Correlation of Systemic Immune-Inflammation Index and Systemic Inflammatory Response Index with Microalbuminuria in Middle-Aged and Elderly Health Check-Up Population: A Postprint

Authors: Huang Ya, Ni Wenji, Zhang Rui, Li Dandan, Zhou Ying, Jin Tao, Zhong Yong, Zhong Yong

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Abstract

Background: Microalbuminuria is a sensitive indicator of early renal microvascular damage and an independent risk factor for cardiovascular disease. Previous studies have demonstrated that chronic inflammation plays an important role in the occurrence and development of microalbuminuria; however, few reports have addressed the correlation between blood inflammatory markers and microalbuminuria.

Objective: To investigate the correlation between the Systemic Immune-Inflammation Index (SII) and Systemic Inflammation Response Index (SIRI) with microalbuminuria in a middle-aged and elderly health examination population.

Methods: This cross-sectional study enrolled 2,105 examinees over 40 years of age who underwent health examinations at the Department of Health Medicine, General Hospital of Eastern Theater Command between April and July 2023. Based on the urinary albumin-to-creatinine ratio (UACR), participants were divided into two groups: a non-microalbuminuria group (1,857 cases, UACR<30 mg/g) and a microalbuminuria group (248 cases, UACR=30~300 mg/g). SII was categorized into tertiles T1 (0.09~0.27), T2 (0.28~0.40), and T3 (0.41~1.38), and SIRI was categorized into tertiles t1 (0.11~0.41), t2 (0.42~0.66), and t3 (0.67~3.52). General information and laboratory findings were collected and compared between the two groups. Linear regression analysis was employed to explore the association between SII, SIRI levels and logarithmically transformed UACR (log UACR), while multivariate logistic regression analysis was used to investigate the relationship between SII, SIRI and the risk of microalbuminuria.

Results: No statistically significant differences were observed between the two groups in terms of gender, waist-to-hip ratio, total cholesterol, low-density lipoprotein cholesterol, or uric acid levels (P>0.05). The microalbuminuria group exhibited higher levels of age, BMI, systolic blood pressure, diastolic blood pressure, fasting blood glucose, 2-hour postprandial blood glucose, glycated hemoglobin, triglycerides, homocysteine, glomerular filtration rate, erythrocyte sedimentation rate, SII, and SIRI, and lower levels of high-density lipoprotein cholesterol compared with the non-microalbuminuria group (P<0.05). Linear regression analysis revealed that both SII and SIRI levels were positively correlated with log UACR (P<0.05). Multivariate logistic regression analysis demonstrated that after adjusting for all control variables, SII level was positively associated with the risk of microalbuminuria (OR=1.17, 95%CI=1.01~1.35, P=0.031). Compared with patients at the T1 level, those at the T3 level showed an increased risk of microalbuminuria (OR=1.43, 95%CI=1.01~2.03, P=0.046), with a trend of increasing risk associated with higher SII (P for trend=0.038). After adjusting for all control variables, SIRI level was also positively associated with the risk of microalbuminuria (OR=1.18, 95%CI=1.03~1.35, P=0.019). Compared with patients at the t1 level, those at the t3 level exhibited an elevated risk of microalbuminuria (OR=1.45, 95%CI=1.01~2.09, P=0.046), with a trend of increasing risk associated with higher SIRI (P for trend=0.032).

Conclusion: In middle-aged and elderly health examination populations, SII and SIRI levels are positively correlated with log UACR and the risk of microalbuminuria.

Full Text

Correlation between Systemic Immune Inflammatory Index and Systemic Inflammatory Response Index with Microalbuminuria in Middle-Aged and Elderly Health Examination Populations

HUANG Ya, NI Wenji, ZHANG Rui, LI Dandan, ZHOU Ying, JIN Tao, ZHONG Yong*

Health Medicine Department, Jinling Hospital, Affiliated Hospital of Medical School, Nanjing University / General Hospital of Eastern Theater Command, Nanjing 210018, China

*Corresponding author: ZHONG Yong, Chief physician; E-mail: zhongyongnj@163.com

Abstract

Background: Microalbuminuria is a sensitive indicator of early renal microvascular damage and an independent risk factor for cardiovascular diseases. Previous studies have shown that long-term chronic inflammation plays an important role in the occurrence and development of microalbuminuria; however, reports on the correlation between blood inflammatory markers and microalbuminuria are scarce. **Objective:** To investigate the correlation between systemic immune inflammatory index (SII) and systemic inflammatory response index (SIRI) with microalbuminuria in middle-aged and elderly health examination populations. **Methods:** This cross-sectional study enrolled 2,105 individuals aged over 40 years who underwent health check-ups at the Department of Health Medicine, General Hospital of Eastern Theater Command from April to July 2023. Participants were divided into two groups based on urinary microalbumin/urinary creatinine ratio (UACR): non-microalbuminuria group (1,857 cases, UACR<30 mg/g) and microalbuminuria group (248 cases, UACR=30-300 mg/g). SII was categorized into T1 (0.09-0.27), T2 (0.28-0.40), and T3 (0.41-1.38), while SIRI was categorized into t1 (0.11-0.41), t2 (0.42-0.66), and t3 (0.67-3.52) according to tertiles. General information and laboratory findings were collected and compared between groups. Linear regression analysis was used to explore the correlation between SII, SIRI levels and log-transformed UACR (log UACR), while multivariate logistic regression analysis was used to examine the association between SII, SIRI and microalbuminuria risk. **Results:** No statistically significant differences were observed between groups in gender, waist-to-hip ratio, total cholesterol, low-density lipoprotein cholesterol, or uric acid levels (P>0.05). The microalbuminuria group showed significantly higher levels of age, BMI, systolic blood pressure, diastolic blood pressure, fasting blood glucose, 2-hour postprandial blood glucose, glycated hemoglobin, triglycerides, homocysteine, glomerular filtration rate, erythrocyte sedimentation rate, SII, and SIRI, along with lower high-density lipoprotein cholesterol levels compared to the non-microalbuminuria group (P<0.05). Linear regression analysis revealed that both SII and SIRI levels were positively correlated with log UACR (P<0.05). Multivariate logistic regression analysis showed that after adjusting for control variables, SII level was positively associated with microalbuminuria risk (OR=1.17, 95%CI=1.01-1.35, P=0.031). Compared with T1 level, T3 level was associated with increased microalbuminuria risk (OR=1.43, 95%CI=1.01-2.03, P=0.046), with a significant trend of increasing risk across SII categories (P-trend=0.038). Similarly, after adjustment, SIRI level was positively correlated with microalbuminuria risk (OR=1.18, 95%CI=1.03-1.35, P=0.019). Compared with t1 level, t3 level showed elevated microalbuminuria risk (OR=1.45, 95%CI=1.01-2.09, P=0.046), with risk increasing across SIRI categories (P-trend=0.032). **Conclusion:** In middle-aged and elderly health examination populations, SII and SIRI levels are positively correlated with both log UACR and microalbuminuria risk.

Keywords: Albuminuria; Microalbuminuria; Systemic immune inflammatory

index; Systemic inflammatory response index; Middle-aged and elderly

Introduction

Inflammatory response is a defensive natural reaction of the body, while immune response is the body' s reaction to eliminate foreign harmful antigens through the simultaneous action of the immune system and immune cells. Immune-inflammatory reactions participate in the occurrence, development, and prognosis of various diseases and represent a current research hotspot. As a sensitive indicator reflecting early renal microvascular damage, microalbuminuria is influenced by hemodynamic and several metabolic factors (such as hypertension, dyslipidemia, and abnormal glucose metabolism) and serves as an important marker of systemic vascular endothelial cell injury as well as an independent risk factor for cardiovascular diseases. Although the mechanisms underlying microalbuminuria remain unclear, literature indicates that innate immune-mediated low-level inflammatory responses play a crucial role in its development and progression. Consequently, various blood inflammatory markers, as objective indicators reflecting the body's inflammatory state, may be correlated with microalbuminuria to some extent. However, current epidemiological evidence regarding the relationship between blood inflammatory markers and microalbuminuria is limited.

As inflammatory biomarkers, peripheral blood inflammatory cell counts and their derived indicators are now widely used in clinical practice. In 2014, Hu et al. first proposed the concept of systemic immune inflammatory index (SII), which is based on peripheral platelet, neutrophil, and lymphocyte counts to comprehensively reflect systemic immune-inflammatory status. In 2016, Qi et al. introduced a novel systemic inflammatory response index (SIRI) that incorporates absolute values of peripheral neutrophils, monocytes, and lymphocytes to distinguish immune-inflammatory responses through three different pathways, providing a more comprehensive reflection of the body' s immune-inflammatory state. SII and SIRI, as comprehensive novel inflammatory biomarkers, are now considered accurate indicators of inflammatory status, with increasing research demonstrating their significant correlation with the occurrence and prognosis of cardiovascular diseases.

Therefore, this study aims to investigate the correlation between these novel inflammatory biomarkers and microalbuminuria in middle-aged and elderly health examination populations, hoping to provide new insights into the pathogenesis, prevention, and treatment of microalbuminuria.

Methods

Study Design and Participants

This cross-sectional study enrolled 2,105 middle-aged and elderly individuals who underwent health examinations at the Department of Health Medicine, General Hospital of Eastern Theater Command from April to July 2023. Inclusion criteria were: (1) age $ $40 years; (2) complete health examination information including health status, medical history, height, body weight, waist circumference, hip circumference, and blood pressure measured by uniformly trained medical staff following standardized procedures; and (3) complete laboratory examinations including routine blood and urine tests, blood biochemical indices, and urinary microalbumin/urinary creatinine ratio (UACR) testing. Exclusion criteria included: (1) acute diseases, advanced malignant tumors, or other severe consumptive diseases; (2) chronic kidney disease or macroalbuminuria (UACR>300 mg/g). This retrospective study involved only collection of clinical data without clinical intervention, posing no health risks to participants and without disclosing personal information. The study was approved by the Ethics Committee of General Hospital of Eastern Theater Command (No. 2024DZKY-015-01), and informed consent was waived.

Data Collection

Physical Examination: All participants underwent physical examination including measurements of height, body weight, waist circumference, and resting blood pressure [systolic blood pressure (SBP), diastolic blood pressure (DBP)]. Height was measured to the nearest 0.1 cm and body weight to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). For waist circumference measurement, participants wore light underwear and measurement was taken horizontally around the umbilicus to the nearest 0.1 cm. Hip circumference was measured using a soft tape around the hips at the level of the symphysis pubis and gluteus maximus muscle, also to the nearest 0.1 cm. Waist-to-hip ratio (WHR) was calculated as waist circumference (cm)/hip circumference (cm). Blood pressure was measured using a calibrated Omron electronic sphygmomanometer.

Laboratory Tests: After at least 8 hours of fasting, venous blood samples were collected by uniformly trained nurses the following morning. All laboratory tests were performed at the Clinical Laboratory of General Hospital of Eastern Theater Command. Tests included complete blood count, liver function, kidney function, fasting blood glucose (FBG), 2-hour postprandial blood glucose (2hBG), glycated hemoglobin (HbA1c), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), homocysteine (HCY), and erythrocyte sedimentation rate (ESR). Random urine samples were collected for UACR measurement. SII was calculated as (peripheral platelet count × neutrophil count)/lymphocyte count/1000, and SIRI as (peripheral neutrophil count

× monocyte count)/lymphocyte count. Glomerular filtration rate (GFR) was estimated using the modified MDRD formula for Chinese population: GFR=186×(serum creatinine)$^{-1}$.^{154}×(age)$^{-0}$.^{203}$×0.742(if female)×$1.233 (Chinese coefficient).

Diagnostic Criteria: Microalbuminuria was defined using the widely accepted criterion of UACR 30-300 mg/g. Participants were divided into two groups based on UACR: non-microalbuminuria group (1,857 cases, UACR<30 mg/g) and microalbuminuria group (248 cases, UACR=30-300 mg/g). SII and SIRI were categorized into tertiles: SII T1 (0.09-0.27), T2 (0.28-0.40), and T3 (0.41-1.38); SIRI t1 (0.11-0.41), t2 (0.42-0.66), and t3 (0.67-3.52).

Quality Control

All measurements of height, body weight, waist circumference, hip circumference, and blood pressure were performed by uniformly trained medical staff following standardized procedures. Data entry was conducted by two independent personnel to ensure accuracy.

Statistical Analysis

Statistical analysis was performed using SAS 9.4 software. The Kolmogorov-Smirnov test was used to assess normality of continuous variables. Normally distributed continuous variables were expressed as mean±standard deviation and compared between groups using independent samples t-test. Non-normally distributed continuous variables were expressed as median (P25, P75) and compared using rank-sum test. Categorical variables were expressed as frequencies and compared using ^{2} test. Linear regression analysis was used to examine the correlation between SII, SIRI levels and log-transformed UACR (log UACR). Binary logistic regression analysis was used to explore the association between SII, SIRI and microalbuminuria risk. P<0.05 was considered statistically significant.

Results

General Characteristics

Among the 2,105 participants, 1,826 (86.7%) were male and 279 (13.3%) were female, with a mean age of 54.3$±$12.9 years. No significant differences were observed between groups in gender, WHR, TC, LDL-C, or uric acid levels (P>0.05). The microalbuminuria group showed significantly higher levels of age, BMI, SBP, DBP, FBG, 2hBG, HbA1c, TG, HCY, GFR, ESR, SII, and SIRI, along with lower HDL-C levels compared to the non-microalbuminuria group (P<0.05) .

Linear Correlation of SII and SIRI with log UACR

Linear regression analysis demonstrated that SII level was positively correlated with log UACR (P<0.05) [Figure 1: see original paper]A. Similarly, SIRI level was positively correlated with log UACR (P<0.05) [Figure 1: see original paper]B.

Association of SII and SIRI with Microalbuminuria Risk

Binary logistic regression analysis was performed with microalbuminuria occurrence as the dependent variable (yes=1, no=0), and SII level (continuous) and its categories (T1=0, T2=1, T3=2) or SIRI level (continuous) and its categories (t1=0, t2=1, t3=2) as independent variables, adjusting for control variables including gender (male=1, female=0), age, BMI, SBP, DBP, FBG, 2hBG, HbA1c, TG, HCY, GFR, and ESR.

After adjustment, SII level was positively associated with microalbuminuria risk (OR=1.17, 95%CI=1.01-1.35, P=0.031). Compared with T1 level, T3 level was associated with increased microalbuminuria risk (OR=1.43, 95%CI=1.01-2.03, P=0.046), with a significant upward trend in risk across SII categories (P-trend=0.038) .

Similarly, after adjustment, SIRI level was positively correlated with microalbuminuria risk (OR=1.18, 95%CI=1.03-1.35, P=0.019). Compared with t1 level, t3 level showed elevated microalbuminuria risk (OR=1.45, 95%CI=1.01-2.09, P=0.046), with risk increasing across SIRI categories (P-trend=0.032) .

Discussion

Microalbuminuria is an early clinical marker of renal damage resulting from persistent early intrarenal hemodynamic abnormalities. Previous studies have confirmed that microalbuminuria is an early marker of widespread microvascular damage, associated with high prevalence of diabetes, hypertension, metabolic syndrome, and increased cardiovascular disease risk. Most kidney diseases are initiated or accompanied by immune-inflammatory responses, and dysregulated immune-inflammatory regulation represents an important pathological mechanism in the development and progression of renal disease. Following renal tissue injury from external or internal causes, systemic immune cells or intrinsic renal cells can mediate inflammation through expression or release of various inflammatory mediators such as interleukin-1β, interleukin-1, and vascular endothelial growth factor, leading to irreversible structural changes in the kidneys. As comprehensive novel inflammatory biomarkers capable of objectively reflecting the body' s inflammatory state, SII and SIRI were investigated in this study for their correlation with microalbuminuria in middle-aged and elderly health examination populations, aiming to provide new insights into the pathogenesis, prevention, and treatment of microalbuminuria.

Our findings demonstrated that after adjusting for control variables, both SII and SIRI levels were positively associated with microalbuminuria risk. Compared with low-level groups, high-level groups of both SII and SIRI showed significantly increased microalbuminuria risk, with a dose-dependent relationship observed for both indices. White blood cells and their components, including neutrophils, monocytes, and lymphocytes, play crucial roles in systemic immune-inflammatory responses. Neutrophils can secrete large amounts of inflammatory mediators, chemokines, and oxygen free radicals, thereby inducing endothelial cell injury and subsequent tissue ischemia. Monocyte activation and transformation into lipid-laden macrophages constitute an important process in atherosclerotic lesion formation, while lymphocytes have regulatory functions in inflammation. Therefore, the significant correlations between these two novel systemic inflammatory indices calculated from blood inflammatory cell parameters and microalbuminuria suggest that systemic immune-inflammatory responses may play an important role in early renal injury.

This large-sample cross-sectional study adjusted for confounding factors including gender, age, blood glucose, blood lipids, and GFR, enhancing the scientific reliability of our results. However, several limitations should be acknowledged. First, as a cross-sectional study, we cannot determine the temporal sequence between systemic immune-inflammatory response and microalbuminuria, pre causal inference. Second, as a retrospective study, lifestyle information such as smoking, alcohol consumption, physical activity, and sleep was incomplete and not included in the analysis. Additionally, our participants were primarily from a health examination population, and due to the occupational characteristics of our hospital' s examination population (predominantly male), their socioeconomic status and occupational features may not represent the broader Chinese middle-aged and elderly population, potentially introducing bias. Large-sample, multicenter epidemiological surveys and cohort studies are needed for validation.

Notably, microalbuminuria detection is not universally performed in clinical and health examination settings. However, complete blood count, as the most basic laboratory test in clinical practice and health examinations, can provide information on systemic immune-inflammatory status that may identify individuals requiring further microalbuminuria screening, thereby reducing healthcare costs and facilitating early detection, diagnosis, and treatment of microalbuminuria and early kidney disease. Furthermore, SII and SIRI calculated from routine blood tests offer advantages of high accessibility, minimal invasiveness, low cost, and good reproducibility, making them valuable not only in medical research but also in routine clinical care.

Future large cohort studies and basic research are warranted to elucidate the causal relationship and biological mechanisms between systemic inflammatory response and microalbuminuria, ultimately aiming to reduce microalbuminuria risk and prevent or delay kidney disease progression through active control of systemic inflammatory responses.

Conclusion

In summary, SII and SIRI levels are positively correlated with log UACR and microalbuminuria risk in middle-aged and elderly health examination populations. These correlations further support the notion that inflammatory responses may play an important role in the development and progression of microalbuminuria. Given the insidious nature of microalbuminuria symptoms, SII and SIRI derived from routine blood tests may help identify individuals at risk who would benefit from further screening, representing a cost-effective approach for early detection and intervention.

Author Contributions

Huang Ya conceptualized the study, designed the research, implemented the investigation, and drafted the manuscript. Huang Ya, Ni Wenji, Zhang Rui, Li Dandan, and Zhou Ying collected and organized data, performed statistical analysis, and prepared figures and tables. Jin Tao revised the manuscript. Zhong Yong was responsible for quality control and review, supervised the overall project, and provided administrative support.

This article has no conflict of interest.

HUANG Ya: https://orcid.org/0000-0002-9499-2922

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