Association of sarcopenic obesity and body composition with metabolically unhealthy overweight/obese phenotypes among Iranian women: A cross-sectional study

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Research

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Abstract

Background

Obesity is a major risk factor for metabolic syndrome, with its prevalence has increased over the past decade. Major changes in body composition with aging have a significant effect on many clinical outcomes. Sarcopenic obesity consists of both the presence of abnormal adipose tissue with a deficit of muscle mass.

Methods

This cross-sectional study was conducted among a total of 241 overweight/obese women aged between 18–48 years in Tehran, Iran, registered by the use of the multistage cluster random sampling method. Blood samples were taken following standard procedures. Body composition was assessed through a multi-frequency bioelectrical impedance analyzer. The metabolic risk was assessed according to Karelis criteria and the subjects were classified as either MHO or MUO phenotypes.

Results

Of the 241 subjects in this study (average age 35.32 years), 176 (73.03%) were classified as MUO phenotype. Based on this study, the prevalence of sarcopenic obesity was 7.88%. We found that high fat-free mass was more strongly and significantly associated with MUO phenotype. Furthermore, we found that individuals with high fat-free mass and high skeletal muscle mass had a significantly low prevalence of MUO phenotype. A significant positive correlation between metabolic phenotypes and sarcopenic obesity was also observed after all potential covariates were adjusted for.

Conclusion

These results of this study suggest that increased adiposity and decreased skeletal muscle mass are associated with unfavorable metabolic traits among overweight and obese Iranian women. SO was also found to be associated with a greater risk of developing MUO phenotype.

Background

Obesity has been defined according to the World Health Organisation (WHO) as an abnormal accumulation of fat that affects health negatively (1). Obesity is a major risk factor for metabolic and cardiovascular morbidity and mortality, and its prevalence has doubled since 1980 in middle-aged and older adults (2). Individuals who are obese are at greater risk of developing the metabolic disease compared to individuals of normal weight (3), while obesity has also been related to the incidence of various cancers, respiratory disorders, arteriosclerosis, arthritis, and fatty liver (4). According to a study by

Fallahzadeh and associates on estimating the prevalence and trends of obesity in the Iranian population, it was reported that 16.5% of Iranian subjects older than 18 years were obese (5). Furthermore, as part of the Jahrom Health Study (JHS), 24.8% of women aged 30 years and above were obese (6). In obese women, it has been reported that a small decline in muscle strength may cause difficulties in bearing their excess weight and in moving efficiently (7). Obese subjects have been reported to have heterogeneous phenotypes with different degrees of metabolic risk (8). A sub-group of obese individuals without associated metabolic complications have been phenotypically described as metabolically healthy obese (MHO) individuals (9, 10). On the other hand, is the metabolically unhealthy obese individuals characterized by obesity-related metabolic complications (11). Previous studies have reported MHO phenotype to be associated with a healthy metabolic profile, characterized by a lower amount of visceral adipose tissue (VAT) and liver fat (12), favorable lipid profile, high insulin sensitivity, and low pro-inflammatory cytokine levels in plasma (12, 13) than metabolically unhealthy obese (MUO) subjects. Growing evidence however has shown that healthy obese adults without metabolic risk factors may progress to unhealthy obesity over time (14). Schroder et al., in a 10-year follow-up of Spanish obese cohort patients, found half of their subjects with an MHO phenotype at the beginning acquire an unhealthy phenotype (15). There is not a universal criterion to determine MUO and MHO, however, some studies have shown that BMI, blood pressure, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, fasting blood glucose, c-reactive protein, and homeostatic model assessment of insulin resistance (HOMA-IR) can be used as a criterion to diagnose obesity phenotype (3).

Aging is a continuous process characterized by a decline in most physiological functions (16). Major changes associated with aging in body composition include a decline in both fat-free mass and muscle strength, which has been referred to as sarcopenia (17); and, an increase in body fat and a decline in skeletal muscle, referred to as sarcopenic obesity (SO) (18). Sarcopenia and obesity are both related to metabolic disorders, morbidity, and mortality (19). It has therefore been hypothesized that sarcopenic obesity may have a greater impact on metabolic diseases and cardiovascular morbidity and mortality than either sarcopenia or obesity alone (2, 20). Sarcopenic obesity has been linked to increased production of inflammatory substances such as leptin, IL-6, tumor necrosis factor [TNF] α , IL-1 α known to alter insulin sensitivity, growth hormone secretion, and energy metabolism (18, 21). Furthermore, Chung *et al.*, in a study of elderly Koreans found that the sarcopenic obese group was more closely associated with insulin resistance, metabolic syndrome, and cardiovascular disease risk factors than any other group in both men and women (22). Moreover, numerous studies have also reported a significantly higher risk of mortality (23) worse cardiovascular risk profiles including hyperglycemia, hypertension, dyslipidemia, insulin resistance, and lower cardiorespiratory fitness (22, 24, 25) in sarcopenic obese individuals compared to non-sarcopenic or non-obese subjects.

In a study of the Iranian adult population, Rahmanian and colleagues reported a 10.9% and a 7.2% prevalence of MUO and MHO respectively in this group (26). Rasaei and associates also reported a 9.9% prevalence of SO among Tehranian overweight and obese women (27). Despite the high prevalence of SO and MUO in this population, information regarding their association with body composition is scarce. The aim of this study therefore was to determine the association of metabolically healthy and unhealthy

obesity with sarcopenic obesity and measures of body composition among overweight and obese Iranian women.

Methods

Study sample

This cross-sectional study was conducted among 241 overweight and obese women who were referred to health centers affiliated to Tehran University Medical Science in Iran. Subjects were registered by use of the multistage cluster random sampling method. All participants answered a questionnaire developed and administered by well-trained investigators. Inclusion criteria were age 18–48 years, being overweight or obese (body mass index (BMI) $\geq 25 \text{ kg/m}^2$, and not being pregnant. Exclusion criteria included having; an acute or chronic inflammatory disease, regular use of medication, history of hypertension, cardiovascular disease, diabetes mellitus, impaired renal and liver function, intake of alcohol or drug abuse, smoking, thyroid disease, malignancies, pregnancy, and lactation. Also, individuals with chronic diseases affecting their dietary intake as well as those following a special dietary pattern over the past year were excluded from this study and whose daily energy consumption was 800 kcal/day or 4200 kcal/day were registered. All participants were informed about the study aims and procedures and provided written informed consent. The Medical Research Ethics Committee of Tehran University of Medical Sciences approved the study with the following identification IR.TUMS.VCR.REC.1398.692.

Measurements

Dietary Assessment

A semi-quantitative food frequency questionnaire (FFQ) which contains 147-item food was applied to evaluate usual dietary intake and nutritional status over the past year. Household methods were used to transform portion sizes of the used up foods into grams (28), and a predictable average daily intake of food parameters (including macro and micronutrients) was computed from the FFQ using NUTRITIONIST IV software (version 7.0; N-Squared Computing, Salem, OR), modified for Iranian foods. This procedure was designed according to the Willett study including a list of 147 food items along with a standard serving size for each nutrient which its reliability and validity had been approved in Iran (29).

Measurement of blood samples

Blood samples were collected following overnight fasting and the serum was centrifuged, liquated, and stored at a temperature of -80°C until the analysis was performed. All samples were analyzed using a single assay according to the manufacturer's protocol. The GOD PAP method and the GPO-PAP method were used for measuring the respective fasting blood sugar (FBS) and triglyceride (TG) amounts. Total cholesterol (T-chol) and cholesterol with high-density lipoprotein (HDL) were calculated using the enzymatic endpoint process and the enzymatic clearance assay. All calculations were made with the usage of a package from Randox Laboratories (Hitachi 902). An immunoturbidimetric assay (high

sensitivity assay, Hitachi 902) was used to test high-sensitive C-reactive protein (hs-CRP). All measurements were taken at the Endocrinology and Metabolism Research Institute (EMRI) - Bio-nanotechnology Laboratory of Tehran University of Medical Science.

Body composition and anthropometric measurements assessment

Bioelectrical impedance analyzer (BIA) (InBody 720, South Korea) was used to calculate body composition indicators, including body fat-free mass and fat mass. This bioelectrical impedance analyzer (BIA) is considered to emit a very weak current to assess body impedance (resistance). Anthropometric measurements were performed on all participants, such as weight, BMI, waist circumference (WC), and waist-to-hip ratio (WHR). Weight was measured with digital scales and recorded to the nearest 0.1 kg while the subjects were in minimal clothing and without shoes. Height was measured using a tape measure while the subjects were standing erect, without shoes, and with shoulders in a normal position and, head, shoulders, heels, and buttocks are in contact with the wall. BMI was calculated by dividing the weight (kg) by the square of the height (m). Waist circumference (WC) and hip circumference (HC) were recorded to the nearest 0.1 cm in the central point of the iliac crest and rib cage with tape with an accuracy of 0.1 cm. To reduce error, all measurements were taken by the same technician. All measurements were carried out by professionally trained technicians and according to specific guidelines to reduce the difference between subjects.

Assessment of blood pressure

The blood pressure was assessed after the participants rested for 10 minutes. Hypertension was defined as blood pressure >130/85 mmHg. This category includes patients taking antihypertensive medicines, even if treatment achieves a blood pressure level that is within the target range.

The HOMA-IR calculation

The insulin resistance homeostatic model assessment (HOMA-IR) was based on the following equation: $[\text{fasting plasma glucose (mmol/l)} \times \text{fasting plasma insulin (mIU/l)}] / 22.5$ (30).

Definition of metabolic health and sarcopenic obesity

The Karelis criteria were used because all inflammation criteria are tested. The existence of four or more of the following five is described as metabolic abnormality according to the requirements of Karelis, composition: TG 1.7 mmol/l, HDL 1.3 mmol/l, without treatment; LDL 2.6 mmol/l, without treatment, 3.0 mg/l hs-CRP and 2.7 HOMA-IR (31). According to the definition, sarcopenic obesity in women is referred to as two lower quintiles of SMM and two highest quintiles of FM (32). In this study, we measured SMM and FM by BIA (Inbody Co., Seoul, Korea) according to guidelines.

Other baseline measurements

The socio-demographic and lifestyle characteristics assessed included age, gender, educational level attained, physical activity status, and smoking habits by questionnaire. A validated International Physical Activity Questionnaire (IPAQ) was used to assess the level of physical activity. For weekly physical activity assessment, a short form (9 items) was applied using MET (metabolic equivalent) scores for each type of activity. For reporting the total physical activity from all activity categories, MET scores across all these sub-components were summed and MET-minutes per week (MET-min/wk) were estimated (33).

Statistical Analysis

All statistical analyses were performed using the IBM SPSS software version 25.0 (SPSS, Chicago, IL, USA), and p-values less than 0.05 were considered statistically significant. Normal distribution of data was checked by the Kolmogorov-Smirnov test. Continuous variables information was represented by mean $\pm$ standard deviations (SDs) and mean $\pm$ standard errors (SEs), and categorical feature information represented by percentage and number. An independent sample t-test was used for assessed differences between groups with the Metabolically Healthy and Metabolically Healthy obese and chi-square (χ^2) tests for categorical variables. Analysis of covariance (ANCOVA) was used for adjusting potential confounders such as age, BMI, physical activity, and energy intake. Spearman bivariate correlation between body composition variables and sarcopenic obesity was performed. Association between metabolic healthy statuses with measures of body composition and sarcopenic obesity were assessed by the Binary logistic regression model, adjust for confounders in crude and 2 adjust models. Results were presented as beta and odds ratios (ORs) and 95% confidence intervals (CIs) compared with the metabolic unhealthy status group.

Results

General characteristics of study participants

The general characteristics of the study subjects according to metabolically healthy and unhealthy phenotypes were shown in **Table1**. In total, 241 women aged 18–48 years, mean $\pm$ SD age of 35.32 $\pm$ 8.68 years, participated in our study. Among these, 78.99% were married and 1.26%, 10.50%, 38.66%, and 49.58%, respectively, were illiterate, under diploma education level, diploma education level, and bachelor and a higher academic degree. A significant difference was observed among the study participants in terms of their economic status ($p=0.02$). After controlling for potential confounders (age, physical activity (PA), energy intake, and BMI, this significance disappeared. The prevalence of sarcopenic obesity was 7.88%. The aforementioned demographic characteristics and prevalence of sarcopenic obesity were marginally different across the two groups ($p=0.06$). However, after adjusting for potential confounders, a significant difference was observed between the two groups ($p=0.04$). Subjects in the MUO group had a significantly higher body weight, BMI, WC, body fat mass (BFM), and visceral fat area (VFA) compared to subjects in the metabolically healthy (MHO) group ($p<0.001$). Similar findings were observed after adjusting for potential confounding variables. The FFM, fat mass index (FMI), and skeletal muscle mass

(SMM) were significantly higher in the MUO group, $p=0.004$, $p=0.001$, and $p=0.002$ respectively. FBS was seen to be significantly higher in the MUO group after potential confounders were controlled for ($p=0.03$). TG, LDL, and total cholesterol were significantly higher ($p<0.001$) in the unhealthy group, while the levels of HDL were significantly higher ($p<0.001$) in the healthy group compared with the unhealthy group. After controlling for potential confounders, the results remained unchanged. A significant difference was also observed among the groups based on HOMA-IR ($p<0.001$) and insulin level ($p=0.001$), with the observed outcome remaining unchanged even after confounders were controlled for. While a non-significant difference was observed across the groups base on systolic blood pressure (SBP), a significantly higher diastolic blood pressure (DBP) was observed among the unhealthy group ($p<0.001$). (hs-CRP levels in the MUO group was significantly higher than in the MHO group ($p<0.001$). We, however, did not observe a statistically significant difference in physical activity among the two groups ($p=0.33$).

Table 1. General characteristics of study participants

variables	Metabolically Healthy	Metabolically Unhealthy	P- value*	P value ^{†**}
	(mean ± SD)			
Demographic characteristic				
Age (year) ^a	35.92 ±7.55	36.32 ±8.68	0.74	0.84
Marital status ^b				
Single (%)	17 (34.0)	33 (66.0)	0.21	0.80
Married (%)	47 (25.0)	141 (75.0)		
Education ^b				
Illiterate (%)	1 (33.3)	2 (66.7)	0.57	0.73
Under diploma (%)	4 (16.0)	21 (84.0)		
Diploma (%)	24 (26.1)	68 (73.9)		
Bachelor and above (%)	35 (27.7)	83 (70.3)		
Economic status ^b				
Low class (%)	6 (19.4)	25 (80.6)	0.02	0.16
Middle class (%)	20 (48.8)	21 (51.2)		
High class (%)	7 (29.2)	17 (70.8)		
Sarcopenic obesity ^b				
Non-sarcopenic obese (%)	61 (27.5)	161 (72.5)	0.06	0.04
Sarcopenic obese (%)	4 (21.1)	15 (78.9)		
Anthropometry and Body Composition				
Weight (kg) ^a	74.89 ±8.71	81.03 ±11.02	<0.001	<0.001
Height (cm) ^a	161.09±5.18	161.51±5.83	0.06	0.92
BMI (kg/m ²) ^a	28.75±2.86	31.11±3.64	<0.001	<0.001
WC (cm) ^a	93.38±7.01	99.64±9.27	<0.001	<0.001
Body fat mass (kg) ^a	29.76±5.96	34.03±7.34	<0.001	<0.001
Visceral fat area(cm ²) ^a	14.04±2.89	15.72±3.25	<0.001	0.001

Fat-free mass (kg) ^a	44.84±4.68	47.10±5.57	0.004	0.01
Skeletal muscle mass (kg) ^a	24.42±2.69	25.89±3.32	0.002	0.008
Fat free mass index (kg) ^a	17.26±1.21	18.75±9.88	0.23	0.27
Fat mass index (kg) ^a	11.65±2.62	13.06±2.78	0.001	<0.001
Blood Parameters				
FBG (mg/dL) ^a	4.68±0.40	4.86±0.49	0.05	0.03
TG (mg/dL) ^a	0.90±0.28	1.52±0.82	<0.001	<0.001
HDL (mg/dL) ^a	1.34±0.24	1.14±0.26	<0.001	<0.001
LDL (mg/dL) ^a	2.19±0.50	2.53±0.62	<0.001	0.001
Total cholesterol (mg/dL) ^a	4.37±0.74	4.89±0.93	<0.001	0.003
Insulin (mIU/l)	1.13±0.24	1.24±0.22	0.001	0.01
HOMA index ^a	2.47±0.85	3.66±1.24	<0.001	<0.001
Blood Pressure				
SBP (mmHg) ^a	109.01±12.44	112.66±13.92	0.06	0.18
DBP (mmHg) ^a	73.74±8.29	79.39±10.05	<0.001	0.007
Inflammatory parameter and other variables				
Hs-CRP (mg/L) ^a	1.33±1.18	5.37±4.91	<0.001	<0.001
Physical activity (MET min/week) ^a	989.33±1078.53	1304.14±2404.33	0.33	0.29

SD, standard deviation; BMI, body mass index; WC, waist circumference; FBG, fasting blood glucose; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, High sensitive c-reactive protein; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Data are presented as mean ± standard deviation (SD) or percent.

‡Collinear variables did not enter into the model and this P-value obtained from ANCOVA analysis

*p-value obtained from independent T-test

** p-value obtained from ANCOVA test, variable adjust for age, physical activity, energy intake, and BMI

Chi-square and analysis of variance were used for qualitative and quantitative variables respectively, and the p-value was set to <0.05.

^a Mean $\pm$ SD

^b Sample size (%)

Dietary intake of study subjects according to metabolic statuses

As shown in **Table 2**, the food groups, mean dietary intakes, and the mean nutrient intakes of the study participants were not statistically significantly different between the MHO and MUO groups even after controlling for potential confounding variables ($p>0.05$).

Table 2. Dietary intake of study subjects according to metabolic statuses

Variables	Metabolic healthy		Metabolic unhealthy		P-value*	P-value**
	Mean	SD	Mean	SD		
Food groups						
Fruits (g/d)	508.45	373.30	505.83	352.66	0.96	0.34
Vegetables(g/d)	379.99	227.11	387.94	248.29	0.82	0.12
Cereal(g/d)	422.18	195.27	427.86	226.56	0.86	0.61
Whole grains(g/d)	58.64	53.41	65.77	62.43	0.42	0.31
Refined grains(g/d)	363.54	203.95	362.45	211.23	0.97	0.43
Nuts(g/d)	15.23	16.91	19.06	28.03	0.96	0.67
Legumes(g/d)	51.64	55.38	48.23	34.54	0.57	0.62
Red meat (g/d)	21.61	17.70	22.53	19.75	0.74	0.60
White meat(g/d)	38.34	32.02	47.34	42.68	0.12	0.54
Salt and salty snacks(g/d)	36.79	38.78	41.18	47.54	0.51	0.99
Dairy(g/d)	274.24	234.54	301.84	214.28	0.39	0.70
Tea(g/d)	637.96	463.59	793.25	912.36	0.19	0.19
Dietary intake						
Energy intake (kcal/d)	2505.26	727.89	2615.62	754.66	0.31	-
Carbohydrate (g/d)	362.65	126.42	370.55	117.74	0.65	0.20
Carbohydrate (% energy)	57.16	6.58	56.57	6.64	0.54	0.44
Protein (g/d)	83.30	26.04	89.26	28.26	0.14	0.58
Protein (% energy)	13.43	2.61	13.75	2.33	0.36	0.64
Fat (g/d)	88.66	27.49	94.91	33.61	0.18	0.33
Fat (% energy)	32.38	5.79	32.75	6.66	0.82	0.62
MUFA (g/d)	28.93	8.47	31.39	11.69	0.12	0.24
PUFA(g/d)	18.84	6.71	20.12	9.06	0.30	0.64
SFA (g/d)	25.99	9.76	28.43	11.60	0.13	0.14
Fiber (g/d)	45.18	20.05	44.30	17.86	0.74	0.15
Nutrients						
Vitamin A (RAE)	729.58	351.47	795.26	428.82	0.27	0.84

Thiamine (mg/d)	2.01	0.65	2.05	0.63	0.63	0.39
Riboflavin (mg/d)	2.05	0.71	2.23	0.84	0.14	0.30
Niacin (mg/d)	23.59	7.09	25.25	9.30	0.19	0.74
Vitamin B6 (mg/d)	2.06	0.67	2.17	0.72	0.28	0.80
Folic acid (µg/d)	585.20	181.26	606.54	171.92	0.40	0.66
Vitamin B12 (µg/d)	3.99	2.00	4.47	2.36	0.15	0.29
Vitamin C (mg/d)	190.26	124.40	195.71	132.75	0.77	0.19
Vitamin E (mg/d)	15.91	6.73	17.32	9.28	0.26	0.37
Vitamin D (µg/d)	2.05	1.73	1.87	1.47	0.44	0.22
Iron (mg/d)	18.28	6.03	18.63	5.90	0.68	0.14
Selenium (µg/d)	114.81	36.86	119.67	42.80	0.42	0.95
Zinc (mg/d)	12.33	4.13	13.12	4.30	0.20	0.94
Magnesium (mg/d)	443.71	144.98	463.73	150.39	0.36	0.65
Calcium (mg/d)	1117.99	423.03	1158.55	410.52	0.50	0.82
Potassium (mg/d)	4208.43	1662.90	4345.83	1538.23	0.55	0.44
Caffeine (g/d)	147.13	105.55	157.53	178.52	0.66	0.72

MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, Saturated fatty acid

Data are presented as mean ± standard deviation (SD).

^a Calculated by analysis of variance and p-value<0.05 indicates a significant level.

*Obtained from Independent T-test

**Obtained from ANCOVA analysis

Food group adjusted by age, BMI, physical activity, and energy intake (Kcal)

Dietary intake (macronutrient and micronutrient) adjusted by energy intake (Kcal)

Correlation of main variables with sarcopenic obesity

Table 3 contains the correlation between sarcopenic obesity with the variables of interest in this study. A simple correlation revealed a significant inverse associations between FFM and FFMI with correlation coefficient ($r=-0.30$, $p<0.001$) and ($r=-0.12$, $p=0.01$) respectively with sarcopenic obesity, while significant

positive correlations were observed between BFM ($r=0.27$, $p<0.001$) and FMI ($r=0.33$, $p<0.001$) with sarcopenic obesity. A non-significant association was however observed between metabolic healthy obesity statuses with sarcopenic obesity.

Table 3. Spearman bivariate correlation of main variables with sarcopenic obesity

Variables	Spearman's correlation coefficient (r)	P-value
Fat Free Mass	-0.30**	<0.001
Body Fat Mass	0.27**	<0.001
FFMI	-0.12*	0.01
FMI	0.33**	<0.001
Metabolic Healthy Obesity	0.04	0.45

Spearman Correlation Analysis

FFMI, fat-free mass index; FMI, fat mass index

** . Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Association between obesity statuses with measures of body composition

With the binary logistic regression analysis, beta (β), odds ratio (OR), and confidence interval (CI) for the association of sarcopenic obesity with measures of body composition in crude and adjusted models are presented in **Table 4**. In the crude model, participants with MUO had greater odds of increasing FFM ($\beta=0.76$, OR=0.27, 95% CI=0.13-0.56, $p=0.001$) than the MHO subjects. However, after controlling for age, total energy intake, and physical activity level, the MUO groups had 0.29 folds decreased odds of FFM ($\beta=-0.89$, OR=0.29, 95% CI=0.13-0.62, $p=0.008$) compared to the MHO group. After additionally controlling for weight and economic status, the observed association disappeared ($\beta=-0.55$, OR=0.26, 95% CI=0.11-0.59, $p=0.07$). In the crude model, participants with MUO were observed to be positively associated with greater odds of increasing BFM ($\beta=1.31$, OR: 3.73, 95% CI=1.27-10.91, $p=0.01$) than those with MHO. Also, after controlling for age, total energy intake, and physical activity level, subjects with MUO phenotype had 4.44 greater odds for BFM, compared to those with MHO phenotype ($\beta=1.49$, OR=4.44, 95% CI=1.31-15.00, $p=0.01$). Even after additional control for weight and economic status, the positive association of the MUO score with higher odds for the BFM remained significant ($\beta=0.95$, OR=2.60, 95% CI=1.39-17.20, $p=0.02$). Subjects with MUO phenotype in the crude model were observed to have a 0.87 kg lower SMM compared with the MHO subjects ($\beta=-0.87$, OR=0.50, 95% CI=0.27-0.90, $p=0.006$). After age, total energy intake, and physical activity had been controlled for, the MUO participants had a 0.83 lower SMM compared with the MHO subjects ($\beta=-0.83$, OR=0.46, 95% CI=0.22-0.84, $p=0.01$). Furthermore, after

additional adjustment for weight and economic status, the association remained significant ($\beta=-0.73$, $OR=0.47$, $95\% CI=0.24-0.94$, $p=0.03$). In the crude model, a non-significant association was seen between metabolic healthy statuses with sarcopenic obesity scores ($\beta=0.35$, $OR=1.42$, $95\% CI=0.45-4.45$, $p=0.54$). However, after controlling for age, total energy intake, physical activity level, weight, and economic status, we observed MUO subjects to have 4.21 fold greater odds for sarcopenic obesity compared to the MHO subjects ($\beta=1.43$, $OR=4.21$, $95\% CI=1.28-62.26$, $p=0.02$).

Table 4. Association between metabolic healthy statuses with measures of body composition and sarcopenic obesity

Variables		β	OR (95% CI)	P-value
Fat-Free Mass				
Crude	MUO	0.76	0.27 (0.13,0.56)	0.001
	MHO	Ref	Ref	
Model 1	MUO	-0.89	0.29 (0.13,0.62)	0.008
	MHO	Ref	Ref	
Model 2	MUO	-0.55	0.26 (0.11,0.59)	0. 07
	MHO	Ref	Ref	
Body Fat Mass				
Crude	MUO	1.31	3.73 (1.27, 10.91)	0.01
	MHO	Ref	Ref	
Model 1	MUO	1.49	4.44 (1.31, 15.00)	0.01
	MHO	Ref	Ref	
Model 2	MUO	0.95	2.60 (1.39, 17.20)	0.02
	MHO	Ref	Ref	
Skeletal Muscle Mass				
Crude	MUO	-0.87	0.50 (0.27, 0.90)	0.006
	MHO	Ref	Ref	
Model 1	MUO	-0.83	0.46 (0.22, 0.84)	0.01
	MHO	Ref	Ref	
Model 2	MUO	-0.73	0.47 (0.24, 0.94)	0.03
	MHO	Ref	Ref	
Sarcopenic obesity				
Crude	MUO	0.35	1.42 (0.45, 4.45)	0.54
	MHO	Ref	Ref	
Model 1	MUO	0.42	1.52 (0.40, 5.70)	0.53
	MHO	Ref	Ref	
Model 2	MUO	1.43	4.21 (1.28, 62.26)	0.02
	MHO	Ref	Ref	

MUO; metabolic unhealthy obese, MH; metabolic obese

P-values are reported base on the Binary logistic regression test and are considered significant at ≤ 0.05

Healthy obese is a reference group

Model 1: Adjusted for age, kcal, and physical activity

Model 2: Model 1 confounders with further adjustment with weight and economic status

Discussion

This study was conducted on overweight and obese Iranian women who were between the ages of 18–50 years, with a BMI greater than or equal to 25 kg/m². The metabolic risk was assessed according to Karelis criteria and the subjects were classified as either MHO or MUO. Of the 241 subjects in this study (average age 35.32 years), 176 (73.03%) were classified as MUO phenotype. Based on this study, the prevalence of sarcopenic obesity was 7.88%. Our study found that high fat-free mass was more strongly and significantly associated with MUO phenotype. Furthermore, we found that individuals with high fat-free mass and high skeletal muscle mass had a significantly low prevalence of MUO phenotype. Consistently, the significant association between high SMM and MUO phenotype persisted even after all potential confounders (age, total energy intake, physical activity, weight, and economic status) were controlled for. Also, we found a significant positive correlation between metabolic phenotypes with sarcopenic obesity after all potential covariates were adjusted for.

Previous epidemiological studies have addressed the issue of fat mass, muscle mass, and sarcopenic obesity in relation to metabolic phenotypes in both Asian and Western populations. The body composition analysis of the two phenotype groups (MUO and MHO) showed that BFM, VFM, FFM, SMM, and FMI, as measured by BIA, were significantly higher in the MUO group than in the MHO group. Previous studies have found that MUO women had significantly higher body fat mass, visceral fat mass, and muscle mass than MHO women [21] and healthy obese people [29].

Despite the fact that some studies (9, 34, 35) have observed a non-significant difference in the measures of adiposity in “healthy” and “unhealthy” phenotypes, in line with other previous studies (3, 10), we observed a significant increase in body fat mass in the MUO phenotype even after all potential confounders were controlled for. Body fat mass has been reported as an independent predictor of insulin resistance and dyslipidemia (36) among postmenopausal women. Moreover, higher body fat has been reported as an increased risk factor for type 2 diabetes (37, 38), as well as increase metabolic risk and the risk of cardiovascular disease (39, 40) in both men and women. Furthermore, researches have shown increasing body fat to be correlated with an increase in fasting blood glucose, triglyceride, LDL cholesterol, and total cholesterol, and a decrease in HDL cholesterol (41, 42).

There have been conflicting results regarding SMM accumulation among the metabolic phenotype groups. While in some studies, no significant differences in SMM indices between metabolic phenotypes of either obese or non-obese postmenopausal women (35) were found, some studies have reported SMM to significantly increase in the MUO phenotype of postmenopausal women (11, 43), and significantly decrease in the metabolic non-obese phenotype of young women (5). Also, Estrella *et al.*, (44) among Hispanic/Latino women, found higher lean body mass to be independently associated with a lower prevalence of the MHO phenotype. In our study, however, each increase of 1-SD in skeletal muscle mass was associated with a lower prevalence of the MUO phenotype. The result from the fourth and fifth Korean National Health and Nutrition Examination Survey indicated a protective association of muscle mass with metabolic syndrome, which was attenuated by high-fat mass (45). Additionally, Burrows *et al.* found in a Chilean birth cohort that low muscle mass is associated with cardiometabolic risk factors independent of dietary intake (46). Furthermore, in a 7-year retrospective cohort study, Kim and colleagues (47) found that an increase in relative skeletal muscle mass over time has a potential preventive effect on developing metabolic syndrome, independently of baseline skeletal muscle mass and glycometabolic parameters. In a nationally representative sample of 4,449 US adults aged 50 years and older from the NHANES surveys, Li and associates (48) found that only participants with low muscle mass but without metabolic syndrome had a significantly increased risk of all-cause mortality. Earlier studies have reported maintenance of muscle mass in the elderly as crucial, as it serves as a metabolic reservoir that is needed to effectively withstand disease (49, 50). The outcome of our study supports the suggestion from a previous report about the importance of skeletal muscle mass in glucose regulation (51), and thus its protection from the development of cardiometabolic abnormalities (45).

After all potential confounders were adjusted for, each increase of 1-SD in sarcopenic obesity was found to be associated with a higher prevalence of MUO phenotype in the current study. Earlier epidemiological studies have shown that the odds of metabolic syndrome was 6 to 8 times higher in postmenopausal Korean women, elderly Korean men and women, and adult Caucasian subjects with sarcopenic obesity (SO) compared to those without sarcopenic obesity (24, 52–54). Furthermore, Kim *et al.*, (55) reported an increased risk of metabolic syndrome in subjects with sarcopenic obesity. In their study, compared with normal subjects among women, they found that SO subjects had significantly higher values for a number of metabolic syndrome components. Furthermore, they found SO to be independently associated with metabolic syndrome among women after adjustment for age.

Strengths And Limitations

Our study has inherent strengths and limitations. A validated food frequency questionnaire was used to assess participants' usual dietary intake. Also, all measurements and interviews were conducted by trained personnel.

Even though this study provides valuable information regarding metabolic phenotypes with sarcopenic obesity and measures of body composition among Iranian subjects, we acknowledge limitations that need to be addressed. First, the cross-sectional nature of this study does not permit the assessment of

causality. Only a prospective study would provide a better understanding of the observed associations. Another limitation of our study is that we used BIA in order to assess body composition and not dual X-ray absorptiometry (DXA) which is considered the gold standard method. However, BIA is also a validated and reliable method for the measurement of body composition in the adult population (56). Furthermore, the result of the current study cannot be generalized since only females were included in the study.

Conclusion

In conclusion, increased adiposity and decreased skeletal muscle mass was associated with unfavorable metabolic traits among overweight and obese Iranian women. SO was also found to be associated with a greater risk of developing MUO phenotype after controlling for potential confounders.

Abbreviations

BFM body fat mass

BIA Bioelectrical impedance analyzer

BMI body mass index

CI confidence intervals

DBP diastolic blood pressure

DXA dual X-ray absorptiometry

FBS fasting blood sugar

FFM fat-free mass

FFMI fat-free mass index

FFQ food frequency questionnaire

FM fat mass

FMI fat mass index

HC hip circumference

HDL high-density lipoprotein

HOMA-IR homeostatic model assessment of insulin resistance

hs-CRP high-sensitive C-reactive protein

IPAQ International Physical Activity Questionnaire

JHS Jahrom Health Study

LDL low-density lipoprotein

MET metabolic equivalent

MHO metabolically healthy obese

MUO metabolically unhealthy obese

OR odds ratios

SBP systolic blood pressure

SDs standard deviations

SE standard errors

SMM skeletal muscle mass

SO sarcopenic obesity

T-choI Total cholesterol

TG triglyceride

TNF tumor necrosis factor

VAT visceral adipose tissue

WC waist circumference

WHO World Health Organization

WHR waist-to-hip ratio

Declarations

Ethical approval

This study was approved by the ethics committee of Tehran University of Medical Sciences (TUMS) with the following identification IR.TUMS.VCR.REC.1398.692.

Consent for publication

Not applicable.

Availability of data and materials

Participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

Competing interests

All authors declared that they have no competing interests

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Author's contributions

ATJ wrote the article, AM and NR revised the article, FSH performed the statistical analyses, KhM had full access to all of the data in the study and took responsibility for the integrity and accuracy of the data. All authors read and approved the final manuscript.

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