458: 187–93.
[41] García-Escobar A, Vera-Vera S, Tébar-Márquez D, *et al*. Neutrophil-to-lymphocyte ratio an inflammatory biomarker, and prognostic marker in heart failure, cardiovascular disease and chronic inflammatory diseases: New insights for a potential predictor of anti-cytokine therapy responsiveness. *Microvasc Res* 2023; 150: 104598.
[42] Cupido AJ, Kraaijenhof JM, Burgess S, *et al*. Genetically Predicted Neutrophil-to-Lymphocyte Ratio and Coronary Artery Disease: Evidence From Mendelian Randomization. *Circ Genom Precis Med* 2022; 15: e003553.
[43] Dong CH, Wang ZM, Chen SY. Neutrophil to lymphocyte ratio predict mortality and major adverse cardiac events in acute coronary syndrome: A systematic review and meta-analysis. *Clin Biochem* 2018; 52: 131–136.
[44] Qin P, Ho FK, Celis-Morales CA, Pell JP. Association between systemic inflammation biomarkers and incident cardiovascular disease in 423, 701 individuals: evidence from the UK biobank cohort. *Cardiovasc Diabetol* 2025; 24: 162.
[45] Angkananard T, Anothaisintawee T, McEvoy M, *et al*.

Neutrophil lymphocyte ratio and cardiovascular disease risk: a systematic review and meta-analysis. *Biomed Res Int* 2018; 2018: 2703518.

[46] Wang Z, Wang J, Cao D, Han L. Correlation of neutrophil-to-lymphocyte ratio with the prognosis of non-ST-segment elevation in patients with acute coronary syndrome undergoing selective percutaneous coronary intervention. *J Int Med Res* 2020; 48: 300060520959510.

[47] Zhou E, Wu J, Zhou X, Yin Y. The neutrophil-lymphocyte ratio predicts all-cause and cardiovascular mortality among U. S. adults with rheumatoid arthritis: results from NHANES 1999-2020. *Front Immunol* 2023; 14: 1309835.

[48] Gu N, Chen P, Wang X, *et al*. Association between the neutrophil-to-lymphocyte ratio and in-stent neoatherosclerosis and plaque vulnerability: an optical coherence tomography study. *J Cardiovasc Pharmacol* 2024; 84: 506–514.

Please cite this article as: LIU Y, FENG XX, GUO QY, ZHOU YJ. Sleep-inflammation-coronary plaque phenotype axis: clinical validation and inflammation-mediated mechanisms based on optical coherence tomography. *J Geriatr Cardiol* 2026; 23(9): 576–589. DOI: 10.26599/1671-5411.2026.09.002