Original Article

Relationship between the number of atherosclerosis risk factors and body composition classification including skeletal muscle mass

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Summary

This study aimed to examine the relationship between skeletal muscle mass and atherosclerosis risk according to body composition considering skeletal muscle mass, obesity, and visceral fat accumulation. A total of 4347 men and 1097 women were included. The participants were classified into eight body composition pattern groups within or outside the reference levels (body mass index, waist circumference, and percentage of skeletal muscle). Atherosclerosis risk was defined as hypertension, hyperglycemia, and dyslipidemia. The relationship between average number of atherosclerosis risk factors and body composition was investigated in the eight groups. Decreased skeletal muscle mass may be an independent risk factor for atherosclerosis in both men and women, in that order (percentage of skeletal muscle was a negative contributor). In cases in which body mass index and waist circumference were at the same level, a relatively low skeletal muscle mass may be associated with an increased risk of atherosclerosis. Further sex-based pathophysiological studies are required.

Key Words: atherosclerosis risk factor, skeletal muscle mass, BMI (Body mass index), visceral fat

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I. Introduction

Atherosclerosis, a localized change that occurs primarily in the arterial intima, is caused by various combinations of lipid acidic mucopolysaccharides, blood and its derived substances, fibrous connective tissue proliferation, and calcification[1]. Epidemiological evidence indicates that the major risk factors for atherosclerosis include obesity, visceral fat accumulation, hypertension, diabetes, and dyslipidemia[2]. Current evaluation methods used in the diagnosis and primary prevention of atherosclerosis can be broadly classified into morphological examination methods such as vascular ultrasonography, multidetector-row computed tomography (MDCT), magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), and vascular function tests such as the ankle brachial pressure index, pulse wave velocity, cardio-ankle vascular index, and flow-mediated dilation (FMD)[2]. However, these tests are complicated and time-consuming, making them difficult to use in general practice.

Previous studies reported that obesity and visceral fat accumulation are essential body composition risk factors for atherosclerosis[3]. Furthermore, it was recently reported that decreased skeletal muscle mass, a body composition component, is an independent risk factor for atherosclerosis[4]. We also previously reported that decreased skeletal muscle mass is independently associated with an increased risk of atherosclerosis[5–7]. However, there is little evidence of the relationship between atherosclerotic risk factors and body composition in terms of skeletal muscle mass.

This study aimed to evaluate the relationship between atherosclerosis risk factors and body composition (body mass index [BMI], waist circumference, and skeletal muscle mass) in Japanese individuals.

II. Participants and Methods

1. Participants

A total of 6327 men and 1518 women participants who underwent a comprehensive health examination (Ningen Dock) at a hospital in Kyoto were recruited. Participants lacking relevant data (362 men and 177 women) and those taking medication for hypertension, dyslipidemia, or diabetes (1618 men and 244 women) were excluded. Thus, a total of 4347 men and 1097 women were included in this study.

2. Methods

(1) Data

The health examination included physical measurements

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(height, body weight, waist circumference as an index of visceral fat accumulation, and percentage of skeletal muscle, as an index of skeletal muscle mass), blood pressure (while seated), and fasting blood tests (triglyceride, high-density lipoprotein [HDL] cholesterol, and blood glucose). The physical examination and blood sampling were performed after an overnight fast. The percentage of skeletal muscle was measured using the upper and lower limb impedance method[8] (modified HBF-354; Omron Healthcare).

(2) Classification of body components

The participants were classified into Groups A–H within or outside the reference levels (BMI, waist circumference, and percentage of skeletal muscle) (Table 1).

In Groups A and B, Groups C and D, Groups E and F, and Groups G and H, BMI and waist circumference were at the same level, and the percentage of skeletal muscle was classified into two groups within or outside the reference levels. The reference levels were BMI < 25 kg/m^2 and waist circumference < 85 cm for men (< 90 cm for women) using the diagnostic criteria of the Specific Health Examination[3,9,10]. The percentage of skeletal muscle was evaluated in terms of the weight ratio of skeletal muscle mass to body weight. In our previous study, the reference levels for the percentage of skeletal muscle were ≥32.5% for men and ≥25.5% for women obtained in our previous study[11].

(3) Atherosclerosis risk

Atherosclerosis risk, defined as the presence or absence of hypertension, hyperglycemia, and dyslipidemia (presence = 1 point; absence = 0 points), was used as the average number of atherosclerosis risk factors. The reference level was determined using the Japanese metabolic syndrome criteria (hypertension: systolic blood pressure, <130 mmHg and diastolic blood pressure, <85 mmHg; hyperglycemia: fasting blood glucose <110 mg/dL; dyslipidemia: triglyceride <150 mg/dL and HDL cholesterol ≥40 mg/dL)[3,9,10]. The average number of atherosclerosis risk factors was calculated for each of the eight groups (Groups A–H) and compared between two groups with the same BMI and waist circumference, and percentage of skeletal muscle within or outside the reference levels.

3. Statistical analyses

IBM SPSS Statistics 24 was used for the statistical analyses. Spearman's correlation analysis was used to examine the relationship between the average number of atherosclerosis risk factors and age, BMI, waist circumference, and percentage of skeletal muscle. A multiple regression analysis was performed of age, waist circumference, and percentage of skeletal muscle as independent variables and the average number of atherosclerosis risk factors as the dependent variable.

Multicollinearity between the independent variables was determined using a variance inflation factor (VIF) ≥ 10. The Mann–Whitney U-test was used to compare the two groups. Values of $p < 0.05$ were considered significant.

4. Ethical Considerations

Informed consent was obtained from all participants. This study was approved by the ethical committee of Kyoto Women's University (approval numbers: 27-3, 30-16) and performed in accordance with the Helsinki Declaration.

III. Results

Table 1 presents the participants' characteristics of body composition and numbers in the eight groups. The largest percentages of both men and women were in Group A (BMI, waist circumference, and percentage of skeletal muscle were all within the reference ranges [men, 36.5%; women, 60.3%]), followed by Group B (BMI and waist circumference were within reference levels, while the percentage of skeletal muscle was outside the reference levels for both men and women [men, 22.1%; women, 23.4%]).

Table 2 shows the patients' characteristics. The men had significantly greater mean height, body weight, BMI, waist circumference, percentage of skeletal muscle, systolic and diastolic blood pressures, triglycerides, and fasting blood glucose levels and significantly lower HDL cholesterol levels than the women.

Table 1. Paticipants' characteristics and numbers in the eight groups

	Group	A	B	C	D	E	F	G	H	Total number
	BMI	○		○		×		×		
	Waist circumference	○		×		○		×		
	Percentage of skeletal muscle	○	×	○	×	○	×	○	×	
Men	number	1587	962	237	507	21	45	118	870	4347
	%	36.5	22.1	5.5	11.7	0.5	1	2.7	20	100
Women	number	662	257	8	19	11	39	14	87	1097
	%	60.3	23.4	0.7	1.7	1	3.6	1.3	7.9	100

○ BMI < 25 kg/m^2, Waist circumference < 85 cm for men or < 90 for women, Percentage of skeletal muscle ≥ 32.5% for men and 25.5% for women

× BMI ≥ 25 kg/m^2, Waist circumference ≥ 85 cm for men or ≥ 90 cm for women, Percentage of skeletal muscle < 32.5% for men or < 25.5% for women

Table 2. Patients' characteristics

	Men (n = 4347)	Women (n = 1097)	p
Age (years)	48.6 ± 9.5	48.3 ± 11.2	0.670
Height (cm)	171.7 ± 6.1	158.2 ± 5.6	<0.001
Body weight (kg)	68.6 ± 10.4	54.2 ± 9	<0.001
BMI (kg/m²)	23.2 ± 3.1	21.6 ± 3.4	<0.001
Waist circumference (cm)	83.4 ± 8.3	78.4 ± 9.4	<0.001
Skeletal muscle mass (kg)	22.2 ± 3.2	14.2 ± 2.2	<0.001
Percentage of skeletal muscle (%)	32.4 ± 2.3	26.4 ± 2.3	<0.001
Systolic blood pressure(mmHg)	124.5 ± 14.6	116.4 ± 16.6	<0.001
Diastolic blood pressure(mmHg)	78.8 ± 11.5	71.1 ± 12	<0.001
Triglyceride (mg/dl)	124.9 ± 105.3	83.7 ± 57.5	<0.001
HDL cholesterol(mg/dl)	59.4 ± 14.6	70.2 ± 15.7	<0.001
Fasting glucose (mg/dl)	101.9 ± 12.9	97.3 ± 12.9	<0.001

(Mean ± SD)

Table 3 shows the simple correlation between the average number of atherosclerosis risk factors and age, waist circumference, and percentage of skeletal muscle. The average number of atherosclerosis cases was significantly positively correlated with age, BMI, and waist circumference in both men and women but significantly negatively correlated with the percentage of skeletal muscle.

Multiple regression analysis showed multicollinearity for BMI and waist circumference (VIF ≥ 10). Therefore, age, waist circumference, and percentage of skeletal muscle were considered dependent variables. Waist circumference, age, and percentage of skeletal muscle were significant contributors to the risk of atherosclerosis in both men and women (percentage of skeletal muscle was a negative contributor) (Table 4).

Fig.1 shows the average number of atherosclerosis risk factors based on body composition. Among the men, the average number of atherosclerosis risk factors was significantly higher in Groups B, D, and H than in Groups A, C, and G. Among the women, the average number of atherosclerosis risk factors was significantly higher in Groups B, F, and H than in Groups A, E, and G.

Table 3. The simple correlation between the average number of atherosclerosis risk factors and age, waist circumference, and percentage of skeletal muscle.

	Men (n = 4347)		Women (n = 1097)	
	r	p	r	p
Age	0.231	<0.001	0.367	<0.001
BMI	0.343	<0.001	0.312	<0.001
Waist circumference	0.371	<0.001	0.333	<0.001
Percentage of skeletal muscle	-0.373	<0.001	-0.388	<0.001

Atherosclerosis risk : Hypertension, Diabetes, dyslipidemia

IV. Discussion

In this study, a decreased skeletal muscle mass was an independent risk factor for atherosclerosis, aging, BMI, and visceral fat accumulation. Furthermore, when BMI and waist circumference were at the same level, groups outside the standard level range of percentage of skeletal muscle showed significantly higher average number of atherosclerosis risk factors than those within the standard level among both men and women.

It is widely known that insulin resistance with obesity and visceral fat accumulation is associated with atherosclerosis[12]. Some studies reported that a decreased skeletal muscle mass might also cause insulin resistance[13–18] due to mitochondrial dysfunction. Decreased mitochondrial function reduces lipid metabolism in skeletal muscle mitochondria, causing an accumulation of lipid metabolites such as long-chain acyl coenzyme A and ceramide in muscle cells of the elderly, obese individuals, and patients with type 2 diabetes[13,14]. Furthermore, the accumulation of fat in skeletal muscle cells by impaired mitochondrial function in the elderly and type 2 diabetics is associated with insulin resistance[14].

Table 4. Multiple regression analysis between the average number of atherosclerosis and age, waist circumference and percentage of skeletal muscle

	Men (n = 4347)			Women (n = 1097)		
	β	p	VIF	β	p	VIF
Age	0.149	<0.001	1.561	0.204	<0.001	1.394
Waist circumference	0.29	<0.001	1.661	0.22	<0.001	1.553
Percentage of skeletal muscle	-0.125	<0.001	2.282	-0.144	<0.001	2.011

Independent values: age, waist circumference, percentage of skeletal muscle
Dependent values: numbers of atherosclerotic risk

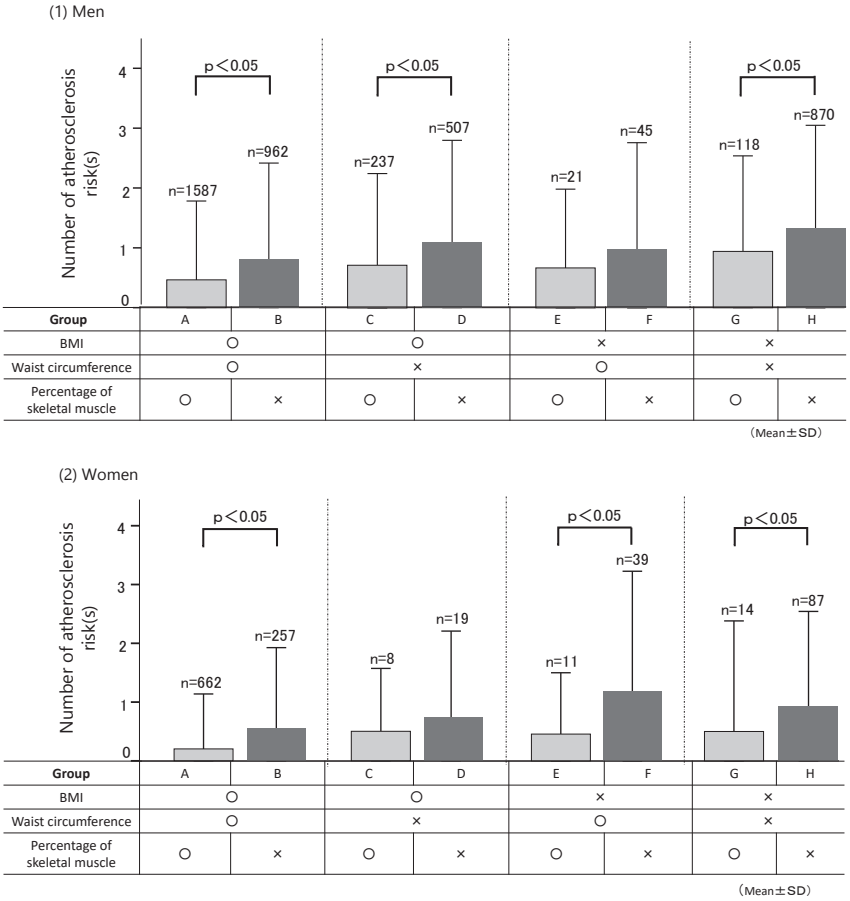

Fig 1. Average number of atherosclerosis risk factors by body composition type. The participants were classified into Groups A–H based on body composition (BMI, waist circumference, and percentage of skeletal muscle).

Some myokines, hormones secreted by skeletal muscles, reportedly have various effects on metabolism related to atherosclerosis. First, the functions of interleukin-6 differ among organs, promoting glucose uptake by the skeletal muscle[17] and insulin secretion by stimulating the secretion of glucagon-like peptide-1, an incretin[19]. Second, irisin is produced and released in the skeletal muscle with increased secretion of peroxisome proliferator-activated receptor-gamma coactivator-1α, a transcriptional coactivator, and increases energy expenditure by changing white fat cells to brown in the subcutaneous fat[18]. Third, β-aminoisobutyric acid increased energy expenditure by turning white fat cells brown and increasing β-oxidation of fatty acids in the liver[20]. Thus, myokines may have a suppressive effect on the risk of atherosclerosis by promoting glucose metabolism and energy expenditure, while a decrease in skeletal muscle mass may lower myokine function. However, myokines reportedly function differently depending on conditions such as exercise[17]. Thus, further studies are required to investigate their function under various conditions.

Recent studies reported that myosteatosis (low attenuation muscle area and intramuscular adipose tissue) underlying muscle quality also plays a more critical role than changes in skeletal muscle mass in the decline of skeletal muscle function and risk of adverse effects[21,22]. This study showed sex-based differences in the relationship between skeletal muscle mass and atherosclerosis risk. One of the reasons for this may be that skeletal muscle mass in women is relatively low (about two-thirds that of men). Therefore, the skeletal muscle has a little effect on atherosclerosis. Another reason is that sex-based differences in muscle fiber composition might lead to different physiological roles of skeletal muscles in cardiovascular diseases[23–25].

Skeletal muscle mass index (SMI), the amount of skeletal muscle in the limbs (kg) divided by the height squared (m^2), is used to diagnose sarcopenia[26]. However, this study used the percentage of skeletal muscle to assess skeletal muscle mass because SMI has a significant positive correlation with insulin resistance but a significant negative correlation with the percentage of skeletal muscle[27].

This study had some limitations. First, it did not evaluate the degree of arteriosclerosis. Second, insulin resistance, mitochondrial function in the skeletal muscle, and myokine secretion were not measured. Third, this study investigated only the relationship between skeletal muscle mass and atherosclerosis, whereas muscle strength, quality, and physical activity were not considered. Fourth, the relationship between insulin resistance and SMI or the percentage of body mass was not examined. Fifth, this was a cross-sectional study; thus, causal relationships remain unknown.

Despite these limitations, this study's findings suggest that a decrease in skeletal muscle mass may be an independent risk

factor for atherosclerosis in both men and women. In cases in which BMI and waist circumference are at the same level, a relatively low skeletal muscle mass may be associated with an increased risk of atherosclerosis. Further sex-based pathophysiological studies are required to validate our findings.

Conflict of Interest

The authors declare no conflicts of interest.

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