

**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<sup>2</sup>) 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.

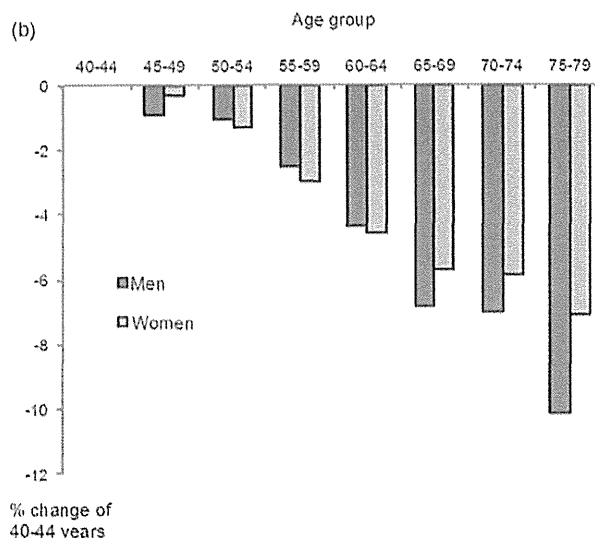
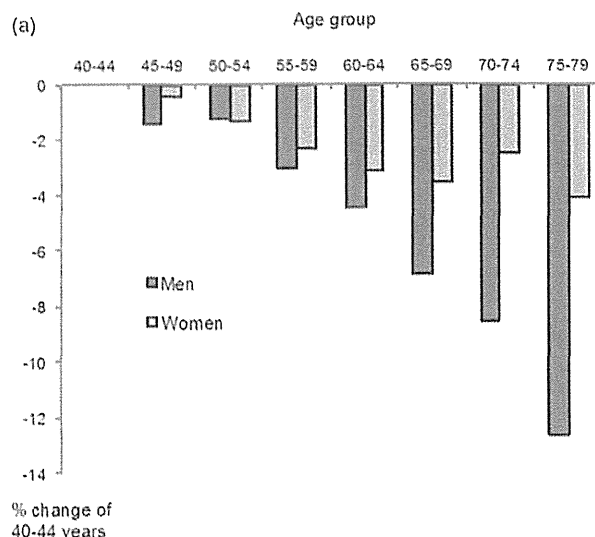
age-dependent decrease in both sexes (Fig. 2, Table 1). The age-dependent changes in the leg SMI were similar in men and women. However, the age-dependent changes in the arm SMI were greater in men than in women.

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

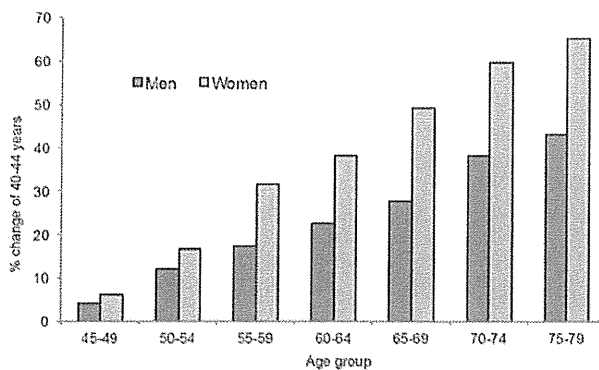


**Figure 2** The percentage of change in the (a) arm and (b) leg skeletal muscle mass index (SMI) in each sex and each age group using 40–44 years-of-age as a reference.

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.<sup>19,20</sup> The age-dependent increases in inflammatory cytokines, such as IL-6 and TNF- $\alpha$ , can result in increased skeletal muscle breakdown.<sup>23</sup> 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

mass.<sup>27,28</sup> 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  $5.97 \pm 0.75$  and  $5.01 \pm 0.67$  in men, and  $3.56 \pm 0.54$  and  $3.24$  in women aged in their 40s and 70s, respectively.<sup>29</sup> 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



**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.

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.<sup>30</sup> 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.<sup>31</sup> 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.

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- $\alpha$  and IL-6.<sup>22</sup> 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.<sup>32</sup> 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  $7.02 \text{ kg/m}^2$  and  $5.61 \text{ kg/m}^2$ , respectively. These values were slightly higher than those determined by the young adult mean in our database (men  $6.75 \text{ kg/m}^2$ ; women  $5.07 \text{ kg/m}^2$ ).<sup>18</sup> 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 ( $\text{cm}^2$ )	$-0.586^{**}$	$-0.627^{**}$
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<sup>2</sup> in men and 4.79–5.80 kg/m<sup>2</sup> in women,<sup>13,33–35</sup> 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.<sup>36</sup> 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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## Arterial Stiffness Predicts Cognitive Decline in Japanese Community-dwelling Elderly Subjects: A One-year Follow-up Study

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**Aim:** The purpose of this study was to determine whether arterial stiffness can be used to predict one-year changes in the cognitive function in Japanese community-dwelling elderly subjects.

**Methods:** A total of 103 Japanese community-dwelling elderly patients joined this study. Information regarding the age, height, weight, gender and past medical history of each participant was obtained. Additionally, arterial stiffness was determined according to the cardio-ankle vascular index (CAVI), and the cognitive function was assessed with the Mini-Mental State Examination (MMSE). One year later, we performed the MMSE in the same subjects. After dividing the cohort according to the 80th percentile of the CAVI (normal and arterial stiffness [AS] groups), we examined whether the degree of cognitive decline, as determined using the pre- and post-MMSE, was significantly different based on the severity of arterial stiffness, adjusted for age, BMI, gender and the pre-MMSE scores.

**Results:** Of the 103 subjects who participated in the pre-data collection, 74 (38 men and 36 women,  $73.4 \pm 4.0$  years) joined the post-data collection. We found a significant difference in the change in the post-MMSE scores between the normal and AS groups (pre-MMSE: normal group [ $27.4 \pm 2.1$ ] and AS group [ $26.9 \pm 2.4$ ] and post-MMSE: normal group [ $27.2 \pm 2.1$ ] and AS group [ $25.5 \pm 2.3$ ],  $F=5.95$ ,  $p=0.02$ ). For each domain of the MMSE, the changes in MMSE-attention-and-calculation ( $F=5.11$ ,  $p=0.03$ ) and MMSE-language ( $F=4.32$ ,  $p=0.04$ ) were significantly different according to an ANCOVA.

**Conclusions:** We found that arterial stiffness predicts cognitive decline in Japanese community-dwelling elderly subjects regardless of the initial level of the global cognitive function. This finding indicates the potential use of the degree of arterial stiffness as an indicator for preventing or delaying the onset of dementia in the elderly.

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**Key words:** Arterial stiffness, Cognitive impairment, Elderly, Dementia

### Introduction

Dementia is a serious issue, especially in community-dwelling elderly subjects<sup>1</sup>. Thirty-five million people worldwide suffered from dementia in 2012 according to the World Health Organization. Approx-

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imately 48% of patients with Alzheimer's disease (AD), the most common form of dementia, are estimated to live in Asia, and this percentage is expected to increase to 59% by 2050<sup>2</sup>. Elderly people with dementia are typically frail due to their poor mobility and body composition, and the transitional stage between normal aging and AD, called mild cognitive impairment (MCI), results in frailty<sup>3</sup>, depression<sup>4</sup>, lower levels of physical activity<sup>1</sup> and higher mortality<sup>5</sup>. Preventing cognitive decline is therefore crucial.

Of risk factors for cognitive decline, cardiovascular risk factors have received more attention in recent

years<sup>6, 7</sup>). High blood pressure<sup>8</sup>), dyslipidemia<sup>8</sup>), obesity<sup>9</sup>) and diabetes mellitus<sup>9</sup>) have been proposed to be risk factors for cognitive decline. Among these factors, arterial stiffness is a comparatively easy-to-modify risk factor in community-dwelling elderly subjects. Madden *et al.* reported that three months of aerobic training reduces the degree of multifactorial arterial stiffness without generating any significant improvements in aerobic fitness, weight, BMI, waist-to-hip ratio or blood pressure in community-dwelling older individuals<sup>10</sup>). Additionally, previous studies have demonstrated the effectiveness of antihypertensive agents in improving arterial stiffness in both short- and long-term trials<sup>11</sup>). Community-dwelling elderly can improve their arterial stiffness; therefore, focusing on treating arterial stiffness may be effective for preventing cognitive decline.

Most older adults with MCI live in the community, and more than half of MCI cases progress to dementia within five years<sup>12</sup>). Therefore, a desired goal is the early detection of cognitive decline, especially in the community-dwelling elderly. When evaluating the degree of arterial stiffness in community-dwelling elderly subjects, the most important property is the ease of measurement. Arterial stiffness is one of the most easily measured vascular risk factors in community-dwelling elderly patients due to its non-invasive nature; therefore, it can be used as a predictor of cognitive decline in this population. Previous studies have also shown arterial stiffness to be a predictor of cognitive decline. However, the subjects in these studies were not elderly individuals living in the community<sup>13, 14</sup>). Additionally, other authors have reported that they were unable to validate arterial stiffness as an independent risk factor for cognitive decline, as measured according to the global cognitive function using the Mini-Mental State Examination (MMSE)<sup>15-17</sup>). Yamamoto *et al.* reported a relationship between the cognitive function and arterial stiffness determined according to the CAVI in community dwelling elderly<sup>18</sup>), although the mean age was approximately 80 years, which is a bit high considering the mean age of community-dwelling elderly individuals in Japan. It may be more important to focus on healthier and younger older adults when discussing community-dwelling elderly<sup>19</sup>). The efficacy of arterial stiffness as a predictor of cognitive decline, especially in community-dwelling elderly patients, is less well investigated<sup>4</sup>).

The purpose of this study therefore was to address whether the degree of arterial stiffness can be used to predict one-year changes in the cognitive function in Japanese community-dwelling elderly subjects.

We used the CAVI to assess arterial stiffness, as this parameter was found to significantly correlate with cognitive decline in a cross-sectional study<sup>18, 19</sup>).

## Methods

### Participants

Participants were recruited for this study through local press that requested healthy community-dwelling volunteers 65 years of age or older, and data collection was performed on two occasions: November 2012 (pre-data collection) and November 2013 (post-data collection). Interviews were conducted to exclude participants from both data collections based on the following exclusion criteria: severe cardiac, pulmonary or musculoskeletal disorders; comorbidities associated with a higher risk of falls, such as Parkinson's disease or stroke; and the use of psychotropic drugs. Written informed consent was obtained from each participant in accordance with the guidelines approved by the Kyoto University Graduate School of Medicine and the Declaration of Human Rights, Helsinki, 1995 during both data collection periods. The study protocol was approved by the ethics committee of Kyoto University Graduate School of Medicine.

### Measurements—Pre-data Collection

#### Demographic Data

Each patient's age, height, weight, gender, past medical history (cardiovascular disease, hypertension, diabetes mellitus and hyperlipidemia), smoking status (number of cigarettes smoked per day and total number of years smoked) and educational background (elementary school, junior high school, high school, career college or university) were obtained as demographic data. All data were collected at the first data collection time point. We directly asked about each participant's age and gender and measured their height and weight using standardized height and weight scales.

#### Arterial Stiffness

The degree of arterial stiffness was determined based on the CAVI using the VaSera-1500 device (Fukuda Denshi Co., Ltd., Tokyo, Japan). The details of this procedure have been described previously<sup>20, 21</sup>). After the participants had rested for five minutes in the sitting position, we obtained these measurements as previously described. Higher CAVI values indicate a higher degree of arterial stiffness. The measurements were obtained once, and the mean values of the right and left CAVI scores for each patient were used for the analysis<sup>19</sup>).

**Table 1.** Baseline characteristics and post-MMSE scores in the study population

	All (n=74)		p
	Normal group n=59	AS group n=15	
Demographic data			
Age, year	72.8 ± 3.8	76.1 ± 3.6	< 0.01
BMI, kg/m <sup>2</sup>	23.2 ± 2.6	23.2 ± 3.2	0.99
Gender, male	28 (47.5%)	10 (66.7%)	0.25
Mean CAVI	8.83 ± 0.61	10.6 ± 0.51	< 0.01
Cognitive function			
Pre-MMSE	27.4 ± 2.1	26.9 ± 2.4	0.40
Post-MMSE	27.2 ± 2.0	25.5 ± 2.3	< 0.01
Pre-MMSE (orientation)	9.6 ± 0.6	9.7 ± 0.5	0.89
Post-MMSE (orientation)	9.7 ± 0.7	9.7 ± 0.5	0.89
Pre-MMSE (registration)	2.9 ± 0.4	3.0 ± 0.0	0.53
Post-MMSE (registration)	2.9 ± 0.3	3.0 ± 0.0	0.49
Pre-MMSE (attention and calculation)	3.2 ± 1.7	2.9 ± 1.8	0.55
Post-MMSE (attention and calculation)	3.4 ± 1.7	2.3 ± 1.5	0.03
Pre-MMSE (recall)	2.6 ± 0.6	2.4 ± 0.8	0.30
Post-MMSE (recall)	2.5 ± 0.6	2.4 ± 0.7	0.69
Pre-MMSE (language)	8.9 ± 0.3	8.9 ± 0.4	0.73
Post-MMSE (language)	8.7 ± 0.5	8.2 ± 1.3	0.15
Comorbidities			
Cardiovascular disease	6 (10.2%)	4 (26.7%)	0.11
Hypertension	23 (39.0%)	8 (53.3%)	0.39
Diabetes mellitus	5 (8.5%)	4 (26.7%)	0.08
Hyperlipidemia	9 (15.3%)	2 (13.3%)	1.00
Brinkman index	0 (0-800)	0 (0-400)	0.63
Educational background			
Elementary school	0 (0.0%)	1 (6.7%)	n.s.
Junior high school	16 (27.1%)	4 (26.7%)	
High school	35 (59.3%)	9 (60.0%)	
Career college	3 (5.1%)	0 (0.0%)	
University	5 (8.5%)	1 (6.7%)	

Mean CAVI = mean value of the right and left CAVI scores. The mean ± SD is shown for age, BMI, mean CAVI and pre- and post-MMSE. n (%) is shown for gender, cardiovascular disease, hypertension, diabetes mellitus, hyperlipidemia and educational background. The median (25% quartile-75% quartile) is shown for the Brinkman index. AS: arterial stiffness; n.s.: not significant.

### Cognitive Function Measurements

The cognitive function was assessed using the Mini-Mental State Examination (MMSE)<sup>22</sup>. The MMSE is a short screening test that consists of the following five areas for detecting cognitive impairment: orientation, registration, attention and calculation, recall and language. The scores range from 0 to 30, with higher scores indicating better cognitive performance. The MMSE was performed at both the pre- and post-data collection time points.

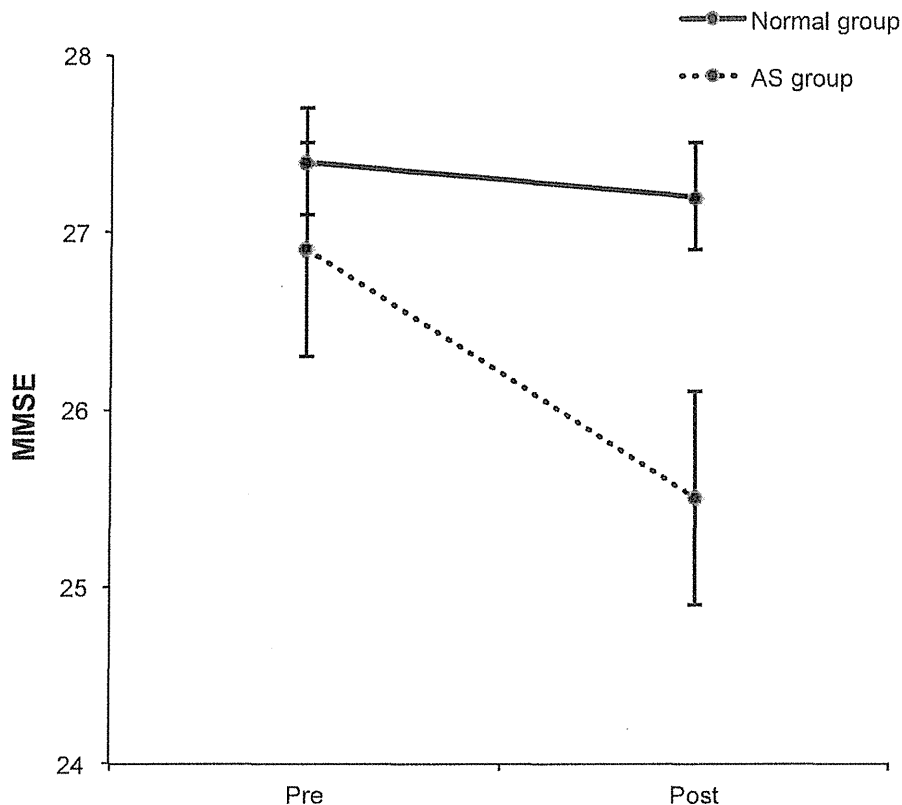
### Measurements—Post-data Collection

#### Cognitive Function Measurements

One year later, the cognitive function was also assessed using the MMSE<sup>22</sup>. We performed the MMSE using the same inclusion and exclusion criteria as that used at the pre-data collection time point.

#### Statistical Analysis

The patients were divided into two groups based on the 80th percentile of the CAVI values: the normal and arterial stiffness [AS] groups. We analyzed the differences between these two groups using the unpaired



**Fig. 1.** Two-way analysis of variance showing the differences in the changes in the post-MMSE scores between the normal and AS groups. These findings indicate that the elderly subjects in the AS group experienced greater cognitive decline than those in the control group ( $F=5.95$ ,  $p=0.02$ ).

*t*-test for age, body mass index (BMI), mean CAVI values on both sides and the pre- and post-MMSE scores (total score and scores for each domain), the  $\chi^2$  test for gender, past medical history and educational background and the Mann Whitney *U*-test for the Brinkman index (number of cigarettes smoked per day  $\times$  total number of years smoked). A repeated measures two-way analysis of covariance (ANCOVA) was used to analyze whether the degree of cognitive decline determined according to the pre- and post-MMSE scores (total score and scores for each domain) differed significantly according to the severity of arterial stiffness, adjusted for age, BMI, gender and the pre-MMSE score. A *p* value of  $<0.05$  was considered to be statistically significant for all analyses.

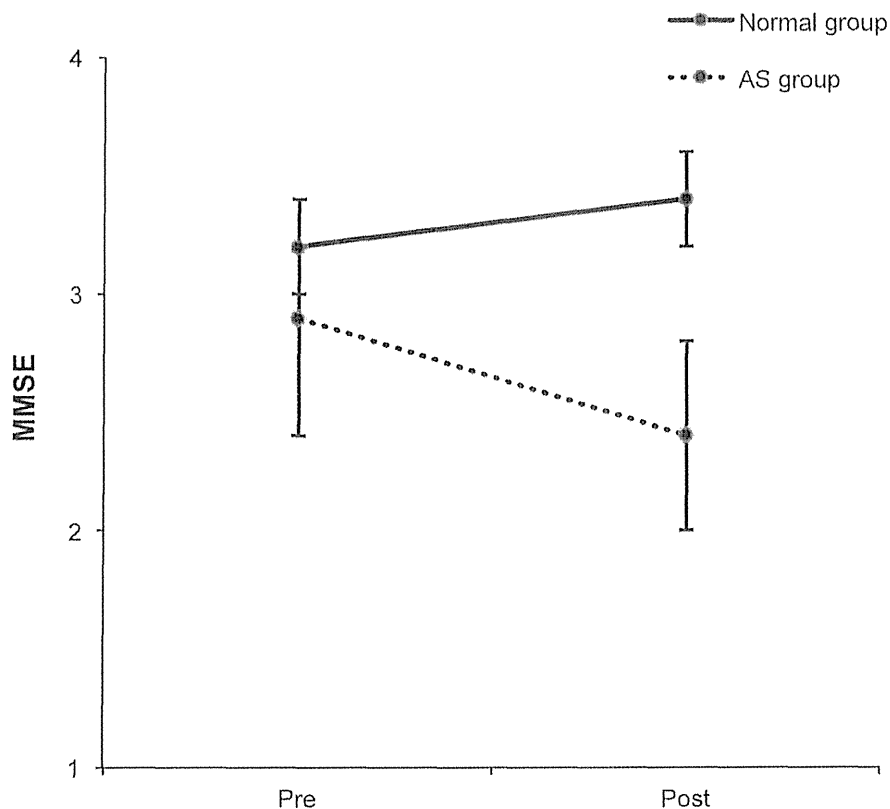
## Results

In total, 74 individuals (38 men and 36 women,  $73.4 \pm 4.0$  years) participated in both data collection

events. Of these individuals, none were excluded. We assigned 59 elderly individuals (28 men and 31 women) to the normal group and 15 (10 men and five women) to the AS group. **Table 1** shows the differences in each variable between the two groups. While there were no significant differences in BMI, gender, pre-MMSE, educational background or past medical history, we found significant differences in age ( $p < 0.01$ ) and the mean CAVI values ( $p < 0.01$ ). Additionally, the normal group had a significantly higher total post-MMSE scores (normal group:  $27.2 \pm 2.1$ , AS group:  $25.5 \pm 2.3$ ,  $p < 0.01$ ) and higher post-MMSE scores for the attention-and-calculation domain (normal group:  $3.4 \pm 1.7$ , AS group:  $2.3 \pm 1.5$ ,  $p = 0.03$ ) than the AS group.

The ANCOVA adjusted for age, BMI, gender and pre-MMSE showed a significant difference in the changes in the post-MMSE scores between the normal and AS groups ( $F=5.95$ ,  $p=0.02$ ) (**Fig. 1**), indicating that elderly individuals with a higher degree of arterial





**Fig. 2.** Two-way analysis of variance showing the differences in the changes in the post-MMSE (attention and calculation) scores between the normal and AS groups. These findings indicate that the elderly subjects in the AS group experienced greater cognitive decline than those in the control group ( $F=5.11$ ,  $p=0.03$ ).

stiffness may experience greater levels of cognitive decline, even after adjusting for age, BMI, gender and the pre-MMSE score. Additionally, the changes in the MMSE-attention-and-calculation ( $F=5.11$ ,  $p=0.03$ ) (Fig. 2) and MMSE-language ( $F=4.32$ ,  $p=0.04$ ) (Fig. 3) domains were shown to be significantly different according to the ANCOVA. The other areas did not show any differences between the two groups (orientation;  $F=0.27$ ,  $p=0.60$ ; registration;  $F=2.69$ ,  $p=0.11$ , recall;  $F=0.16$ ,  $p=0.69$ ).

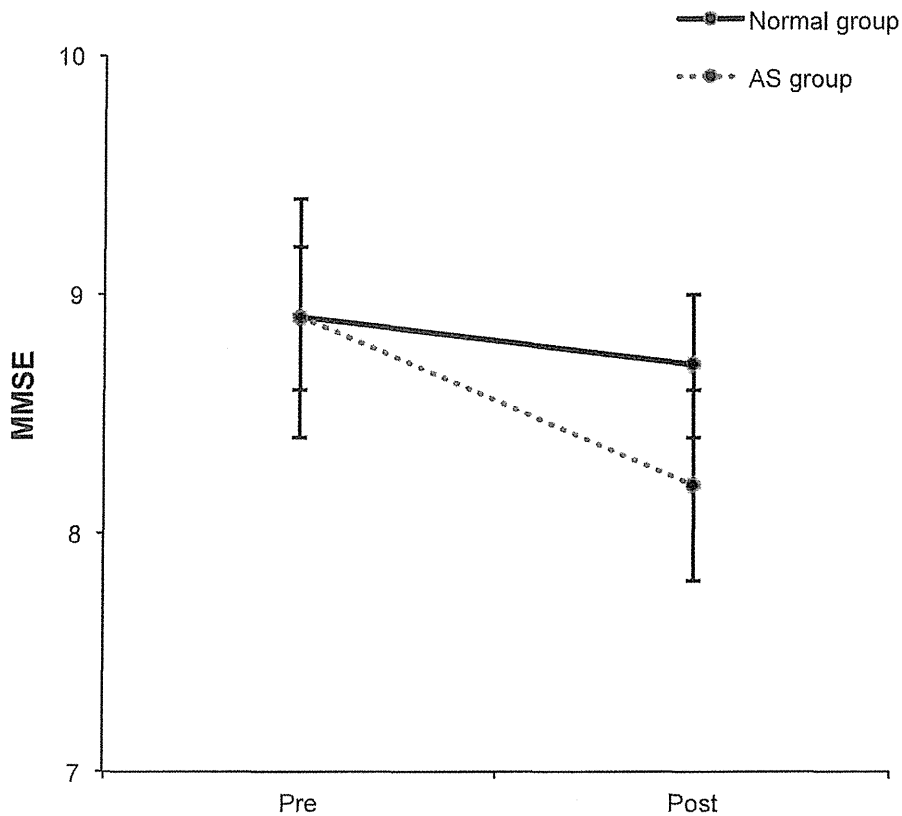
### Discussion

In this study, we analyzed whether the degree of cognitive decline differs significantly according to the severity of arterial stiffness, adjusted for age, BMI, gender and the cognitive function at baseline and at the one-year follow-up. Consequently, we found that arterial stiffness predicts cognitive decline in Japanese community-dwelling elderly subjects, regardless of the

initial level of the global cognitive function. Previous studies have demonstrated that arterial stiffness has a predictive effect on cognitive decline in the non-community-dwelling elderly<sup>13-15, 18</sup>); however, few reports have found arterial stiffness to be a predictor of cognitive decline in this group.

There are hypotheses regarding pathways linking arterial stiffness and cognitive decline, wherein augmented pressure pulses penetrate and damage small cerebral vessels in the global brain<sup>23</sup>). Brain lesions, such as ischemic lesions and white matter abnormalities resulting from augmented pressure, are thought to cause cognitive decline, thereby leading to dementia<sup>24</sup>). The augmented pressure caused by arterial stiffness independently predicts cognitive performance<sup>25</sup>), and many previously published studies evaluating the association between arterial stiffness and the cognitive function have discussed the causal relationship with this phenomenon<sup>14, 17, 18, 23</sup>).

Several studies have examined whether the sever-



**Fig. 3.** Two-way analysis of variance showing the differences in the changes in the post-MMSE (language) scores between the normal and AS groups. These findings indicate that the elderly subjects in the AS group experienced greater cognitive decline than those in the control group ( $F=4.32$ ,  $p=0.04$ ).

ity of arterial stiffness longitudinally predicts cognitive decline. For example, one study targeting people older than 80 years of age in nursing homes showed results similar to the current findings<sup>13</sup>). The mean baseline MMSE score of these subjects was  $23.7 \pm 4.9$ , which is lower than that observed in the current study. Another study, in which the subjects were older patients in the hospital with complaints of memory loss, also reported that arterial stiffness has a strong predictive ability for cognitive decline<sup>14</sup>). Furthermore, Yamamoto *et al.* performed a similar analysis in community-dwelling elderly patients; however, the mean age was higher than that noted in our study<sup>18</sup>). Notably, we found that arterial stiffness predicts cognitive decline in community-dwelling elderly subjects with a comparably preserved cognitive function, even after adjusting for age, gender, BMI and the baseline cognitive function. In addition, we observed the scores for the attention-and-calculation and language domains of the MMSE to be significantly decreased in the AS group. It has

been reported that these MMSE domains are not affected by impairment of the hippocampus<sup>26</sup>). Therefore, we assume that the cognitive dysfunction resulting from arterial stiffness is not attributed to dysfunction of the hippocampus. However, other studies have reported that measurements of arterial stiffness do not predict performance for the global cognitive function, as measured according to the MMSE<sup>15-17</sup>). There are various possible reasons for this discrepancy: 1) the mean age of the subjects was 57.1 years and the participants were relatively high functioning (ceiling effect of the MMSE)<sup>15</sup>); 2) many participants dropped out from the follow-up survey and selection bias may have affected the results for the change in the cognitive function<sup>16</sup>); 3) memory tasks that are more demanding for the executive function and attention may be more sensitive to cerebrovascular alterations due to aging and the MMSE may be too insensitive to accurately detect cognitive changes<sup>17, 27</sup>). As a result, further studies are needed to establish evidence clarify-

ing the association between arterial stiffness and the cognitive function.

The most important clinical implication of our findings is that one of the most easily measured and non-invasive parameters, especially in community-dwelling elderly individuals, arterial stiffness, predicted cognitive decline after one year. These results imply that maintaining the arterial function may prevent or delay the onset of dementia in the community-dwelling elderly. Additionally, it may be possible to identify individuals at risk of dementia by evaluating the degree of arterial stiffness. Interventional and longitudinal studies examining improvements in arterial stiffness with the aim of preventing cognitive decline are required to establish effective strategies for inhibiting the onset of dementia.

This study is associated with several limitations. First, because we were unable to perform neuroimaging assessments, it was not possible to make a specific diagnosis of dementia subtypes. In addition, we only performed MMSE as a cognitive test, and the cognitive function was not fully investigated. There may be asymptomatic brain lesions and specific cognitive domains that exhibit a strong relationship with arterial stiffness. Second, the age at baseline in the AS group was significantly higher than that observed in the normal group. Although we tried to minimize the impact of this difference by adjusting for age, the effect may have been insufficient. Third, the small number of subjects may also have affected the results, and more samples are needed to confirm the results of this study. Finally, many studies have investigated the relationship between arterial stiffness and the cognitive function; therefore, this study may not have adequate novelty. Nevertheless, we regard our findings as providing evidence that strengthens the close relationship between arterial stiffness and cognitive decline.

### Conclusions

This study showed that arterial stiffness predicts cognitive decline in Japanese community-dwelling elderly subjects regardless of the initial level of the global cognitive function. These findings indicate the potential of improving arterial stiffness in order to prevent or delay of the onset of dementia in the elderly.

### Conflicts of Interest

None.

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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.<sup>1</sup> 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.<sup>2</sup> 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,<sup>3</sup> inflammation,<sup>4</sup> and insulin resistance,<sup>1</sup> are also associated with atherosclerosis.<sup>5</sup> However, only a few studies have been carried out to verify such associations.<sup>5–8</sup> 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.<sup>6</sup> Other studies have verified the associations of peripheral lean mass and visceral fat mass with atherosclerosis,<sup>7</sup> and the relationships between regional fat and lean mass and large artery properties in young men and women.<sup>8</sup>

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,<sup>2,9,10</sup> 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.<sup>11</sup>

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  $\leq 21$  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)<sup>12</sup> 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<sup>2</sup>, normal weight, BMI 18.5–25 kg/m<sup>2</sup>, and obese, BMI  $\geq 25$  kg/m<sup>2</sup>).<sup>13</sup> 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.<sup>14,15</sup>

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

GS was collected with a standard handgrip dynamometer (Smedley'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.<sup>16,17</sup> 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.<sup>2,10</sup>

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.<sup>18</sup> The validity, reproducibility, and blood pressure-independent nature of this system have been widely documented by other researchers.<sup>2,9,10</sup>

### 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<sup>2</sup>) and females (7.57 kg/m<sup>2</sup>). 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  $\chi^2$ -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;<sup>5–8</sup> 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 ( <i>n</i> = 140)	Low SMI ( <i>n</i> = 35)	<i>P</i>
Age (years)	73 [70–77]	76 [71–78]	0.01
Females	52.1 (73)	51.4 (18)	0.94
Regular physical activity <sup>†</sup>	65.4 (83)	63.3 (19)	0.83
Alcohol consumption <sup>‡</sup>	39.4 (52)	36.7 (11)	0.78
Smoking <sup>‡</sup>	9.1 (12)	6.7 (2)	1.00
No. medications <sup>§</sup>	76.6 (95)	52 (13)	0.01
	23.4 (29)	48 (12)	
Morbidities <sup>‡</sup>			
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

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

**Table 2** Bivariate comparisons of the participants' health indicators

Variables	Normal ( <i>n</i> = 140)	Low SMI ( <i>n</i> = 35)	<i>P</i>
BMI (kg/m <sup>2</sup> )	23.6 ± 2.71	20.7 ± 2.61	<0.001
SMI (kg/m <sup>2</sup> )	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 <sup>2</sup> )	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.<sup>5</sup> Furthermore, Kohara *et al.* found that men with sarcopenic obesity had higher baPWV

than normal, sarcopenic, or obese men.<sup>19</sup> In theory, changes in arterial stiffness might mediate the association between body composition and cardiovascular risk.<sup>8</sup> 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.<sup>6</sup>

Some researchers have linked the higher prevalence of low muscle mass in men<sup>20</sup> to their findings of arterial stiffness in men, but not in women.<sup>5,19</sup> 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,<sup>1</sup> whereas SW represents aerobic capacity.<sup>16,17</sup> 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.<sup>21</sup>

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.<sup>22</sup>

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,<sup>23</sup> 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.<sup>24</sup> 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.<sup>25</sup>

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,<sup>1,4</sup> 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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ORIGINAL ARTICLE: EPIDEMIOLOGY,  
CLINICAL PRACTICE AND HEALTH**Comparison of frailty among Japanese, Brazilian Japanese descendants and Brazilian community-dwelling older women**Priscila Yukari Sewo Sampaio,<sup>1</sup> Ricardo Aurélio Carvalho Sampaio,<sup>1</sup> Minoru Yamada,<sup>1</sup> Mihoko Ogita<sup>2</sup> and Hidenori Arai<sup>1</sup><sup>1</sup>Department of Human Health Sciences, Kyoto University Graduate School of Medicine, and <sup>2</sup>Department of Health Science, Kyoto Koka Women's University, Kyoto, Japan**Aim:** To investigate frailty in Japanese, Brazilian Japanese descendants and Brazilian older women.**Methods:** The collected data included sociodemographic and health-related characteristics, and the frailty index Kihon Checklist. We analyzed the differences between the mean scores of Kihon Checklist domains (using ANCOVA) and the percentage of frail women (using  $\chi^2$ -test). We carried out a binary logistic regression with Kihon Checklist domains.**Results:** A total of 211 participants (Japanese  $n = 84$ , Brazilian Japanese descendants  $n = 55$ , Brazilian  $n = 72$ ) participated in this research. The Brazilian participants had the highest total Kihon Checklist scores (more frail), whereas the Brazilian Japanese descendants had the lowest scores ( $P < 0.001$ ). Furthermore, the Brazilian group had more participants with oral dysfunction ( $P < 0.001$ ), seclusion ( $P < 0.001$ ), cognitive impairment ( $P < 0.001$ ) and depression ( $P < 0.001$ ). They were more likely to be frail (OR 5.97, 95% CI 2.69–13.3,  $P < 0.001$ ), to have oral dysfunction (OR 3.18, 95% CI 1.47–6.85,  $P = 0.003$ ), seclusion (OR 9.15, 95% CI 3.53–23.7,  $P < 0.001$ ), cognitive impairment (OR 3.87, 95% CI 1.93–7.75,  $P < 0.001$ ) and depression (OR 6.63, 95% CI 2.74–16.0,  $P < 0.001$ ) than the Japanese group.**Conclusions:** The older Brazilian women were likely to be more frail than the participants in other groups. More than the environment itself, the lifestyle and sociodemographic conditions could affect the frailty of older Brazilian women. *Geriatr Gerontol Int* 2014; ●●: ●●–●●.**Keywords:** cross-cultural study, frailty, Kihon Checklist, older women.**Introduction**

Because the aging process is a worldwide trend, frailty has become a global concern. In general, there are two predominant approaches to define frailty: (i) frailty is treated as a count of health impairments;<sup>1,2</sup> and (ii) the frailty phenotype is identified to detect people who find themselves between the independent and the dependent life stages.<sup>3</sup>

Several assessments have been developed to identify frail older adults, such as the "Kihon Checklist" (KCL) proposed by the Japanese Ministry of Health, Labor and

Welfare that identifies vulnerable older adults as those who have a higher risk of becoming dependent<sup>4,5</sup> based on the needs of the Japanese long-term care insurance (LTCI) system.<sup>6</sup> The KCL showed a good concurrent validity against the Fried's criteria for evaluating frailty, in which the KCL had a sensitivity of 60% and a specificity of 86.4%.<sup>7</sup> Furthermore, another study verified that the risk groups detected by the KCL were associated with lower ADL, lower subjective quality of life scores and higher scores on the geriatric depression scale.<sup>8</sup>

Despite the global concern on frailty, the features of each country have not been adequately explored. Therefore, it is intriguing to analyze such differences from a cross-cultural perspective. In the present study, we compared Japan and Brazil because of the different ethnic and cultural backgrounds. Brazil is a Latin American country with a miscegenated population. It is the largest and the most populous country in South

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America, and has become South America's leading economic power by exploiting vast natural resources and by utilizing the large labor pool; where Japan is an Asian, modern and industrialized country with a homogeneous population. Despite the recent economic slowdown; it still remains a major economic power.<sup>9</sup> The link between both countries started when the Japanese immigrated to Brazil in 1908, generating a community of approximately 1.3 million people of Japanese descent in Brazil.<sup>10</sup> Thereon, many Japanese descendants have experienced a different lifestyle in Brazil. Because of the lack of evidence regarding frailty in Japanese immigrants, we hypothesized that the living environment and culture play an important role in the aging process and the development of frailty; thus, the present study aimed to investigate frailty in native Japanese, Brazilian Japanese descendants and native Brazilian older adults.

## Methods

This was a cross-sectional observational study.

### Participants

The inclusion criteria were women living in the community, aged 60 years or older and able to respond to the questionnaires. The participants who did not match these criteria or those who did not want to participate in the research procedures were excluded from the present study.

The Japanese participants were recruited in the western area of Japan through a local press advertisement that requested community-dwelling older female volunteers to collaborate in this research. The Brazilian and Brazilian Japanese descendant participants were recruited by municipal health units and by a recreational club that promotes Japanese culture in the south part of Brazil, chosen because of the large population of Japanese subjects present in the region. Furthermore, the total population (Japanese region with approximately 1 500 000 citizens and Brazilian region with approximately 1 800 000 citizens) and the economic pattern (based on industry and tourism) of both regions were similar.<sup>11,12</sup>

The older women received oral and written explanations about the research procedures. Participation in this study was voluntary, and all participants signed an informed consent form. We recruited the participants from April to November 2012, and conducted data collection from June to November 2012.

A total of 228 older women were recruited to participate in the present study; however, 17 participants were excluded from the analysis (Brazilian  $n = 7$ , Brazilian Japanese Descendants  $n = 4$ , Japanese  $n = 6$ ) because of age lower than 60 years and poor responses in

questionnaires. The resulting 211 participants who met the criteria for the study (Brazilian  $n = 72$ , mean age  $69.0 \pm 6.41$  years; Brazilian Japanese descendants  $n = 55$ , mean age  $70.8 \pm 8.38$  years; and Japanese  $n = 84$ ; mean age  $73.2 \pm 4.21$  years). The study protocol was approved by the university ethical committee where it was carried out (E-1575, E-1470).

### Assessments

The participants answered a questionnaire regarding sociodemographic information, such as age, living arrangement, educational level and work status (worker, volunteer, retired); health-related characteristics, such as body mass index (BMI), use and number of medications, frequency of medical consultation in the past 6 months, hospitalization in the past year, self-rated health, life satisfaction and the frailty index KCL. The Japanese participants completed the original KCL version in the Japanese language, and the Brazilian and the Brazilian Japanese descendants completed the translated and validated KCL Brazilian Portuguese version.<sup>13</sup>

The KCL has 25 yes/no questions that are divided into the following domains: instrumental activities of daily living (IADL), physical strength, nutrition, eating, socialization, memory and mood. In the present study, we set the cut-off points based on our previous finding that determined the KCL cut-offs regarding an elevated risk for requiring LTCI service in community-dwelling older adults.<sup>14</sup> For the KCL total score (sum of the scores of all questions: 1–25), we used the cut-off of  $>6$  points; in question number 12 (nutrition domain), we used the cut-off of BMI  $<20.5$ ; and in the socialization domain, we used the cut-off as having one negative answer in question number 16 or question number 17 or more. To the best of our knowledge, there is no published cut-off point for the IADL domain; therefore, in the present study, we determined the cut-off point as a score higher than two points. For the other domains, the cut-off points remained the same, as scoring three points or more in the physical domain represents the clustering of physical inactivity; scoring two points in the nutrition domain indicates malnutrition; scoring two points or more in the oral domain suggests oral dysfunction; one point or more in the memory domain suggests cognitive impairment; and finally, scoring two points or more in the mood domain indicates depression.<sup>4</sup>

### Statistical analysis

Regarding sociodemographic and health-related characteristics, we analyzed the differences of age, BMI, and number of medications among Brazilian, Brazilian Japanese descendants and Japanese using one-way ANOVA and the Tukey post-hoc test. For categorical variables,