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# Association between systemic immune-inflammation index and sarcopenic obesity in middle-aged and elderly Chinese adults: a cross-sectional study and mediation analysis

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## Abstract

**Background** Despite the known association between chronic inflammation and reduced muscle mass, there is a gap in research regarding the association between the systemic immune-inflammation index (SII) and sarcopenic obesity (SO). This study aims to assess the relationship between SII and SO in middle-aged and elderly adults and the mediating role of triglyceride-glucose index (TyG).

**Methods** This cross-sectional study involved 2,719 participants aged 45–90 years who underwent health check-ups. SO was evaluated by combining sarcopenia [assessed by handgrip strength and appendicular skeletal muscle index (ASMI)] with obesity (determined by body fat percentage). Association between SII and SO, sarcopenia, and obesity in middle-aged and elderly individuals was examined using multivariable logistic regression, restricted cubic spline analysis, and subgroup analysis. Bidirectional mediation analysis was conducted to determine the direct and indirect effects through SII and TyG.

**Results** The study included 2,719 participants, of which 228 had SO (8.4%). SO prevalence increased as the SII quartiles rose ($P_{for\ trend}$ <0.001). SII (per SD increase) had a significantly positive association with SO in both middle-aged individuals (OR = 1.69, 95% CI: 1.43 ~ 1.99) and older adults (OR = 2.52, 95% CI: 1.68 ~ 3.77). The relationship between SII and SO was found to be non-linear ($P_{nonlinear}$<0.05). In addition, SII showed a strong negative relationship with both handgrip strength and ASMI across all participants. In subgroup analysis, SII was still shown to significantly increase the risk of SO in all subgroups by gender, body mass index, waist circumference, smoking, drinking, hypertension, diabetes, dyslipidemia. TyG was found to mediate 21.36%, 11.78%, and 9.94% of the associations between SII and SO, sarcopenia, and obesity, respectively. SII had no mediation effect on the association between TyG and SO, sarcopenia, and obesity ($P$>0.05).

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**Conclusions** Elevated levels of SII were associated with an increased risk of SO in middle-aged and elderly adults, especially in the elderly population, and elevated TyG levels played a role in this relationship.

**Keywords** Systemic immune-inflammation index, Sarcopenic obesity, Sarcopenia, Obesity, Mediation analysis

## Introduction

With aging, there are noticeable shift in body composition, like the decline in muscle mass, strength, and overall function [1, 2]. After reaching midlife, there is an estimated 1–2% decline in muscle mass each year, resulting in a reported loss of around 50% of muscle mass by the 8th–9th decades of life [3]. Sarcopenia, a prevalent skeletal muscle disorder in aging populations, is marked by the gradual deterioration of muscle function and mass, resulting in various detrimental outcomes such as an elevated risk of falls, fractures, physical impairment [4], more frequent hospitalizations, diminished quality of life, and potentially death. Sarcopenia impacts a quarter to nearly half of people aged 60 and above [5]. If sarcopenia is combined with an increase in fat mass, it is referred to as SO [6]. This dual condition is linked to various negative health outcomes, including complications after surgery, limited physical function, cognitive decline, and higher mortality rates [7–11]. With increasing age, the likelihood of sarcopenia and SO also increases, particularly when other health conditions are present. Studies indicate that sarcopenia is especially prevalent in individuals who have chronic conditions like cardiovascular disease and diabetes [6].

Previous research has suggested that inflammation may contribute to the decline of muscle mass, impacting the function and composition of skeletal muscle [12]. A recent review found that individuals with sarcopenia tend to have higher levels of inflammation markers compared to those with normal muscle [13]. Inflammation in humans can lead to the breakdown of muscle proteins, potentially leading to sarcopenia and SO [13, 14]. Older adults, particularly those with chronic health issues, tend to experience higher levels of inflammation [14]. As such, the prevalence of sarcopenia and SO in this vulnerable population is a major worry. Recognizing how these conditions are linked to inflammation is essential for enhancing healthcare practices and averting muscle deterioration in the elderly demographic.

Recent studies have highlighted the systemic immune-inflammation index (SII) as a reliable indicator of immune response and inflammation in the body [15, 16]. The SII, which was introduced in 2014 by Hu et al., is calculated using easily accessible blood biomarkers including peripheral lymphocyte (LY), neutrophil (NE), and platelet (PLT) counts [17]. This index has been widely used in clinical research and has correlated to various disease such as osteoporosis, long-term mortality, and hepatic steatosis [18, 19].

Furthermore, a systematic review has demonstrated that insulin resistance is the central mechanism of sarcopenic obesity. While the homeostasis model assessment of insulin resistance (HOMA-IR) has traditionally been used to assess insulin sensitivity in clinical settings, the TyG index has been found to be more effective in identifying various insulin-resistance-related conditions such as type 2 diabetes mellitus, arterial stiffness, and non-alcoholic fatty liver disease [20]. Additionally, a recent study indicated a link between elevated TyG levels and low muscle mass in elderly populations, suggesting a potential contribution of TyG to the development of this condition [21]. Moreover, a large cross-sectional study revealed a positive association between the systemic immune-inflammation index (SII) and the TyG index [22]. Several inflammatory cytokines are known to play a key role in the development of insulin resistance, obesity, and insulin resistance caused by obesity. These cytokines include tumor necrosis factor-alpha (TNF-α), interleukin-6, and interleukin-1 [23, 24]. Insulin resistance leads to muscle protein breakdown and loss of muscle mass, as skeletal muscle is the main tissue for insulin-mediated glucose uptake [25]. Additionally, insulin resistance can lead to the accumulation of advanced glycosylation end products in skeletal muscle, which can impair muscle function. Therefore, the TyG index may indirectly impact the relationship between systemic inflammation and sarcopenic obesity.

Despite previous epidemiological research delving into the association between inflammation and low muscle mass, scarce studies explored the association between SII and SO. Therefore, the purpose of this study is to explore the relationship between SII and SO, and to examine the potential mediation of TyG among middle-aged and older adults with a large sample size.

## Materials and methods

The study involved individuals aged 45 years and above who participated in yearly health check-ups at the health check-up center of Wuxi People's Hospital. Initially, a total of 11,089 middle-aged and elderly Chinese adults were included in this retrospective study. Exclusion criteria for participants included incomplete medical information, lack of access to Bioelectronics Impedance Analyzer (BIA), severe cardiac dysfunction or heart failure or acute inflammatory condition (Fig. 1). Following the exclusion of these individuals, 2,719 participants were finally involved in the study, comprising 1,725 males and 994 females aged between 45 and 90 years. This retrospective

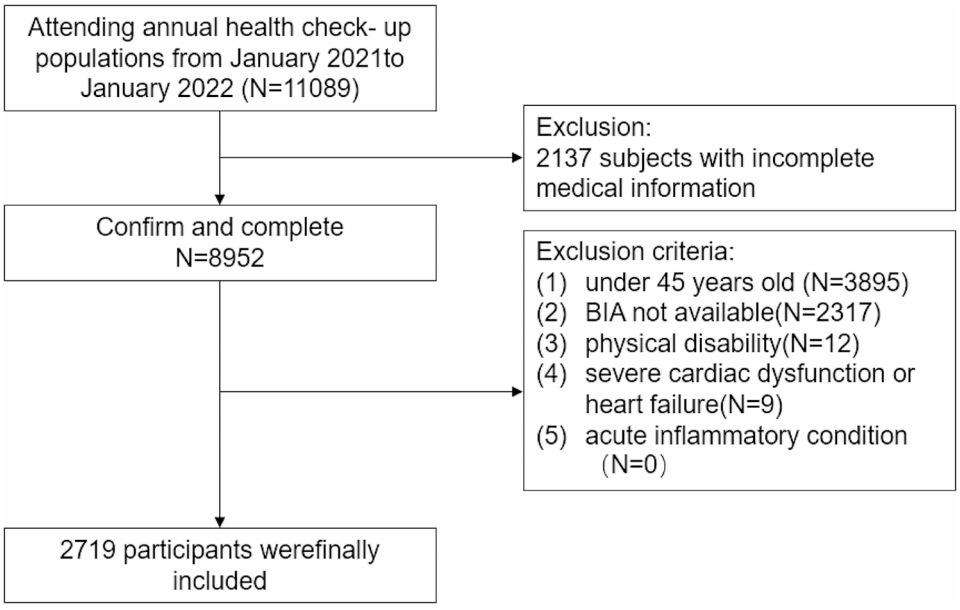


**Fig. 1** Study design flowchart

study followed the Declaration of Helsinki and received approval from the Ethics and Research Committee of the Health Examination Center of Wuxi People's Hospital (approval number. 2022-KY22029). Personal data was anonymized to ensure patient privacy, and statistical analysis was carried out confidentially for scientific purposes. Therefore, the requirement for informed consent was waived.

#### Data measurements

A standard questionnaire was used to collect demographic characteristics such as age, gender, and cigarette/alcohol use. Consuming three or more cigarettes daily for a year was the criteria for defining smoking, whereas drinking at least three times a week for twelve months was considered as alcohol consumption [26]. Following a 12-hour overnight fast, fasting venous blood samples were obtained from all participants. An automatic hematology analyzer was used to measure levels of fasting blood glucose (FBG), platelet counts (PLT), neutrophils (NE), lymphocytes (LY), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C). The laboratory strictly followed quality control procedures, and the systemic immune-inflammation index was calculated by multiplying peripheral platelet counts with neutrophil counts and dividing by lymphocyte counts [17].

Moreover, we gathered health-related data, such as whether individuals had been previously diagnosed with hypertension or diabetes, and if they were currently on any medications. Diabetes was identified by FBG levels≥7.0 mmol/L, the use of insulin or oral hypoglycemic agents for treatment, or a self-reported medical history [27]. Hypertension is diagnosed when the systolic blood pressure (SBP) is 140 mmHg or above, or the diastolic blood pressure (DBP) is 90mmHg or above, and the individual is currently taking antihypertensive medications [28]. Dyslipidemia was defined as having LDL-C≥3.4 mmol/L or TC≥5.2 mmol/L or TG≥1.7 mmol/L or HDL-C<1.0 mmol/L [29]. The physical examination involved taking measurements of height, waist circumference (WC), weight, and blood pressure. Body mass index (BMI) was determined by dividing weight in kilograms by height in meters squared.The calculation formula for the TyG index was as follows: TyG=Ln [fasting triglyceride (mg/dL) × fasting blood glucose (mg/dL)/2]. Systolic and diastolic blood pressure were assessed on the right arm using a sphygmomanometer following a minimum of 5 min of rest, and the mean of two readings was recorded.

We utilized a Bioelectronics Impedance Analyzer (BIA) from Biospace, Korea, to measure appendicular skeletal muscle (ASM) and body fat percentage (BFP). The skeletal muscle mass in each participant was evaluated using the validated equation developed by Janssen et al. [30]. The appendicular skeletal mass index (ASMI) was obtained by dividing ASM by the square of body height ($kg/m^2$). According to the Asian Working Group for Sarcopenia 2019 (AWGS 2019) recommendations, low muscle mass was identified as an ASMI of ≤7.0 $kg/m^2$ for males and ≤5.7 $kg/m^2$ for females [31]. Muscle strength was evaluated using a handgrip dynamometer (EH101, Xiangshan, Guangdong Province, China), and the average grip strength was determined by taking three trials with the dominant hand for the analysis presented. The Asian Working Group on Sarcopenia in Older

People (AWGSOP) established in 2019 that low handgrip strength was characterized by less than 28 kg for men and less than 18 kg for women.

At AWGSOP 2019, it was agreed upon that sarcopenia would be identified in individuals with low muscle mass and low handgrip strength. In contrast, obesity was defined as having a body fat percentage exceeding 25% for men and 30% for women [32]. SO was described as meeting the criteria for sarcopenia along with being obese.

### Statistical analysis

Continuous variables were reported as mean ± standard deviation (SD) or median with interquartile ranges, based on the normal distribution determined by the Kolmogorov–Smirnov test. Meanwhile, categorical variables were displayed as numbers (n) along with their respective percentages (%). Analysis of the data included either one-way ANOVA or Kruskal-Wallis tests for continuous variables, along with chi-square tests for categorical variables. The "P for trend" was calculated by assessing the significance of test for trend on different variables among SII quartiles. To assess the independent relationship between SII and SO, sarcopenia and obesity, multivariable logistic regression analysis was conducted. Two models were used for adjustment: Model 1 included age, sex, BMI, waist circumference (WC), smoking, and drinking; Model 2 added diabetes, hypertension, and dyslipidemia to Model 1. Odds ratios (ORs) and 95% confidence intervals (CIs) were obtained. Furthermore, a restricted cubic spline model was employed to examine potential nonlinear associations between SII and obesity, sarcopenia, and SO in fully adjusted models among middle-aged and older adults, the model was conducted with 4 knots at the 5th, 35th, 65th, 95th percentiles of SII, and the p-value was calculated to determine the nonlinearity of the smooth curve fitting. Stratification analysis was also conducted to explore the relationship between SII and SO among subgroups, based on gender, BMI, WC, drinking, smoking, diabetes, hypertension, and dyslipidemia. Additionally, we carried out a statistical two-way mediation effect model to investigate the direct and indirect relationships between SII and SO, as well as sarcopenia and obesity, through TyG by utilizing the "mediation" R package. Statistical analyses were performed using R software (version 4.0.1). Two-sided p-values were reported, with significance determined at $P<0.05$.

## Results

### Baseline characteristics of participants

Table 1 displays the data of 2719 participants included in the study, with 63.4% being male and 36.6% female. The prevalence of obesity, sarcopenia, and SO among all participants was 48.2%, 8.2%, and 8.4% respectively.

**Table 1** Baseline characteristics of study populations ($n=2719$)

| Variables | Overall ($n=2719$) | Control ($n=956$) | Obesity ($n=1313$) | Sarcopenia ($n=222$) | Sarcopenic obesity ($n=228$) | *P*-value |
|---|---|---|---|---|---|---|
| Age (years) | 56.26 ± 8.36 | 53.91 ± 7.04 | 56.96 ± 8.20 | 56.09 ± 8.31 | 62.23 ± 10.57 | < 0.001 |
| Male (n, %) | 1,725 (63.4%) | 490 (51.3%) | 996 (75.9%) | 89 (40.1%) | 150 (65.8%) | < 0.001 |
| Smoking (n, %) | 923 (33.9%) | 249 (26.0%) | 559 (42.6%) | 46 (20.7%) | 69 (30.3%) | < 0.001 |
| Drinking (n, %) | 548 (20.2%) | 138 (14.4%) | 341 (26.0%) | 28 (12.6%) | 41 (18.0%) | < 0.001 |
| BMI (kg/m$^2$) | 24.73 ± 2.99 | 23.28 ± 1.91 | 26.75 ± 2.43 | 20.48 ± 1.38 | 23.28 ± 1.79 | < 0.001 |
| WC (cm) | 87.81 ± 8.96 | 82.79 ± 5.79 | 93.83 ± 7.40 | 76.54 ± 4.38 | 85.12 ± 6.07 | < 0.001 |
| SBP (mmHg) | 126.03 ± 16.00 | 122.96 ± 15.69 | 128.99 ± 15.55 | 119.83 ± 15.35 | 127.86 ± 16.48 | < 0.001 |
| DBP (mmHg) | 75.77 ± 10.37 | 73.43 ± 10.15 | 78.03 ± 10.21 | 72.41 ± 9.31 | 75.89 ± 10.14 | < 0.001 |
| FPG (mmol/L) | 5.34 (5.02, 5.85) | 5.22 (4.94, 5.60) | 5.49 (5.12, 6.13) | 5.10 (4.83, 5.45) | 5.47 (5.06, 6.11) | < 0.001 |
| Diabetes (n, %) | 287 (10.6%) | 58 (6.1%) | 181 (13.8%) | 16 (7.2%) | 32 (14.0%) | < 0.001 |
| Hypertension (n, %) | 478 (17.6%) | 131 (13.7%) | 287 (21.9%) | 19 (8.6%) | 41 (18.0%) | < 0.001 |
| Dyslipidemia (n, %) | 1,201 (44.2%) | 369 (38.6%) | 632 (48.1%) | 100 (45.0%) | 100 (43.9%) | < 0.001 |
| TG (mmol/L) | 1.36 (0.98, 1.99) | 1.23 (0.87, 1.73) | 1.58 (1.13, 2.26) | 0.99 (0.77, 1.40) | 1.42 (1.06, 1.88) | < 0.001 |
| TC (mmol/L) | 4.92 (4.34, 5.55) | 4.86 (4.34, 5.46) | 4.92 (4.32, 5.57) | 5.18 (4.55, 5.71) | 4.96 (4.36, 5.57) | 0.004 |
| LDL-C (mmol/L) | 3.21 (2.65, 3.76) | 3.15 (2.60, 3.68) | 3.24 (2.67, 3.79) | 3.25 (2.74, 3.78) | 3.35 (2.66, 3.84) | 0.088 |
| HDL-C (mmol/L) | 1.24 (1.04, 1.49) | 1.31 (1.11, 1.57) | 1.16 (0.99, 1.35) | 1.53 (1.29, 1.83) | 1.25 (1.05, 1.46) | < 0.001 |
| NE count (×10$^9$/L) | 3.22 (2.61, 3.93) | 3.07 (2.46, 3.77) | 3.33 (2.75, 4.03) | 2.85 (2.34, 3.66) | 3.35 (2.71, 4.10) | < 0.001 |
| LY count (×10$^9$/L) | 2.08 (1.73, 2.51) | 1.97 (1.67, 2.36) | 2.20 (1.84, 2.64) | 1.98 (1.59, 2.37) | 2.06 (1.65, 2.46) | < 0.001 |
| TyG | 7.24 ± 0.64 | 7.02 ± 0.62 | 7.35 ± 0.61 | 7.35 ± 0.62 | 7.40 ± 0.64 | < 0.001 |
| SII | 323.05(241.85, 428.95) | 293.78(218.73, 398.71) | 327.72(252.32, 427.47) | 344.87(240.63, 456.83) | 384.11(306.03, 523.10) | < 0.001 |

Continuous variables were described as mean ± standard deviation or median (interquartile) or number (proportion, %) IQR interquartile range, P values are calculated by One-way ANOVA or Kruskal-Wallis test for continuous variables, Chi-square test for categorical variables. BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, high-density lipoprotein cholesterol; NE, neutrophil; LY, lymphocyte; TyG, triglyceride-glucose index; SII, systemic immune-inflammation index

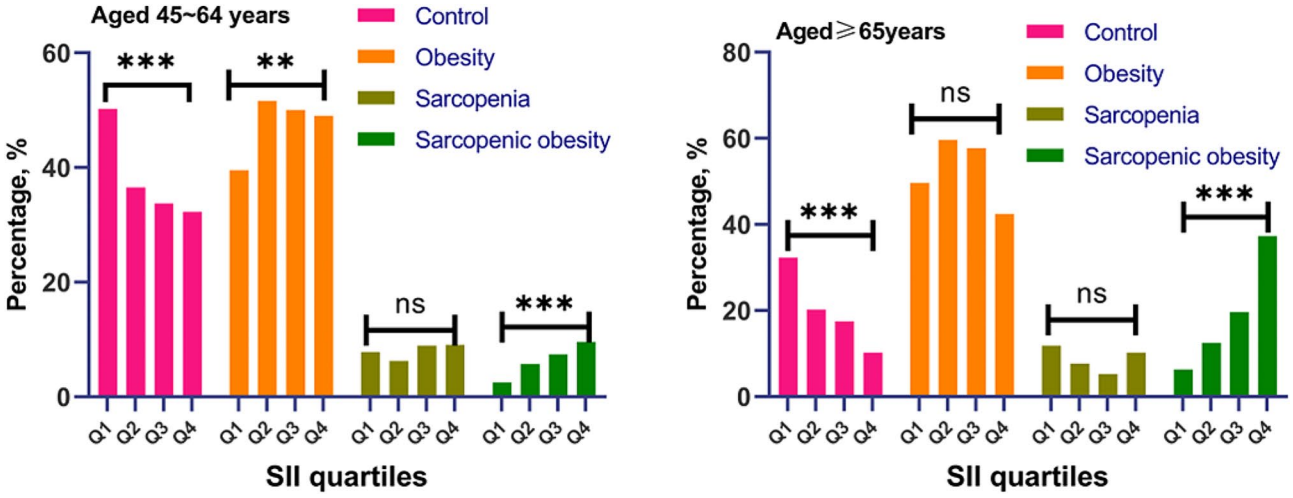


**Fig. 2** Incidence of obesity, sarcopenia, and sarcopenic obesity among SII quartiles separately in middle-aged and older adults. **, P for trend<0.01; ***, P for trend<0.001; ns, no significance

**Table 2** Patient demographics and baseline characteristics according to SII quartiles

| Variables | SII quartiles | | | | *P*-value | *P* for trend |
|---|---|---|---|---|---|---|
| | Q1 (*n* = 679) | Q2 (*n* = 680) | Q3 (*n* = 681) | Q4 (*n* = 679) | | |
| Age(years) | 55.87 ± 9.00 | 55.68 ± 8.27 | 56.23 ± 8.15 | 57.26 ± 7.92 | 0.002 | < 0.001 |
| Male (n, %) | 360 (53.0%) | 437 (64.3%) | 471 (69.2%) | 457 (67.3%) | < 0.001 | < 0.001 |
| BMI (kg/m$^2$) | 24.44 ± 2.92 | 24.86 ± 3.06 | 24.95 ± 3.01 | 24.66 ± 2.92 | 0.009 | 0.158 |
| WC (cm) | 86.68 ± 8.55 | 88.32 ± 9.46 | 88.47 ± 8.91 | 87.76 ± 8.79 | < 0.001 | 0.028 |
| Smoking (n, %) | 179 (26.4%) | 240 (35.3%) | 240 (35.2%) | 264 (38.9%) | < 0.001 | < 0.001 |
| Drinking (n, %) | 100 (14.7%) | 149 (21.9%) | 160 (23.5%) | 139 (20.5%) | < 0.001 | 0.006 |
| Diabetes (n, %) | 58 (8.5%) | 61 (9.0%) | 72 (10.6%) | 96 (14.1%) | 0.003 | < 0.001 |
| Hypertension (n, %) | 117 (17.2%) | 108 (15.9%) | 132 (19.4%) | 121 (17.8%) | 0.397 | 0.419 |
| Dyslipidemia (n, %) | 301 (44.3%) | 306 (45.0%) | 313 (46.0%) | 281 (41.4%) | 0.359 | 0.356 |
| NE count (×10$^9$/L) | 2.56 (2.10, 3.10) | 3.01 (2.56, 3.60) | 3.38 (2.90, 4.00) | 4.01 (3.36, 4.88) | < 0.001 | < 0.001 |
| LY count (×10$^9$/L) | 2.34 (2.00, 2.78) | 2.16 (1.84, 2.58) | 2.03 (1.72, 2.44) | 1.77 (1.50, 2.17) | < 0.001 | < 0.001 |
| TyG | 7.16 ± 0.62 | 7.21 ± 0.61 | 7.29 ± 0.65 | 7.29 ± 0.66 | < 0.001 | < 0.001 |

Significant differences were observed in baseline characteristics such as age, sex, smoking, drinking, BMI, WC, SBP, DBP, diabetes, hypertension, TG, TC, HDL-C, dyslipidemia, NE, LY, TyG index and SII across groups (all $P$<0.01), with no significant difference in LDL-C levels ($P$=0.088). Additionally, the incidence of SO increased with higher SII quartiles in all subjects ($P_{trend}$ <0.001), as illustrated in Fig. 2. Additionally, Table 2 displayed the baseline characteristics of the study population among groups divided by SII quartiles. Dividing the data into four quartile groups: the first group (Q1, $n$=679; SII≤241.85), the second group (Q2, $n$=680; 241.86<SII≤323.05), the third group (Q3, $n$=681; 323.06<SII≤428.95), and the fourth group (Q4, $n$=679; SII>428.95).

The analysis showed that there were statistically significant differences in age, BMI, waist circumference (WC), neutrophil count, lymphocyte count and TyG index across the SII quartiles (all $P$<0.01). Additionally, the distribution of sex, smoking, drinking, and diabetes varied significantly among the quartiles with p-values<0.01. Specifically, individuals in the fourth group tended to be older, male, and have higher levels of WC, neutrophil count, lymphocyte count and TyG index than the Q1 group ( $P_{trend}$<0.05). Furthermore, the proportion of smoking, drinking, and diabetes increased gradually with higher levels of SII (all $P_{trend}$<0.01).

### Dose-response relationship

We utilized restricted cubic spline to analyze and illustrate the associations of SII and obesity, sarcopenia, and SO in middle aged and older Chinese adults (Fig. 3). Even after accounting for confounders such as age, gender, BMI, WC, smoking, drinking, diabetes, hypertension, and dyslipidemia, there was a clear positive association between elevated SII values and the risk of obesity and SO in all participants (all $P_{overall}$ <0.01). In addition, the risk of sarcopenia was found to be higher in individuals

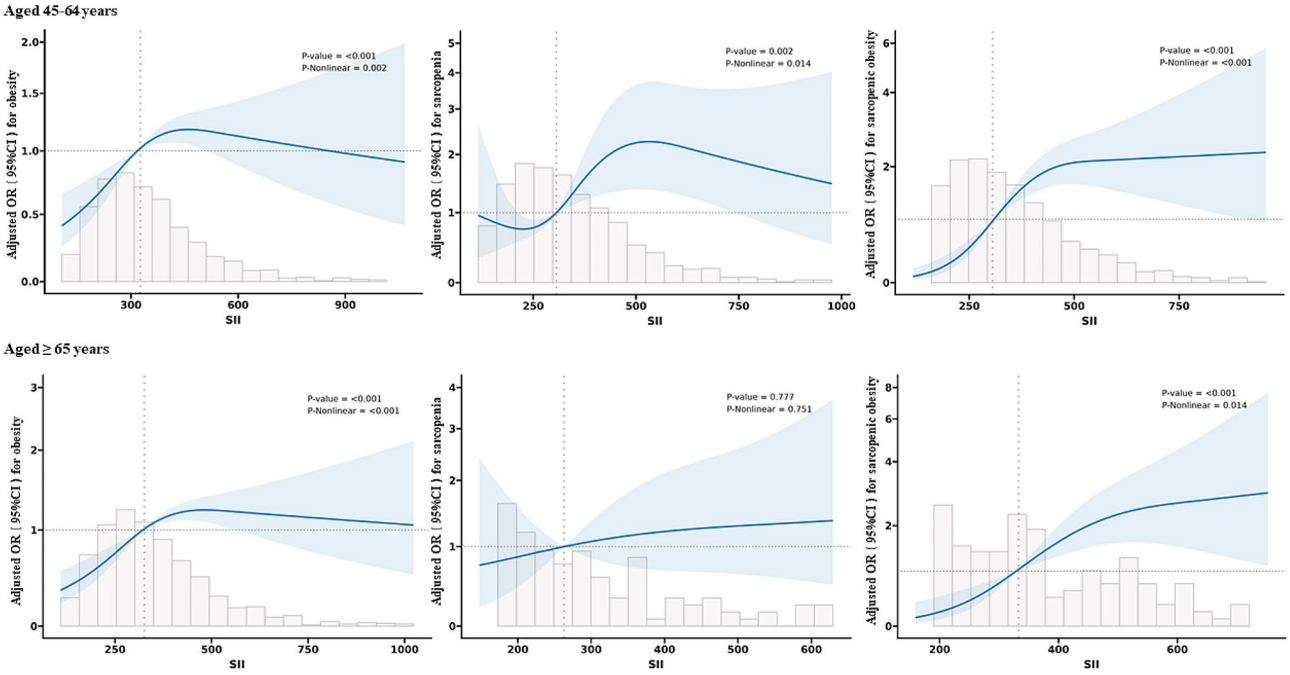


**Fig. 3** The smooth curve fitting between SII and obesity, sarcopenia, and sarcopenic obesity separately in middle-aged and older adults

aged 45 to 64 years with an elevated SII, but not in those over 65 years old. Nonlinear relationships were seen between SII and obesity, as well as SO, in all groups (all $P_{nonlinear}$ <0.01). Conversely, a linear connection between SII and sarcopenia was noted in older adults, while no such relationship was observed in middle-aged individuals. Besides, we also conducted adjusted restricted cubic spline models in relation to SII, ASMI and handgrip in all participants (Fig. 4), there were significantly negative associations between SII and ASMI and handgrip strength (all P overall <0.01). In middle-aged subjects, a significantly nonlinear relationship between SII and ASMI was discovered ($P_{nonlinear}$ =0.013). However, this nonlinear relationship was not observed in elderly subjects. Additionally, there was a linear relationship between SII and handgrip strength in all participants (all $P_{nonlinear}$ >0.05).

### Multivariable logistic analysis

After adjusting for all confounders, the results of multivariable logistic regression showed that SII (per SD increase) was positively associated with obesity [OR=1.21, 95% CI: 1.05 ~ 1.38], sarcopenia [OR=1.35, 95% CI: 1.11 ~ 1.64], and SO [OR=1.69, 95% CI: 1.43 ~ 1.99] in middle-aged populations. In older adults, the odds ratios (95% CI) for obesity and SO were "1.65 (95% CI: 1.13 ~ 2.17)" and "2.52 (95% CI: 1.68 ~ 3.77)", respectively (Table 3). In middle-aged populations, the risk of sarcopenia increased with elevated SII (OR=1.35, 95% CI: 1.11 ~ 1.64), but this association was not observed in older adults (OR=1.90, 95% CI: 0.93 ~ 3.27). When the SII was categorized into quartiles for sensitivity analysis, the fourth quartile had the highest adjusted ORs (95% CI) for obesity [1.89 (1.31 ~ 2.72)], sarcopenia [2.14(1.21 ~ 3.77)], and SO [8.51(4.43 ~ 16.37)] in middle-aged adults compared to the lowest quartile. Among older adults, the ORs (95% CI) for obesity and SO in the fourth quartile were 3.20(1.22 ~ 8.34) and 24.20(7.99 ~ 73.29) respectively, compared to the first quartile of SII. Moreover, the risk of SO, sarcopenia, and obesity among older subjects was found to be more significant than that among middle-aged subjects when considering the fourth quartile of SII in fully adjusted models (all $P_{interaction}$<0.001). Additionally, the findings from the generalized linear regression analysis revealed a significant negative association between the highest quartile of SII and both ASMI and handgrip strength when compared to the lowest quartile of SII in middle-aged and elderly individuals. This association remained steady across different models.

### Subgroup analysis

Subgroup analysis was conducted to determine the reliability of our findings within each group, and the detailed subgroup results were described in Table 4. The results remained consistent cross all subgroups. Additionally, the interaction test revealed that sex, BMI, smoking, drinking, hypertension, and dyslipidemia did not have a significant impact on the association (all $P_{interaction}$>0.05). Stronger associations between SII level and SO were noted in individuals with abnormal WC ($P_{interaction}$<0.01).

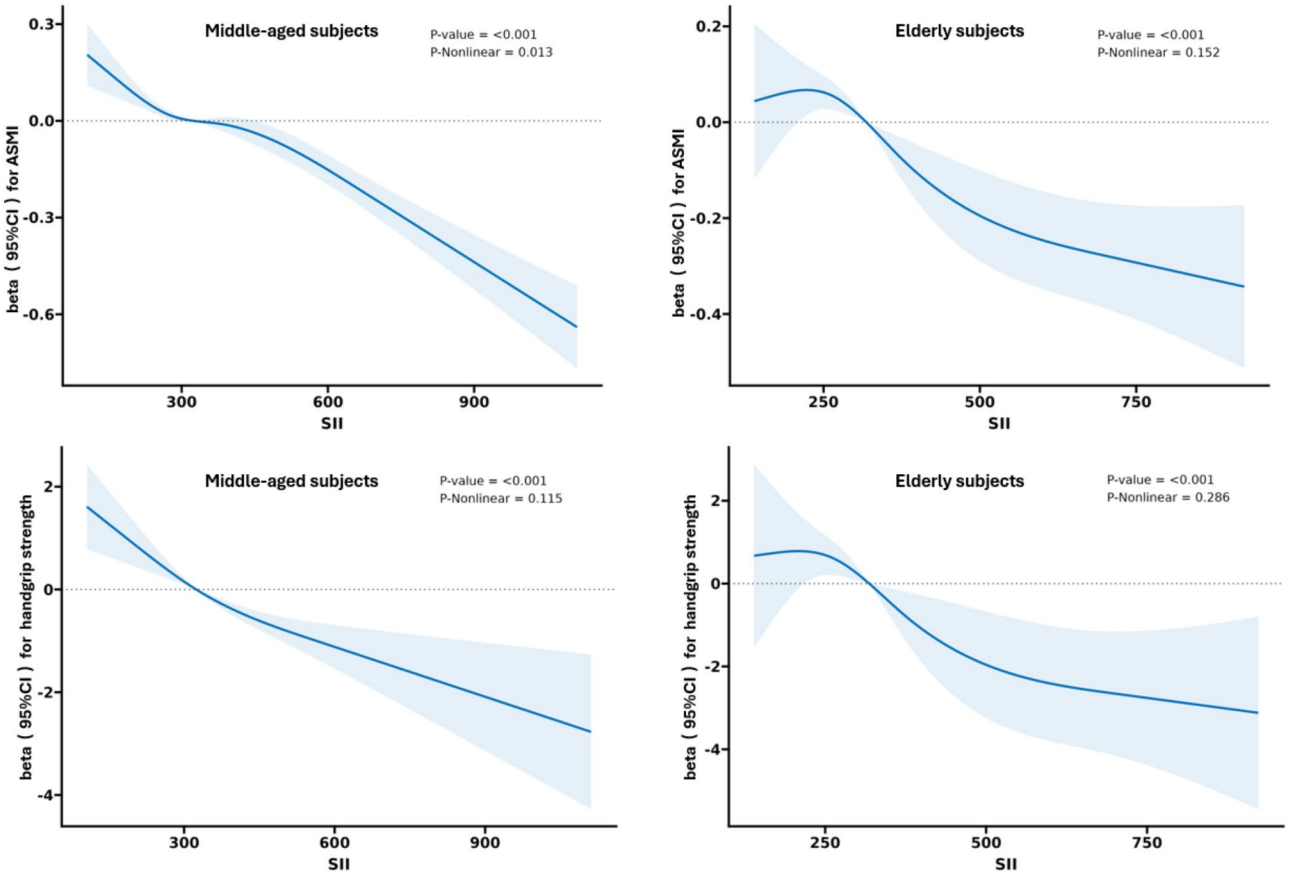


**Fig. 4** Analysis of adjusted restricted cubic spline model in relation to SII, ASMI and handgrip strength in middle-aged and older adults. Solid and long dashed lines represent the estimated regression coefficient Beta and its 95% confidence interval

**Table 3** Odds ratios (95% CI) for obesity, Sarcopenia, and sarcopenic obesity in relation to SII quartiles in all participants

| | Model 1 [OR (95% CI)] | | | Model 2 [OR (95% CI)] | | |
|---|---|---|---|---|---|---|
| | **Obesity** | **Sarcopenia** | **Sarcopenic obesity** | **Obesity** | **Sarcopenia** | **Sarcopenic obesity** |
| **Aged 45 ~ 64 years** | | | | | | |
| SII (Per SD increase) | 1.21(1.06 ~ 1.39) * | 1.34(1.10 ~ 1.64) * | 1.68(1.42 ~ 1.98) ** | 1.21(1.05 ~ 1.38) * | 1.35(1.11 ~ 1.64) * | 1.69(1.43 ~ 1.99) ** |
| SII quartiles | | | | | | |
| Q4 | 1.89(1.31 ~ 2.72) *** | 2.11(1.20 ~ 3.72) ** | 8.38(4.37 ~ 16.05) *** | 1.89(1.31 ~ 2.72) ** | 2.14(1.21 ~ 3.77) ** | 8.51(4.43 ~ 16.37) *** |
| Q3 | 1.53(1.07 ~ 2.20) * | 2.32(1.34 ~ 4.01) ** | 5.60(2.90 ~ 10.81) *** | 1.53(1.07 ~ 2.20) * | 2.29(1.32 ~ 3.98) ** | 5.61(2.90 ~ 10.83) *** |
| Q2 | 1.62(1.13 ~ 2.31) * | 0.82(0.45 ~ 1.49) | 3.61(1.84 ~ 7.07) ** | 1.61(1.13 ~ 2.31) * | 0.82(0.45 ~ 1.49) | 3.61(1.84 ~ 7.10) *** |
| Q1 | 1.00(reference) | 1.00(reference) | 1.00(reference) | 1.00(reference) | 1.00(reference) | 1.00(reference) |
| **Aged ≥ 65 years** | | | | | | |
| SII (Per SD increase) | 1.42(0.95 ~ 2.12) | 1.85(1.07 ~ 3.18) * | 2.43(1.64 ~ 3.61) ** | 1.65(1.13 ~ 2.17) * | 1.90(0.93 ~ 3.27) | 2.52(1.68 ~ 3.77) ** |
| SII quartiles | | | | | | |
| Q4 | 3.04(1.18 ~ 7.81) * | 4.01(0.93 ~ 17.29) | 21.34(7.33 ~ 62.18) *** | 3.20(1.22 ~ 8.34) * | 4.76(0.98 ~ 23.10) | 24.20(7.99 ~ 73.29) *** |
| Q3 | 2.86(1.19 ~ 6.92) * | 0.52(0.09 ~ 3.03) | 5.65(1.94 ~ 16.52) *** | 2.83(1.16 ~ 6.92) * | 0.42(0.07 ~ 2.63) | 6.04(2.03 ~ 18.00) *** |
| Q2 | 2.53(1.09 ~ 5.86) * | 1.28(0.28 ~ 5.81) | 3.51(1.17 ~ 10.47) * | 2.47(1.06 ~ 5.74) * | 1.14(0.24 ~ 5.38) | 3.61(1.20 ~ 10.88) * |
| Q1 | 1.00(reference) | 1.00(reference) | 1.00(reference) | 1.00(reference) | 1.00(reference) | 1.00(reference) |
| $P_{for\ interaction}$ | < 0.001 | | | 0.024 | | |

Model 1: Adjusted for age, sex, BMI, WC, smoking, drinking

Model 2: Model 1 + adjustment for diabetes, hypertension, and dyslipidemia. *$P$ < 0.05, **$P$ < 0.01, ***$P$ < 0.001

**Table 4** Subgroup analysis of the association between SII (per SD increase) and obesity, Sarcopenia, and sarcopenic obesity

| Subgroup | Adjusted OR (95% CI) | | | *P* for interaction |
|---|---|---|---|---|
| | Obesity | Sarcopenia | Sarcopenic obesity | |
| **Sex** | | | | 0.486 |
| Male | 1.19(1.01 ~ 1.40) * | 1.61(1.21 ~ 2.14) ** | 1.77(1.45 ~ 2.16) *** | |
| Female | 1.29(1.04 ~ 1.59) * | 1.35(1.05 ~ 1.74) * | 1.88(1.50 ~ 2.36) *** | |
| **BMI (kg/m$^2$)** | | | | 0.622 |
| <24 | 1.11(0.89 ~ 1.39) | 1.37(1.17 ~ 1.60) *** | 1.64(1.38 ~ 1.95) *** | |
| ≥ 24 | 1.28(1.10 ~ 1.48) ** | 1.61(1.11 ~ 2.14) ** | 1.97(1.56 ~ 2.50) *** | |
| **WC (cm)** | | | | 0.004 |
| male<90/female<85 | 1.07(0.89 ~ 1.28) | 1.34(1.11 ~ 1.61) * | 1.64(1.38 ~ 1.95) *** | |
| male ≥ 90/female ≥ 85 | 1.51(1.21 ~ 1.88) ** | 1.65(1.22 ~ 2.14) ** | 2.38(1.78 ~ 3.18) *** | |
| **Smoking** | | | | 0.522 |
| No | 1.21(1.04 ~ 1.41) * | 1.38(1.11 ~ 1.70) * | 1.72(1.45 ~ 2.04) *** | |
| Yes | 1.26(1.01 ~ 1.59) * | 1.55(1.05 ~ 2.28) * | 2.09(1.56 ~ 2.78) *** | |
| **Drinking** | | | | 0.727 |
| No | 1.21(1.05 ~ 1.39) | 1.40(1.14 ~ 1.71) * | 1.68(1.43 ~ 1.98) *** | |
| Yes | 1.32(0.97 ~ 1.81) | 1.32(0.83 ~ 2.11) | 2.77(1.88 ~ 4.08) *** | |
| **Hypertension** | | | | 0.990 |
| No | 1.18(1.03 ~ 1.36) * | 1.37(1.13 ~ 1.65) * | 1.73(1.48 ~ 2.03) *** | |
| Yes | 1.52(1.06 ~ 2.20) * | 1.56(0.75 ~ 3.27) | 2.30(1.51 ~ 3.49) *** | |
| **Diabetes** | | | | 0.630 |
| No | 1.23(1.08 ~ 1.41) * | 1.38(1.14 ~ 1.67) * | 1.89(1.62 ~ 2.21) *** | |
| Yes | 1.01(0.69 ~ 1.47) | 1.64(1.09 ~ 2.28) * | 2.34(1.64 ~ 3.47) *** | |
| **Dyslipidemia** | | | | 0.139 |
| No | 1.25(1.05 ~ 1.48) * | 1.38(1.11 ~ 1.72) * | 1.94(1.61 ~ 2.34) *** | |
| Yes | 1.17(0.97 ~ 1.41) | 1.47(1.08 ~ 2.00) * | 1.61(1.26 ~ 2.04) *** | |

*Note* Adjusted for age, sex, BMI, WC, smoking, drinking, diabetes, hypertension, and dyslipidemia. *$P$<0.05, **$P$<0.01, ***$P$<0.001

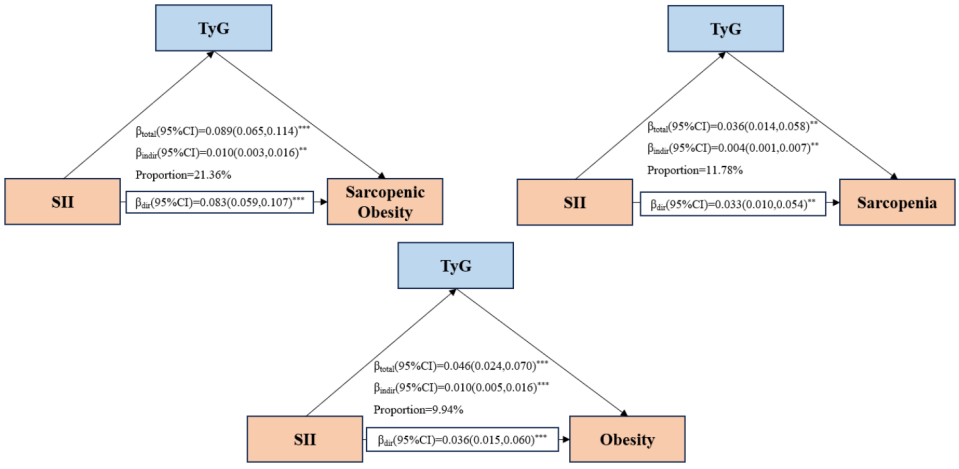


**Fig. 5** Mediation analyses of the association between SII and sarcopenic obesity, sarcopenia and obesity through TyG: adjusted for age, sex, BMI, WC, smoking, drinking, diabetes, hypertension, and dyslipidemia

### Bidirectional mediation analysis through TyG

The study examined the bidirectional mediation effects of SII and TyG on their relationships with SO, sarcopenia, and obesity in all participants. Figure 5 demonstrates how TyG acts as a mediator in the relationship between SII and SO, as well as between sarcopenia and obesity. The results revealed a significant indirect effect of SII on the risk of SO, sarcopenia, and obesity through TyG (all P values < 0.05). TyG was found to mediate 21.36%, 11.78%, and 9.94% of the associations between SII and SO, sarcopenia, and obesity, respectively. Additionally, as depicted in Fig. 6, TyG had a significant direct effect on the risk of SO, sarcopenia, and obesity (all P values < 0.001), with no significant mediation effect observed between TyG and SO, sarcopenia, and obesity through SII (all P values > 0.05). Moreover, there was no significant interaction

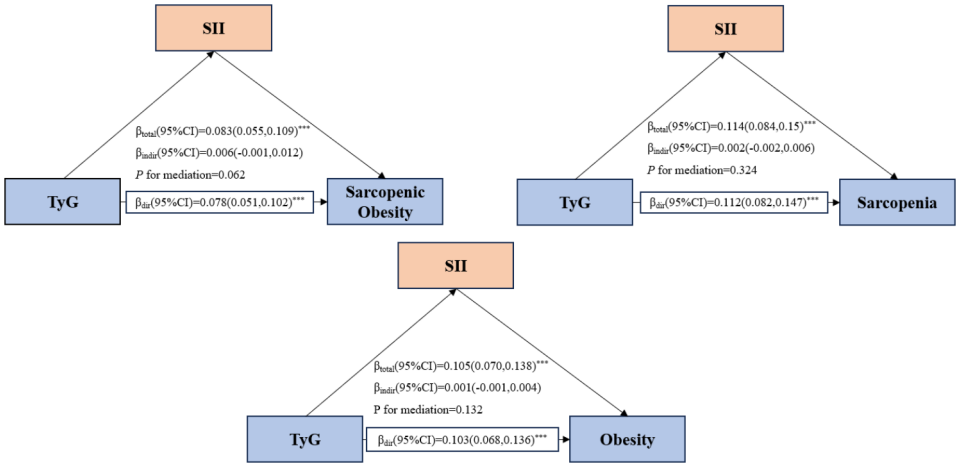


**Fig. 6** Mediation analyses of the association between TyG and sarcopenic obesity, sarcopenia and obesity through SII: adjusted for age, sex, BMI, WC, smoking, drinking, diabetes, hypertension, and dyslipidemia

effect between SII and TyG in SO ($P_{interaction}$ =0.544), sarcopenia ($P_{interaction}$ =0.908), and obesity ($P_{interaction}$ =0.416).

## Discussion

In this cross-sectional study, we examined the relationship between SII and SO in middle-aged and older adults. Our findings revealed a rise in SO cases as SII quartiles increased ($P_{for\ trend}$<0.001). The results showed a positive non-linear relationship between SII and SO in middle-aged subjects (OR=1.69,95% CI: 1.43 ~ 1.99) and elderly individuals (OR=2.52, 95% CI: 1.68 ~ 3.77), with a stronger association observed in the elderly population, indicating that individuals who have high levels of systemic inflammation may be more likely to develop SO in comparison to those with lower inflammation levels. Moreover, there were negatively association between SII and ASMI and handgrip in all participants. Besides, the interaction tests show that the relationship between elevated SII values and the risk of SO remains consistent regardless of sex, BMI, smoking, drinking, hypertension, diabetes, and dyslipidemia. Furthermore, in bidirectional mediation analysis, it is evident that TyG acts as a partial mediator in the link between SII and SO. TyG also influences the risk of SO directly, without the involvement of SII.

SO is characterized by both reduced skeletal muscle mass and excessive adiposity [6]. A chronic pro-inflammatory state is commonly found in both obesity and sarcopenia, potentially disrupting metabolic processes and impacting the function of adipose tissue and muscles [14, 33, 34]. It is acknowledged that either low muscle mass and strength or obesity can each individually lead to a decline in physical capacity and quality of life [35]. Hence, it can be inferred that the combination of muscle damage and obesity may have a compounding impact on the likelihood of mortality, metabolic disorders, and overall well-being [36]. A meta-analysis of 23 prospective studies showed that SO increases the risk of all-cause mortality in adults (pooled HR=1.21, 95% CI: 1.01 ~ 1.32), particularly in hospitalized older adults [37]. Additionally, research has indicated that individuals with SO exhibit higher waist circumference, elevated insulin resistance, increased blood pressure, fasting blood glucose, and dyslipidemia when compared to individuals with sarcopenia or obesity alone [38, 39]. Furthermore, previous research has highlighted the various complications associated with SO, which is considered a significant risk factor for disability, frailty, and cardiometabolic diseases, particularly in older populations [40, 41]. The loss of muscle mass and the accumulation of excess fat may have similar underlying risk factors and can exacerbate each other's effects. Additionally, the combination of sarcopenia and obesity can lead to more harmful metabolic consequences than either condition alone. Despite having similar body mass index or waist circumference, individuals with sarcopenia have been found to have a more significant effect on cardiovascular disease than those without sarcopenia [42].

Many studies have explored the relationship between inflammation and muscle metabolism, but the exact mechanisms of this process are not fully understood. Previous research has shown that chronic inflammation is linked to decreased skeletal muscle mass and function [13]. Inflammation is closely associated with apoptosis, as laboratory studies have shown that tumor necrosis factor-α (TNF-α), a marker of systemic inflammation, rises with age and is correlated with muscle atrophy and cell depletion in rats [43]. TNF-α hinders the synthesis of muscle proteins by regulating the PI3K/Akt/mTOR signalling pathway. This leads to muscle atrophy as it stimulates the expression of muscle growth inhibitory factors such as atrogin-1, NF-κB, and myostatin [44, 45]. Muscle mass is maintained through a delicate equilibrium

between protein synthesis and degradation, but pro-inflammatory agents like TNF-α can disrupt this balance and promote protein degradation in skeletal muscle. Studies have indicated that individuals with low muscle mass display elevated TNF-α levels when compared to those in the control group [46]. Moreover, prior studies have indicated that individuals who exhibit elevated levels of systemic inflammation tend to possess a greater fat mass [47]. Schrager et al. found that excessive visceral fat was linked to increased inflammatory markers, reduced muscle strength, and the development of SO [48]. Our study also found that the relationship between systemic inflammation and SO was influenced by waist circumference (WC). This association was stronger in individuals with abnormal WC compared to those with normal WC ($P_{interaction}$<0.01), indicating that abnormal accumulation of visceral fat may worsen the inflammatory response.

Determined through the evaluation of lymphocytes, neutrophils, and platelets in the peripheral blood, SII acts as a comprehensive inflammatory index that provides insight into the immune and inflammatory status of the host [49]. Consequently, the data acquisition and calculation of SII yield benefits in terms of accuracy, objectivity, efficiency, and ease of implementation. Elevated SII values suggest a rise in platelet and neutrophil counts, coupled with an increase in various cytokine levels or a decrease in lymphocyte counts. The drop in lymphocytes during inflammation can trigger an increase in the production of oxidative stress, proinflammatory cytokines and cell apoptosis [50], potentially worsening inflammation and playing a role in disease progression. As people age, they often experience higher levels of inflammatory markers and factors, and conditions like sarcopenia or SO are considered age-related diseases [51]. Elevated levels of inflammation and oxidative stress are thought to play a significant role in the development of sarcopenia in middle-aged and elderly individuals [52]. Among non-elderly populations in the US, the SII may be a useful tool for identifying subjects at risk of sarcopenia, and further research is needed to explore SII as a biomarker for this condition [53].

The results of the study revealed that TyG plays a role in mediating the relationship between SII and SO, sarcopenia, and obesity, accounting for 21.36%, 11.78%, and 9.94% respectively., while relationships between TyG and SO, sarcopenia and obesity were not mediated by SII. Factors such as physical inactivity, insulin resistance, oxidative stress, and chronic inflammation are known risk factors for SO [54]. Studies have shown that proinflammatory molecules can induce obesity-associated insulin resistance by affecting cytokine receptors and insulin receptor signaling pathways [55, 56]. Additionally, intramuscular fat infiltration has been linked to insulin resistance in obese individuals [57, 58]. TyG, a reliable indicator of insulin resistance, may be a useful marker for sarcopenic obesity in older adults. Systemic inflammation, characterized by elevated levels of inflammatory cytokines like TNF-α, IL-6, and CRP, can lead to insulin resistance in tissues such as skeletal muscle and adipose tissue [59]. This insulin resistance can disrupt the balance of muscle tissue, causing a loss of muscle protein and a decrease in muscle mass [60]. Additionally, insulin resistance in adipose tissue can increase lipolysis, releasing free fatty acids into the bloodstream. These fatty acids can contribute to ectopic fat deposition in tissues like muscle, further worsening insulin resistance [61]. This cycle of events can also trigger the production of more inflammatory cytokines, creating a loop that sustains systemic inflammation and insulin resistance. In sarcopenic obesity, the loss of muscle mass is accompanied by an increase in adiposity. Systemic inflammation-induced insulin resistance can promote fat accumulation by affecting adipose tissue function and impairing lipolysis [62]. The interaction between muscle and adipose tissue in the context of insulin resistance and systemic inflammation likely plays a role in the development and progression of SO. In conclusion, systemic inflammation impacts SO by reducing insulin sensitivity, which in turn affects muscle protein metabolism and adipose tissue function, resulting in a decrease in muscle mass and an increase in fat mass.

There are several limitations that need to be addressed in our study. Firstly, the study's cross-sectional design prevented us from determining a causal relationship between exposure and outcome. Therefore, a high-quality prospective study is necessary to further investigate this relationship. Secondly, we used BIA instead of the "gold standard" devices (computed tomography, dual-energy x-ray, or magnetic resonance imaging) for estimating muscle mass. However, BIA has been found to be comparable to DXA and is recommended as an alternative option for measuring muscle mass by AWGS 2019 [62]. Finally, despite adjusting for several confounding factors, there may still be other factors such as dietary patterns or physical activity that could impact the results.

## Conclusion

To summarize, this cross-sectional study found a relationship between elevated SII levels and an increased risk of SO in middle-aged and older adults. The analysis also revealed that this relationship is partially influenced by TyG, indicating that TyG may be a potential influencing factor in the association between systemic inflammation and SO.

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**Author contributions**
The original manuscript writing was carried out by XW and YJ, with XW also responsible for the statistical analysis. RW and HY were assigned to validate the statistical analysis results. SL and XC played crucial roles in the study design and manuscript revision. All authors participated in the final manuscript review and approval.

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**Data availability**
The data generated and analyzed in the current study are not publicly available due to privacy and ethical limitations, but can be requested from the corresponding authors upon reasonable request.

## Declarations

**Ethics approval and consent to participate**
This study was carried out following the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of the Affiliated Health Examination Center of Wuxi People's Hospital, Nanjing Medical University (approval number. 2022-KY22029). Informed consent was not required due to the retrospective nature of the study.

**Consent for publication**
Not applicable.

**Competing interests**
The authors have disclosed that they have no conflicts of interest in this work.

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