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Association between systemic Immune-inflammation index, systemic inflammation response index and adult osteoarthritis: national health and nutrition examination survey

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Abstract

Background Osteoarthritis (OA) is a degenerative and inflammatory joint disease caused by multiple factors, the underlying mechanisms of which are not fully understood. The systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI) are both novel biomarkers and predictors of inflammation. Thus, this study aimed to evaluate the relationship between SII, SIRI and OA in adult.

Objective The ultimate goal is to gain a deeper understanding of how SII, SIRI influences OA and the implications of this relationship.

Materials and methods We analyzed data from 7204 participants aged 20 and older from the NHANES surveys conducted in 1999–2020, all of whom provided comprehensive data for this study. Standardized surveys assessed the presence of osteoarthritis and SII, SIRI. To thoroughly understand their relationship, we employed statistical techniques including multivariable logistic regression, stratified analysis with interaction, restricted cubic splines (RCS), and threshold effect analysis.

Results A total of 7204 adult participants were enrolled, composing of 2830 (39.3%) male and 4374 (60.7%) female with a median age of 62.2 ± 13.9 years, 2955 (41.0%) were diagnosed with OA. Accordingly, A linear relationship between SII and OA was discovered after adjusting for underlying confounders, ($p > 0.05$) in RCS, and the association

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between the SIRI and OA exhibited a nonlinear relationship ($p = 0.042$) in RCS. In the threshold analysis, the OR of developing OA was 1.648 (95% CI: 1.144 ~ 2.374, $p < 0.05$) in participants with SIRI of < 0.99 10^3 cells/ml. There was no significantly association between the SIRI and OA when the SIRI was ≥ 0.99 10^3 cells/ml. Further sensitivity analyses provided confidence that the results are robust and not likely to be substantially influenced by unmeasured confounding factors.

Conclusions This cross-sectional study demonstrated that a linear relationship between SII and OA, and the association between the SIRI and OA was found to be nonlinear.

Clinical trial number Not applicable.

Highlights

- In observational studies, the systemic immune-inflammation index and systemic inflammation response index has been associated with a increased risk of death from osteoarthritis.
- The systemic immune-inflammation index was linearly associated with the risk of osteoarthritis.
- The association between the systemic inflammation response index and osteoarthritis exhibited a nonlinear relationship.

Keywords Osteoarthritis, Systemic immune inflammation index, Systemic inflammation response index, NHANES

Introduction

Osteoarthritis (OA) is a widespread chronic condition that impacts millions of individuals worldwide [1]. It is characterized by a range of primary symptoms that typically develop gradually over time if left untreated [2]. The exact cause of OA is multifaceted, involving a complex interplay of genetic and environmental factors, as well as unhealthy lifestyle habits [3]. With an estimated global prevalence of over 10%, OA represents a significant public health concern with detrimental impacts on individuals' quality of life [4]. Early identification of risk factors associated with OA presents an opportunity to delay or prevent the onset of the disease [5].

The Systemic Immune-Inflammation Index (SII) and Systemic Inflammation Response Index (SIRI) are critical blood biomarkers that provide valuable insights into human health [6]. These dynamic parameters fluctuate in response to various stimuli, offering clinicians a sensitive measure of the body's homeostatic mechanisms. Regular monitoring of SII and SIRI levels enables healthcare professionals to assess a wide range of metabolic processes and organ functions [7]. The values of SII and SIRI are influenced by genetic predisposition, lifestyle choices, and environmental factors. Deviations from their normal reference ranges can indicate underlying pathophysiological imbalances requiring medical intervention [8]. Given their responsiveness to health status changes, measuring SII and SIRI levels is crucial for diagnosing and managing various acute and chronic diseases [9]. These biomarkers are often included in standard blood panels to screen for health conditions and evaluate treatment effectiveness [10]. Ongoing research continues to enhance our understanding of the clinical significance of SII and SIRI, exploring their potential as prognostic indicators and optimizing their use in personalized healthcare. Additionally, understanding the physiological determinants of SII and SIRI levels improves clinicians' ability to interpret results accurately and make informed decisions regarding patient care [11].

Despite the recognized importance of SII and SIRI in assessing overall health, their specific impacts on OA across different populations remain unclear. Research exploring the relationship between these biomarkers and OA symptoms is crucial for advancing clinical practice beyond a symptom-based approach [3]. Previous studies have often relied on traditional universal scales that may lack disease specificity, potentially introducing bias. Currently, evidence regarding the correlation between SII, SIRI, and OA is insufficient.

To address this knowledge gap, our primary objective is to investigate the relationship between SII, SIRI, and OA, along with their clinical implications. Additionally, we aim to determine an appropriate cutoff value for assessing the impact of SIRI on OA. We conducted a retrospective cross-sectional study involving 7,204 adult participants in the United States.

Materials and methods

Study population

This cross-sectional study utilized NHANES data collected from 1999 to 2022 by the Centers for Disease Control and Prevention [12]. The NHANES project's aim was to assess the health and nutritional status of non-institutionalized Americans through a stratified multistage probability survey [13]. Demographic and comprehensive health information was gathered through home visits, screening, and laboratory testing at a mobile examination center (MEC). The NHANES was approved by the National Center for Health Statistics (NCHS) Ethics Review Committee, and participants provided written informed consent prior to participation. Additional Institutional Review Board approval was not required

for the secondary analysis [14]. The NHANES data can be accessed through the NHANES website (http://www.cdc.gov/nchs/nhanes.htm) (accessed on 1 April 2024). Our study included individuals over 20 years old who completed an interview, excluding those with missing data on OA, SII, SIRI, or covariates. The exclusion criteria comprised individuals under the age of 20, those with missing OA diagnosis, SII or SIRI data, and missing data on other covariates. Ultimately, a total of 7204 participants were analyzed, and the detailed inclusion and exclusion process is depicted (Fig. 1).

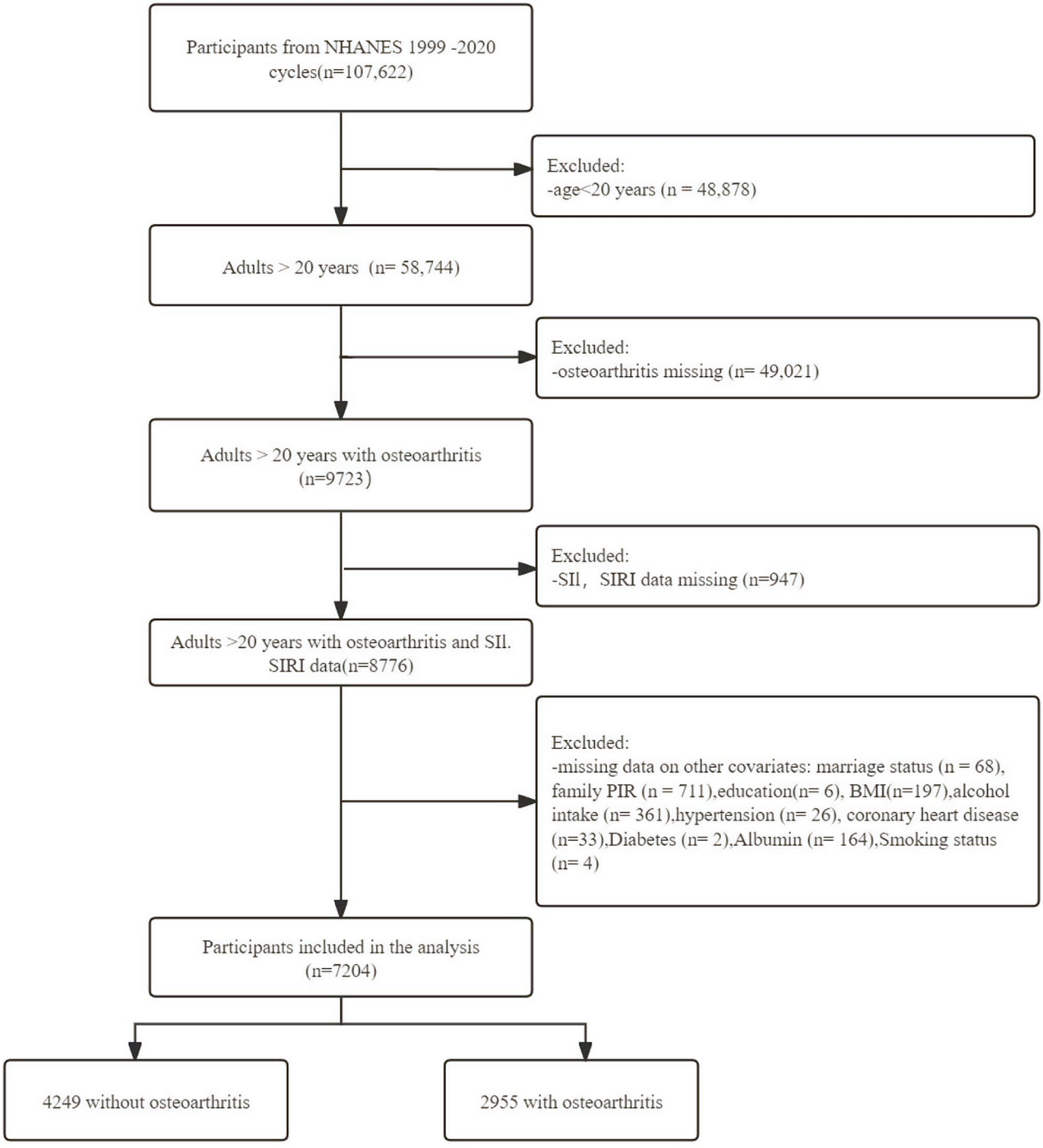

Fig. 1 The study's flow diagram. Abbreviations: NHANES, National Health and Nutrition Examination Survey; SII, systemic immune inflammation index; SIRI, systemic inflammation response index; PIR, poverty income ratio; BMI, body mass index

Assessment of OA

OA status was determined through a questionnaire survey [15], where participants were asked if a healthcare professional had diagnosed them with arthritis. Those who answered "no" were considered as not having OA. If the response was "yes," participants were further asked to specify the type of arthritis, and those who self-reported "osteoarthritis" was classified as having OA.

Definition of SII and SIRI

Peripheral blood samples from NHANES participants were analyzed at the Mobile Examination Centers (MEC) using a Beckman Coulter HMX Hematology Analyzer. Lymphocyte, neutrophil, monocyte, and platelet counts were obtained via complete blood count and reported as $\times 10^3$ cells/ml [16]. SII and SIRI levels were calculated using the following formulas: platelet count × neutrophil count/lymphocyte count, and monocyte count × neutrophil count/lymphocyte count, respectively [17]. These values were expressed as $\times 10^3$ cells/mL based on previous studies and were utilized as exposure variables in this study.

Covariates

Based on existing literature, we evaluated potential confounders that may affect OA. These variables included age, sex, marital status, race/ethnicity, education level, family income, smoking status, physical activity, hypertension, diabetes, coronary heart disease, and body mass index (BMI), Albumin (g/dL). Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Mexican American, or other races. Marital status was classified as married, living with a partner, or living alone. Educational attainment was grouped into less than 9 years, 9 to 12 years, and more than 12 years of education. Family income was categorized by the poverty income ratio (PIR) into low (PIR ≤ 1.3), medium (PIR > 1.3 to 3.5), and high (PIR > 3.5), according to a US government report. Smoking status was classified as never smokers (fewer than 100 cigarettes smoked), current smokers, and former smokers (more than 100 cigarettes smoked but quit). Physical activity was classified as sedentary, moderate (at least 10 min of light activity within the last 30 days), and vigorous (at least 10 min of intense activity within the last 30 days). The presence of hypertension, diabetes, stroke, and coronary heart disease was determined based on self-reported physician diagnoses. BMI was computed using standardized techniques based on weight and height measurements [18].

Statistical analysis

This study is a secondary analysis of publicly accessible datasets. Categorical variables were presented as proportions (%) while continuous variables were described using means (standard deviation, SD) or medians (interquartile range, IQR), as appropriate. Although NHANES data is designed to be nationally representative through a complex sampling design, considering the potential reduction in estimate precision and over adjustment bias introduced by weighting, as well as our primary focus on exploring associations rather than generating precise national population prevalence estimates, we chose to present unweighted results. We acknowledge that this approach may limit the generalizability of our findings to prevalence estimates for the adult population in the United States. To compare group differences, we employed one-way analyses of variance (for normally distributed data), Kruskal–Wallis tests (for skewed data), and chi-square tests (for categorical variables). Logistic regression models were used to determine the odds ratios (OR) and 95% confidence intervals (95% CIs) for the relationship between. For the right-skewed distribution of SII/SIRI levels, SII/SIRI levels were natural logtransformed (lnSII/lnSIRI) when assessing the association between SII/SIRI levels (continuous variable) and OA risk. Model 1 was adjusted for gender, BMI, marital status, age, education, PIR, physical activity, smoking, and alcohol consumption. Model 2 included adjustments for the same variables as Model 1, plus hypertension, diabetes, and coronary heart disease. Model 3 was fully adjusted, incorporating all variables from Model 2 along with albumin levels.

In addition, we performed restricted cubic spline (RCS) regression to assess linearity and examine the dose–response relationship between SII, SIRI, and OA, adjusting for variables in Model 3. A two-piecewise logistic regression model with smoothing was used to analyze the association threshold between SIRI and OA, also adjusted for variables in Model 3. Inflection points were determined using a likelihood-ratio test and the bootstrap resampling method.

We evaluated potential modifications in the relationship between lnSII, lnSIRI, and OA across various subgroups, including sex, age (20–50 vs. >50 years), marital status (married/partnered vs. living alone), education level (≤ 12 years vs. >12 years), family income (low vs. medium/high), and BMI (< 25 vs. ≥25 kg/m²). Heterogeneity among subgroups was assessed using multivariate logistic regression, and interactions between subgroups and lnSII, lnSIRI were examined via likelihood ratio tests. To address multiple comparisons in the subgroup interaction analysis, the Bonferroni correction was applied, adjusting the significance threshold to $p \leq 0.0038$ (0.05/13).

Due to the dataset's predetermined nature, no a priori statistical power estimates were conducted. All statistical analyses were conducted using R Statistical Software (Version 4.2.2, http://www.R-project.org, The R Founda

tion) and Free Statistics Analysis Platform (Version 1.9, Beijing, China, http://www.clinicalscientists.cn/freestatistics). Free Statistics is a user-friendly software package that offers intuitive interfaces for common analyses and data visualization. It leverages R as the underlying statistical engine, with the graphical user interface (GUI) developed in Python. The platform allows for reproducible analysis and interactive computing, enabling users to perform analyses with ease. Statistical significance was defined as a two-sided P value < 0.05.

Results

Description of crowd characteristics

A total of 7204 patients were included after strict screening according to the inclusion and exclusion criteria. Of these, the overall prevalence of OA disease was 2955(41%). The baseline characteristics of the groups stratified by SII, SIRI are shown in Table 1. In summary, significant differences were observed between participants with and without OA, notably in terms of age, BMI, race/ethnicity, smoking status, alcohol intake, and albumin levels (all $P < 0.05$).

Table 1 Baseline characteristics of participants in the NHANES follow-up study from 1999 to 2020 ($n = 7204$).

Association between SII/SIRI levels and the risk of OA

Table 2 displays the findings of the multivariable logistic regression analysis investigating the relationship between the SII/SIR and OA. The analysis revealed that a lnSII were significantly associated with a heightened risk of OA (OR = 1.10, 95% CI: 1.01 ~ 1.19, $P = 0.025$), even after controlling for potential confounding factors (see Table 2, model III). No significant associations were found among lnSIRI and OA (OR = 1.01, 95% CI: 0.93 ~ 1.09, $P = 0.819$).

Curve fitting and inflection point analysis

Multivariate smooth splines analysis revealed that the association between the SIRI and OA exhibited a nonlinear relationship in RCS (nonlinear, $p = 0.042$), and a linear relationship between SII and OA was discovered after adjusting for underlying confounders, $p > 0.05$) in RCS (P for linearity = 0.507, Fig. 2).

In the threshold analysis, the OR of developing OA was 1.648 (95% CI: 1.144 ~ 2.374, $p = 0.007$) in participants with SIRI levels of < 0.99 10^3 cells/mL (Table 3). This means that the risk of OA is increased by 64.8% with every 1×10^3 cells/mL SIRI increase. There was no association between SIRI and OA when the SIRI levels were ≥ 0.99 10^3 cells/mL ($P > 0.05$) (Table 3). This means that the risk of OA no longer increases with increasing SIRI.

Subgroup and sensitivity analysis

In several subgroups, stratified analysis was performed to assess potential effect modifications on the relationship between SII/SIRI and OA. we did not find any significant interactions between SII/SIRI levels and those potential confounders (all p value for interaction > 0.0038) (Figs. 3 and 4).

Discussion

This cross-sectional study is the first to explore the association between SII and SIRI and the risk of OA in a large, nationally representative sample. The findings indicate that changes in SII/SIRI are independently linked to an increased risk of OA in the NHANES population. Notably, a linear relationship between SII and OA was observed in RCS, whereas SIRI and OA exhibited a nonlinear relationship. Subgroup analysis revealed no significant interactions between subgroups. Our results suggest that monitoring SII and SIRI levels could facilitate early identification of individuals at high risk for OA. These findings carry important implications for OA management strategies, highlighting the potential value of prioritizing inflammation management to mitigate OA risk.

OA is a common chronic systemic autoimmune disease characterized by joint swelling, pain, and impaired mobility [1]. Immuno-inflammatory mechanisms are crucial in OA pathogenesis [17]. During OA onset and progression, the immune and inflammatory systems are activated, involving platelets, neutrophils, lymphocytes, and monocytes [19]. Neutrophil infiltration is a typical histopathological hallmark of OA, with their cytokines, chemokines, enzymes, and elastase driving chronic inflammation [20]. Monocytes are central to innate immunity and inflammation orchestration [21]. Lymphocytes, key to adaptive immunity, link innate and adaptive responses [22]. Platelets maintain homeostasis and mediate both acute and chronic inflammation, contributing to an inflammatory environment [23]. SII/SIRI has been used to assess disease activity in inflammatory conditions such as systemic lupus erythematosus, ankylosing spondylitis, gout, and rheumatoid arthritis [24, 25].

Previous studies have linked changes in peripheral blood neutrophils, monocytes, lymphocytes, and platelets to OA [26–28]. SII and SIRI, as emerging inflammation indicators, are easily detectable, cost-effective, and accessible through routine blood tests. They have shown promise as biomarkers for predicting stroke prognosis and various cancers [29–32]. SII is also associated with OA comorbidities such as body fat mass, BMI, circulating vaspin, follistatin/FSTL1, activin A/FSTL1, high-sensitivity C-reactive protein, and elevated fasting blood glucose [33, 34]. However, the literature on SII and OA is limited to two small retrospective cohort studies focusing on predictive ability and disease severity [33, 34]. We hypothesize that SII/SIRI may be associated with OA occurrence.

Table 1 Baseline characteristics of the study participants

Characteristics	All participants (*N* = 7204)	Patients without osteoarthritis (*N* = 4249)	Patients with osteoarthritis (*N* = 2955)	*P*-value
Sex, n (%)				0.813
Male	2830 (39.3)	1674 (39.4)	1156 (39.1)	
Female	4374 (60.7)	2575 (60.6)	1799 (60.9)	
Age(years), Mean (SD)	62.2 ± 13.9	61.4 ± 14.0	63.2 ± 13.7	< 0.001
BMI(kg/m$^{2)}$, Mean (SD)	30.8 ± 7.7	31.0 ± 7.9	30.4 ± 7.2	0.001
Race/ethnicity, n (%)				< 0.001
Non-Hispanic white	4168 (57.9)	2376 (55.9)	1792 (60.6)	
Non-Hispanic black	1414 (19.6)	860 (20.2)	554 (18.7)	
Mexican American	759 (10.5)	464 (10.9)	295 (10)	
Others	863 (12.0)	549 (12.9)	314 (10.6)	
Education level (year), n (%)				0.546
< 9	749 (10.4)	445 (10.5)	304 (10.3)	
9–12	2793 (38.8)	1625 (38.2)	1168 (39.5)	
> 12	3662 (50.8)	2179 (51.3)	1483 (50.2)	
Marital status, n (%)				0.645
Married or living with a partner	4214 (58.5)	2476 (58.3)	1738 (58.8)	
Living alone	2990 (41.5)	1773 (41.7)	1217 (41.2)	
Family income, n (%)				0.062
Low	2150 (29.8)	1305 (30.7)	845 (28.6)	
Medium	2813 (39.0)	1662 (39.1)	1151 (39)	
High	2241 (31.1)	1282 (30.2)	959 (32.5)	
hypertension, n (%)	3660 (50.8)	2145 (50.5)	1515 (51.3)	0.511
Diabetes, n (%)	1478 (20.5)	902 (21.2)	576 (19.5)	0.073
Coronary heart disease, n (%)	651 (9.0)	378 (8.9)	273 (9.2)	0.618
Physical activity, n (%)				0.058
Sedentary	4109 (57.0)	2458 (57.8)	1651 (55.9)	
Moderate	2072 (28.8)	1177 (27.7)	895 (30.3)	
Vigorous	1023 (14.2)	614 (14.5)	409 (13.8)	
Smoking status, n (%)				0.003
Never	3280 (45.5)	1899 (44.7)	1381 (46.7)	
Current	2535 (35.2)	1474 (34.7)	1061 (35.9)	
Former	1389 (19.3)	876 (20.6)	513 (17.4)	
Alcohol intake, n (%)	5145 (71.4)	3105 (73.1)	2040 (69)	< 0.001
Monocyte(10^3 cells/mL), Mean (SD)	2.1 ± 1.6	2.1 ± 1.6	2.1 ± 1.6	0.203
Neutrophils(10^3 cells/mL), Mean (SD)	4.4 ± 1.8	4.4 ± 1.8	4.3 ± 1.7	0.388
Peripheral platelet (10^3 cells/mL), Mean (SD)	250.8 ± 72.6	249.8 ± 72.1	252.2 ± 73.2	0.183
Albumin(g/L), Mean (SD)	4.1 ± 0.3	4.1 ± 0.3	4.2 ± 0.3	0.005
Osteoarthritis, n (%)	7204	4249 (59.0)	2955 (41.0)	< 0.001
Lymphocyte, (10^3 cells/mL), Median (IQR)	0.5 (0.4, 0.7)	0.5 (0.4, 0.7)	0.5 (0.4, 0.7)	0.352
SII(10^3 cells/mL), Median (IQR)	500.7 (348.7, 717.2)	500.8 (345.8, 710.1)	500.0 (351.8, 722.5)	0.298
SIRI(10^3 cells/mL), Median (IQR)	1.1 (0.8, 1.7)	1.1 (0.8, 1.7)	1.1 (0.8, 1.6)	0.760

Abbreviations: BMI, body mass index; SII, Systemic immune-inflammation index, SIRI, systemic inflammation response index

Table 2 Association between LnSII, LnSIRI and osteoarthritis in multiple regression model

Outcome	Model I		Model II		Model III	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
lnSII	1.09(1.01 ~ 1.18)	0.031	1.09(1.01 ~ 1.18)	0.037	1.10(1.01 ~ 1.19)	0.025
lnSIRI	1 (0.91 ~ 1.09)	0.999	1.00 (0.93 ~ 1.08)	0.982	1.01(0.93 ~ 1.09)	0.819

Model I: Adjust for variables, including gender, BMI, marital status, age, education, PIR, activity, smoke, alcohol

Model II: Adjust for variables, including gender, BMI, marital status, age, education, PIR, activity, smoke, alcohol, hypertension, diabetes, coronary heart disease

Model III: Adjust for all of these variables, including gender, BMI, marital status, age, education, PIR, activity, smoke, alcohol, hypertension, diabetes, coronary heart disease, albumin

Abbreviations: OR, odd ratio; CI, confidence interval; BMI, body mass index; SII, Systemic immune-inflammation index, SIRI, systemic inflammation response index

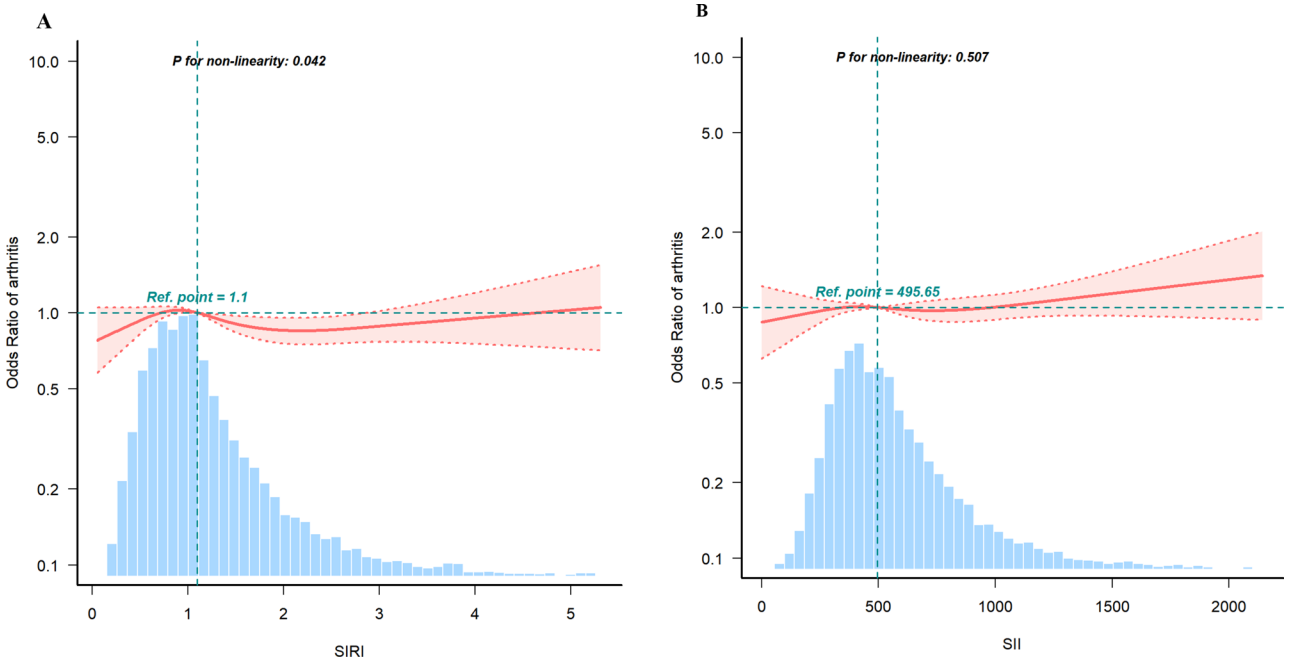

Fig. 2 RCS analysis of SIRI (**A**) and SII (**B**) with the odds ratio of osteoarthritis. Solid and dashed lines represent the predicted value and 95% confidence intervals. They were adjusted for age, Gender, Family income, BMI, Race, Education, Marital status, hypertension, Diabetes, Coronary heart disease, Activity, Smoke, Alcohol. Only 99% of the data is shown. Abbreviations: OR, odd ratio; CI, confidence interval; BMI, body mass index; SII, Systemic immune-inflammation index, SIRI, systemic inflammation response index

Table 3 Threshold analysis of the relationship of systemic inflammation response index and osteoarthritis

SIRI levels (10^3 cells/mL)	Adjusted Model	
	OR (95%CI)	P-value
< 0.99	1.648 (1.144 ~ 2.374)	0.007
≥ 0.99	1.006 (0.947 ~ 1.069)	0.835
Likelihood Ratio test	-	0.009

Adjusted for age, gender, Family income, BMI, race, education, marital status, hypertension, diabetes, coronary heart disease, activity, smoke, alcohol. Only 99% of the data is displayed

Abbreviations: OR, odd ratio; CI, confidence interval; BMI, body mass index; SII, Systemic immune-inflammation index, SIRI, systemic inflammation response index

Our study found that the SII pattern was positively associated with OA, while restricted cubic spline analysis revealed a non-linear association between SIRI levels and OA. To aid clinical interpretation of our findings, we will provide an example: "When SII increases by 50%, the risk of OA increases by approximately 4% (OR = 1.04), and this change is statistically significant. However, changes in SIRI do not significantly affect the probability of OA occurrence. In threshold analysis, the OR for developing OA was 1.648 (95% CI: 1.144–2.374, p = 0.007) in participants with SIRI levels < 0.99×10^3 cells/mL, indicating a 64.8% increased risk of OA with every 1×10^3 cells/mL increase in SIRI. No association was found between SIRI and OA at levels ≥ 0.99×10^3 cells/mL, suggesting that the risk does not increase further. Previous studies have reported non-linear dose-response relationships between SII and conditions like hyperlipidemia, all-cause mortality in nonalcoholic fatty liver disease, and a 'U-shaped' association with mortality in cardiovascular disease patients [19, 35, 36]. These findings highlight the complex, dose-dependent relationship between SII/SIRI and OA, warranting further research. Notably, previous studies are limited to case reports or series, with no comprehensive investigation in the general population. NHANES provides a unique opportunity to assess the association and dose-response link between SII/SIRI and OA, fully adjusted for numerous covariates and stratified analyses. The threshold effect analysis of SIRI identified a cut-off value of 0.99×10^3 cells/mL as critical, while statistically significant in our study, its biological and clinical relevance requires further investigation. Future research should focus on validating this threshold in independent cohorts, exploring its applicability to different OA phenotypes (e.g., different joint types), and elucidating the underlying mechanisms driving the observed threshold effect. We acknowledge that this threshold may not represent a definitive clinical breakpoint and should be considered as a potential area for further investigation rather than a definitive diagnostic criterion.

Our study offers several notable advantages. Firstly, the large sample size and appropriate covariate adjustments enhance the reliability and representativeness of our findings. Secondly, we thoroughly assessed the individual effects of SII and SIRI on OA risk. Lastly, SII and SIRI were measured using standard methodologies, making

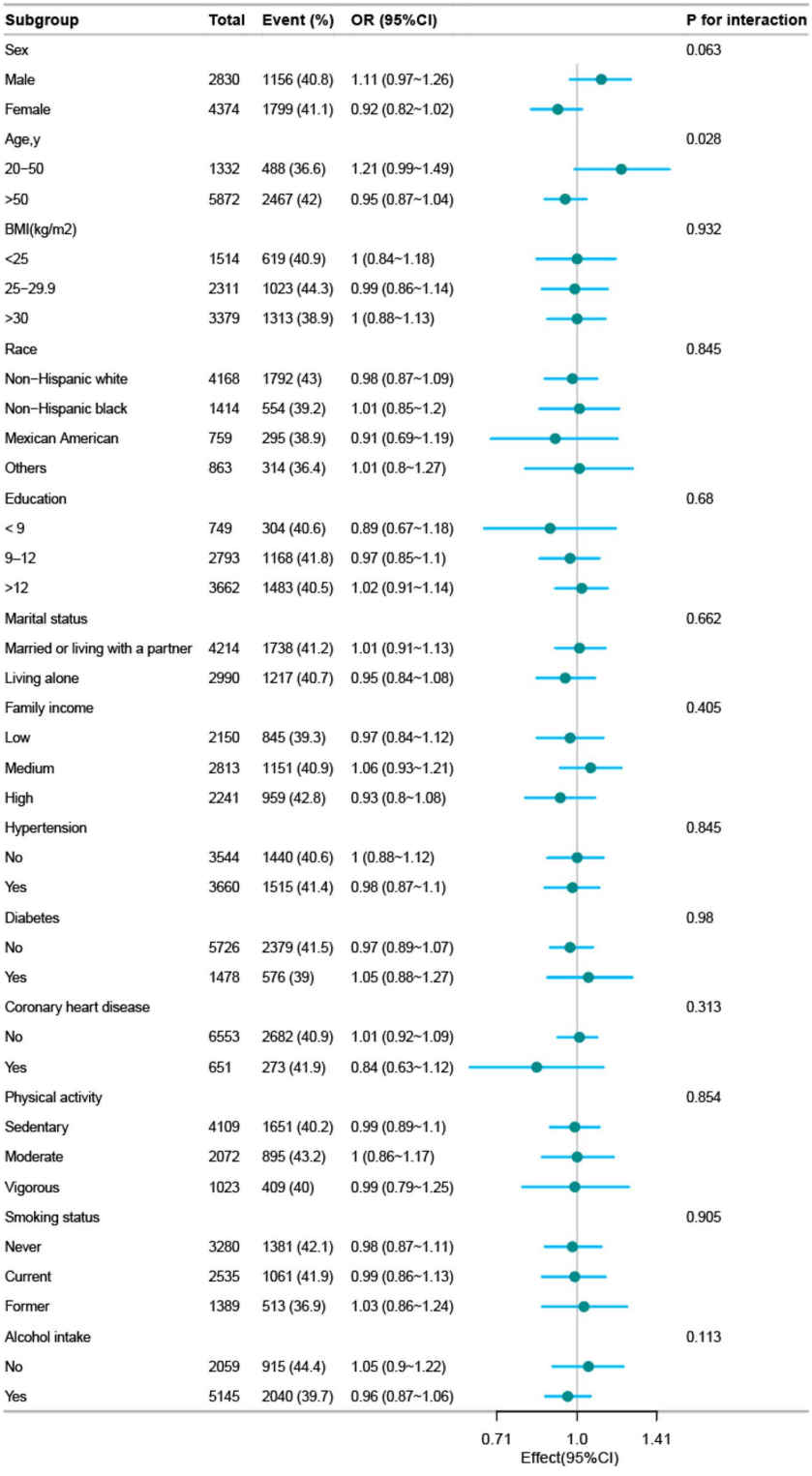

Fig. 3 Forest plot depicting subgroup analysis of the association between lnSII and OA

them accessible and low-cost biomarkers with potential clinical utility.

However, there are limitations worth noting. Firstly, although NHANES is a representative sample of the U.S. population, the study's findings may not fully translate to other populations, particularly those in developing countries or different ethnic backgrounds, further validation is needed in multi-center, multi-ethnic populations in the

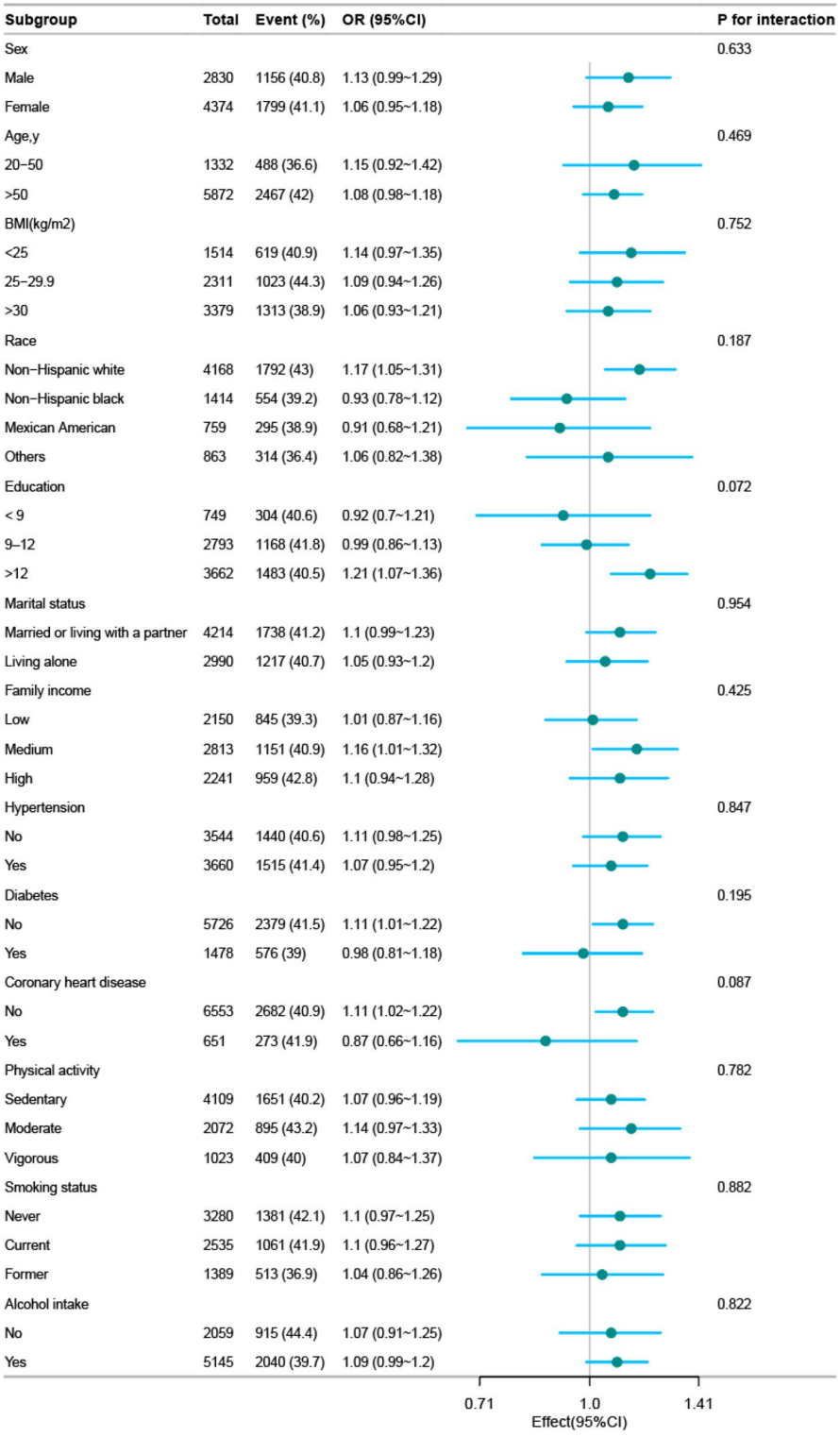

Fig. 4 Forest plot depicting subgroup analysis of the association between lnSIRI and OA

future. Secondly, the cross-sectional design of NHANES precludes our ability to determine a causal relationship between SII/SIRI and OA, and the absence of longitudinal data on OA progression and detailed functional outcome measures limits our capacity to evaluate the impact of SII/SIRI on disease severity and functional limitations. Future studies should incorporate longitudinal designs and functional assessments to further elucidate

the relationships between systemic inflammation, OA progression, and patient-reported outcomes. and the diagnosis of OA was based on self-reports, which may be subject to recall bias. Lastly, despite our findings suggest a link between systemic inflammation and OA, and adjusting for numerous confounders, residual or unmeasured confounders may still influence our findings, due to data availability limitations, we were unable to compare the predictive performance of SII/SIRI with other specific inflammatory markers, future prospective studies incorporating more cytokine detections are needed to validate the mechanistic hypothesis, and required to fully disentangle the contributions of different inflammatory pathways and to determine whether SII/SIRI can serve as a specific biomarker for OA. SII and SIRI are composite indices that provide an indirect assessment of systemic inflammation. While they have been validated in various disease backgrounds, their application in OA requires further investigation due to the heterogeneity of the disease and the potential influence of local joint inflammation. Compared to direct measurements of inflammatory mediators, these indices may not fully capture the complexity of inflammatory processes in OA. Therefore, future prospective studies with larger sample sizes and more comprehensive data collection are necessary to confirm the association between SII/SIRI and OA risk.

Conclusions

This cross-sectional study provides evidence that SII / SIRI associated with the risk of OA, a linear relationship between SII and OA, and the association between the SIRI and OA was found to be nonlinear. These results revealed that underscoring SII/SIRI may play a role as a risk factor for OA, and may be a relevant biomarker. However, given the limitations of our study, further research with well-designed prospective designs is needed to confirm these findings.

Abbreviations

BMI	Body mass index
SII	Systemic immune-inflammation index
SIRI	Systemic inflammation response index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12891-025-08792-9.

Supplementary Material 1

Supplementary Material 2

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Author contributions

Conceptualization, P.W. and S.L.; Data curation, N.L., Q. O., G.H.; Formal analysis, X.C., P.W., Q.G. and J.L.; Funding acquisition, F. G. and L.H.; Methodology, X.C., N.L., S.Z. and Y.S.; Writing original draft, X.C., N.L., and Q. O.; Writing review and editing, X.C., N.L., Q. O., L.H., S.L. and F.G. All authors made a significant contribution to the work reported and agreed to be accountable for all aspects of the work.

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Data availability

Publicly available datasets are available online for this study. The repository/repositories name and accession numbers are available online at http://www.cdc.gov/nchs/nhanes.htm (accessed on 1 March 2024).

Declarations

Ethics approval and consent to participate

This study adhered to the Declaration of Helsinki. The NHANES protocol was approved by the NCHS IRB (Continuation of Protocol #2011-17), and all participants provided informed consent. Ethical approval was waived by the NCHS IRB under 45 CFR 46.104(d)(4) because the study used de-identified, publicly available data.

Consent for publication

All participating authors give their consent for this work to be published.

Competing interests

The authors declare no competing interests.

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