we used the χ^2-test. In the items that showed a significant difference ($P < 0.05$), we dichotomized the items and carried out a χ^2 analysis separately for each category. Additionally, we analyzed the differences of KCL domains (mean scores) among the three groups using ANCOVA adjusted by age.

We calculated the differences in the percentage of frail older women among the groups using the χ^2-test. Furthermore, we carried out a binary logistic regression analysis adjusted by age with each KCL domain as a dependent variable. The Japanese group was determined to be the reference group; for the total KCL score and for each domain, the robust condition was coded as 0 and frailty was coded as 1. Statistical significance was set at $P < 0.05$. All analyses were carried out using the Statistical Package for the Social Sciences (version 21.0; SPSS, IBM, Chicago, IL, USA).

Results

A total of 211 participants completed the research procedures (Brazilian $n = 72$; Brazilian Japanese descendants $n = 55$; Japanese $n = 84$). The Japanese were the oldest (mean age 73.2 ± 4.21 years), whereas the Brazilians were the youngest (mean age 69.0 ± 6.41 years; $P < 0.001$). There were differences in living arrangement ($P = 0.023$), educational level ($P < 0.001$) and work activity ($P < 0.001$) among the three groups. More Brazilian participants were living alone ($P = 0.029$), whereas more Japanese women were living with a partner ($P = 0.015$). Additionally, more than 50% of the Brazilian participants had received education at the elementary school level ($P < 0.001$), whereas the majority of the Japanese participants had finished high school ($P < 0.001$), and the majority of the Brazilian Japanese descendants had a university degree ($P < 0.001$). In terms of employment, a higher proportion of Brazilian and Brazilian Japanese descendants were retired compared with the Japanese women ($P = 0.042$), who were more engaged in informal work ($P < 0.001$; Table 1).

Regarding the health-related characteristics among the groups, there were differences in BMI ($P < 0.001$), number of medications ($P = 0.028$), frequency of medical consultation ($P < 0.001$) and life satisfaction ($P < 0.001$). The Brazilian participants had the highest BMI ($P < 0.001$) and took the greatest number of medications ($P = 0.028$), whereas the Japanese participants had the lowest BMI and took fewer medications. The Japanese women consulted a doctor more frequently ($P < 0.001$) and had a poorer life satisfaction ($P < 0.001$) than the other groups (Table 2).

We compared frailty among the three groups using the KCL (Japanese or Brazilian Portuguese version).

Table 1 Comparison of sociodemographic characteristics among Brazilian, Brazilian Japanese descendants and older Japanese women

Variables	Brazilian ($n = 72$)	Brazilian Japanese descendants ($n = 55$)	Japanese ($n = 84$)	P
Age (years)	69.0 ± 6.41†	70.8 ± 8.38	73.2 ± 4.21†	<0.001
Living arrangement				0.023
Alone	26.4 (19)	14.5 (8)	10.7 (9)	0.029
With partner	23.6 (17)	27.3 (15)	44.0 (37)	0.015
With child	25.0 (18)	27.3 (15)	17.9 (15)	0.369
With partner and child	15.3 (11)	23.6 (13)	13.1 (11)	0.246
Other	9.7 (7)	7.3 (4)	14.3 (12)	0.242
Educational level				<0.001
Elementary school	68.1 (49)	27.5 (14)	–	<0.001
Junior high school	13.9 (10)	17.6 (9)	28.6 (24)	0.053
High school	9.7 (7)	15.7 (8)	56.0 (47)	<0.001
Technical school	–	2.0 (1)	7.1 (6)	0.035
University	6.9 (5)	33.3 (17)	8.3 (7)	<0.001
Other	1.4 (1)	3.9 (2)	–	0.208
Work activity				<0.001
Formal work	6.2 (4)	13.7 (7)	1.4 (1)	0.016
Informal work	12.3 (8)	3.9 (2)	37.8 (28)	<0.001
Volunteer	9.2 (6)	9.8 (5)	5.4 (4)	0.551
Retirement	72.3 (47)	72.5 (37)	55.4 (41)	0.042

Values represent the mean ± standard deviation and valid percentage (n); $n = 211$. Tukey's post-hoc: †$P < 0.001$.

Table 2 Comparison of health-related characteristics among Brazilian, Brazilian Japanese descendants and older Japanese women

Variables	Brazilian (n = 72)	Brazilian Japanese descendants (n = 55)	Japanese (n = 84)	P
BMI (kg/m^2)	28.1 ± 5.39†‡	23.6 ± 2.50†	22.9 ± 2.84‡	<0.001
On medication	84.7 (61)	85.5 (47)	81.9 (68)	0.831
No. medications	2.9 ± 2.1§	2.7 ± 2.4	2.1 ± 1.5§	0.028
Consultations in 6 months				<0.001
None	17.4 (12)	9.3 (5)	14.5 (12)	0.462
1–2 times	50.7 (35)	61.1 (33)	18.1 (15)	<0.001
3–4 times	21.7 (15)	14.8 (8)	16.9 (14)	0.630
5–6 times	8.7 (6)	13 (7)	32.5 (27)	<0.001
7 times or more	1.4 (1)	1.9 (1)	18.1 (15)	<0.001
Hospitalization in 1 year	14.1 (10)	16.4 (9)	7.5 (6)	0.248
Self-rated health				0.467
Very good	11.1 (8)	20.0 (11)	17.1 (14)	
Good	33.3 (24)	34.5 (19)	35.4 (29)	
Normal	34.7 (25)	32.7 (18)	40.2 (33)	
Not so good	18.1 (13)	12.7 (7)	7.3 (6)	
Bad	1.4 (1)	–	–	
Life satisfaction				<0.001
Very satisfied	43.1 (31)	47.3 (26)	21.7 (18)	0.002
Satisfied	41.7 (30)	52.7 (29)	43.4 (36)	0.405
Normal	9.7 (7)	–	30.1 (25)	<0.001
A bit unsatisfied	5.6 (4)	–	3.6 (3)	0.220
Unsatisfied	–	–	1.2 (1)	0.468

Values represent the mean ± standard deviation and valid percentage (n); n = 211. Tukey's post-hoc: †‡P < 0.001; §P = 0.027.

Table 3 Comparison of Kihon Checklist scores by analysis of covariance adjusted by age among Brazilian, Brazilian Japanese descendants and Japanese women

Variables	Brazilian (n = 72)	Brazilian Japanese descendants (n = 55)	Japanese (n = 84)	P
Total KCL score	6.22 ± 3.83	3.22 ± 2.75	3.43 ± 2.72	<0.001
IADL domain	0.58 ± 0.84	0.29 ± 0.57	0.18 ± 0.50	<0.001
Physical strength domain	1.58 ± 1.15	1.11 ± 1.18	1.38 ± 1.24	0.047
Nutrition domain	0.35 ± 0.48	0.23 ± 0.47	0.40 ± 0.60	0.252
Eating domain	1.07 ± 0.98	0.51 ± 0.77	0.67 ± 0.90	0.001
Socialization domain	0.39 ± 0.52	0.18 ± 0.39	0.01 ± 0.28	<0.001
Memory domain	0.88 ± 0.84	0.51 ± 0.72	0.36 ± 0.61	<0.001
Mood domain	1.42 ± 1.62	0.40 ± 0.78	0.52 ± 0.93	<0.001

Values represent the mean ± standard deviation; n = 211. IADL, instrumental activities of daily living; KCL, Kihon Checklist.

The Brazilian participants had the highest total KCL scores (more frail), whereas the Brazilian Japanese descendants had the lowest scores (P < 0.001). Additionally, when we compared each domain adjusted by age, the Brazilian participants showed the poorest condition in IADL (P < 0.001), physical (P = 0.047), oral (P = 0.001), socialization (P < 0.001), cognitive (P < 0.001) and mood (P < 0.001) domains (Table 3).

Reviewing the results that identified frailty using our determined cut-off points, we observed that the Brazilian group had the higher prevalence of frail women according to their total KCL score (P < 0.001) compared with the other groups. Furthermore, this group also had more participants with oral dysfunction (P < 0.001), seclusion (P < 0.001), cognitive impairment (P < 0.001) and depression (P < 0.001). There were no significant

Table 4 Logistic regression analysis of frail condition among Japanese, Brazilian Japanese descendants and Brazilian participants using Kihon Checklist scores as dependent variables and nationality as covariate – adjusted by age

	Frailty % (*n*)	*P*	OR (95% CI)	*P*
Total KCL score (cut-off >6 points)		<0.001		
Japanese (reference for OR)	16.7 (14)		1	
Brazilian Japanese descendants	10.9 (6)		0.65 (0.23–1.84)	0.417
Brazilian	45.8 (33)		5.97 (2.69–13.3)	<0.001
IADL domain (cut-off >2 points)		0.194		
Japanese (reference for OR)	1.2 (1)		1	
Brazilian Japanese descendants	0		–	–
Brazilian	4.2 (3)		5.15 (0.51–52.2)	0.165
Physical strength domain		0.242		
Japanese (reference for OR)	21.4 (18)		1	
Brazilian Japanese descendants	10.9 (6)		0.44 (0.16–1.22)	0.114
Brazilian	20.8 (15)		0.95 (0.42–2.13)	0.892
Nutrition domain (cut-off BMI<20.5)		0.090		
Japanese (reference for OR)	6 (5)		1	
Brazilian Japanese descendants	1.9 (1)		0.22 (0.018–2.57)	0.226
Brazilian	0		–	
Eating domain		<0.001		
Japanese (reference for OR)	19 (16)		1	
Brazilian Japanese descendants	9.1 (5)		0.45 (0.15–1.33)	0.148
Brazilian	37.5 (27)		3.18 (1.47–6.85)	0.003
Socialization Domain (cut-off >1 point)		<0.001		
Japanese (reference for OR)	8.3 (7)		1	
Brazilian Japanese descendants	18.2 (10)		2.70 (0.95–7.73)	0.063
Brazilian	37.5 (27)		9.15 (3.53–23.7)	<0.001
Memory domain		<0.001		
Japanese (reference for OR)	29.8 (25)		1	
Brazilian Japanese descendants	38.2 (21)		1.49 (0.72–3.08)	0.279
Brazilian	61.1 (44)		3.87 (1.93–7.75)	<0.001
Mood domain		<0.001		
Japanese (reference for OR)	10.7 (9)			
Brazilian Japanese descendants	9.1 (5)		0.89 (0.28–2.83)	0.844
Brazilian	38.9 (28)		6.63 (2.74–16.0)	<0.001

Values represent percentage (*n*) and OR (95% CI); $n = 211$. BMI, body mass index; IADL, instrumental activities of daily living; KCL, Kihon Checklist.

differences regarding IADL performance, and physical and nutritional conditions among the groups (Table 4).

The results of the logistic regression confirmed that older Brazilian women were more inclined to be frail than Japanese women. The Brazilian participants were fivefold more likely to be frail (OR 5.97, 95% CI 2.69–13.3, $P < 0.001$), threefold more likely to have oral dysfunction (OR 3.18, 95% CI 1.47–6.85, $P = 0.003$), ninefold more likely to have seclusion (OR 9.15, 95% CI 3.53–23.7, $P < 0.001$), threefold more likely to have cognitive impairment (OR 3.87, 95% CI 1.93–7.75, $P < 0.001$) and sixfold more likely to have depression (OR 6.63, 95% CI 2.74–16.0, $P < 0.001$) than the older Japanese women. However, no difference was found between the Japanese and Brazilian Japanese descendants. No difference was found in terms of IADL, physical or nutritional domains among the groups (Table 4).

Discussion

In the present study, we observed a higher prevalence of frail participants in the Brazilian group ($P < 0.001$); and that older Brazilian women were more inclined to be frail than Japanese women (OR 5.97, 95% CI 2.87–13.3, $P < 0.001$). To the best of our knowledge, the present study is the first that compares frailty among Brazilian, Brazilian with Japanese genetic background and older Japanese women. To substantiate our

findings, we discussed our observations and results separately, detailing each KCL domain and linking it to the participants' sociodemographic and lifestyle characteristics.

According to the KCL domains, we observed differences regarding the mean scores in IADL ($P < 0.001$) and physical ($P = 0.047$) domains among the three groups; however, such differences failed to remain statistically significant when we dichotomized them according to the cut-off points to determine frailty. A similar pattern was observed in the nutritional domain; no group showed a significantly different risk level to develop frailty. Although no differences were found in the physical and nutritional domains among the groups, we can discuss the significant difference observed in BMI ($P < 0.001$), especially because BMI is an important indicator of physical and nutritional status, and an increased BMI could be an alarming sign of imminent frailty evaluated by both domains. In the present study, the Brazilian participants were more obese (BMI 28.1 ± 5.39 kg/m^2) than the other groups. Although the KCL considers low bodyweight to be a frailty symptom, epidemiological studies show that both overweight and underweight are negative health outcomes associated with a greater risk for morbidity and mortality.[15]

There are some data showing that the Brazilian environment might pose a risk for developing obesity compared with the Japanese environment; a study verified that the risk for developing central obesity was 2.8-fold higher among Japanese Brazilians living in Brazil.[8] Although that study did not include Brazilian natives, there is evidence supporting concurrent increases in obesity in Brazil.[16]

Furthermore, we found that Brazilian participants were threefold more likely to be frail in terms of oral health (eating domain) than the Japanese group (OR 3.18, 95% CI 1.47–6.85, $P = 0.003$). In this case, the educational level of the participants seems to be related to their poor oral condition; considering the evidence that older adults who received elementary school level education had a significantly larger number of missing teeth and significantly fewer healthy gingival units compared with those who received higher than elementary school level education.[17] Another study showed that not only educational level, but also living arrangement influenced the participants' oral health; concluding that poorly educated and divorced women had fewer remaining teeth than better-educated and married women.[18] In the present study, the most favored group in terms of educational and living arrangement conditions was the Japanese cohort that were also more concerned about dehydration (consuming liquids, especially tea, as one of the Japanese habits), another included aspect in the oral domain.

Regarding the socialization domain, the Brazilian participants also showed a greater risk for becoming frail compared with the Japanese participants (OR 9.15, 95% CI 3.53–23.7, $P < 0.001$). A study showed that a partner relationship, such as marriage, might impact women's health status in numerous ways and could confer health-related benefits, such as providing nurturing conditions and socialization through a spouse,[19] and building a network with the partner's family.[20] Furthermore, a relationship possibly includes access to material resources and other social support.[21] These privations could lead Brazilian women to a poorer condition not only in the seclusion domain, but also in the mood domain, as the study concluded that individuals who lack social connections or report frequent feelings of loneliness tend to suffer higher rates of depression as well.[22]

Although the older Brazilian women showed a higher life satisfaction ($P = 0.002$), they presented a higher risk for being frail in terms of depression (OR 6.63, 95% CI 2.74–16.0, $P < 0.001$) than the Japanese group. Evidence showed that living alone or with other(s) than a partner could lead to depression and anxiety disorders in women.[23]

Finally, the results that we found in the memory domain did not differ from those aforementioned. The Brazilian participants were threefold more likely to be frail compared with the Japanese group (OR 3.87; 95% CI 1.93–7.75, $P < 0.001$). It is widely recognized that low education is one of the conditions that affect cognitive performance, especially phonological verbal fluency, calculation and working memory[24,25] that are required when processing the tasks assessed by the KCL cognitive domain. Another factor that might be related to the lowest scores achieved by Brazilian women in the memory domain is their highest number of medication use (Brazilian participants 2.9 ± 2.1 *vs* Japanese participants 2.1 ± 1.5, $P = 0.028$). Although we did not investigate the drug classes, the cognitive impairment is repeatedly reported to be a side-effect among medications prescribed for the elderly.[26,27]

We discerned that the majority of the differences in the present study were shows between Japanese and Brazilian natives. However, we must emphasize that an improved condition in terms of frailty was observed in the Brazilian Japanese descendants. This result might be linked to their higher educational level that predicts a higher-level financial status and better living conditions, which might in turn reflect a better health education, as they showed the lowest total KCL score ($P < 0.001$), and also the lowest mean KCL score in physical strength ($P = 0.047$), eating ($P = 0.001$) and mood ($P < 0.001$) domains.

We emphasize that the native Brazilian participants might be more vulnerable and frail because of the sociodemographic disadvantages that they are exposed to and their adopted lifestyle. However, such conditions are reversible; and an early detection of the frail aspects

is essential to reverse it in older adults. For this purpose, the KCL was designed to monitor the health conditions and to detect negative health outcomes at the earliest stage, thereby assuring prompt prevention or rehabilitation interventions, being an accurate, cheap, easy and fast diagnostic tool.

The present study had several limitations: (i) the present study was a cross-sectional design, which did not enable us to determine a cause–effect relationship; (ii) the present study was carried out in only one Brazilian and one Japanese region, which did not allow us to extend our findings to the national level; and finally, (iii) we only analyzed older women with heterogeneous characteristics, which complicated our comparisons. We recommend prospective studies to include a greater sample size, with male participants recruited from several regions of Brazil and Japan, and that future studies investigate important aspects that could be related to frailty, such as the financial situation of the participants.

In summary, we found that Brazilian natives were more frail than Japanese natives, but not Brazilian Japanese descendants. In addition to the environment, we believe that the lifestyle and the sociodemographic conditions could reflect the frailty of older Brazilian women in the present study. Hence, we recommend the dissemination of general health education among these older adults, including incentives for regular engagement in physical activity and a well-balanced diet, the principles of oral health safety and social and cognitive approaches to warrant a healthy aging process.

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Disclosure statement

The authors declare no conflict of interest.

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Original Article

Arterial Stiffness Determined According to the Cardio-Ankle Vascular Index (CAVI) is Associated with Mild Cognitive Decline in Community-Dwelling Elderly Subjects

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Aims: The purpose of this study was to determine the cross-sectional relationship between the cognitive function and cardio-ankle vascular index (CAVI) in Japanese community-dwelling elderly subjects.
Methods: A total of 179 Japanese community-dwelling elderly subjects were recruited for this study. The age, height, weight, gender and past medical history (cardiovascular disease, hypertension, diabetes mellitus, hyperlipidemia) of each participant was recorded. In addition, the degree of arterial stiffness was determined according to the CAVI, while the cognitive function was assessed using the Mini-Mental State Examination (MMSE). After dividing the cohort into two groups according to the MMSE score (≤ 26, >26), we used a multiple regression analysis to assign the level of the cognitive function as a dependent variable.
Results: The data were statistically analyzed for the 174 participants (84 men and 90 women) who completed the data collection process without omissions. A multivariate logistic regression analysis showed that a higher weight (Odds Ratio [OR]: 1.05, 95% Confidence Interval [95% CI]: 1.00-1.11, $p=0.03$), male gender (OR: 3.13, 95% CI: 1.05-9.34, $p=0.04$) and lower CAVI (OR: 0.68, 95% CI: 0.48-0.96, $p=0.03$) were significantly correlated with a higher MMSE score. We also found significant correlations between the MMSE and weight (OR: 1.11, 95% CI: 1.03-1.19, $p=0.01$) and CAVI (OR: 0.57, 95% CI: 0.33-0.98, $p=0.04$) in elderly men only using a gender-specific analysis.
Conclusions: We found that the elderly subjects with a high CAVI exhibited a worse cognitive function even after adjusting for age, height, weight and gender. This finding therefore indicates the usefulness of the CAVI in the early detection of dementia.

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Key words: Cognitive function, Arterial stiffness, Community-dwelling elderly

Introduction

Dementia can drastically influence daily life and is currently one of the most common diseases in the elderly. The World Health Organization estimated that 35 million people worldwide suffered from dementia in 2012, and people with dementia have been shown to be frail due to their poor mobility and body composition. Approximately 48% of people with Alzheimer's disease (AD), the most common form of dementia, are estimated to live in Asia, and this percentage will grow to 59% by 2050[1]. The transitional stage between normal aging and AD is called mild cognitive impairment (MCI), and more than half of MCI cases progress to dementia within five years[2, 3]. Therefore, preventing cognitive decline is crucial.

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Identifying risk factors that can predict cognitive decline will help to prevent such decline. Although many studies have attempted to address this issue, evidence supporting the role of modifiable risk factors remains limited[4-6]. Meanwhile, vascular risk factors have received attention in recent years[7, 8]. High blood pressure[9], dyslipidemia[9], obesity[10] and diabetes mellitus[10] have been proposed to be risk factors for cognitive decline. Among these factors, arterial stiffness, specifically, is a comparatively easy-to-modify risk factor. It has been reported that systemic atherosclerosis plays a role in the cognitive function and is directly linked to the pathology of Alzheimer's disease[11]. In one European study, it was found that functional changes in the arterial system may be involved in the onset of dementia[12].

Arterial stiffness is one of the most easily measured vascular risk factors in community-dwelling elderly subjects due to its noninvasive nature. The brachial-ankle pulse wave velocity (baPWV) is widely used for this purpose. In a cross-sectional study of 370 middle-aged Korean participants, the baPWV was found to be significantly correlated with the cognitive function[13]. In addition, in a Japanese study, a high baPWV was shown to be a risk factor for a poor cognitive function in 352 community-dwelling elderly subjects[5]. However, there are several problems associated with the measurement of baPWV, as the value of the parameter depends on the blood pressure (BP) at the time of measurement[14]. Therefore, it is difficult to evaluate arterial stiffness in patients treated with antihypertensive medications or those with masked hypertension. In contrast, the cardio-ankle vascular index (CAVI) is a novel BP-independent parameter of arterial stiffness[15, 16]. This parameter is adjusted for the PWV according to the systolic and diastolic blood pressure and blood density and is therefore a theoretically BP-independent index. Clinicians can ensure the validity of arterial stiffness measurements using this parameter. However, no studies have so far evaluated the relationship between the cognitive function and arterial stiffness using the CAVI. In addition, few studies have evaluated this relationship in community-dwelling elderly patients.

The purpose of this study, therefore, was to determine the cross-sectional relationship between the cognitive function and the CAVI in Japanese community-dwelling elderly subjects.

Methods

Participants

Participants were recruited for this study through local press requesting healthy community-dwelling volunteers, resulting in a total of 179 Japanese participants 65 years of age or older and currently living in the community. Interviews were then performed to exclude participants based on the following exclusion criteria: severe cardiac, pulmonary or musculoskeletal disorders; comorbidities associated with a greater risk of falls, such as Parkinson's disease and stroke; and the use of psychotropic drugs. Written informed consent was obtained from each participant for the trial in accordance with the guidelines approved by the Kyoto University Graduate School of Medicine and the Declaration of Human Rights, Helsinki, 1995. The study protocol was approved by the ethical committee of the Kyoto University Graduate School of Medicine.

Measurements

Demographic Data

Age, height, weight, gender, past medical history (cardiovascular disease, hypertension, diabetes mellitus, 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 and university) were recorded as demographic data. All data were collected at the onset of data collection. We surveyed age and gender from the participant directly and measured the height and weight using standardized height and weight scales.

CAVI

The CAVI was determined using the VaSera-1500 (Fukuda Denshi Co., Ltd., Tokyo, Japan). The procedure has been detailed previously[15, 16]. Briefly, after the participants had rested for five minutes in a sitting position, they were placed in a supine position. Then, cuffs were wrapped around both brachia and ankles to detect the brachial and ankle pulse waves. Electrocardiograms and heart sounds were monitored. The PWV from the heart to the ankle was calculated by measuring the length from the aortic valve to the ankle and dividing by time, which was determined according to the heart sounds and the rise of the brachial and ankle pulse waves. Blood pressure was also measured at the brachial artery. Finally, scale conversion was performed using the following formula:

$$CAVI = a\{(2\rho/\Delta P) \times \ln(Ps/Pd)PWV^2\} + b \text{ (no unit)}$$

ρ: blood density, Ps: systolic blood pressure, Pd; diastolic blood pressure, ΔP: Ps-Pd, PWV: pulse wave velocity, a and b: constants.

The validity, reproducibility and blood pressure-independent nature of this experiment have been well

Table 1. Differences in each variable between the MMSE high/low score groups

	All (n=174)			Men (n=84)			Women (n=90)		
	Low MMSE (≤26) n=56	High MMSE (>26) n=118	p	Low MMSE (≤26) n=30	High MMSE (>26) n=54	p	Low MMSE (≤26) n=26	High MMSE (>26) n=64	p
MMSE	24.6±1.3	28.7±1.1	<0.01**	24.8±1.0	28.8±1.1	<0.01**	24.5±1.5	28.6±1.1	<0.01**
Age, year	74.2±4.6	73.4±4.3	0.26	73.8±5.2	73.8±4.2	0.94	74.5±3.7	73.0±4.4	0.12
Height, cm	155.5±8.7	156.1±8.1	0.65	162.2±5.3	162.8±6.0	0.64	147.8±4.6	150.5±4.7	0.02*
Weight, kg	54.0±8.8	57.3±9.7	0.03*	57.6±9.3	63.6±8.7	0.01*	49.9±6.1	52.0±7.1	0.19
Gender, male	30 (53.6%)	54 (45.8%)	0.21	–	–	–	–	–	–
Mean CAVI	9.61±1.30	9.13±1.16	0.02*	9.97±1.52	9.38±0.87	0.03*	9.19±0.85	9.03±0.93	0.47
Cardiovascular disease	8 (14.3%)	8 (6.8%)	0.16	6 (20.0%)	4 (7.4%)	0.16	2 (7.7%)	4 (6.3%)	1.00
Hypertension	21 (37.5%)	50 (42.4%)	0.62	13 (43.3%)	23 (42.6%)	1.00	8 (30.8%)	27 (42.2%)	0.35
Diabetes mellitus	6 (10.7%)	14 (11.9%)	1.00	2 (6.7%)	8 (14.9%)	0.47	4 (15.4%)	6 (9.4%)	0.47
Hyperlipidemia	8 (14.3%)	18 (15.3%)	1.00	4 (13.3%)	5 (9.6%)	0.72	4 (15.4%)	13 (20.3%)	0.77
Brinkman index	0 (0-762.5)	0 (0-356.3)	0.70	0 (0-787.5)	0 (0-637.5)	0.50	0 (0-612.5)	0 (0-2.25)	0.23
Educational background			n.s.			n.s.			n.s.
Elementary school	2 (3.6%)	1 (0.8%)		2 (6.7%)	1 (1.9%)		0 (0.0%)	0 (0.0%)	
Junior high school	26 (46.4%)	28 (23.7%)		16 (53.3%)	15 (27.8%)		10 (38.5%)	13 (20.3%)	
High school	26 (46.4%)	69 (58.5%)		11 (36.7%)	30 (55.6%)		15 (57.7%)	39 (60.9%)	
Career college	0 (0.0%)	7 (5.9%)		0 (0.0%)	1 (1.9%)		0 (0.0%)	6 (9.4%)	
University	2 (3.6%)	13 (11.0%)		1 (3.3%)	7 (13.0%)		1 (3.8%)	6 (9.4%)	

Mean CAVI = the mean value of the right and left CAVI scores; Mean ± SD values are shown for age, height, weight and mean CAVI; n (%) is shown for gender, cardiovascular disease, hypertension, diabetes mellitus, hyperlipidemia and educational background; Median (25% quartile-75% quartile) is shown for the Brinkman index; n.s.: not significant.
*: $p<0.05$, **: $p<0.01$

documented by several studies[15, 16]. The measurements were obtained once, and the mean value of the right and left CAVI scores for each patient was used for the analysis[17].

Cognitive Function Measurement

The cognitive function was assessed using the Mini-Mental State Examination (MMSE)[18]. The MMSE is a short screening test that consists of five areas of possible cognitive impairment: orientation; registration; attention and calculation; and language. The scores ranged from 0 to 30, with a higher score indicating a better cognitive performance. We tested the participants individually based on the generalized method and used 26/27 as the cutoff score, according to Spering CC *et al.*[19].

Statistical Analysis

The participants were divided into two groups based on the MMSE score: ≤26 or >26. This cutoff of 26/27 has been shown to be a better balanced score of estimates of diagnostic accuracy for educated individuals[19]. Because our participants were community-dwelling and highly educated and all lived independently, we adopted this 26/27 cutoff.

We statistically analyzed the differences between the two groups using the unpaired *t*-test for age, height, weight and the mean CAVI on both sides, the χ^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 × total number of years smoked). A multivariate logistic regression model was performed to investigate whether the CAVI was independently associated with the MMSE score. We assigned a high MMSE score as the dependent variable adjusted for age, height, weight and gender. A value of $p<0.05$ was considered to be statistically significant for all analyses.

Results

In total, there were 179 elderly participants (85 men and 94 women) in this study. Of the 179 patients, 84 men and 90 women completed the data collection without omissions, for a total of 174 data points.

We assigned 56 elderly subjects (30 men and 26 women) into the low MMSE group and 118 elderly subjects (54 men and 64 women) into the high MMSE group. **Table 1** shows the differences in each variable between the two groups. While there were no significant differences in age, height, gender or past medical history, a higher weight was associated with a higher MMSE score ($p=0.03$). In addition, the low

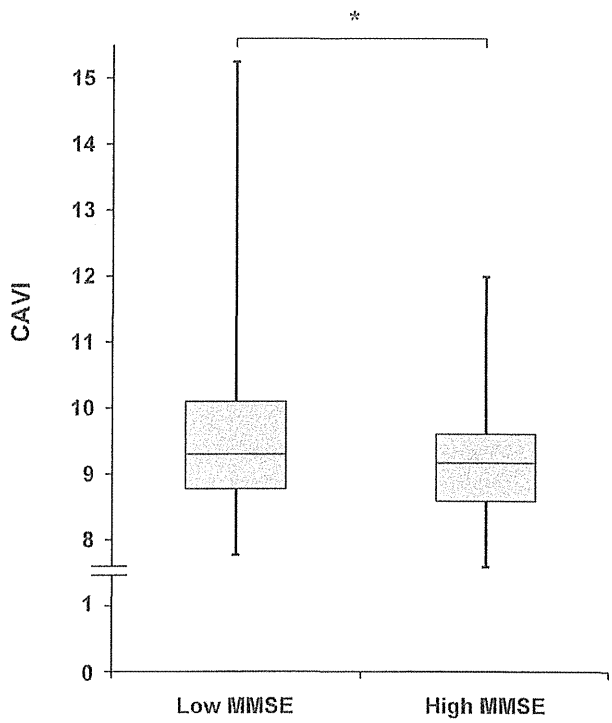

Fig. 1. Differences in the mean CAVI values between the high and low MMSE groups.

We statistically analyzed the differences between the two groups using the unpaired *t*-test for the mean CAVI on both sides.
*: $p=0.02$

MMSE group had significantly higher CAVI values than the high MMSE group (**Fig. 1**, the low group: 9.61 ± 1.30, the high group: 9.13 ± 1.16, $p=0.02$).

The multivariate logistic regression analysis showed that a higher weight (odds ratio [OR]: 1.05, 95% confidence interval [95% CI]: 1.00-1.11, $p=0.03$), female gender (OR: 3.13, 95% CI: 1.05-9.34, $p=0.04$) and lower CAVI (OR: 0.68, 95% CI: 0.48-0.96, $p=0.03$) were significantly correlated with a higher MMSE score (**Table 2**), indicating that elderly subjects with a higher CAVI have a lower cognitive function, even after adjustment for age, height, weight and gender. In the multivariate logistic regression analysis of each gender, we found a significant correlation between the MMSE score and weight (OR: 1.11, 95% CI: 1.03-1.19, $p=0.01$) and CAVI (OR: 0.57, 95% CI: 0.33-0.98, $p=0.04$) in the elderly men only (**Table 2**).

Discussion

We analyzed the relationship between the cogni-

Table 2. Multivariate logistic regression model to determine the association with a high MMSE score

	All (n=174)		Male (n=84)		Female (n=90)	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age, year	1.00 (0.92-1.09)	1.00	1.08 (0.95-1.12)	0.25	0.96 (0.85-1.09)	0.51
Height, cm	1.04 (0.97-1.12)	0.27	0.97 (0.88-1.08)	0.60	1.13 (1.00-1.28)	0.05
Weight, kg	1.05 (1.00-1.11)	0.03*	1.11 (1.03-1.19)	0.01*	1.01 (0.94-1.09)	0.82
Gender	–	0.04*	–	–	–	–
men	1 [Reference]	–	–	–	–	–
women	3.13 (1.05-9.34)	–	–	–	–	–
Mean CAVI	0.68 (0.48-0.96)	0.03*	0.57 (0.33-0.98)	0.04*	0.73 (0.44-1.23)	0.24

Mean CAVI = the mean value of the right and left CAVI scores; OR = Odds Ratio, 95% CI = 95% confidence interval.
*: $p<0.05$

tive function and the CAVI in Japanese community-dwelling elderly subjects. In this study, we found a negative correlation between the CAVI and the cognitive function, even after adjusting for age, height, weight and gender. Many studies have demonstrated a relationship between arterial stiffness and a decreased cognitive function[5, 12, 13]; however, there are no reports using the novel index of arterial stiffness, the CAVI, in community-dwelling elderly subjects.

Several mechanisms may potentially explain why arterial stiffness is associated with the cognitive function. First, the development of dementia is associated with organic brain lesions, such as ischemic lesions and white matter abnormalities[20]. Because stiff blood vessels lose their capacity to buffer pulse pressure, the pulsatile flow is increased, causing damage to the fragile small vessels in the brain[21]. This phenomenon has been demonstrated in animal studies, in which locally induced isolated alterations in pressure pulsatility have been shown to have major effects on the cerebral microvascular structure and function[22]. Pase *et al.*[23] reported that the augmented pressure caused by arterial stiffness independently predicts the cognitive function. In addition, some studies have shown evidence that asymptomatic cerebral microvascular lesions caused by augmented pressure are associated with an increased risk of AD[24, 25]. Our major finding indicating a correlation between the CAVI and the cognitive function is consistent with the results of these previous reports. However, this relationship was found only in elderly men in a gender-specific analysis; therefore, cognition may be more strongly affected by arterial stiffness in men than in women. Larger studies should address the effects of the CAVI on the cognitive function in elderly women.

The peculiarity of the CAVI is that it indicates BP-independent arterial stiffness, unlike the baPWV. Therefore, it is conceivable that the CAVI is a useful parameter in patients who are subject to variation in BP at various times due to masked hypertension or the use of antihypertensive medications. Masked hypertension is defined as a normal BP in the clinic or office (<140/90 mmHg) with an elevated BP out of the clinic (ambulatory daytime BP or home BP> 135/85 mmHg)[26]. This phenomenon can occur in up to 8-38% of the general population and is observed at all ages[27]. In addition, antihypertensive medication use has recently increased. Men have seen the greatest increase in antihypertensive medication use (47.5%, 1988-1994 versus 57.9%, 1999-2002) among hypertensive adults[28]. Moreover, Takaki *et al.* demonstrated the superiority of the CAVI to the baPWV in measurement sensitivity[29]. They found that the CAVI was better correlated with the parameters of left ventricular diastolic indices, low-density lipoprotein cholesterol and angina pectoris than the baPWV.

When evaluating arterial stiffness in community-dwelling elderly subjects, the most important properties of an instrument for assessment are ease of measurement and validation. The clinical advantage of our study is the indication of a significant relationship between arterial stiffness and the cognitive function in community-dwelling elderly subjects based on the use of a better arterial stiffness index, the CAVI. In order to early detect cognitive decline, clinicians should conduct screening exams for community-dwelling elderly patients. This is why we adopted the 26/27 cutoff point for our patients, all of whom lived independently and were highly educated. This index has the potential to be used to detect cognitive decline earlier in community-dwelling elderly subjects due to its validity and noninvasive nature.

This study is associated with several limitations. First, because this study is a cross-sectional study, the

cause-effect relationship between the CAVI and the cognitive function is unknown. Second, we were unable to perform neuroimaging procedures. The participants may have had asymptomatic brain lesions that we could not fully investigate. In addition, we did not distinguish between the types of dementia. Different types of dementia may affect the results. Further investigations, such as prospective studies, are required to confirm the findings of the present study.

Conclusion

This is the first study to determine the relationship between the cognitive function and the CAVI in community-dwelling elderly subjects. We found a significant relationship between a higher CAVI and mild cognitive decline. This finding indicates the usefulness of the CAVI in the early detection of dementia.

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.[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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Original article

Spot the Difference for Cognitive Decline: A quick memory and attention test for screening cognitive decline

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ABSTRACT

Background: Dementia is currently one of the most common conditions in older adults, and early detection of cognitive decline is crucial for identifying dementia. We developed a new type of short-term memory and attention test that uses a spot-the-difference task: Spot the Difference for Cognitive Decline (SDCD). The purpose of the present study was to examine the accuracy of the SDCD test for the identification of cognitive impairment in community-dwelling older adults.

Methods: The participants were 443 Japanese community-dwelling older adults. The SDCD test uses two scenery pictures. Participants were instructed to memorize the details of the first picture for 30 seconds, after which the first picture was taken away and the second picture was shown. Next, the participants were asked to identify as many differences as possible between the first and second pictures, which were presented sequentially. The number of correct responses comprises the SDCD score (scores: 0–10). The Mini-Mental State Examination and Scenery Picture Memory Test were used to measure the participants' cognitive function. We used receiver-operating characteristic analysis to examine the power of the SDCD test and identify the optimal cutoff value of the SDCD score.

Results: Of the 443 participants, 30 (6.77%) had some cognitive impairment based on the Mini-Mental State Examination scores. Participants without cognitive impairment had higher SDCD scores than those with cognitive impairment ($p < 0.001$). The SDCD scores were significantly associated with the Mini-Mental State Examination ($r = 0.333$) and Scenery Picture Memory Test ($r = 0.402$) results. The receiver-operating characteristic curve used for the identification of cognitive impairment had a comparatively high area under the curve (0.798) for the SDCD score with a cutoff value of 1/2 (with >1 being normal; sensitivity: 70.5%; and specificity: 80.0%).

Conclusion: The present study found that the SDCD test could be an effective clinical tool for the identification of cognitive impairment in older adults.

1. Introduction

Dementia can drastically influence one's daily life and is currently one of the most common conditions in older adults. Dementia affects 5–8% of the population over 65 years of age[1] and up to 30% of the people aged ≥85 years.[2] Currently, the number of people with dementia is increasing. It has been estimated that approximately 48% of the patients with Alzheimer's disease (AD), the most common form of dementia, live in Asia, and this percentage is projected to grow to 59% by 2050.[3] Dementia and AD have been associated with mortality[4]; therefore, prevention and early detection of cognitive decline are crucial.

The presence of cognitive decline increases the risk of progression to mild cognitive impairment (MCI) and AD.[5,6] It is generally agreed that older adults with early AD, compared to healthy older adults, exhibit a greater decline in memory function[7] and working memory[8] than in other major domains of cognitive function._ENREF_7 A central feature of AD is the decline in episodic memory.[9] Visual memory, which is included in episodic memory, is

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