small sample of older adults.[24] However, the association of skeletal muscle mass with age-dependent changes in visceral fat in a large population has not previously been shown.

The primary aim of the present study was to evaluate the age-dependent changes in skeletal muscle mass and visceral fat area using a large cross-sectional cohort of Japanese adults between 40 and 79 years-of-age. We also evaluated sex differences in skeletal muscle loss in the arms and legs. The secondary aim of the present study was to evaluate the association between the skeletal muscle mass and visceral fat area.

Methods

Participants

Participants were recruited by advertisements at several fitness and community centers. The participants in the present study were limited to visitors to these centers in the Kyoto, Osaka, and Hyogo prefectures in Japan. The inclusion criteria were an age of 40–79 years, living in the community and the ability to walk independently (including with a cane). The exclusion criteria were a certification of frailty status by the long-term care insurance service in Japan and artificial implants, such as cardiac pacemakers and replacement joints, which would interfere with accurate bioimpedance measurements. An interview was also used to identify those with the following exclusion criteria: severe cognitive impairment; severe cardiac, pulmonary, or musculoskeletal disorders; and comorbidities associated with greater risk of falls, such as Parkinson's disease or stroke. Because the purpose of the present study was to address physiological age-dependent changes in body composition, we excluded frail elderly and adults with those comorbidities. The present study was carried out in accordance with the guidelines of the Declaration of Helsinki, and the study protocol was reviewed and approved by the Ethics Committee of the Kyoto University Graduate School of Medicine.

Healthy men (n = 16 379) and women (n = 21 660) aged 40–79 years participated in the present study. The male participants were divided into eight groups according to age: 40–44 (n = 3697), 45–49 (n = 3151), 50–54 (n = 2202), 55–59 (n = 1952), 60–64 (n = 2274), 65–69 (n = 1683), 70–74 (n = 1030), and 75–79 (n = 390) years. The female participants were similarly divided into eight groups according to age: 40–44 (n = 3828), 45–49 (n = 3686), 50–54 (n = 3597), 55–59 (n = 3002), 60–64 (n = 3490), 65–69 (n = 2314), 70–74 (n = 1269), and 75–79 (n = 474) years.

Skeletal muscle mass index and visceral fat area

A bioelectrical impedance data acquisition system (Inbody 720; Biospace, Seoul, Korea) was used to determine bioelectrical impedance.[25] This system uses an electrical current at different frequencies (5, 50, 250, 500, and 1000 kHz) to directly measure the amount of extracellular and intracellular water in the body. The study participants stood on two metallic electrodes and held metallic grip electrodes. Using segmental body composition and muscle mass, a value for the appendicular skeletal muscle mass was determined and used for further analysis. The muscle mass was converted into the skeletal muscle mass index (SMI) by dividing the weight by the height squared (kg/m^2). This index has been used in several epidemiological studies.[6,26] Additionally, the SMI of the arms and legs was calculated. The visceral fat area was determined by evaluating a transverse cross-section of the fourth and fifth abdominal lumbar area.

Statistical analysis

Differences in the total SMI, arm SMI, leg SMI, and visceral fat area among the eight age groups were examined using an analysis of variance. Multiple regression models were applied to determine the relationship between the visceral fat area and the SMI, adjusted for age and weight in each sex. The data were managed and analyzed using SPSS (Windows version 18.0; SPSS, Chicago, IL, USA). A P-value of <0.05 was considered to show statistical significance for all analyses.

Results

The mean age of the study participants was 54.5 ± 9.9 years, and 21 660 (56.9%) of the participants were women. The total SMI showed an age-dependent decrease in both sexes (men, F = 251.1, P < 0.001; women, F = 135.6, P < 0.001; Table 1). The percentage change in the total SMI at 40–44 years showed an age-dependent decrease in both sexes (Fig. 1, Table 1). In those aged over 65 years, the percentage change in the total SMI was greater in men than in women. In addition, the 20th percentile of total SMI in men and women aged 65–79 years was 7.02 kg/m^2 and 5.61 kg/m^2, respectively (Table 2).

To compare the age-dependent changes in muscle mass in the upper and lower limbs in this cohort, we analyzed the arm and leg SMI. The arm SMI showed an age-dependent decrease in both sexes (men, F = 132.1, P < 0.001; women, F = 24.1, P < 0.001; Table 1). The percentage change in the arm SMI using the 40–44 years group as a reference also showed an age-dependent decrease in both sexes (Fig. 2, Table 1).

Similarly to the arm SMI, the leg SMI also showed an age-dependent decrease in both sexes (men, F = 273.2, P < 0.001; women, F = 192.2, P < 0.001; Table 1). The percentage change in the leg SMI also showed an

Table 1 Participant characteristics by age half decade

		Overall Men (n = 16 379) Women (n = 21 660)			40–44 years Men (n = 3697) Women (n = 3828)			45–49 years Men (n = 3151) Women (n = 3686)			50–54 years Men (n = 2202) Women (n = 3597)			55–59 Men (n = 1952) Women (n = 3002)		
		Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years
Total SMI (kg/m^2)	Men	7.97	0.73	–	8.20	0.78	–	8.11	0.66	−1.0	8.11	0.67	−1.1	7.98	0.64	−2.7
	Women	6.26	0.64	–	6.41	0.67	–	6.39	0.64	−0.3	6.33	0.64	−1.3	6.23	0.59	−2.8
Arm SMI (kg/m^2)	Men	2.08	0.28	–	2.14	0.31	–	2.11	0.26	−1.4	2.11	0.26	−1.2	2.08	0.24	−3.0
	Women	1.47	0.22	–	1.49	0.24	–	1.49	0.23	−0.5	1.47	0.22	−1.4	1.46	0.21	−2.3
Leg SMI (kg/m^2)	Men	7.98	0.73	–	6.06	0.51	–	6.00	0.46	−0.9	5.99	0.46	−1.1	5.91	0.45	−2.5
	Women	6.26	0.64	–	4.92	0.48	–	4.91	0.45	−0.3	4.85	0.46	−1.3	4.77	0.42	−3.0
Visceral fat area (cm^2)	Men	100.6	29.2	–	88.4	28.8	–	91.9	27.1	4.0	98.9	28.8	11.9	103.5	25.7	17.1
	Women	84.7	27.4	–	68.0	25.3	–	72.1	23.9	6.0	79.3	23.6	16.5	89.4	23.0	31.5

		60–64 years Men (n = 2274) Women (n = 3490)			65–69 years Men (n = 1683) Women (n = 2314)			70–74 years Men (n = 1030) Women (n = 1269)			75–79 years Men (n = 390) Women (n = 474)			ANOVA	
		Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	F-value	P-value
Total SMI (kg/m^2)	Men	7.84	0.68	−4.3	7.64	0.67	−6.9	7.59	0.66	−7.4	7.32	0.62	−10.8	251.1	<0.001
	Women	6.14	0.61	−4.2	6.08	0.60	−5.2	6.09	0.55	−5.1	6.00	0.60	−6.4	135.6	<0.001
Arm SMI (kg/m^2)	Men	2.05	0.25	−4.4	1.99	0.25	−6.9	1.96	0.24	−8.5	1.87	0.26	−12.6	132.1	<0.001
	Women	1.45	0.22	−3.1	1.44	0.21	−3.6	1.46	0.20	−2.5	1.43	0.21	−4.1	24.1	<0.001
Leg SMI (kg/m^2)	Men	5.80	0.48	−4.3	5.64	0.46	−6.9	5.64	0.51	−7.0	5.45	0.45	−10.1	273.2	<0.001
	Women	4.69	0.43	−4.6	4.64	0.44	−5.7	4.63	0.41	−5.9	4.57	0.45	−7.1	192.2	<0.001
Visceral fat area (cm^2)	Men	108.3	26.2	22.5	113.0	25.7	27.8	122.3	25.1	38.3	126.4	25.2	42.9	376.9	<0.001
	Women	94.0	23.3	38.2	101.6	23.0	49.4	108.5	24.1	59.5	112.4	29.3	65.3	966.7	<0.001

Percentage change of 40–44 years = (absolute change value / 40–44 years value) × 100. SMI, skeletal muscle mass index.

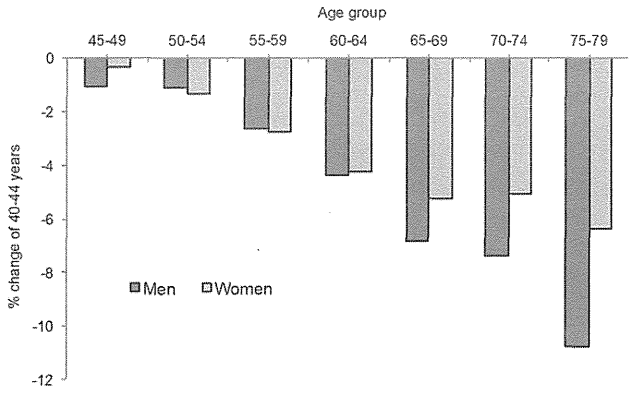

Figure 1 The percentage of change in the total skeletal muscle mass index in each sex and each age group, using 40–44 years-of-age as a reference.

Table 2 20th percentile of total skeletal muscle mass index (kg/m^2) in both sexes

Age group (years)	20th percentile of SMI	
	Men	Women
65–69	7.06	5.61
70–74	7.09	5.63
75–79	6.83	5.54
65–79	7.02	5.61

SMI, skeletal muscle mass index.

age-dependent decrease in both sexes (Fig. 2, Table 1). The age-dependent changes in the leg SMI were similar in men and women. However, the age-dependent changes in the arm SMI were greater in men than in women.

Next, we examined the age-dependent changes in visceral obesity. The visceral fat area showed an age-dependent increase in both sexes (men, $F = 376.9$, $P < 0.001$; women, $F = 966.7$, $P < 0.001$; Table 1). The percentage change from 40–44 years in the visceral fat area showed an age-dependent increase in both sexes (Fig. 3, Table 1).

To examine the association between skeletal muscle mass and visceral obesity, we carried out a multiple regression analysis using the SMI as an outcome. We found that the visceral fat area, age, and weight were significant and independent determinants of the SMI in both men ($\beta = -0.586$) and women ($\beta = -0.627$; Table 3). Therefore, the age-dependent change in the SMI was negatively associated with the visceral-fat area in both sexes.

Discussion

The current cross-sectional study was carried out to evaluate the SMI in Japanese adults aged between 40 and 79 years. Our data show that the SMI decreased age-dependently in both sexes. Notably, regarding the age-dependent decreases in the total SMI and in those aged over 65 years, the percentage change in the total SMI was greater in men than in women. From 40 to 79 years, the total SMI decreased by 10.8% in men and by 6.4% in women. Previous epidemiological studies of body composition have shown that between 40 and 79 years, the fat-free mass decreases by 6.6–23.3% in both sexes.[19,20] The age-dependent increases in inflammatory cytokines, such as IL-6 and TNF-α, can result in increased skeletal muscle breakdown.[23] In contrast, the age-dependent decrease in anabolic hormones, such as testosterone, growth hormone, and insulin-like growth factor-1 (IGF-1), might lead to a loss of skeletal muscle

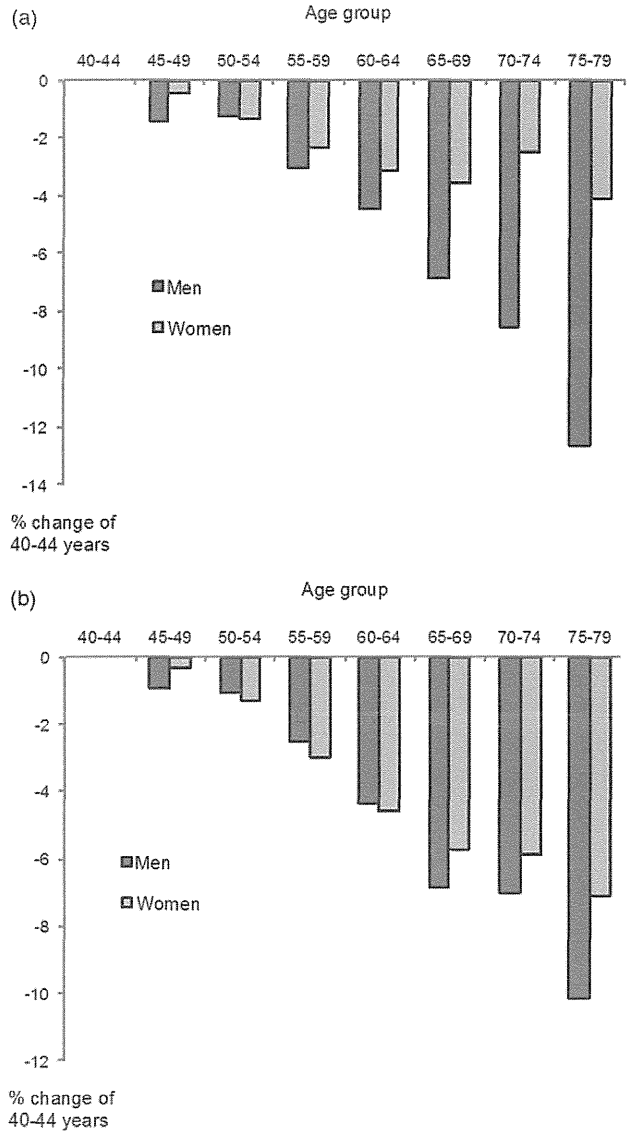

Figure 2 The percentage of change in the (a) arm and (b) leg skeletal muscle mass index (SMI) in each sex and each age group using 40–44 years-of-age as a reference.

mass.[27,28] In addition, there is also an age-dependent decrease in the amount of physical activity and energy intake. These behavioral changes can enhance the age-dependent reduction in skeletal muscle mass.

Interestingly, in those aged over 65 years, age-dependent decreases in total SMI were greater in men than in women. Furthermore, this age-dependent sex difference was more prominent in the arm than in the leg. From 40 to 79 years, the arm SMI decreased by 12.6% in men and by 4.1% in women. This is consistent to the previous studies in Japanese older adults. Kitamura *et al.* reported that the arm lean tissue mass was 5.97 ± 0.75 and 5.01 ± 0.67 in men, and 3.56 ± 0.54 and 3.24 in women aged in their 40s and 70s, respectively.[29] Based on their data, the percentage change in the arm lean tissue mass in men is −16.0% and is −8.9% in women. However, there is no sex difference in the percentage change in the leg lean tissue mass. The mechanism of this sex difference in the arm and leg lean tissue mass change is not clear. In general, older Japanese women frequently use the upper limbs, such as when washing and cooking. However, older Japanese men usually do not carry out such work. Therefore, it is possible that these behavioral differences lead to greater age-dependent decreases in the arm SMI in men than in women. As another possibility, Baumgartner reported that the sex hormone signal is an important factor for muscle mass in men, but not in women; however, physical activity is an important factor for muscle mass in both sexes.[30] Furthermore, previous studies have shown that 20% of men older than 60 years, 30% of men older than 70 years, and 50% of men older than 80 years have serum testosterone levels below the normal range.[31] Thus, it is also possible that the sex hormone-dependent changes in muscle mass are greater in men than in women. Therefore, age-dependent gender differences in the SMI might be influenced by daily activity or alterations in sex hormone levels.

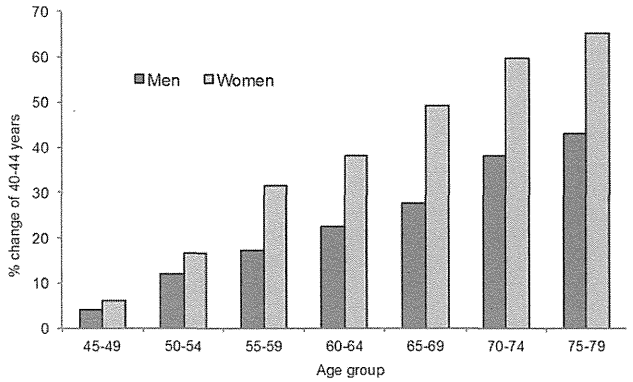

Figure 3 The percentage of change in the visceral fat area in each sex and each age group using 40–44 years-of-age as a reference.

The present data show that aging is associated with a progressive increase in visceral fat area in both sexes. From 40 to 79 years of age, the visceral fat area increased by 42.9% in men and by 65.3% in women. Furthermore, the SMI was negatively associated with the visceral fat area when adjusted for age and body weight in both sexes. The visceral adipose tissue produces many catabolic factors, such as TNF-α and IL-6.[22] Therefore, the age-dependent increases in both visceral adipose tissue and inflammatory cytokines might lead to a loss of skeletal muscle mass. Recently, sarcopenic obesity has been defined as both low muscle mass and high adipose tissue in older adults, and the health-related risk is higher in sarcopenic obesity than in sarcopenia.[32] The current data show that the age-dependent changes in body composition can accelerate sarcopenic obesity. These results suggest that it is very important to begin prevention of sarcopenia and sarcopenic obesity as early as possible.

According to our analysis of this cohort, we found that the 20th percentile of total SMI in men and women aged 65–79 years was 7.02 kg/m^2 and 5.61 kg/m^2, respectively. These values were slightly higher than those determined by the young adult mean in our database (men 6.75 kg/m^2; women 5.07 kg/m^2).[18] That these values were lower than the 20th percentile of total SMI

Table 3 Multiple regression analysis for the association with skeletal muscle mass index in both sexes

Independent variables	Men Adjusted R^2 value = 0.781** standard regression value	Women Adjusted R^2 value = 0.627** standard regression value
Visceral fat area (cm^2)	−0.586**	−0.627**
Age (year)	0.212**	0.252**
Weight (kg)	1.180**	1.169**

**$P < 0.01$.

is probably because we did not use the data of SMI in participants aged 80 years and older. Other studies on sarcopenia in Asia also show that the cut-off of SMI is 6.08–7.27 kg/m^2 in men and 4.79–5.80 kg/m^2 in women,[13,33–35] which is quite consistent with the present results. Thus, the 20th percentile of total SMI in men and women in our data can be used for the cut-off of SMI in Asians; however, further studies are required to address whether these cut-off points are associated with adverse health outcomes in Asian older adults.

There were several limitations to the present study that warrant mention. First, physical performance data were not measured. The European Working Group on Sarcopenia in Older People (EWGSOP) has recommended using the presence of both low muscle function (low physical performance or muscle strength) and low muscle mass to diagnose sarcopenia.[36] Therefore, the prevalence of sarcopenia could not be determined. Second, the study design was cross-sectional, and no outcome data are available. Further research with a longitudinal design will be required to clarify whether low muscle mass can predict adverse health outcomes in older Japanese adults. Third, the SMI measurement was estimated using BIA, which is not a method that is recommended by the EWGSOP for assessing muscle mass. However, it is very challenging to measure muscle mass in community-dwelling older adults using dual-energy X-ray absorptiometry (DXA); thus, BIA is a more practical screening method to use in large samples, especially in a community setting. However, to determine the specific effect of an intervention, a more accurate measurement, such as DXA, computed tomography, or magnetic resonance imaging, should be used in future studies. Serum outcomes were not measured. Therefore, the relationship between the SMI and hormone signals could not be determined. Finally, the participants in the present study were limited to visitors to fitness and community centers. Therefore, the participants of this study might not be a representative sample of community-dwelling adults.

In conclusion, the SMI showed an age-dependent decrease in both sexes, and the total SMI decreased by 10.8% in men and by 6.4% in women aged 40–79 years. Notably, age-dependent sex differences were more pronounced in the arm SMI; from 40 to 79 years, the arm SMI decreased by 12.6% in men and 4.1% in women. These results suggest that the age-dependent loss of skeletal muscle mass begins at approximately 40 years-of-age, and becomes prominent after 50 years-of-age in Japanese adults. Furthermore, the visceral fat area showed an age-dependent increase in both sexes, and the visceral fat area increased by 42.9% in men and by 65.3% in women of 40–79 years-of-age. Finally, the SMI was negatively associated with the visceral fat area in both sexes. Thus far, no studies have reported age-dependent changes and the association of muscle mass and visceral fat in Asian populations. Therefore, the current data could be used as the reference value for Asian adults.

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Disclosure statement

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Arterial stiffness is associated with low skeletal muscle mass in Japanese community-dwelling older adults

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Aim: To examine whether arterial stiffness, measured by the cardio-ankle vascular index (CAVI), is associated with skeletal muscle mass index (SMI) in Japanese community-dwelling older adults.

Methods: Data were collected from 175 participants through questionnaires and specific tests; the data included demographic, lifestyle and health characteristics, body mass index (BMI), and body composition features determined by the bioelectrical impedance analysis, ankle-brachial index, the Mini-Nutritional Assessment, handgrip strength (GS), walking speed and shuttle walking tests (SW), and arterial stiffness determined by the CAVI. Absolute SMI was dichotomized according to the first quintile, which determined low ($n = 35$) and normal ($n = 140$) SMI.

Results: Participants with low SMI were older ($P = 0.01$), had more polypharmacy ($P = 0.01$), a lower BMI ($P < 0.001$), and fat mass index ($P = 0.02$), and had a greater risk of malnutrition ($P < 0.001$) than the normal group. Additionally, they showed poorer physical performance (GS and SW, $P = 0.007$ and 0.01, respectively) than the normal group. Furthermore, CAVI was associated with SMI even after adjustments (OR 1.82, 95% CI 1.14–2.90, $P = 0.01$).

Conclusions: Our data showed that arterial stiffness is associated with low SMI in community-dwelling older adults, even when adjusting by multiple factors, showing a close interaction of vascular aging and muscle mass decline. **Geriatr Gerontol Int 2014; 14 (Suppl. 1): 109–114.**

Keywords: arterial stiffness, cardio-ankle vascular index, older adults, sarcopenia, skeletal muscle mass.

Introduction

The progressive loss of skeletal muscle mass is the primordial factor to determine sarcopenia, a syndrome that combines low skeletal muscle mass and strength, and can lead to adverse health outcomes, such as physical disability, poor quality of life and mortality.[1] In addition, the elderly might experience several adverse health outcomes as a result of vascular aging, such as increased arterial stiffness, which can contribute to the development of cardiovascular and cerebrovascular diseases.[2] It is known that both the loss of skeletal muscle mass and arterial stiffness worsen with age, and that some of the predisposing factors and mechanisms underlying low muscle mass and sarcopenia; for example, oxidative stress,[3] inflammation,[4] and insulin resistance,[1] are also associated with atherosclerosis.[5] However, only a few studies have been carried out to verify such associations.[5–8] A study showed that arterial stiffness is associated with an increase in the loss of muscle mass index over time independent of age, body fat, peripheral arterial disease, chronic inflammation, and cardiac disease.[6] Other studies have verified the associations of peripheral lean mass and visceral fat mass with atherosclerosis,[7] and the relationships between regional fat and lean mass and large artery properties in young men and women.[8]

A novel measurement tool to assess arterial stiffness is the cardio-ankle vascular index (CAVI), which reflects the stiffness of the aorta, femoral artery, and tibial artery, and involves the measurement of the brachial-ankle pulse wave velocity (baPWV) and blood pressure (BP). The most important feature of CAVI is its independence from BP during examination,[2,9,10] which shows that it is a useful tool to assess those who are

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subject to variation in blood pressure at different times of the day, suffer from masked hypertension or are taking antihypertensive medications.[11]

Therefore, the objective of the present study was to examine whether arterial stiffness, measured by CAVI, is associated with skeletal muscle mass index (SMI) in Japanese community-dwelling older adults. We hypothesized that arterial stiffness is associated with a low SMI independent of sex, nutritional status, and physical performance in community-dwelling older adults.

Methods

The present study had a cross-sectional design.

Participants

The participants of the present study were community-dwelling Japanese older adults ($n = 175$; male = 84, female = 91) recruited through local press announcements requesting healthy volunteers. Recruited participants were 65 years-of-age or older, and were able to carry out the activities of daily living (ADL) and answer the proposed questionnaires. The exclusion criteria at the first screening were the following: (i) moderate cognitive impairment (i.e. Mini-Mental State Examination score ≤21 points); (ii) uncontrolled cardiovascular, pulmonary, or metabolic diseases; (iii) any orthopedic conditions that could restrain the ADL; and (iv) comorbidities associated with a greater risk of falls (e.g. Parkinson's disease and stroke). Additionally, in the present study, none of the participants had peripheral artery disease as evidenced by an ankle-brachial index (ABI) of less than 0.9. All participants were informed of the purpose and procedures of the study, and signed a written consent. The data were collected in November 2012.

The study protocol was approved by the Kyoto University Graduate School of Medicine Ethics Committee (No. E1245, E1583).

Assessments

The participants answered a self-administered questionnaire about demographic, lifestyle, and health characteristics, including age, regular physical activity engagement, alcohol consumption, smoking, current number of medications, and morbidities (i.e. diabetes, hypertension, hyperlipidemia and coronary artery disease; determined by the assumption that the prescribed medications they reported in the analysis were being used for the morbidity).

Additional relevant health indicators, such as (i) body mass index (BMI); (ii) body composition features determined by bioelectrical impedance analysis (Inbody 430; Biospace, Seoul, Korea); (iii) ABI; and (iv) the Mini-Nutritional Assessment short-form (MNA)[12] were also collected.

The bioelectrical impedance instrument made use of octapolar tactile electrodes, two in contact with the palm and thumb of each hand, and two with the anterior and posterior aspects of the sole of each foot. The participants were instructed to stand with their soles in contact with the foot electrodes and to grasp the hand electrodes. The resistance of the arms, trunk, and legs was measured at frequencies of 5, 50, and 250 kHz. The participants' ID number, height (measured with a standard stadiometer), age, and sex were also inserted in the analyzer. Then, body mass and consequently BMI were automatically measured by the "InBody". For classification purposes, the BMI cut-offs used were those proposed by the Japan Society for Study of Obesity (i.e. underweight, BMI <18.5 kg/m^2, normal weight, BMI 18.5–25 kg/m^2, and obese, BMI ≥25 kg/m^2).[13] The bioelectrical impedance examination provided values for absolute skeletal muscle mass, body fat percentage, absolute fat mass, and segmental muscle mass (right and left arms/legs and trunk). From these measurements, absolute skeletal muscle mass and absolute fat mass were posteriorly adjusted by height to determine the SMI and fat mass index (FMI), respectively. The "InBody" system uses direct segmental multifrequency technology, and had previously been validated as having a strong correlation to muscle volume and fat mass as measured by dual energy X-ray absorptiometry.[14,15]

Physical performance was investigated by the following: (i) handgrip strength (GS); (ii) walking speed (WS); and (iii) shuttle walking tests (SW).[16,17]

GS was collected with a standard handgrip dynamometer (Smedlay's Dynamo Meter; TTM, Tokyo, Japan). The participants were asked to stand up and hold the dynamometer with their arms parallel to their bodies without touching their bodies. GS was measured once for each hand, and the higher value was used to characterize his/her maximum muscle strength. GS was expressed in kilograms (kg).

In the WS test, outside marks of 12 m in length were clearly placed on the ground. Inside this distance, another 10 m long delimitation was marked. The participants were asked to walk the entire distance at their usual pace, but only the time to complete the inner 10 m distance was measured. Such measurement was intended to avoid the acceleration and deceleration stages of the participant's walking.

Finally, the SW test was carried out; two cones were placed 10 m apart. The participants were instructed to walk around the cones without stopping at a pace set by a timed signal played on a CD player. The SW test consists of 102 shuttles divided into 12 levels, each lasting approximately 1 min. The first level consists of three shuttles with a subsequent one-shuttle (i.e. 10 m)

increase at each following level. At each level, the speed is increased by 0.17 m/s, with an initial speed of 0.5 m/s rising to a maximum speed of 2.37 m/s.[16,17] The test ended if the participant was unable to continue (due to breathlessness or any other reason) or was unable to reach the next cone before the timer sounded. If none of these mentioned factors occurred, we stopped the test at shuttle 50 (or 500 m, half of the total) to assure the participants' safety due to fatigue issues. Then, the values in meters were included in the analysis. A resting time of at least 3 min was provided between each assessment, and a longer time was provided if the participant claimed fatigue.

CAVI

CAVI was determined using VaSera1500 (Fukuda Denshi, Tokyo, Japan). The procedures started with the participants resting for 5 min in a sitting position. Afterwards, they were placed supine on a standard stretcher. Cuffs were wrapped around both arms and ankles to detect the brachial and ankle pulse waves. An electrocardiogram was carried out, and the heart sound was monitored. The pulse wave velocity (PWV) from the heart to the ankle was determined by measuring the length from the aortic valve to the ankle divided by time, according to the heart sound and the rise of the brachial and ankle pulse wave. The BP was measured at the four limbs alternately, first at the right arm and ankle, and then at the left arm and ankle. This procedure is important not only because it reduces the burden of the examinees, but also because it enables a more accurate measurement. Finally, a scale conversion was carried out using the following formula: $CAVI = a\{(2\rho/\Delta P) \times \ln(Ps/Pd)PWV^2\} + b$ (no unit), in which "ρ" is blood density, "Ps" is systolic blood pressure, "Pd" is diastolic blood pressure, "ΔP" is Ps – Pd, "PWV" is pulse wave velocity, and "a" and "b" are specific constants. This procedure has also been detailed in previous studies.[2,10]

This measurement was carried out once for each participant, and the mean of the right and left values of CAVI for each participant was used for analytical purposes.[18] The validity, reproducibility, and blood pressure-independent nature of this system have been widely documented by other researchers.[2,9,10]

Statistical analysis

The Kolmogorov–Smirnov test was carried out to determine the normality of the data. Absolute SMI was dichotomized according to the first quintile for males (8.81 kg/m^2) and females (7.57 kg/m^2). Then, we arbitrarily assumed that those in the first quintile had a low SMI (n = 35), coded 1, and the others were considered normal SMI (n = 140), coded 0.

We analyzed the relationship between the two groups using the unpaired t-test for the age, BMI, body fat percentage, FMI, and ABI variables, and the Mann–Whitney U-test for the SMI, CAVI, GS, WS, and SW tests. Furthermore, the χ^2-test was used for sex, regular physical activity engagement, alcohol consumption, smoking, number of medications, morbidities, and malnutrition. In addition, a univariate logistic regression was carried out to verify the association of each variable and the muscle mass condition, except for the number of medications as a result of missing values in the variable; then, a stepwise multivariate logistic regression was carried out to investigate whether CAVI was associated with low SMI. We assigned the status of muscle mass as the dependent variable, CAVI as the main covariate, and sex, age, BMI, MNA, GS, and SW as adjusted covariates. Differences were considered statistically significant at $P < 0.05$. All analyses were carried out using the Statistical Package for the Social Sciences software (SPSS; IBM, Chicago, IL, USA) version 20.0.

Results

A total of 175 subjects participated in the present study; we divided them into two groups: low SMI older adults (n = 35) and normal SMI (n = 140) participants. The participants in the first group were older and had more polypharmacy (four or more concurrent medications) than the normal participants. No significant differences were found for the lifestyle characteristics or morbidities (Table 1).

The results of the health indicators showed that low SMI participants had a lower BMI and FMI, and were at a higher risk of malnutrition than the normal group. Additionally, they presented with poorer physical functioning, such as low muscle strength and lower SW test scores. Regarding the CAVI results, the low SMI older adults had higher CAVI (Table 2).

The findings of the multivariate logistic regression showed that females were less likely to have low SMI than males. Similar conditions were verified in the participants with higher BMI and GS. Additionally, CAVI showed an independent association with SMI, even when adjusted for age, sex, BMI, MNA, GS, and SW. Thus, a higher CAVI was associated with low SMI in older adults (Table 3).

Discussion

The present study supported the hypothesis that arterial stiffness (assessed by CAVI) is associated with low SMI in community-dwelling older adults. Other studies have been carried out to ascertain this association;[5–8] however, none of them considered arterial stiffness as measured by CAVI, a non-invasive and BP-independent tool.

Table 1 Bivariate comparisons of the participants' demographic and lifestyle characteristics

Variables	Normal (n = 140)	Low SMI (n = 35)	P
Age (years)	73 [70–77]	76 [71–78]	0.01
Females	52.1 (73)	51.4 (18)	0.94
Regular physical activity[†]	65.4 (83)	63.3 (19)	0.83
Alcohol consumption[‡]	39.4 (52)	36.7 (11)	0.78
Smoking[‡]	9.1 (12)	6.7 (2)	1.00
No. medications[§]	76.6 (95)	52 (13)	0.01
	23.4 (29)	48 (12)	
Morbidities[‡]			
Diabetes	12.1 (16)	10 (3)	1.00
Hypertension	42.4 (56)	36.7 (11)	0.56
Hyperlipidemia	14.4 (19)	20 (6)	0.41
Coronary artery disease	7.6 (10)	10 (3)	0.71

[†]n = 157; [‡]n = 162; [§]n = 149; values are expressed as medians [interquartile range] or valid percentages (n).

Table 2 Bivariate comparisons of the participants' health indicators

Variables	Normal (n = 140)	Low SMI (n = 35)	P
BMI (kg/m^2)	23.6 ± 2.71	20.7 ± 2.61	<0.001
SMI (kg/m^2)	9.00 [8.20–9.81]	7.54 [7.39–8.43]	<0.001
Body fat percentage	29.0 ± 7.72	28.1 ± 8.80	0.56
FMI (kg/m^2)	7.06 ± 2.37	6.03 ± 2.42	0.02
ABI	1.10 ± 0.07	1.08 ± 0.07	0.10
MNA at risk	20.0 (28)	51.4 (18)	<0.001
Handgrip strength (kg)	28.7 [25–35]	24.5 [22.5–31]	0.007
Walking speed (m/s)	1.39 [1.25–1.50]	1.39 [1.22–1.48]	0.48
Shuttle walking (m)	400 [360–470]	360 [300–440]	0.01
CAVI	9.13 [8.52–9.71]	9.57 [8.93–10.4]	0.008

Values are means ± SD, medians [interquartile range] or valid percentages (n). ABI, ankle-brachial index; BMI, body mass index; CAVI, cardio-ankle vascular index; FMI, fat mass index; MNA, mini-nutritional assessment; SMI, skeletal muscle mass index.

A previous study investigated the occurrence of a specific association between arterial stiffening (analyzed by baPWV) and peripheral skeletal muscle mass, and concluded that arterial stiffness was associated with a higher loss of muscle mass index over time independent of age, total body fat, peripheral arterial disease, chronic inflammation, or cardiac disease. Ochi *et al.* hypothesized that age-related decline of muscle mass and atherosclerosis share common pathological processes and interact with each other. In fact, the authors verified a direct association with baPWV and thigh muscle sarcopenia in men, but that association was not confirmed in women.[5] Furthermore, Kohara *et al.* found that men with sarcopenic obesity had higher baPWV than normal, sarcopenic, or obese men.[19] In theory, changes in arterial stiffness might mediate the association between body composition and cardiovascular risk.[8] However, it is unclear how arterial stiffness and the loss of muscle mass relate to each other. Authors suggested that because basal limb blood flow declines with aging, in part due to arterial stiffening, dysfunction in blood vessel dynamics could have a predictive role in muscle mass decline.[6]

Some researchers have linked the higher prevalence of low muscle mass in men[20] to their findings of arterial stiffness in men, but not in women.[5,19] To examine any sex effect on CAVI, we carried out further analysis and verified that men had higher CAVI than women (data

Table 3 Stepwise multivariate logistic regression considering skeletal muscle mass index (normal or low condition) as dependent variable and cardio-ankle vascular index, age, gender, body mass index, Mini-Nutritional Assessment, handgrip strength, and shuttle walking as covariates

Variables	OR (95% CI)	*P*
Sex		
Female	0.23 (0.61–0.90)	0.03
BMI	0.71 (0.59–0.85)	<0.001
Handgrip strength	0.83 (0.74–0.94)	0.002
CAVI	1.82 (1.14–2.90)	0.01

Values are odds ratio (95% confidence interval). BMI, body mass index; CAVI, cardio-ankle vascular index; SMI, skeletal muscle mass index.

not shown). However, in our fully adjusted analysis, we verified the association of CAVI and low SMI independent of sex.

Regarding physical performance, those with normal muscle mass presented better physical functioning, such as a higher GS, higher SW test scores, and a lower CAVI, than the group with low SMI. GS is a representative measure of strength and is an important screening tool for sarcopenia,[1] whereas SW represents aerobic capacity.[16,17] Regarding SW, a previous study showed that endurance-trained older men demonstrated lower arterial stiffness than their sedentary age peers despite similar systolic blood pressures, suggesting that age-associated augmentation of arterial stiffness might be mitigated by regular aerobic exercise.[21]

Furthermore, polypharmacy was observed more frequently among participants in the low SMI group. Although we did not deeply investigate the classes of medications to which they were exposed, our results were in agreement with previous studies that identified the association of concomitant medications and impaired physical functioning in older adults.[22]

Based on the present results, we would like to emphasize the importance of physical activity, mainly the combination of progressive resistance exercise and aerobic exercise,[23] in accordance with well-balanced nutrition in relation to low SMI and arterial stiffness, especially because the participants with low SMI in the present study had lower physical performance, lower BMI, and a higher risk for malnutrition. Nutritional status is widely known to be associated with both muscular and vascular health. Thus, aiming to reverse low muscle mass, Yamada *et al.* verified that a diet rich in proteins and vitamin D in combination with resistance exercise was more effective at improving muscle mass than resistance exercise alone.[24] In addition, evidence showed that lower levels of 25-hydroxyvitamin D, an established marker of vitamin D status, are associated with abnormalities in the indices of arterial stiffness.[25]

Although the low SMI participants had lower BMI and FMI than the normal group, both groups presented similar results for body fat percentage. This result might show that lean body mass is lost, and fat could be preserved or even increased in people with low muscle mass or sarcopenia. As intramuscular and visceral fat increase, and subcutaneous fat decreases with age,[1,4] the association with muscle mass decline and arterial stiffness might also be perceived from the standpoint of the relationship between fat mass and cardiovascular risks.

Some limitations of the present study should be mentioned: (i) its cross-sectional design did not permit the determination of a cause–effect relationship between CAVI and the low SMI condition; and (ii) the small number of participants limited further group subdivision (i.e. to differentiate pre-sarcopenic and sarcopenic older adults) as a result of the low statistical power achieved when further dividing the groups. However, the present study showed that a relationship between CAVI and low SMI does exist, and might serve as a basis for further studies with a larger sample size, analyzing the time effect on muscle, and physical performance decline, and also investigating the role of sex on such an association.

To our knowledge, this is the first study to verify the interaction of CAVI and total SMI in Japanese older adults. The main clinical advantage of the present study was that it clearly showed the important relationship between arterial stiffness and low SMI in community-dwelling older adults as measured by CAVI, a non-invasive reliable method and blood pressure independent measure. It would be useful to perform further health analyses in older adults with arterial stiffness, including body composition features and physical performance measurements, to aid in the early detection of people with the risk of developing sarcopenia; and also to verify arterial stiffness in older adults already in a progressive muscle loss condition. We believe that a suitable intervention for the promotion of improvements in vascular and muscular parameters would be aimed at increasing physical fitness levels and improving nutrition; this combined intervention might reduce the probability of a person developing systolic hypertension and the associated risk of cardiovascular events, and could help maintain SMI and function, especially in older adults.

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Disclosure statement

The authors declare no conflict of interest.

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