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Association of Systemic Inflammatory Indices NLR, SIRI, and MHR with Carotid Plaque in Middle-Aged and Elderly Individuals: A Cross-Sectional Study

Putian Zhang
Nanjing Medical University
Yi Fang
Department of Geriatric Cardiology, The First Affiliated Hospital of Nanjing Medical University
Teng Cui
Department of Geriatric Medicine, Kunshan Second People's Hospital
Yudong Xia
Department of Cardiology, The First Affiliated Hospital of Nanjing Medical University
An Yan
Department of Geriatric Cardiology, The First Affiliated Hospital of Nanjing Medical University
Jialu Wang
Department of Geriatric Cardiology, The First Affiliated Hospital of Nanjing Medical University
Jun Wu
wujun9989@njmu.edu.cn

Department of Geriatric Cardiology, The First Affiliated Hospital of Nanjing Medical University

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Abstract

Objective

To examine the associations of the neutrophil-to-lymphocyte ratio (NLR), systemic inflammation response index (SIRI), and monocyte-to-high-density lipoprotein cholesterol ratio (MHR) with carotid plaque in middle-aged and older adults.

Methods

This retrospective study included 433 patients aged ≥ 40 years who underwent carotid ultrasonography at Kunshan Second People's Hospital between **2024-01-01** and **2026-02-28**. Participants were classified as plaque or non-plaque based on imaging findings. Clinical and laboratory data were collected, and NLR, SIRI, and MHR were calculated. Multivariable logistic regression was used to assess associations with carotid plaque. The primary analysis was conducted in complete cases (n = 374), with sensitivity analyses in the full cohort (n = 433). Associations were examined per standard deviation increment, and restricted cubic spline models were used to evaluate nonlinear dose–response relationships.

Results

NLR, SIRI, and MHR were higher in the plaque group (n = 244) than in the non-plaque group (n = 189) (all $P < 0.001$). In fully adjusted models based on complete cases, both NLR (OR 1.35, 95% CI 1.02–1.79, $P = 0.038$) and SIRI (OR 1.47, 95% CI 1.05–2.07, $P = 0.026$) were associated with carotid plaque, whereas MHR was not (OR 1.19, 95% CI 0.84–1.70, $P = 0.326$). In the full cohort, associations for NLR and SIRI remained directionally consistent but were attenuated ($P = 0.059$ and 0.095). Risk of carotid plaque increased across SIRI quartiles (P for trend < 0.05), and spline analysis supported a linear association (P for non-linearity > 0.05). No interactions were observed by sex, age, or body mass index.

Conclusion

Higher NLR and SIRI were associated with carotid plaque, with SIRI showing a dose–response relationship, while MHR exhibited no independent association. These routinely calculated indices may facilitate early risk stratification for carotid plaque in middle-aged and elderly populations, supporting their utility as easily accessible systemic inflammatory biomarkers.

1. Introduction

Cardiovascular disease remains a leading cause of mortality and long-term disability worldwide, imposing a substantial and growing burden on healthcare systems and populations[1, 2].Among its

underlying pathological processes, atherosclerosis plays a central role in the initiation and progression of both cardiovascular and cerebrovascular events. This chronic condition evolves over decades through complex interactions between lipid metabolism, vascular biology, and immune regulation, ultimately leading to plaque formation, vascular narrowing, and, in some cases, acute thrombotic complications.The carotid artery provides a unique and accessible site for the in vivo assessment of atherosclerosis[3]. Due to its superficial anatomical location and the feasibility of noninvasive imaging, carotid ultrasonography has become a widely used tool for evaluating vascular structure and early pathological changes[4]. Carotid atherosclerotic plaque (CAP) is not merely a localized vascular abnormality but reflects the systemic nature of atherosclerosis. Its presence indicates an advanced stage of arterial remodeling and is strongly linked to generalized vascular risk[5]. Epidemiological and longitudinal studies have consistently demonstrated that individuals with CAP are at increased risk of major adverse cardiovascular events, including myocardial infarction and ischemic stroke[6]. In clinical practice, imaging evidence of atherosclerosis has therefore been incorporated into risk assessment frameworks. Current guidelines emphasize that subclinical vascular changes, including plaque detection, can refine cardiovascular risk stratification, particularly among individuals initially categorized as having low or intermediate risk[7]. In this context, early identification of carotid plaque has important implications for preventive strategies and individualized risk management[8].

The burden of CAP increases markedly with age. Population-based studies suggest that approximately one quarter to one third of individuals older than 40 years have detectable carotid plaque, with prevalence rising to nearly half or more among those over 60 years of age[9, 10]. Despite its high prevalence, management strategies for early or asymptomatic plaque remain suboptimal. Current approaches largely target conventional risk factors such as hypertension, dyslipidemia, and hyperglycemia, which are well-established contributors to atherosclerotic disease. However, these strategies primarily slow disease progression rather than reverse established lesions. Pharmacological therapies may reduce lipid burden or stabilize plaque but are often insufficient to eliminate existing atherosclerotic changes and may carry risks when used long term[11]. Interventional procedures, including carotid endarterectomy and stenting, are typically reserved for patients with significant luminal stenosis or high-risk clinical features. As a result, a considerable proportion of individuals with subclinical or early-stage plaque remain without targeted interventions, underscoring the need for improved tools to identify high-risk patients at an earlier stage.

In recent years, increasing attention has been directed toward the role of chronic inflammation in atherosclerosis. Beyond lipid accumulation, atherosclerosis is now widely recognized as a dynamic and immune-mediated process involving both innate and adaptive immune responses[12]. Metabolic disturbances such as hypertension, dyslipidemia, and hyperglycemia can trigger endothelial dysfunction, enhance oxidative stress, and promote the recruitment and activation of inflammatory cells within the vascular wall[13]. These processes contribute not only to plaque initiation but also to its progression and destabilization. In this framework, circulating biomarkers that capture systemic inflammatory activity may provide additional insight into disease risk beyond traditional clinical factors.

Among such biomarkers, composite inflammatory indices derived from routine blood tests have gained increasing interest. These indices integrate information from different immune cell populations and, in some cases, lipid parameters, thereby reflecting the balance between pro-inflammatory and regulatory mechanisms. The neutrophil-to-lymphocyte ratio (NLR) represents the interplay between neutrophil-mediated inflammatory activation and lymphocyte-mediated immune regulation. The systemic inflammation response index (SIRI), which incorporates neutrophil, monocyte, and lymphocyte counts, provides a broader representation of inflammatory status. The monocyte-to-high-density lipoprotein cholesterol ratio (MHR) links immune cell activity with lipid metabolism and has been proposed as an indicator of vascular inflammation. Collectively, these indices are inexpensive, readily available, and reproducible in routine clinical practice.

Previous studies have demonstrated that these inflammatory markers are associated with the severity and prognosis of coronary artery disease, including plaque burden and adverse cardiovascular outcomes[14]. However, most existing evidence has focused on coronary circulation, while their relevance to carotid atherosclerosis remains less well defined. Given that carotid plaque serves as a surrogate marker of systemic atherosclerosis and is directly related to cerebrovascular risk, it is important to clarify whether these indices can provide meaningful information in this context. Moreover, comparative evaluation of multiple inflammatory indices within the same population is limited, and their relative performance in relation to carotid plaque has not been fully established.

Against this background, the present study aimed to investigate the associations of NLR, SIRI, and MHR with carotid atherosclerotic plaque in a cohort of middle-aged and older adults. Using a cross-sectional design, we sought to evaluate the independent relationships between these indices and plaque presence, examine potential dose–response patterns, and assess their potential utility for early risk identification. By focusing on routinely available laboratory parameters, this study may contribute to the development of accessible and clinically applicable strategies for improving the detection and stratification of atherosclerotic risk.

2. Materials and Methods

2.1 Study population

2.1.1 Participants

This retrospective study enrolled a total of 433 consecutive patients aged 40 years and older who received carotid ultrasonography at Kunshan Second People’s Hospital from January 2024 to February 2026. The study was conducted in accordance with the principles of the Declaration of Helsinki. The protocol was approved by the Ethics Committee of Kunshan Second People’s Hospital (Approval No. KSEHLLSP2026-001). Due to the retrospective nature of the study and the use of anonymized clinical data, the requirement for written informed consent was waived by the Ethics Committee.

Clinical trial number: not applicable.

2.1.2 Inclusion Criteria

Participants were eligible if they met the following criteria: (1) age ≥ 40 years; (2) complete demographic, clinical, and laboratory data; (3) underwent carotid ultrasonography.

2.1.3 Exclusion Criteria

Participants were excluded if they had any of the following conditions: (1) hepatic or renal dysfunction; (2) congenital heart disease; (3) malignant tumors; (4) autoimmune diseases; (5) infectious diseases; (6) cardiomyopathy, cor pulmonale, rheumatic valvular disease, or other severe cardiac diseases; (7) incomplete clinical or laboratory data.

2.2 Data Collection

2.2.1 Clinical and Laboratory Data

Demographic information including sex, age, and medical history such as hypertension and diabetes was collected through medical records and interviews. Blood pressure, height, and weight were measured, and BMI was calculated.

All participants fasted for at least 8 hours before venous blood samples were collected in the morning for laboratory analysis.

2.2.2 Carotid Ultrasonography

Carotid ultrasonography was performed using a Siemens ACUSON Sequoia color Doppler ultrasound system with a probe frequency of 5 to 10 MHz. Bilateral carotid intima media thickness (IMT) was measured, and ultrasound images were evaluated to determine the presence of plaque and vascular stenosis. Plaque location, size, and echogenic characteristics were recorded.

All examinations were performed by trained sonographers following standardized procedures based on the Chinese Guidelines for Ultrasound Assessment of Carotid Intima Media Thickness and Plaque. To evaluate interobserver reliability, a subset of participants was randomly selected for repeated measurements by two or more independent qualified sonographers in a blinded manner. Interobserver agreement was assessed using the intraclass correlation coefficient (ICC) and Cohen's Kappa statistics. The preliminary evaluation showed acceptable ICC and Kappa values, indicating good interobserver consistency and reliable measurements.

2.2.3Definition of Carotid Plaque

Carotid plaque was defined as a focal structure identified on ultrasonography that met at least one of the following criteria[15]: (1)IMT ≥ 1.5 IM mm measured from the lumen intima interface to the media adventitia interface; (2) focal protrusion into the lumen of at least 0.5 mm; (3) localized IMT thickening greater than 50 percent of the surrounding IMT value.

2.3Statistical analysis

Statistical analyses were performed using SPSS version 27.0 and R version 4.5.1. All tests were two-sided, and a P value < 0.05 was considered statistically significant.Continuous variables are reported as mean ± standard deviation or median with interquartile range, as appropriate, and were compared using the independent samples t-test or Mann–Whitney U test. Categorical variables are presented as counts and percentages and were compared using the chi-square test.Multivariable logistic regression models were used to assess the associations of inflammatory indices with carotid plaque. Three models with increasing levels of adjustment were constructed. Associations are presented per standard deviation increase in each index.Covariates included in the multivariable models were selected a priori based on clinical relevance and prior evidence, including established cardiovascular risk factors and variables associated with both inflammatory status and atherosclerotic disease. This approach was adopted to minimize residual confounding while avoiding overadjustment.Potential multicollinearity among covariates was assessed before model construction. Correlations between variables were examined, and variance inflation factors were calculated. All variables included in the final models showed acceptable values, indicating that collinearity was unlikely to influence the regression estimates.Model performance was evaluated using complementary approaches. Calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test, and discrimination was evaluated by calculating the area under the receiver operating characteristic curve. Additional diagnostic procedures were performed to identify influential observations and to verify model assumptions.To investigate potential effect modification, interaction terms between inflammatory indices and key clinical variables, including age, sex, and body mass index, were incorporated into the fully adjusted models. Where interaction effects were suggested, stratified analyses were conducted.Restricted cubic spline models were used to explore potential nonlinear relationships between inflammatory indices and carotid plaque. Knots were placed at predefined percentiles to ensure model stability, and the median value was used as the reference. Both overall and nonlinear effects were formally tested.Missing data were evaluated prior to analysis. The primary analysis was conducted using a complete-case approach. Sensitivity analyses were performed in the full cohort to assess the robustness of the findings under different model specifications. As the proportion of missing data was low and no systematic pattern was identified, imputation was not performed.

3. Results

3.1 Baseline characteristics of the study population

A total of 433 participants were included; 244 (56.4%) had carotid plaque and 189 (43.6%) did not. Participants with plaque were older, more often male, and had a higher prevalence of hypertension and diabetes (all $P < 0.001$).Creatinine, uric acid, neutrophil count, and monocyte count were higher in the plaque group, whereas high-density lipoprotein cholesterol was lower (all $P < 0.05$). NLR, SIRI, and MHR

were also higher among participants with plaque (all $P < 0.001$). Additional characteristics are shown in Table 1 and Fig. 1.

Table 1
Comparison of baseline characteristics between the plaque and non-plaque groups

Variable	Plaque group (n = 244)	Non-plaque group (n = 189)	Statistic	Pvalue
Age[1]	67.42 ± 8.99	59.97 ± 9.96	8.050	< 0.001
Male, n (%)	123 (50.4)	66 (34.9)	10.388	< 0.001
BMI (kg/m^2)[2]	24.77 (22.45, 26.67)	24.34 (22.63, 26.37)	-0.540	0.589
Systolic blood pressure [1]	140 ± 15	137 ± 17	1.689	0.092
Diastolic blood pressure[1]	80.64 ± 12	79.60 ± 10	0.986	0.325
Hypertension, n (%)	184 (75.4)	95 (50.3)	29.385	< 0.001
Diabetes, n (%)	145 (59.4)	82 (43.4)	10.986	< 0.001
HbA1c (%)[2]	6.6 (5.7, 8.1)	6.2 (5.5, 7.7)	-2.547	0.011
ALT (U/L)[2]	15 (11, 22)	16 (12, 22)	-0.686	0.493
AST (U/L)[2]	18 (15, 22)	17 (15, 20)	-1.478	0.140
ALB (g/L)[2]	41.6 (39.8, 43.8)	43.1 (40.2, 45.3)	-3.145	0.002
Cr (μmol/L)[2]	73.45 (60.95, 85.20)	66.30 (57.80, 79.20)	-3.625	< 0.001
UA(μmol/L)[2]	314.55 (264.83, 366.45)	297.90 (232.15, 355.35)	-2.352	0.019
HDL-C (mmol/L)[2]	1.13 (0.96, 1.34)	1.22 (1.02, 1.46)	-2.634	0.008
LDL-C (mmol/L)[2]	2.62 (2.04, 3.20)	2.66 (2.05, 3.22)	-0.029	0.977
Neu (×10^9/L)[2]	3.37 (2.72, 4.12)	3.02 (2.48, 3.69)	-3.478	< 0.001
Mon(×10^9/L)[2]	0.45 (0.36, 0.54)	0.41 (0.33, 0.51)	-2.882	0.004
NLR[2]	1.92 (1.44, 2.44)	1.65 (1.37, 2.10)	-3.994	< 0.001
SIRI[2]	0.84 (0.61, 1.29)	0.63 (0.48, 1.03)	-4.664	< 0.001

Variable	Plaque group (n = 244)	Non-plaque group (n = 189)	Statistic	Pvalue
MHR [2]	0.40 (0.29, 0.51)	0.33 (0.25, 0.45)	-3.864	< 0.001

3.2Association between inflammatory indices and carotid plaque based on logistic regression analysis

All inflammatory indices were standardized and analyzed per standard deviation increase in multivariable models (Fig. 2). In the primary analysis (n = 374), after full adjustment for age, sex, body mass index, hypertension, diabetes, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and high-sensitivity C-reactive protein, both NLR (OR 1.35, 95% CI 1.02–1.79, *P* = 0.039) and SIRI (OR 1.47, 95% CI 1.05–2.07, *P* = 0.026) were associated with carotid plaque, whereas MHR was not (OR 1.19, 95% CI 0.84–1.70, *P* = 0.326).In sensitivity analyses using the full cohort (n = 433), effect estimates for NLR and SIRI remained directionally consistent (OR 1.27 and 1.26, respectively), although statistical significance was attenuated.

3.3Quartile analysis and trend test of inflammatory indices

After categorization into quartiles, the lowest quartile was used as the reference. The risk of carotid plaque increased across higher levels of SIRI, with a significant trend (*P* for trend = 0.031). In the highest quartile, SIRI was associated with an increased odds of carotid plaque (OR 2.11, 95% CI 1.08–4.14). A similar pattern was observed for NLR (*P* for trend = 0.055), although the trend did not reach statistical significance; the corresponding odds ratio in the highest quartile was 1.94 (Table 2, Fig. 3).

Table 2
Quartile analysis of systemic immune-inflammation indices and the risk of carotid plaque (n = 374)

Index	Group	OR(95%CI)	Pvalue	P for trend
NLR	Q1 (≤ 1.54)	1.00 (reference)	-	0.055
	Q2 (1.54–2.06)	0.98 (0.51–1.86)	0.944	
	Q3 (2.02–2.73)	1.26 (0.65–2.45)	0.488	
	Q4 (> 2.73)	1.94 (0.96–3.93)	0.064	
SIRI	Q1 (≤ 0.53)	1.00 (reference)	-	0.031
	Q2 (0.53–0.81)	0.95 (0.49–1.83)	0.887	
	Q3 (0.81–1.28)	1.34 (0.71–2.54)	0.364	
	Q4 (> 1.28)	2.11 (1.08–4.14)	0.029	

3.4Dose–response relationship analysis

Restricted cubic spline analysis indicated a significant linear association between SIRI and carotid plaque risk (overall *P* = 0.026; *P* for non-linearity = 0.089). The risk increased progressively across the range of SIRI values, with no evidence of a threshold or saturation effect (Fig. 4).

3.5Predictive performance evaluation

Receiver operating characteristic curves were constructed to assess the discriminative performance of each inflammatory index for carotid plaque. SIRI showed the highest area under the curve (0.639), followed by NLR (0.617) and MHR (0.610). The combined model incorporating all three indices yielded a modest increase in discrimination (AUC 0.642) (Table 3, Fig. 5).

Table 3
ROC analysis of different inflammatory indices for predicting carotid plaque (n = 374)

Predictor	AUC	95%CI
NLR	0.617	0.560–0.674
SIRI	0.639	0.584–0.694
MHR	0.610	0.553–0.667
Combined model (NLR + SIRI + MHR)	0.642	0.587–0.697

3.6Subgroup analysis and interaction

Subgroup analyses showed generally consistent associations of NLR and SIRI with carotid plaque across predefined strata. For NLR, the association appeared stronger in women (OR 1.57, 95% CI 1.04–2.47, *P* = 0.036) than in men (OR 1.19, *P* = 0.355). Similarly, stronger associations were observed among participants without diabetes (OR 1.74, *P* = 0.045) and without hypertension (OR 1.86, *P* = 0.041). However, tests for interaction were not statistically significant (all P for interaction > 0.05), indicating no evidence of effect modification by age, sex, body mass index, or metabolic conditions (Table 4, Fig. 6).

Table 4
Subgroup analysis of the association between NLR and carotid plaque (n = 374)

Subgroup variable	Category	OR(95%CI)	P value
Sex	Male	1.19(0.84–1.79)	0.355
	Female	1.57(1.04–2.47)	0.036
Age	< 65 years	1.19(0.80–1.78)	0.39
	> 65 years	1.51(1.01–2.46)	0.066
Diabetes	No	1.74(1.06–3.11)	0.045
	Yes	1.20(0.85–1.72)	0.312
Hypertension	No	1.86(1.09–3.52)	0.041
	Yes	1.19(0.85–1.70)	0.320

4. Discussion

Carotid atherosclerotic plaque is an important subclinical manifestation of atherosclerosis and has substantial value for identifying individuals at increased vascular risk [1]. In recent years, composite inflammatory indices derived from routine blood tests, including NLR, SIRI, and MHR, have attracted growing attention because they are inexpensive, easily obtainable, and capable of capturing multiple dimensions of immune-inflammatory status[4]. In the present study, we evaluated the associations of these three indices with carotid plaque in middle-aged and older adults. After adjustment for conventional cardiovascular risk factors, both NLR and SIRI remained independently associated with plaque, whereas MHR did not. These findings support the view that systemic inflammation is closely involved in the development of carotid atherosclerosis and suggest that inflammatory imbalance may provide clinically relevant information beyond traditional metabolic indicators[16].

The importance of inflammation in atherosclerosis has been well established. Rather than representing a simple process of lipid deposition, atherosclerosis is now understood as a chronic inflammatory disorder involving persistent interactions among endothelial cells, circulating leukocytes, platelets, and vascular smooth muscle cells[17]. Landmark epidemiologic work by Ridker and colleagues showed that circulating inflammatory markers are strongly linked to cardiovascular risk, thereby helping to establish inflammation as a major determinant of vascular disease[18]. Mechanistic studies further demonstrated that both innate and adaptive immune responses participate in atherogenesis, influencing lesion initiation, growth, and destabilization[19]. The clinical significance of these pathways was underscored by the CANTOS trial, in which targeted inhibition of interleukin-1β reduced recurrent cardiovascular events, providing direct evidence that inflammation is not merely associated with atherosclerosis but actively contributes to its clinical consequences[20]. Within this biological framework, it is reasonable

that blood-derived composite inflammatory indices would show meaningful relationships with carotid plaque.

Our results suggest that indices incorporating neutrophils and monocytes may be particularly informative. Prior work has shown that monocyte count is independently associated with subclinical carotid atherosclerosis, even after adjustment for conventional inflammatory markers such as C-reactive protein[21]. Other studies have linked inflammatory cell activity to intraplaque neovascularization and microembolization, both of which are relevant to plaque progression and vulnerability[22]. In addition, Mendelian randomization analyses have provided genetic support for the contribution of neutrophil-related pathways to cardiovascular disease[23]. Taken together, these studies provide biological plausibility for the associations observed in our cohort.

NLR is one of the most widely studied composite inflammatory indices and reflects the balance between neutrophil-mediated pro-inflammatory activity and lymphocyte-associated immune regulation. Horne and colleagues first highlighted the prognostic significance of leukocyte subtype patterns in cardiovascular disease, laying the foundation for later interest in NLR as a vascular risk marker[24]. In our study, NLR remained independently associated with carotid plaque after multivariable adjustment, suggesting that it captures clinically relevant inflammatory information not fully reflected by conventional covariates. Although its effect estimates were somewhat weaker than those observed for SIRI, the overall pattern supports the relevance of neutrophil-lymphocyte imbalance in carotid atherosclerosis.

Among the three indices evaluated, SIRI showed the strongest and most consistent association with carotid plaque. This may be because SIRI integrates three key cellular components: neutrophils, monocytes, and lymphocytes. By combining information on both innate inflammatory activation and adaptive immune regulation, SIRI may provide a broader reflection of systemic inflammatory burden than NLR alone. Our findings are consistent with those of Nai and colleagues, who reported a significant association between SIRI and carotid atherosclerosis in a Chinese population[25]. Similar results were observed by Sun and colleagues in a large cross-sectional health screening cohort[26]. More recently, Tao and colleagues suggested that SIRI may outperform several other inflammatory indices in predicting incident carotid atherosclerosis[27]. In another vascular context, Dziedzic and colleagues found that SIRI was associated with the severity of coronary artery disease[28]. Viewed together, these studies and our present findings suggest that SIRI may be a particularly sensitive marker of inflammation-related vascular injury.

In contrast, MHR did not remain independently associated with carotid plaque after full adjustment. Although previous studies have suggested that MHR may have predictive value in atherosclerotic disease[29], its performance appears less stable across populations and analytical models. One possible explanation is that MHR captures a narrower biological axis centered on monocyte-related inflammation and lipid metabolism. While this pathway is relevant, it may not fully represent the broader inflammatory network involved in plaque formation. In addition, part of the information conveyed by MHR may overlap with lipid-related covariates already included in multivariable models, thereby

weakening its apparent independent contribution. From a mechanistic standpoint, monocytes promote plaque formation through uptake of oxidized low-density lipoprotein and transformation into foam cells, but this process occurs within a more complex inflammatory milieu that may be better represented by indices incorporating multiple leukocyte subsets, such as SIRI[30].

The biological interpretation of our findings is also supported by current understanding of leukocyte function in atherosclerosis. Neutrophils are increasingly recognized as active participants in vascular injury. They release reactive oxygen species, proteases, and inflammatory mediators that damage the endothelium and amplify local inflammation. Neutrophil extracellular traps may further destabilize plaques by promoting fibrous cap thinning, thrombogenicity, and vascular inflammation[31]. In contrast, regulatory T cells exert anti-inflammatory effects and contribute to plaque stabilization[32]. Composite indices such as NLR and SIRI may therefore serve as accessible surrogates for the balance between pro-inflammatory and protective immune processes.

In our subgroup analyses, the overall associations of inflammatory indices with carotid plaque were broadly similar across strata, although some effect estimates appeared stronger in specific subgroups. In the original analysis, the association involving MHR appeared more pronounced in women. This observation should be interpreted cautiously, but it may be biologically plausible. Sex-related variation in lipid metabolism and vascular protection, particularly the decline in estrogen after menopause, may influence both high-density lipoprotein function and inflammatory responses[33]. At the same time, the absence of statistically significant interaction tests suggests that these subgroup differences should not be overinterpreted and require confirmation in larger studies.

An additional finding of interest was the linear association observed in spline analyses. The absence of an apparent threshold effect suggests that the relationship between inflammatory burden and carotid plaque may be continuous rather than confined to a narrow high-risk range. This interpretation is consistent with the broader concept that atherosclerosis develops under conditions of persistent low-grade inflammation that accumulates over time, rather than appearing abruptly once a single inflammatory marker exceeds a fixed cutoff[34]. From a clinical perspective, this may explain why even moderate elevations in inflammatory indices could still be relevant to vascular risk.

These findings may have practical implications. Carotid ultrasonography remains an important tool for plaque detection, but imaging is not always available in all clinical settings. By contrast, NLR and SIRI can be derived from routine laboratory testing at minimal additional cost. Their discriminative performance in this study was modest, and they should not be viewed as standalone diagnostic tools. However, they may still be useful as accessible adjunctive markers for identifying individuals who warrant closer vascular assessment, especially in resource-limited settings or in combination with established clinical risk factors.

Several limitations should be acknowledged. First, the cross-sectional design precludes causal inference. Second, this was a single-center study, which may limit external generalizability. Third, the sample size, particularly in subgroup analyses, may have limited statistical precision. Finally, detailed

plaque characteristics, such as lipid core burden and fibrous cap morphology, were not assessed, which restricted further evaluation of the relationship between inflammatory indices and plaque vulnerability.

In conclusion, NLR and SIRI were independently associated with carotid plaque in middle-aged and older adults, whereas MHR was not after multivariable adjustment. SIRI showed the most robust association and appeared to capture a graded increase in plaque risk. These findings support the potential value of selected blood-derived inflammatory indices as accessible markers of subclinical atherosclerosis and justify further validation in prospective studies.

Abbreviations

NLR
Neutrophil-to-Lymphocyte Ratio
SIRI
Systemic Inflammatory Response Index
MHR
Monocyte-to-HDL Cholesterol Ratio
HDL
High-Density Lipoprotein
LDL
Low-Density Lipoprotein
BMI
Body Mass Index
BP
Blood Pressure
CVD
Cardiovascular Disease.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the principles of the Declaration of Helsinki. The protocol was approved by the Ethics Committee of Kunshan Second People's Hospital (Approval No. KSEHLLSP2026-001). Due to the retrospective nature of the study and the use of anonymized clinical data, the requirement for written informed consent was waived by the Ethics Committee.

Consent for publication

Not applicable. All data analyzed in this study are anonymized and do not contain any identifiable personal information of individual participants.

Competing interests

All authors declare no conflicts of interest.

AuthorContributions

ZP:Data curation, Formal analysis, Writing – original draft, Writing – review &editing.FY:Data analysis, Interpretation, Writing – original draft.XY: Supervision, Formal analysis, Writing – original draft.CT: Data curation.YA: Formal analysis, Writing – review &editing.WJ: Formal analysis, Writing – review & editing.

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Author Contribution

ZP: Data curation, Formal analysis, Writing – original draft, Writing – review & editing.FY: Data analysis, Interpretation, Writing – original draft.XY: Supervision, Formal analysis, Writing – original draft.CT: Data curation.YA: Formal analysis, Writing – review & editing.WJ: Formal analysis, Writing – review & editing.All authors read and approved the final manuscript.

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Availability of data and materials

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

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Figures

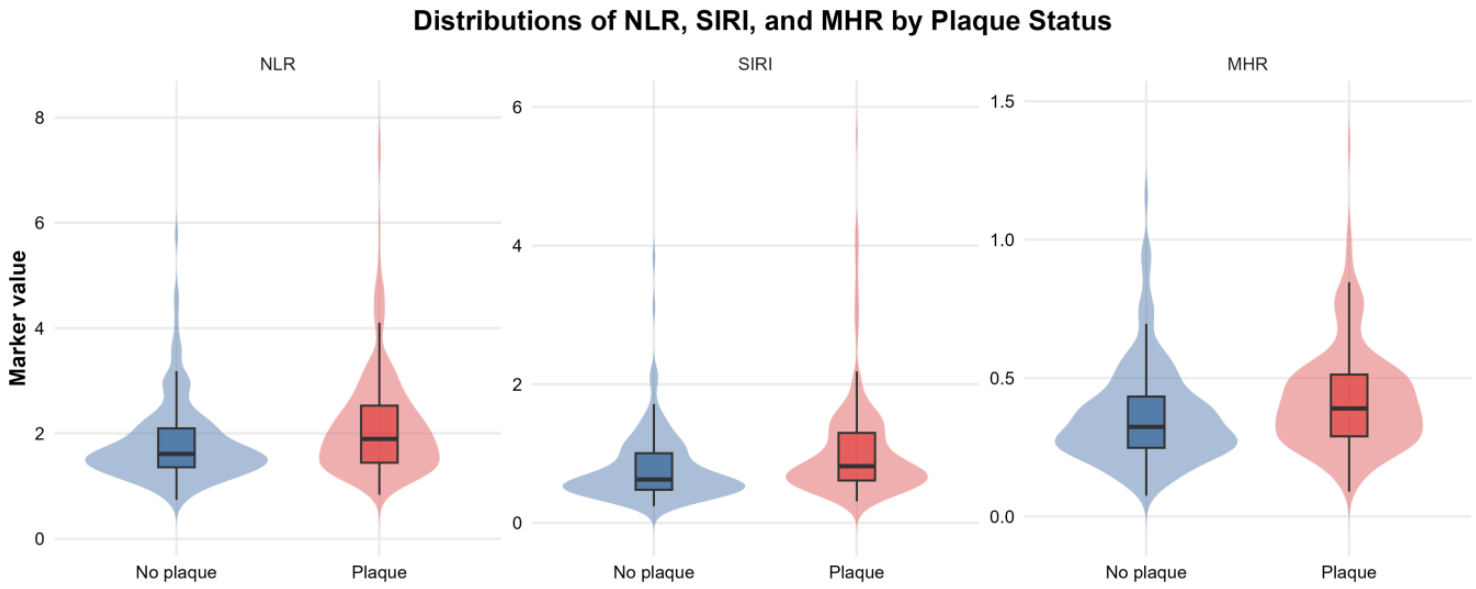


Figure 1

Distribution of NLR, SIRI, and MHR

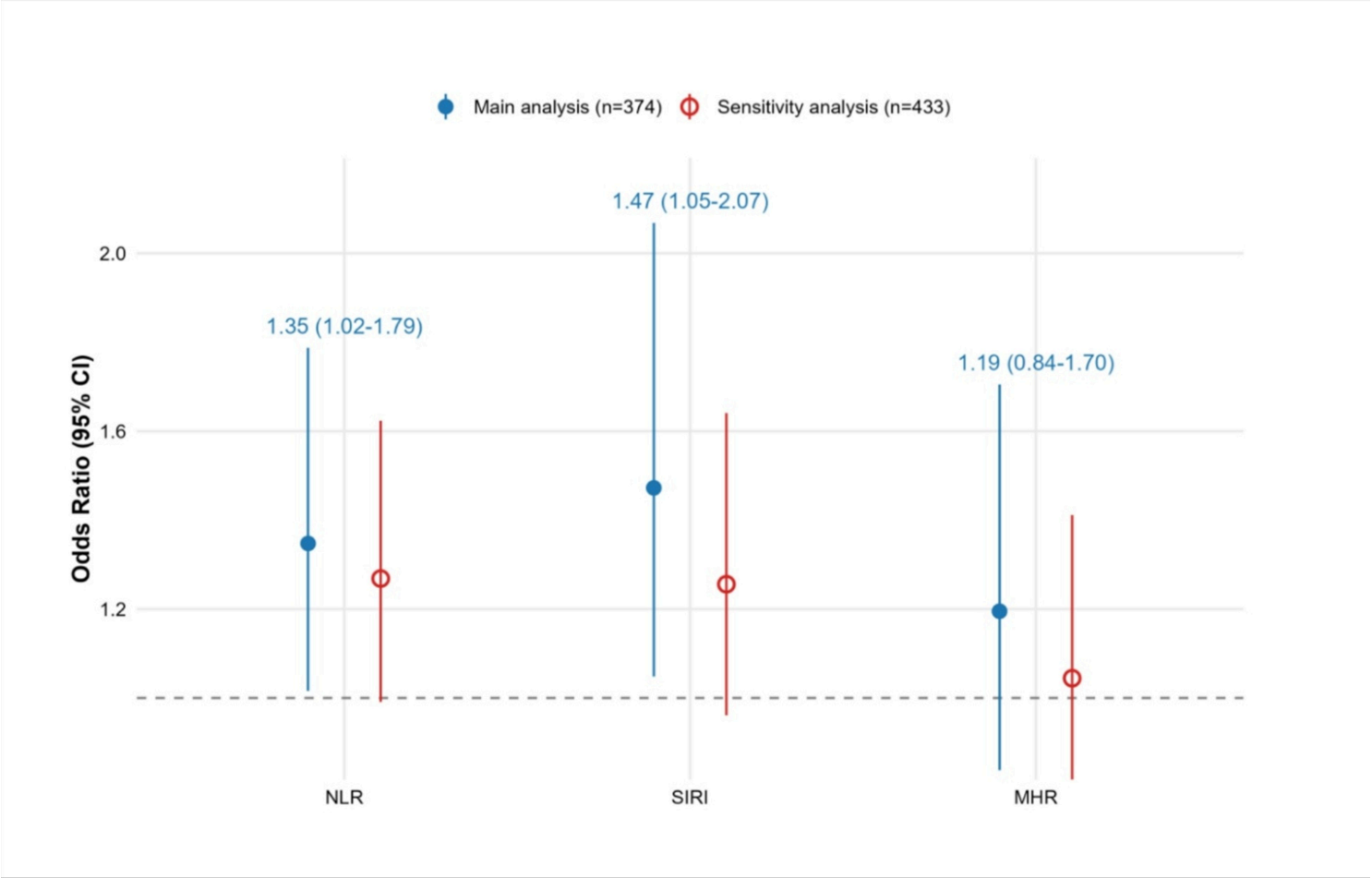


Figure 2

Association Between Systemic Inflammatory Indices and the Risk of Carotid Plaque

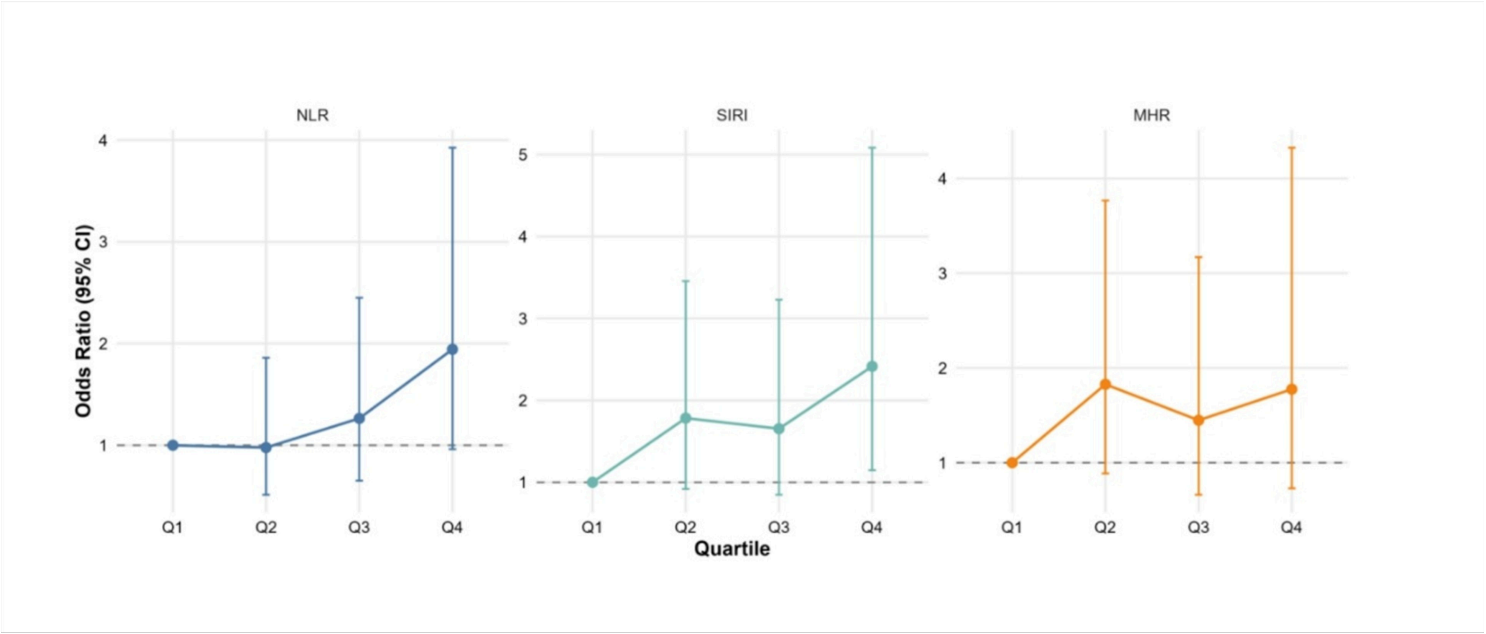


Figure 3

Distribution of Odds Ratios Across Quartiles of the Inflammatory Indices

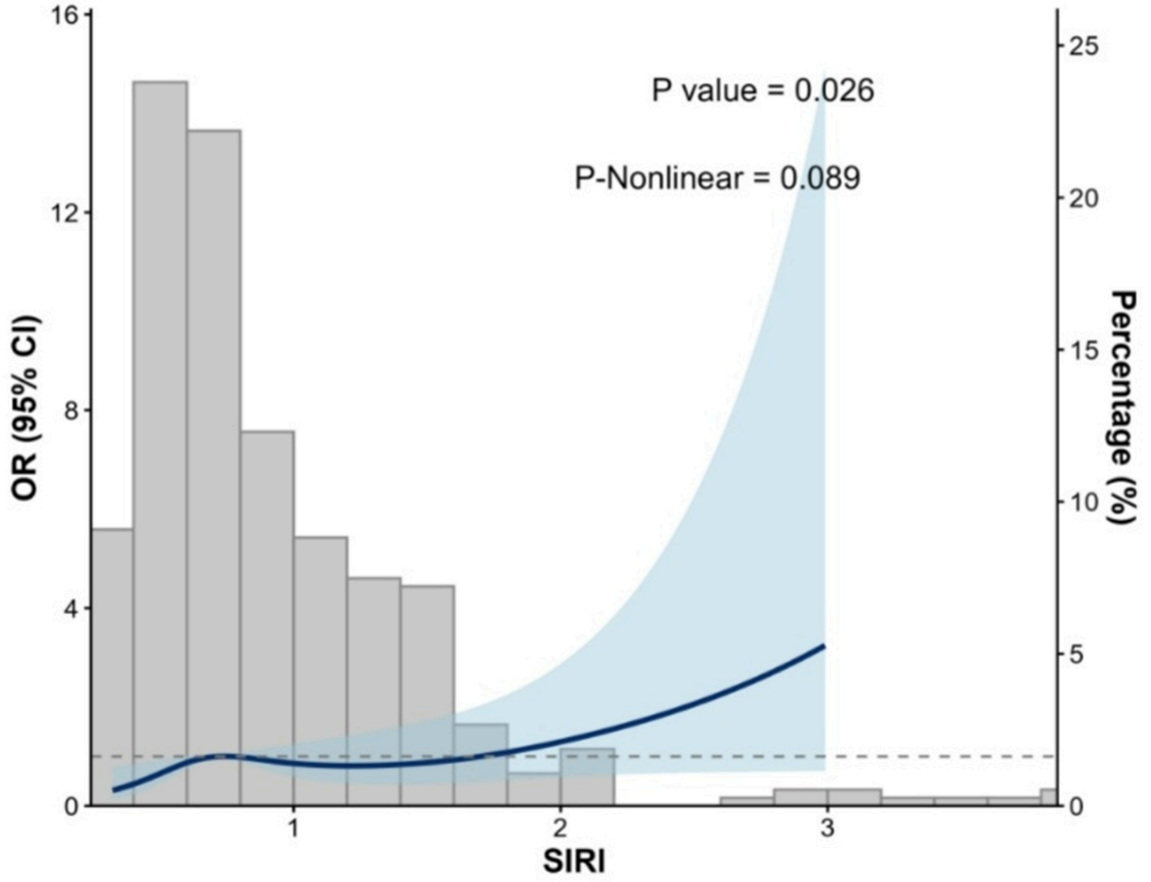


Figure 4

Restricted Cubic Spline Curve for the Association Between SIRI and the Risk of Carotid Plaque

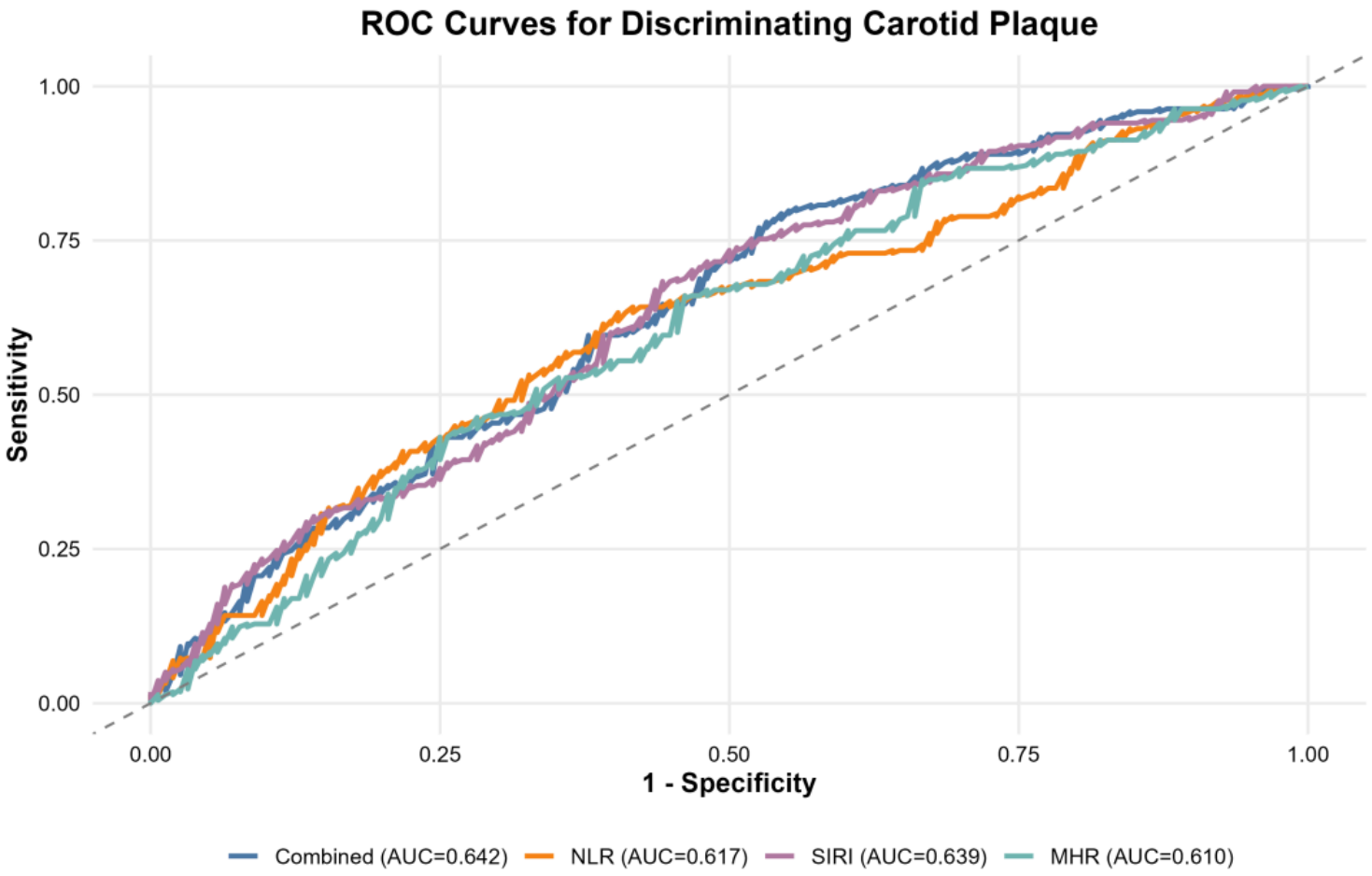


Figure 5

ROC Curves of Different Inflammatory Indices for Predicting the Risk of Carotid Plaque

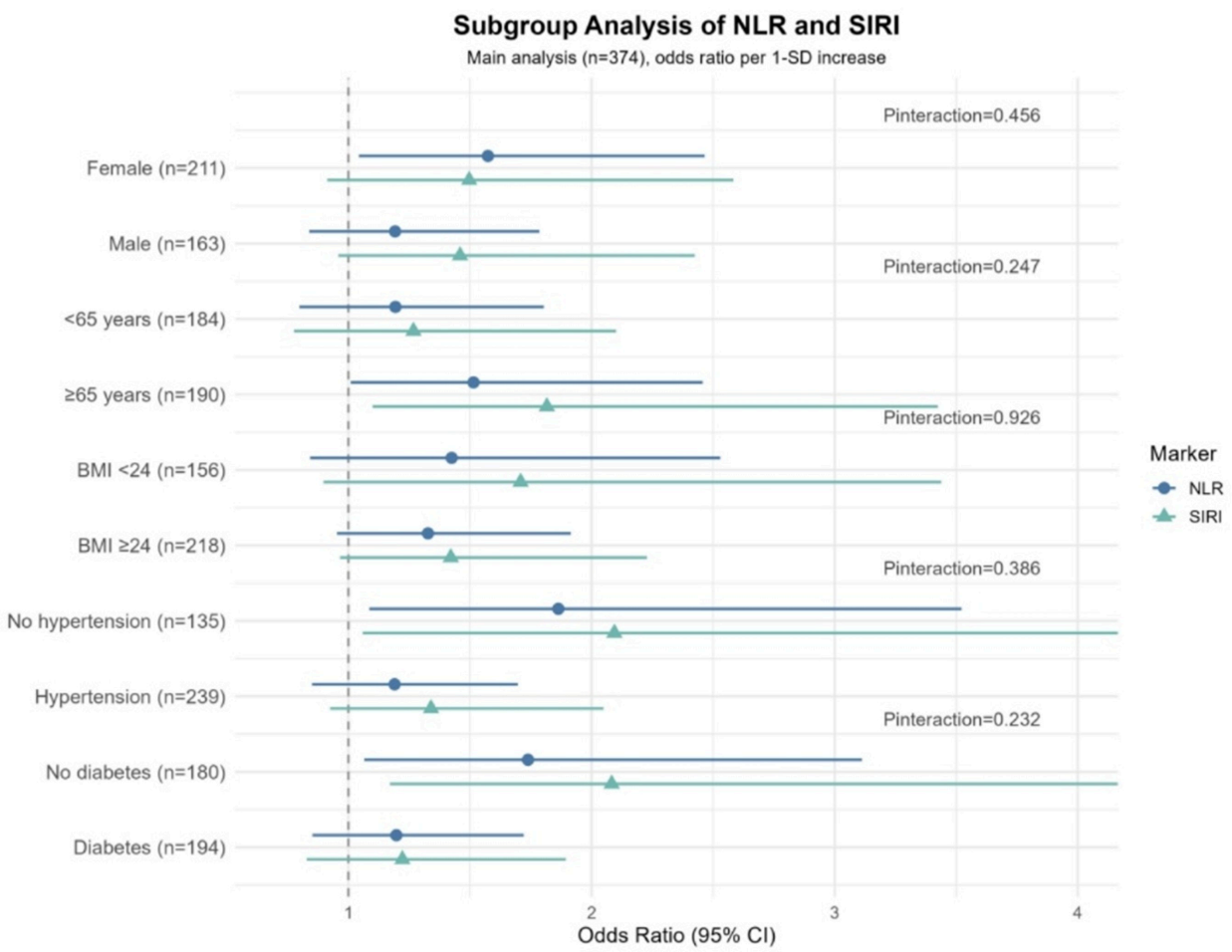


Figure 6

Forest Plot of the Subgroup Analyses of the Associations of NLR and SIRI With Carotid Plaque