

Association Between Sarcopenia Index and Central Obesity: Age- and Gender-Specific Patterns and Clinical Implications

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Background: Central obesity is a major contributor to cardiometabolic diseases. The sarcopenia index (SI), derived from serum creatinine and cystatin C, is a biomarker reflecting muscle mass, but its relationship with obesity phenotypes across age and sex remains unclear.

Objective: To examine the association between SI and central versus peripheral obesity, determine whether SI is independently associated with central obesity, and identify optimal SI cut-off values in a large Chinese population.

Methods: This retrospective cross-sectional study analyzed 10,054 adults undergoing health examinations at Xiamen Chang Gung Hospital. Anthropometric data, biochemical profiles, and body composition by bioelectrical impedance analysis were collected. Participants were categorized as non-obese, peripheral obese, or central obese based on body fat percentage and visceral fat degree. Logistic regression assessed associations between SI tertiles and central obesity stratified by age and sex. Receiver operating characteristic (ROC) curves determined optimal SI cut-off values.

Results: Central obesity was present in 24.4% of participants and correlated with adverse cardiometabolic profiles. Individuals with central obesity exhibited lower SI levels, most notably in men <50 years and women ≥50 years. After multivariable adjustment, the lowest SI tertile was independently associated with central obesity in younger men (adjusted OR 1.27; 95% CI 1.06–1.52) and older women (adjusted OR 3.03; 95% CI 2.04–4.50). SI demonstrated moderate discriminatory ability in women (AUC 0.687; optimal cut-off 79.52) but limited performance in men (AUC 0.534; cut-off 96.60).

Conclusion: Lower SI is independently associated with a higher prevalence of central obesity, particularly among younger men and older women. SI may provide a simple and practical supplementary marker for identifying individuals at risk of central adiposity, especially in women. Prospective studies are needed to validate its predictive utility.

Keywords: central obesity, sarcopenia index, cystatin C, visceral adiposity, age-specific patterns

Introduction

Recently, the negative impact of obesity on physical health has received increasing attention. According to the Global Burden of Disease Obesity Collaborators, the worldwide population of obese individuals reached 603.7 million, with obesity prevalence doubling in over 70 countries since 1980.¹ Obesity, particularly central obesity, is associated with an elevated risk of several chronic diseases, such as diabetes, hypertension, hyperlipidemia, non-alcoholic fatty liver disease, obstructive sleep apnea, cardiovascular disease (CVD), and chronic renal failure.² Ian Janssen et al reported that waist circumference, not body mass index (BMI), represents obesity-related risk.³ Therefore, people with abdominal obesity (central obesity) have a higher risk of comorbidities, even at a normal BMI. Moreover, the diagnostic criteria for metabolic syndrome incorporate waist circumference, rather than BMI or body weight.⁴

Sarcopenia is linked to heightened adverse outcomes, including falls, functional decline, frailty, mortality,^{5,6} and diabetes.⁷ Recently, the concept of sarcopenic obesity, characterized by the combination of obesity and sarcopenia, has gained attention. This condition is associated with an increased risk of mortality and cardiovascular risk factors.⁸ Previous studies have shown that the ratio of creatinine (Cr) to cystatin C (CysC) is associated with muscle mass and strength, serving as an indicator of sarcopenia,⁹ and is associated with CVD events and mortality.^{10,11} CysC, a cysteine protease inhibitor, is synthesized by nucleated cells at a constant rate¹² and is found to be elevated in obese individuals due to the contribution of adipose tissue.¹³ Cr is known as a marker of not only kidney function but also muscle mass.¹⁴ Hence, sarcopenia index (SI, serum Cr/CysC * 100) may also be associated with obesity.

Therefore, the primary aim of this study was to examine the association between the sarcopenia index and central obesity in a large adult population. Secondary aims included exploratory analyses of age- and sex-specific patterns, as well as comparisons across sarcopenia index tertiles, to further characterize potential heterogeneity in this association.

Materials and Methods

Study Populations

This retrospective cross-sectional study included Chinese participants aged 18 or older who underwent health examinations at Xiamen Chang Gung Hospital between 2014 and 2016. Enrollment criteria required complete data, including past medical and medication history, sufficient fasting duration, and measurements such as body height, body weight, waist circumference, blood pressure, bioelectric impedance analysis (BIA), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), fasting blood glucose (FBG), serum creatinine (sCr), and cystatin C (CysC). Exclusion criteria included incomplete data, inadequate fasting duration (less than 12 hours), chronic diseases that could significantly impact metabolism, such as thyroid dysfunction or chronic hepatitis, current use of hypoglycemic drugs or steroids affecting metabolism, and pregnancy. This study protocol was approved by the Institutional Review Board (IRB) of Xiamen Chang-Gung Hospital (approval number: XMCGIRB2022102). The requirement for written informed consent was waived by the IRB due to the retrospective nature of the study and the use of de-identified data.

Measurements

All participants completed uniformly designed questionnaires detailing their medical history, including age, previous diseases or medication usage, pregnancy status, and fasting duration. Trained nurses, adhering to standard operating procedures, collected venous blood samples and administered the questionnaires to ensure accurate data collection. Body height and weight were precisely measured to the nearest 0.1 cm and 0.01 kg, respectively. BMI was defined as the body weight (kg) divided by the square of height (m). Waist circumference was measured at the midpoint between the lower rib margin and the iliac crest. Blood pressure was measured using an automated sphygmomanometer while seated, following a resting period of at least 15 minutes. Three measurements were taken, and the average of the three readings was recorded as the final value. Mean arterial pressure (MAP) was calculated using the equation: $(2/3) \times$ diastolic blood pressure (DBP) + $(1/3) \times$ systolic blood pressure (SBP).

Laboratory Assessment

All laboratory data were collected after a 12-hour fasting period, during which participants were instructed to refrain from consuming high-fat diets and alcohol for at least 24 hours before blood withdrawal. Biochemical analysis included fasting FBG (mmol/L), measured using a modified hexokinase enzymatic assay (Cobas Mira Chemistry System; Roche Diagnostic Systems, Montclair, New Jersey, USA), and sCr (μ mol/L), TC (mmol/L), LDL-C (mmol/L), HDL-C (mmol/L), and TG (mmol/L), determined using a biochemical autoanalyzer (DxC 800, Beckman Coulter UniCel DxCSYNCHRON, Ireland). CysC (mg/L) was assessed via a turbidimetric inhibition immunoassay on an ARCHITECT c16000 biochemical autoanalyzer from Abbott Laboratories (Illinois, USA). In our study setting, CysC was measured as part of a standardized health examination program. The measurement was not restricted to specific clinical indications or predefined disease groups but

was included in routine health examinations for individuals undergoing comprehensive metabolic and renal assessments. The SI was calculated as follows: $(sCr (\mu\text{mol/L})/\text{CysC} (\text{mg/L})) \times 1.13 \times 100$.

The Body Composition

All subjects underwent BIA (MC 180 mo Tanita, Tokyo, Japan). To ensure measurement accuracy, participants were instructed to abstain from physical exercise and alcohol consumption for at least 24 hours before the examinations. The MC-180 device estimates visceral fat degree using segmental, multi-frequency impedance measurements combined with proprietary prediction algorithms. The visceral fat degree is a semi-quantitative index reflecting relative visceral adipose tissue accumulation rather than a direct measurement of visceral fat area. According to the definitions established by the Taiwan Medical Association for the Study of Obesity, gender-specific percentage body fat (BF%) cutoffs were as follows: (1) low BF%: men <17% and women <20%; (2) normal BF%: men 17–23% and women 20–27%; and (3) high BF%: men >23% and women >27%. In our study, non-obese were defined as BF% \leq 23% in males and \leq 27% in females. Central obesity was defined as BF% >23% with a visceral fat degree >10 in males and BF% >27% with a visceral fat degree >10 in females, while peripheral obesity was defined as BF% >23% with a visceral fat degree \leq 10 in males and BF% >27% with a visceral fat degree \leq 10 in females. These definitions were applied as study-specific operational classifications to distinguish obesity phenotypes with predominant visceral versus peripheral fat accumulation.

Statistical Analysis

Baseline characteristics of males and females were compared with the Chi-squared test for categorical variables, Student's *t*-test for normally distributed continuous variables, and Mann–Whitney *U*-test for non-normally distributed variables. Participants were stratified into three groups based on BF% and visceral fat (ie, non-obese, central obese, and peripheral obese) and compared using a Chi-squared test for categorical variables and one-way ANOVA for continuous variables. The Bonferroni post hoc test was utilized for pairwise comparisons between specific pairs of groups when the overall relationship was significant. Subgroup analyses for SI tertiles by sex and age were conducted as follows: for males under 50 years old, lowest tertile <91.9; middle tertile 105.1–91.9; highest tertile >105.1; for males over 50, lowest tertile <82.9; middle tertile 96.3–82.9; highest tertile >96.3; for females under 50, lowest tertile <83.5; middle tertile 95.7–83.5; highest tertile >95.7; for females over 50, lowest tertile <72.2; middle tertile 84.2–72.2; highest tertile >84.2. Logistic regression models were used to identify the association between central obesity and SI levels, with data presented as odds ratios (OR) with 95% confidence intervals. Participants were categorized into sex- and age-specific tertiles of the sarcopenia index to ensure adequate sample size and stable estimates in stratified analyses. Given the absence of validated SI cut-off values across age and sex groups, tertiles were used as a pragmatic approach to explore graded associations. Lastly, the ability of SI to identify central obesity was evaluated using receiver operating characteristic (ROC) analysis to ascertain the optimal cut-off value. All analyses were conducted using SPSS version 26.0 (SPSS, Chicago, IL, USA). A two-sided *p*-value <0.05 was considered statistically significant.

Results

Comparison of Baseline Characteristics by Gender

A total of 10,054 participants, comprising 5638 males (56.1%) and 4416 females (43.9%) were included. As shown in Table 1, significant differences were observed between males and females across all variables, except for age (*P* = 0.058). Male subjects exhibited higher BMI, waist-to-height ratio (WHtR), MAP, FBG, TC, LDL, TG/HDL-C, sCr, CysC, and SI, while HDL-C and BF% were lower than females. Despite females presenting higher BF%, males displayed a higher proportion of central obesity (39.04% in males and 5.71% in females, *P*<0.001).

Table 1 Main Characteristics of the Study Subjects by Gender

Characteristics	Total	Men	Women	P value
Number of subject	10054	5638	4416	
Age (years)	47.54 ± 10.40	47.37 ± 10.27	47.77 ± 10.57	0.058
BMI (kg/m ²)	23.82 ± 3.31	24.47 ± 3.21	22.99 ± 3.25	<0.001
WHtR	0.51 ± 0.06	0.51 ± 0.05	0.50 ± 0.06	<0.001
MAP (mmHg)	87.4 ± 13.42	90.35 ± 12.88	83.63 ± 13.15	<0.001
FBG (mmol/L)	5.33 ± 1.38	5.44 ± 1.54	5.20 ± 1.13	<0.001
TC (mmol/L)	5.23 ± 0.99	5.28 ± 0.98	5.15 ± 0.99	<0.001
TG (mmol/L)	1.57 ± 1.4	1.84 ± 1.54	1.22 ± 1.10	<0.001
LDL-C (mmol/L)	3.35 ± 0.86	3.47 ± 0.86	3.20 ± 0.84	<0.001
HDL-C (mmol/L)	1.32 ± 0.32	1.21 ± 0.28	1.45 ± 0.31	<0.001
TG/HDL-C	1.38 ± 1.78	1.72 ± 1.98	0.94 ± 1.37	<0.001
BF (%)	25.77 ± 7.32	21.69 ± 5.33	30.98 ± 6.12	<0.001
Central obese type, n (%)	2453 (24.40%)	2201 (39.04%)	252 (5.71%)	<0.001
sCr (μmol/L)	72.97±13.92	81.65 ± 11.26	61.90 ± 7.77	<0.001
CysC (mg/L)	0.93±0.21	0.99 ± 0.20	0.85 ± 0.19	<0.001
SI	91.34±17.93	95.88 ± 17.37	85.54 ± 16.93	<0.001

Note: Data are presented as mean ± SD or n (%).

Abbreviations: BMI, body mass index; WHtR, waist-to-height ratio; MAP, mean arterial pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; TG, triglyceride; sCr, serum creatinine; CysC, cystatin C; SI, sarcopenia index calculated as (sCr (μmol/L)/CysC (mg/L)) × 1.13 × 100.

Comparison of Male Baseline Characteristics by Body Fat Percentage and Visceral Fat Degree Stratified by Age

All variables displayed significant differences among non-obese, peripheral obese, and central obese groups in younger male subjects. However, in the males over 50 years old, there were no significant differences in age, TC, and SI ($p = 0.247, 0.085, \text{ and } 0.288$, respectively). Among males under 50, individuals with central obesity exhibited higher levels of BMI, WHtR, MAP, BF%, and CysC compared to non-obese and peripherally obese subjects. Conversely, among males older than 50 years, only BMI and WHtR were found to be higher in individuals with central obesity compared to non-obese and peripherally obese subjects.

In males under the age of 50, individuals with central obesity demonstrated significantly higher levels of CysC, while their SI was notably lower compared to non-obese counterparts. Conversely, among males aged 50 and above, those with central obesity exhibited elevated levels of both CysC and Cr in comparison to non-obese individuals. However, the SI did not show a significant difference between central obese and non-obese subjects in this age group. (Table 2).

Comparison of Female Baseline Characteristics by Body Fat Percentage and Visceral Fat Degree Stratified by Age

In younger female subjects, all variables, except for CysC ($P=0.208$), showed statistically significant differences among non-obese, peripheral obese, and central obese groups. However, in the females over 50 years old, no significant differences were observed in sCr levels ($p = 0.147$). Among females under the age of 50, individuals with central obesity displayed elevated levels of BMI, WHtR, MAP, TG, LDL-C, TG/HDL-C ratio, and BF%, along with lower levels of HDL-C, compared to non-obese and peripheral obese subjects. On the other hand, among females aged 50 and above, those with central obesity presented significantly higher levels of BMI, WHtR, MAP, FBG, TG, LDL-C, and BF%.

In females under the age of 50, individuals with central obesity exhibited higher levels of CysC, and their SI was lower than that of non-obese individuals. However, these differences did not reach statistical significance. Conversely, among females aged 50 and above, central obesity was associated with significantly higher levels of CysC, and the SI was significantly lower compared to non-obese individuals. (Table 3).

Table 2 Baseline Characteristics According to Body Fat Type Stratified by Age in Men

Characteristics	Non-Obese	Peripheral Obese	Central Obese	P value
Men < 50 years of age				
Number	2006	156	1335	
Age, years	40.82 ± 5.66	36.75 ± 5.55 ^a	41.40 ± 5.13 ^{ab}	<0.001
BMI (kg/m ²)	22.69 ± 2.38	23.88 ± 1.32 ^a	27.59 ± 2.29 ^{ab}	<0.001
WHtR	0.48 ± 0.04	0.50 ± 0.03 ^a	0.55 ± 0.04 ^{ab}	<0.001
MAP (mmHg)	86.22 ± 11.44	88.42 ± 10.53	94.28 ± 13.08 ^{ab}	<0.001
FBG (mmol/L)	5.12 ± 1.11	5.53 ± 2.12 ^a	5.57 ± 1.67 ^a	<0.001
TC (mmol/L)	5.17 ± 0.92	5.41 ± 1.00 ^a	5.46 ± 1.02 ^a	<0.001
TG (mmol/L)	1.63 ± 1.29	2.04 ± 1.37 ^a	2.38 ± 1.99 ^a	<0.001
LDL-C (mmol/L)	3.36 ± 0.82	3.61 ± 0.87 ^a	3.63 ± 0.88 ^a	<0.001
HDL-C (mmol/L)	1.28 ± 0.30	1.17 ± 0.21 ^a	1.12 ± 0.22 ^a	<0.001
TG / HDL-C	1.44 ± 1.54	1.82 ± 1.29	2.34 ± 2.82 ^{ab}	<0.001
BF %	18.28 ± 3.79	24.46 ± 1.83 ^a	26.68 ± 2.74 ^{ab}	<0.001
sCr (μmol/L)	81.97 ± 10.28	79.16 ± 10.27 ^a	81.76 ± 11.16 ^b	0.006
CysC (mg/L)	0.94 ± 0.17	0.91 ± 0.16	0.97 ± 0.19 ^{ab}	<0.001
SI	100.18 ± 16.52	100.01 ± 15.20	97.91 ± 17.49 ^a	<0.001
Men ≥ 50 years of age				
Number	1265	10	866	
Age, years	57.83 ± 6.33	56.60 ± 7.32	58.28 ± 7.26	0.247
BMI (kg/m ²)	22.61 ± 2.34	21.98 ± 2.47	26.64 ± 2.29 ^{ab}	<0.001
WHtR	0.49 ± 0.04	0.50 ± 0.04	0.55 ± 0.04 ^{ab}	<0.001
MAP (mmHg)	89.31 ± 12.67	92.83 ± 12.07	95.71 ± 12.76 ^a	<0.001
FBG (mmol/L)	5.47 ± 1.49	6.41 ± 3.03	5.95 ± 1.90 ^a	<0.001
TC (mmol/L)	5.23 ± 0.98	5.62 ± 0.93	5.32 ± 1.00	0.085
TG (mmol/L)	1.52 ± 1.39	1.97 ± 1.71	1.93 ± 1.29 ^a	<0.001
LDL-C (mmol/L)	3.41 ± 0.86	3.71 ± 1.14	3.56 ± 0.87 ^a	<0.001
HDL-C (mmol/L)	1.26 ± 0.30	1.19 ± 0.26	1.13 ± 0.24 ^a	<0.001
TG / HDL-C	1.38 ± 1.71	1.81 ± 1.59	1.86 ± 1.53 ^a	<0.001
BF %	18.14 ± 3.78	30.04 ± 12.19 ^a	26.48 ± 2.83 ^{ab}	<0.001
sCr (μmol/L)	80.59 ± 11.57	73.64 ± 6.71	82.83 ± 13.02 ^a	<0.001
CysC (mg/L)	1.03 ± 0.20	1.01 ± 0.13	1.07 ± 0.25 ^a	<0.001
SI	90.65 ± 16.71	83.08 ± 11.42	89.84 ± 16.77	0.288

Notes: Data are presented as mean ± SD or n (%). ^ap < 0.05 versus non-obese; ^bp < 0.05 versus peripheral obese in the Bonferroni post hoc comparisons.

Abbreviations: BMI, body mass index; WHtR, waist-to-height ratio; MAP, mean arterial pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; TG, triglyceride; sCr, serum creatinine; CysC, cystatin C; SI, sarcopenia index calculated as (sCr (μmol/L)/CysC (mg/L)) × 1.13 × 100.

Risk of Central Obesity Within Different Tertile of CCR Stratified by Age and Gender

Table 4 shows that if the risk of central obesity in the highest tertile is set at 1, the relative risk in the lowest tertile is 1.377 (95% C.I. 1.165–1.628, p < 0.001) in younger males (model 1). After adjustments in models 2 and 3, consistent results were observed, indicating an increasing odds ratio in the lowest tertile. However, significant differences were observed only in models 1, 2, and 3 in younger males (p trend < 0.001, < 0.001, 0.009, respectively), and in model 2 in older males (p trend = 0.040).

In the younger female group, no significant differences in the risk of central obesity were observed across various models. However, among older females, when the risk of central obesity in the highest tertile was considered as 1, the relative risk in the lowest tertile was 2.729 (95% C.I. 1.878–3.968, p < 0.001) (model 1). These results were consistently found in models 2 and 3 in older females, demonstrating a significant trend (p < 0.001) in both models.

Table 3 Baseline Characteristics According to Body Fat Type Stratified by Age in Women

Characteristics	Non-Obese	Peripheral Obese	Central Obese	P value
Women < 50 years of age				
Number	810	1691	48	
Age, years	38.68 ± 6.46	41.20 ± 5.60 ^a	43.02 ± 4.78 ^a	<0.001
BMI (kg/m ²)	19.51 ± 1.59	23.19 ± 2.31 ^a	30.95 ± 3.39 ^{ab}	<0.001
WHR	0.44 ± 0.04	0.49 ± 0.04 ^a	0.59 ± 0.05 ^{ab}	<0.001
MAP (mmHg)	76.03 ± 9.53	80.34 ± 11.44 ^a	90.65 ± 12.39 ^{ab}	<0.001
FBG (mmol/L)	4.82 ± 0.77	5.06 ± 0.87 ^a	5.33 ± 0.71 ^a	<0.001
TC (mmol/L)	4.79 ± 0.87	4.95 ± 0.92 ^a	5.18 ± 1.06 ^a	<0.001
TG (mmol/L)	0.83 ± 0.39	1.15 ± 1.37 ^a	1.75 ± 1.95 ^{ab}	<0.001
LDL-C (mmol/L)	2.83 ± 0.74	3.07 ± 0.76 ^a	3.37 ± 0.70 ^{ab}	<0.001
HDL-C (mmol/L)	1.58 ± 0.29	1.43 ± 0.29 ^a	1.21 ± 0.26 ^{ab}	<0.001
TG/HDL-C	0.56 ± 0.38	0.90 ± 1.87 ^a	1.58 ± 1.92 ^{ab}	<0.001
BF %	23.52 ± 3.25	32.18 ± 3.56 ^a	43.87 ± 4.47 ^{ab}	<0.001
sCr (μmol/L)	61.86 ± 8.51	60.64 ± 6.48 ^a	61.26 ± 9.28	<0.001
CysC (mg/L)	0.78 ± 0.16	0.79 ± 0.15	0.81 ± 0.17	0.208
SI	92.18 ± 16.37	89.78 ± 16.48 ^a	88.65 ± 21.48	0.002
Women ≥ 50 years of age				
Number	298	1365	204	
Age, years	58.03 ± 6.57	57.22 ± 6.02	61.18 ± 7.75 ^{ab}	<0.001
BMI (kg/m ²)	20.19 ± 2.22	24.1 ± 2.145 ^a	29.55 ± 2.63 ^{ab}	<0.001
WHR	0.47 ± 0.05	0.53 ± 0.04 ^a	0.61 ± 0.05 ^{ab}	<0.001
MAP (mmHg)	84.63 ± 12.42	89.77 ± 12.94 ^a	96.80 ± 12.58 ^{ab}	<0.001
FBG (mmol/L)	5.18 ± 0.87	5.47 ± 1.37 ^a	6.01 ± 1.87 ^{ab}	<0.001
TC (mmol/L)	5.41 ± 0.99	5.49 ± 0.99	5.66 ± 1.01 ^a	0.019
TG (mmol/L)	1.14 ± 0.76	1.46 ± 0.96 ^a	1.63 ± 0.94 ^{ab}	<0.001
LDL-C (mmol/L)	3.32 ± 0.82	3.49 ± 0.86 ^a	3.70 ± 0.90 ^{ab}	<0.001
HDL-C (mmol/L)	1.55 ± 0.31	1.40 ± 0.30 ^a	1.35 ± 0.27 ^a	<0.001
TG/HDL-C	0.81 ± 0.75	1.17 ± 1.05 ^a	1.33 ± 1.06 ^a	<0.001
BF %	23.06 ± 4.00	33.49 ± 3.51 ^a	42.55 ± 3.63 ^{ab}	<0.001
sCr (μmol/L)	63.10 ± 7.53	62.92 ± 8.01	64.13 ± 10.66	0.147
CysC (mg/L)	0.92 ± 0.20	0.92 ± 0.20	1.03 ± 0.24 ^{ab}	<0.001
SI	79.97 ± 15.44	79.34 ± 14.66	72.90 ± 14.41 ^{ab}	<0.001

Notes: Data are presented as mean ± SD or n (%). ^a p < 0.05 versus non-obese; ^b p < 0.05 versus peripheral obese in the Bonferroni post hoc comparisons.

Abbreviations: BMI, body mass index; WHtR, waist-to-height ratio; MAP, mean arterial pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; TG, triglyceride; sCr, serum creatinine; CysC, cystatin C; SI, sarcopenia index calculated as (sCr (μmol/L)/CysC (mg/L)) × 1.13 × 100.

SI Cut-Off Value to Identify Central Obesity

Table 5 and Figure 1 presented the ROC analysis of SI values, stratified by gender. The optimal cut-off value for SI, determined by the highest Youden index, was identified as 79.52 for females (sensitivity 56.5%, specificity 65.8%) and 96.60 for males (sensitivity 57.1%, specificity 48.5%). The SI demonstrated satisfactory discriminatory power in females (AUC=0.687, p<0.001), suggesting its potential utility in identifying individuals with central obesity. However, in males, the SI exhibited limited discriminatory power (AUC=0.534, p<0.001).

Discussion

This study uniquely explored the associations between central and peripheral obesity, cardiovascular risk factors, CysC levels, and the SI, while considering age and gender differences in a large Chinese population. Several key findings emerged from this study. First, central obesity was significantly associated with adverse cardiovascular risk profiles, consistent with previous evidence identifying central obesity as a key correlate of metabolic syndrome and cardiovascular

Table 4 Unadjusted and Adjusted Odds Ratios with 95% Confidence Intervals of Having Central Obesity in Men and Women

Group/Type	Central Obesity	Model 1		Model 2		Model 3	
	n (%)	OR (95% C.I.)	P Value	OR (95% C.I.)	P Value	OR (95% C.I.)	P Value
Men < 50 years of age							
SI tertile 3	405 (34.76%)	Reference		Reference		Reference	
SI tertile 2	436 (37.36%)	1.122 (0.948 to 1.329)	0.181	1.157 (0.975 to 1.374)	0.095	1.081 (0.903 to 1.294)	0.396
SI tertile 1	494 (42.40%)	1.377 (1.165 to 1.628)	<0.001	1.455 (1.228 to 1.724)	<0.001	1.268 (1.059 to 1.517)	0.010
P trend		<0.001		<0.001		0.009	
Men ≥ 50 years of age							
SI tertile 3	278 (38.99%)	Reference		Reference		Reference	
SI tertile 2	290 (40.62%)	1.067 (0.863 to 1.319)	0.552	1.148 (0.925 to 1.425)	0.210	1.078 (0.863 to 1.347)	0.508
SI tertile 1	298 (41.74%)	1.125 (0.910 to 1.390)	0.276	1.255 (1.011 to 1.557)	0.040	1.163 (0.928 to 1.456)	0.190
P trend		0.276		0.040		0.189	
Women < 50 years of age							
SI tertile 3	16 (1.88%)	Reference		Reference		Reference	
SI tertile 2	11 (1.29%)	0.683 (0.315 to 1.481)	0.335	0.720 (0.330 to 1.573)	0.411	0.565 (0.256 to 1.246)	0.157
SI tertile 1	21 (2.47%)	1.317 (0.683 to 2.542)	0.411	1.404 (0.720 to 2.740)	0.320	1.034 (0.522 to 2.046)	0.925
P trend		0.376		0.288		0.827	
Women ≥ 50 years of age							
SI tertile 3	43 (6.91%)	Reference		Reference		Reference	
SI tertile 2	56 (8.99%)	1.332 (0.881 to 2.015)	0.174	1.480 (0.968 to 2.261)	0.070	1.433 (0.935 to 2.198)	0.099
SI tertile 1	105 (16.88%)	2.729 (1.878 to 3.968)	<0.001	3.041 (2.067 to 4.475)	<0.001	3.029 (2.041 to 4.496)	<0.001
P trend		<0.001		<0.001		<0.001	

Notes: All 10054 participants (5638 males and 4416 females) were divided into the SI tertiles according to gender and age. Model 1, unadjusted analysis; Model 2, adjusted for fasting glucose level; Model 3, Model 2 + TG, HDL-C, and LDL-C level.

Abbreviations: OR, odds ratio; CI, confidence interval.

Table 5 Cut-Off Value and Prediction Power for SI Stratified by Gender

Variables	AUC (95% CI)	p value	Cut-Off Point According to Youden's Index	Sensitivity (%)	Specificity (%)
Male	0.53	<0.001	96.60	57.1	48.5
SI	(0.52 to 0.55)				
Female	0.69	<0.001	79.52	65.5	65.8
SI	(0.67 to 0.70)				

Abbreviations: SI, sarcopenia index; AUC, area under curve.

diseases.¹⁵ Additionally, individuals with central obesity exhibited higher CysC levels, supporting findings that central adiposity is associated with systemic inflammation and impaired renal and metabolic function.¹⁶ Second, the SI demonstrated significant associations with central obesity, particularly in men under 50 years and women over 50 years, even after adjusting for glucose and lipid parameters. This suggests that SI, a non-invasive marker reflecting muscle mass relative to CysC, may be a valuable marker in identifying individuals with central obesity in specific subpopulations.¹⁷ Notably, while SI was associated with central obesity in younger men, it showed even stronger associations in older women, where the highest SI tertile was linked to over a three-fold higher odds of central obesity, underscoring potential gender and age differences in muscle-fat distribution and their cardiometabolic implications.¹⁸ Third, although the predictive power of SI for central obesity was limited in men (AUC = 0.53), it showed moderate predictive ability in women (AUC = 0.69). The identified cut-off value of 79.52 in women may be clinically useful for screening central obesity, especially in resource-limited settings where advanced imaging modalities for visceral fat assessment are not feasible. The modest sensitivity and specificity observed in the ROC analyses indicate that SI alone

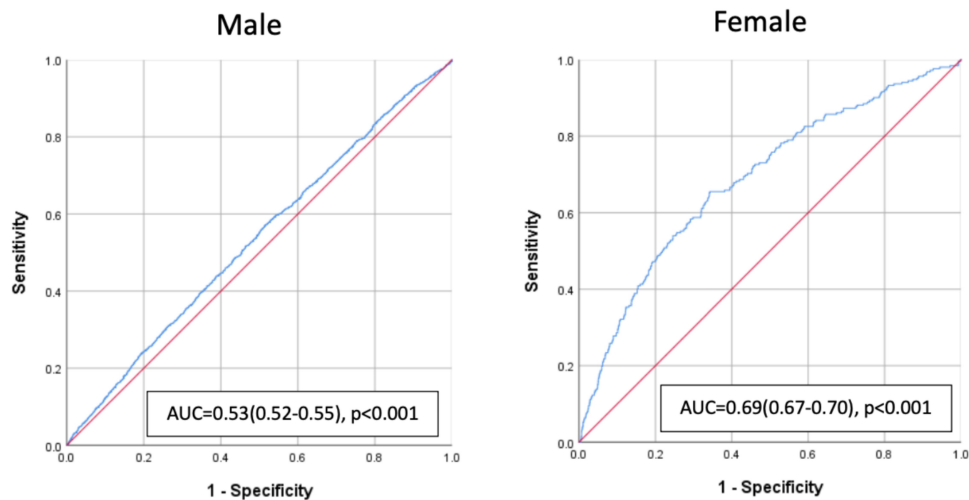


Figure 1 ROC curves assessing diagnostic performance of SI stratified by gender. ROC curves illustrated the discriminatory ability of SI for predicting central obesity with gender-specific analysis.

Abbreviations: SI, sarcopenia index; AUC, area under curve.

has limited discriminatory ability for central obesity, reflecting its multifactorial etiology. Accordingly, SI should not be interpreted as a predictive or screening marker but rather as an associated biomarker that may provide complementary information alongside other anthropometric and metabolic measures.

Central and Peripheral Obesity

Our study findings indicate that males had a higher proportion of central obesity, despite having a lower BF%. Conversely, females tended to exhibit a higher BF%, but a lower proportion of central obesity. These results are consistent with previous research studies, which have demonstrated that women generally have a higher BF% than men. However, at the same level of body fat, men tend to have a higher proportion of visceral fat than women. This phenomenon occurs because women tend to store fat in the subcutaneous tissue of the hips and abdomen, resulting in a higher subcutaneous adipose tissue (SAT)% and a lower visceral adipose tissue (VAT)% than men at the same BMI level.^{19–21} It is important to note that VAT poses a higher risk of CVD compared to SAT. Therefore, men have a twofold higher VAT/SAT ratio than women, putting them at greater risk of CVD.²² Overall, our results are consistent with previous population-based studies reporting significant sex-related differences in baseline characteristics, including body composition, fat distribution, and sarcopenia-related parameters. In particular, men have been shown to exhibit greater visceral fat accumulation at comparable levels of total adiposity, whereas women demonstrate distinct patterns of fat distribution and age-related muscle mass decline.^{19,23,24}

Notably, our findings based on BIA-derived visceral adiposity are directionally consistent with MRI-based studies, which have demonstrated significant sex- and age-related differences in visceral fat accumulation, with men exhibiting greater visceral fat at comparable levels of total adiposity and visceral fat increasing with age.^{25,26} Although MRI provides direct anatomical quantification of visceral adipose tissue, the concordant patterns observed across modalities support the external validity of our BIA-based approach in population-level analyses.

Sarcopenic Index and Central Obesity

Visceral obesity is also associated with a low-grade inflammatory state.^{27,28} The chronic low-grade inflammation induced by visceral obesity leads to metabolic changes in the body, increasing the risk of CVD and type 2 diabetes mellitus.²² Typical adipocytes are associated with M2 macrophages that maintain cellular health and produce anti-inflammatory signals. However, excessive nutritional intake leads to the predominance of M1 macrophages, secreting pro-inflammatory cytokines, including Interleukin (IL)-6, Tumor necrosis factor- α (TNF- α), IL-8, IL-1 β , Interferon- γ (IFN- γ).²⁹ Visceral

adipocytes are more susceptible to obesity-induced inflammation signals and are primarily responsible for the production and secretion of IL-6 and TNF- α , in contrast to SAT.³⁰

Extensive studies have shown that creatinine-to-cystatin C ratio (CCR) is a biomarker for sarcopenia, reflecting muscle quality and strength^{31–33} and is associated with clinical outcomes such as 3-year mortality,¹¹ frailty,³¹ and length of hospital stay.³⁴ Several interrelated mechanisms link central obesity to the loss of skeletal muscle mass and function: (1) Visceral fat is metabolically active and secretes various pro-inflammatory cytokines, including IL-6, TNF- α , and C-reactive protein. These inflammatory markers lead to chronic low-grade inflammation, a key factor in muscle catabolism. Inflammatory cytokines promote muscle protein degradation and inhibit muscle protein synthesis through pathways such as nuclear factor- κ B (NF- κ B) and the ubiquitin-proteasome system.^{35,36} (2) Central obesity is closely linked to insulin resistance, characterized by a reduced responsiveness of muscle, fat, and liver cells to insulin. This impairment hinders muscle protein synthesis and exacerbates inflammation.³⁷ (3) Adipose tissue, particularly visceral fat, influences hormone production, resulting in elevated leptin levels and reduced adiponectin levels. In individuals with central obesity, leptin resistance diminishes the hormone's beneficial effects on muscle metabolism, while decreased adiponectin levels are associated with reduced insulin sensitivity and increased inflammation, ultimately leading to sarcopenia.^{36,38} Research has shown that leptin levels are negatively correlated with muscle mass and positively correlated with visceral obesity, especially in sarcopenic obesity, which is more pronounced than sarcopenia or visceral obesity alone.³⁹ (4) Myosteatosis, characterized by fat infiltration into muscle tissue, impairs muscle mass and function, leading to inflammation, fibrosis, and metabolic dysfunction, thereby further contributing to muscle atrophy.³⁸ (5) Individuals with central obesity often experience reduced physical activity due to decreased mobility and increased fatigue, which leads to muscle atrophy and further exacerbates sarcopenia.³⁵

Although younger men typically have higher absolute skeletal muscle mass, SI is a relative index based on Cr and CysC and may decrease when muscle quality is impaired and/or CysC is elevated. At comparable levels of total adiposity, men generally exhibit greater visceral fat accumulation than women, which may amplify visceral inflammation and insulin resistance even at younger ages.¹⁹ Moreover, adipose tissue has been shown to contribute to elevated circulating CysC in obesity, independent of kidney function, potentially leading to a lower SI despite preserved muscle mass.¹³ In addition to biochemical alterations, central obesity has been linked to early impairment of muscle quality, including myosteatosis and metabolic dysfunction, which may occur before a measurable decline in muscle mass and be reflected by SI.⁴⁰ These mechanisms provide a plausible explanation for the observed SI–central obesity association in younger men.

Our research findings indicate that individuals with lower SI are at a higher risk of central obesity. One study suggests that a higher CCR is associated with greater muscle mass and better clinical outcomes, including reduced risk of falls and lower hospitalization rates.³⁷ This highlights the potential of the CCR in predicting sarcopenic obesity and related health risks. Additionally, studies exploring cross-sectional and longitudinal data have shown that over time, a lower CCR is significantly associated with higher central obesity and poorer muscle function, emphasizing its utility in identifying individuals at risk of sarcopenic obesity.⁴¹ Another study discussing the CCR as a surrogate marker for sarcopenia found that a lower ratio is related to decreased muscle mass and increased obesity, particularly central obesity, making it a valuable tool for early detection and management of sarcopenic obesity in clinical settings.⁴² Furthermore, research investigating the relationship between the CCR, waist circumference, and hypertension concluded that a lower CCR is associated with higher waist circumference and central obesity, which in turn is linked to an increased risk of hypertension. This underscores the importance of the CCR in predicting metabolic health issues related to central obesity.³⁶

Sarcopenic Index and Peripheral Obesity

Our research shows a significant difference in SI between peripheral obesity and central obesity groups among women over 50. Peripheral obesity, also known as lower body obesity, is characterized by fat accumulation in the lower part of the body, such as the hips, thighs, and buttocks. This type of obesity is influenced by various mechanisms, including hormonal regulation, genetic predisposition, differences in fat cell function, metabolic differences, and the role of physical activity. Hormones play a crucial role in fat distribution; for instance, estrogen promotes fat deposition in the

lower body, which explains why premenopausal women are more likely to have peripheral obesity. Estrogen increases the activity of lipoprotein lipase in the lower body, an enzyme responsible for fat storage in adipocytes.^{43,44} Genetic factors significantly affect the location of fat storage, with certain genetic variations predisposing individuals to store fat in the lower body rather than the abdomen. These genetic influences impact fat cell distribution and number, as well as the hormonal response to dietary intake and energy expenditure.⁴⁵ Lower body fat cells function differently from upper body fat cells, often storing fat more efficiently and releasing it more slowly due to lower hormone-sensitive lipase activity. They are also more sensitive to insulin, which promotes fat storage, making fat in these areas harder to mobilize.⁴⁶ Peripheral fat has lower metabolic activity compared to visceral fat and is associated with a lower risk of metabolic diseases such as insulin resistance, type 2 diabetes, and CVD. This is because peripheral fat produces fewer pro-inflammatory cytokines and is less involved in the pathogenesis of metabolic disorders.⁴⁷ Physical activity also influences fat distribution; regular lower body exercises such as walking, running, and resistance training can increase lower body muscle mass, affect fat storage and distribution, and improve overall insulin sensitivity, influencing how fat is stored and mobilized.⁴⁸

Gender Difference in Adipose Tissue

Our research indicates that men have a higher SI than women, and this ratio decreases with age. These observations align with results reported in another study,⁴⁹ supporting the consistency of the identified gender and age-related patterns in the CCR. When using CCR as a marker for sarcopenia, different CCR thresholds may be needed for men and women.^{50,51} Both before and after adjusting for age, women generally have a lower muscle mass index compared to men. Regardless of body weight, men experience a faster loss of muscle mass with age compared to women.⁵² Therefore, we hypothesize that the lack of significant differences in SI among older males may be attributed to the substantial impact of age-related muscle loss.

Before menopause, estrogen in women is primarily secreted by the ovaries. After menopause and in men, estrogen is mainly produced by peripheral tissues, especially adipose tissue.⁵³ Estrogen is believed to suppress pro-inflammatory signals and promote anti-inflammatory effects. In individuals who have undergone oophorectomy and received estrogen treatment, there is an increase in M2 macrophages and elevated anti-inflammatory markers.⁵⁴ Moreover, macrophages lacking estrogen receptor α expression exhibit increased secretion of TNF- α and heightened inflammation in white adipose tissue.^{55,56} The absence of estrogen expression leads to the upregulation of TNF- α and IL-6, along with increased pro-inflammatory signaling.⁵⁷ Additionally, estrogen promotes the growth of subcutaneous fat and inhibits the expansion of visceral fat at both the adipocyte and preadipocyte levels.⁵⁸ In postmenopausal women, the CysC level is higher than in premenopausal women.⁵⁹ In our study, younger females may exhibit no significant differences, potentially due to the protective effects of estrogen and the limited sample size.

Given the mean age of female participants, many were likely undergoing the menopausal transition, which has been linked to visceral fat redistribution and increased inflammation.^{60,61} These changes may partly explain the stronger associations observed in older women, while estrogen-related protection and limited sample size may account for the null findings in younger females.⁵⁹

Strengths and Limitations

The strength of our study lies in its large, population-based sample, which enhances the reliability of our findings. Unlike other studies that select participants from patients visiting hospitals or clinics for treatment, our participants are more representative of the general population. However, several limitations need to be considered. First, the cross-sectional study design does not allow for the assessment and determination of a causal relationship between SI and central obesity. Second, recruiting subjects from health examinations at a single center may introduce selection bias and may not represent the entire population. Third, since our participants were individuals undergoing health examinations, the standardized questionnaire did not collect data on confounding factors such as physical activity, dietary habits, and socioeconomic status, as these items were not mandatory. Fourth, the measurement of creatinine at a single time point introduces the possibility that acute kidney injury could not be ruled out. Fifth, CysC was measured only in participants undergoing comprehensive health examinations rather than in the entire cohort and was not

restricted to specific disease-based indications. This selective testing may have introduced selection bias and limited the generalizability of our findings. Therefore, further prospective studies are needed to improve the sensitivity and specificity of SI in predicting central obesity and to confirm the causal relationship between SI and central obesity by reducing confounding factors.

Conclusion

In this large cross-sectional study, lower sarcopenia index (SI) levels were associated with central obesity, with notable age- and sex-specific patterns, particularly among younger men and older women. These findings suggest that SI may reflect underlying muscle–fat imbalance related to visceral adiposity rather than generalized obesity. However, given the retrospective and cross-sectional design, causal inferences cannot be established. Furthermore, the modest sensitivity and specificity observed in ROC analyses indicate that SI has limited utility as a stand-alone screening or diagnostic tool for central obesity. Accordingly, SI should be interpreted as a complementary biomarker within a multifactorial framework that encompasses hormonal status, metabolic factors, lifestyle behaviors, and systemic inflammation. Future prospective and longitudinal studies incorporating direct measures of visceral adiposity and detailed hormonal and lifestyle data are warranted to clarify the temporal relationships and clinical relevance of SI in obesity-related risk assessment.

Abbreviations

AUC, area under the curve; BIA, bioelectrical impedance analysis; BF%, body fat percentage; BMI, body mass index; CCR, creatinine-to-cystatin C ratio; Cr, creatinine; CVD, cardiovascular disease; CysC, cystatin C; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; IFN- γ , interferon gamma; IL, interleukin; LDL-C, low-density lipoprotein cholesterol; MAP, mean arterial pressure; NF- κ B, nuclear factor kappa B; OR, odds ratio; ROC, receiver operating characteristic; SAT, subcutaneous adipose tissue; SI, sarcopenia index; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; TNF- α , tumor necrosis factor alpha; VAT, visceral adipose tissue; WHtR, waist-to-height ratio.

Data Sharing Statement

Raw data were generated at Xiamen Chang-Gung Memorial Hospital. Derived data supporting the findings of this study are available from the corresponding author on request.

Ethical Approval

This study protocol was approved by the Institutional Review Board (IRB) of Xiamen Chang-Gung Hospital (approval number: XMCGIRB2022102) and conducted by the guidelines laid down in the Declaration of Helsinki. The requirement for written informed consent was waived by the IRB due to the retrospective nature of the study and the use of de-identified data.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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