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Original Study

Differential Association of Frailty With Cognitive Decline and Sarcopenia in Community-Dwelling Older Adults



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ABSTRACT

Keywords: Frailty cognitive decline sarcopenia community-dwelling older adults Objectives: Frailty in older adults is a serious problem because of various adverse health outcomes in many countries with aging populations, such as Japan. The purpose of this study was to determine whether frailty and pre-frailty are associated with cognitive decline and sarcopenia in community-dwelling older adults.

Design: This is a cross-sectional study.

Setting: Japan.

Participants: The participants were 273 Japanese community-dwelling older women aged 65 years and older

Measurements: We used the frailty criteria developed by the Cardiovascular Health Study to define physical frailty. We divided the cohort into nonfrail, prefrail, and frail according to frailty scores. Cognitive decline and memory decline were defined by using the Mini-Mental State Examination and Scenery Picture Memory Test, respectively. Sarcopenia was defined according to the diagnostic algorithm recommended by the Asian Working Group for Sarcopenia.

Results: In the multivariate logistic regression analysis by using non-frail participants as the reference, pre-frail elderly individuals were significantly more likely to have sarcopenia than non-frail elderly individuals [odds ratio (OR): 2.77, 95% confidence interval (CI): 1.05–9.26], but not cognitive decline or memory decline. Frail elderly individuals were significantly more likely to have cognitive decline (OR: 5.76, 95% CI: 1.20–27.6), memory decline (OR: 5.53, 95% CI: 1.64–18.7) and sarcopenia (OR: 19.1, 95% CI: 3.73–98.0) than non-frail elderly individuals.

Conclusions: Sarcopenia was associated with pre-frailty and frailty, whereas cognitive decline was associated only with frailty.

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Frailty in older adults is a serious concern in countries with aging populations, such as Japan. In general, frailty is defined as a vulnerable state that places older adults at high risk for adverse health outcomes, such as falls, hospitalization, and mortality.^{1,2} Using the frailty criteria developed by the Cardiovascular Health Study, the overall prevalence of frailty in community-dwelling adults aged 65 or older in the United States has been found to range from 7% to 12% and

was greater in women than in men.¹ In Japanese, the prevalence of frailty in community-dwelling adults aged 65 or older was 11.3%, and it increased with aging.³ Frail older adults are considered to have a substantially increased risk of disability, dependency, and need for long-term care insurance. Therefore, prevention and early detection of frailty is important for addressing age-related health care issues.

The causes of frailty are not clearly defined, but it has been suggested that age-related physical changes are the main causes of frailty.⁴ Sarcopenia, defined as progressive loss of skeletal muscle mass, strength, and physical function, is regarded as a key component of physical frailty.^{5,6} The Interventions on Frailty Working Group assessed various methods for screening, recruiting, evaluating, and

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retaining frail elderly individuals in clinical trials.⁷ They reported that most researchers focused on the following domains when identifying physical frailty: mobility, such as lower-extremity performance and gait abnormalities; muscle weakness; poor exercise tolerance; unstable balance; and factors related to body composition, such as weight loss, malnutrition, and muscle loss.⁷ Age-dependent loss of skeletal muscle mass is a multifactorial process; contributing factors include physical inactivity, malnutrition, oxidative stress, changes in endocrine function, and increases in inflammatory cytokines.⁵ Thus, the domains of frailty overlap with the factors related to sarcopenia, and both frailty and sarcopenia mutually result in adverse health outcomes.^{5,6}

Of note, some definitions of frailty include cognitive function and dementia. A.S Several cross-sectional studies have reported an association between physical frailty and cognitive function. A.J., In addition, longitudinal studies have revealed that a higher level of physical frailty is associated with increased risk of incident Alzheimer's disease (AD) and mild cognitive impairment. It has been indicated that frailty is associated with AD pathology and its biological mechanisms. However, not all dementia patients become frail; therefore, the association between frailty and cognitive impairment warrants further study.

Frailty is associated with sarcopenia and cognitive decline. Furthermore, frailty has been considered to include other aspects, such as psychosocial issues and comorbidities. However, it is unclear whether the associations between frailty and cognitive decline as well as between frailty and sarcopenia are different according to the level of frailty. Therefore, the purpose of this study was to determine whether frailty and prefrailty are associated with cognitive decline and sarcopenia in community-dwelling older adults.

Methods

Participants

Participants for this study were recruited through the local press; 273 Japanese women aged 65 years and older (mean age 73.0 \pm 5.4 years) responded. We included community-dwelling older adults who were independent in activities of daily living. Participants were interviewed and excluded if they met any of the following criteria: severe cardiac, pulmonary, or musculoskeletal disorders; severe neurologic disorders, such as Parkinson disease and stroke; and participation in Japan's long-term care service. The following data were collected from each participant: age, height, weight, and number of medications being consumed.

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, 1975. The study protocol was approved by the ethical committee of the Kyoto University Graduate School of Medicine.

Assessment of Frailty

We measured physical frailty domains determined in a previous study.³ As in that study, we considered the frailty phenotype to be characterized by limitations in the following 5 domains by using frailty criteria developed by the Cardiovascular Health Study¹: slowness, weakness, exhaustion, low activity, and shrinking. To measure slowness, each participant's 10-m normal walking speed (m/s) was calculated, and a slow walk was defined as <1.0 m/s. To measure weakness, low grip strength was established according to a sex-specific cutoff of the average grip strength in each arm (women: <17 kg). Exhaustion was assessed via self-report by using the Geriatric Depression Scale¹⁶ (ie, exhaustion was defined as a negative ["no"] answer to the

question "do you feel full of energy?)" We evaluated the role of physical activity by asking the following questions about time spent engaged in sports and exercise: (1) "Do you engage in moderate levels of physical exercise or sports aimed at health?" and (2) "Do you engage in low levels of physical exercise aimed at health?" If a participant answered "no" to both of these questions, then we considered their physical activity to be low. Shrinking was established according to self-reports of weight loss in response to the following question: "In the past 2 years, have you lost more than 5% of your body weight irrespective of intent to lose weight?" If a participant answered "yes" to this question, then we considered them to have shrunk. We calculated the number of affected domains and classified participants as follows: prefrailty = 1 or 2, frailty >3.\[^1\]

Measurement of Cognitive Function

Participants' cognitive function was measured by using 2 neuropsychological tests: the Mini-Mental State Examination (MMSE)¹⁷ and the Scenery Picture Memory Test (SPMT).¹⁸

Global cognitive function was assessed by using the MMSE, a standard test in cognitive aging research to assess mental status. The MMSE tests 5 areas of cognitive function: orientation, registration, attention and calculation, recall, and language. It has 11 questions and a possible maximum score of 30. We divided the participants into a normal or a cognitive decline group based on a cut-off of 23/24 as the MMSE score. ¹⁹

The SPMT is a simple memory test that assesses visual memory combined with verbal responses. This test uses a line drawing of a living room in a house with 23 objects commonly observed in daily life on an A4 piece of paper. The examinee is instructed to look at the picture for 1 minute and remember the items. After this encoding period, participants are distracted by completing a brief digits forward test. Participants are then asked to recall the objects in the picture without a time limitation. The recall usually takes approximately 2 minutes. The number of items recalled is the score for the SPMT. We divided the participants into a normal or memory decline group based on a cut-off of 9/10 as the SPMT score. ¹⁸

Definition of Sarcopenia

We defined sarcopenia by using the diagnostic algorithm recommended by the Asian Working Group for Sarcopenia, which assesses the presence of both low muscle function (low physical performance or low muscle strength) and low muscle mass.²⁰ A bioelectrical impedance data acquisition system (Inbody 430; Biospace Co, Ltd, Seoul, Korea) was used to perform bioelectrical impedance analysis.²¹ This system uses electrical current at multiple frequencies (5, 50, 250, 500, and 1000 kHz) to directly measure the amount of extracellular and intracellular water. Participants stood on 2 metallic electrodes and held metallic grip electrodes. Using segmental body composition, appendicular skeletal muscle mass was determined and used for further analysis. Skeletal muscle mass index (SMI) was calculated by dividing muscle mass by height squared in meters (kg/m²). This index has been used in several epidemiological studies. 22,23 If a participant had both low muscle function (slow walking speed, ≤ 0.8 m/s; low grip strength for women, ≤ 18 kg) and low SMI (low muscle mass for women, \leq 5.7 kg/m²), then they were defined as having sarcopenia.²⁰

Statistical Analysis

Prior to the analysis, we classified participants into the following 3 groups according to their frailty score: nonfrailty, prefrailty, and frailty. Differences in the demographic variables, MMSE, SPMT, and

 Table 1

 Demographic Differences According to Frailty Scores

	Total $(n = 273)$	Frailty Level			P for Trend	Post-hoc
		Nonfrailty (n = 89)	Prefrailty (n = 155)	Frailty (n = 57)		
Age (y)	73.0 ± 5.4	73.1 ± 4.6	72.3 ± 5.6	76.6 ± 5.1	<.001 [†]	a, b
BMI (kg/m ²)	22.5 ± 3.2	22.2 ± 3.0	22.7 ± 3.3	21.9 ± 3.8	.291	_
Medications	2.32 ± 2.24	2.18 ± 2.35	2.23 ± 2.10	3.27 ± 2.55	.072	
Walking speed (m/s)	1.40 ± 0.20	1.43 ± 0.18	1.41 ± 0.20	1.21 ± 0.20	<.001 [†]	a, b
Grip strength (kg)	22.4 ± 4.0	23.4 ± 3.4	22.6 ± 3.8	18.3 ± 4.1	<.001	a, b
Cognitive decline (n)	18 (6.56%)	4 (4.49%)	9 (5.81%)	5 (8.77%)	.047*	
Memory decline (n)	20 (7.33%)	6 (6.74%)	4 (2.58%)	10 (17.5%)	<.001 [†]	
Sarcopenia (n)	22 (8.06%)	2 (2.25%)	9 (5.81%)	11 (19.3%)	<.001	

AWGS, Asian Working Group for Sarcopenia; BMI, body mass index.

Nonfrailty was defined as frailty score of 0, prefrailty was score 1 or 2, frailty was score 3 or greater.

Cognitive decline was defined as the cut-off of MMSE score (23/24).

Memory decline was defined as the cut-off of SPMT score (9/10).

Sarcopenia was defined by using the AWGS-recommended diagnostic algorithm.

a, significant difference between frailty and nonfrailty (P < .01).

b, significant difference between score frailty and prefrailty (P < .01).

SMI among the 3 groups were examined by using the analysis of variance. When a significant effect was found, differences were determined with the Tukey-Kramer post-hoc test. Differences in the prevalence of cognitive decline, memory decline, and sarcopenia among the 3 groups were evaluated by using the χ^2 test. In addition, multivariate logistic regression analyses, adjusted for age, body mass index, and medications, were performed to determine whether physical frailty was associated with cognitive decline, memory decline, or sarcopenia. For this analysis, cognitive decline, memory decline, and sarcopenia were dependent variables, whereas the 3 frailty groups (dummy coded with non-frailty group as the reference group) were independent variables. Subsequent multivariate logistic regression analyses were performed to determine the independent association between each level of frailty and the risk of cognitive decline or sarcopenia. In these subsequent analyses (adjusted for age

5.20

Non-frailty

Pre-frailty Frailty level and medications), the frailty groups were the dependent variables, and cognitive decline and sarcopenia were independent variables. Odds ratios (ORs) with 95% confidence intervals (CI) were presented. Statistical analyses were carried out by using SPSS Statistics for Windows, version 20.0 (SPSS Inc, Chicago, IL), with a significance threshold of 0.05.

Results

Demographic data for participants stratified by frailty group are shown in Table 1. There were 89 participants (32.6%) in the nonfrailty group, 155 participants (56.8%) in the prefrailty group, and 29 participants (10.6%) in the frailty group. Analysis of variance showed that there were significant differences in age, walking speed, and grip strength among the 3 groups (Table 1). In the χ^2 test, there were

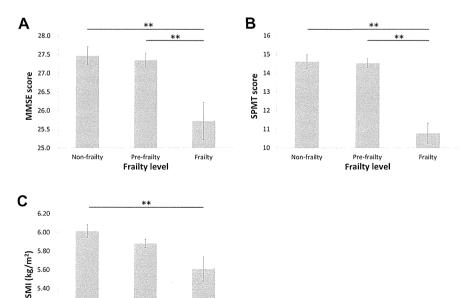


Fig. 1. Comparison of the MMSE, SPMT, and SMI between the groups according to the level of frailty. (A) There were significant differences in the MMSE scores between the 3 groups (F = 6.78, P = .001). (B) There were significant differences in the SPMT scores between the 3 groups (F = 18.5, P < .001). (C) There were significant differences in the SMI between the 3 groups (F = 5.17, P = .006). *P < .05, **P < .05.

^{*}P < .05.

 $^{^{\}dagger}P < .01.$

Table 2Relationship Between the Level of Frailty and Cognitive Decline, Memory Decline, and Sarcopenia

Frailty Level	Cognitive Decline		Memory Decline		Sarcopenia	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Nonfrailty	1 [Reference]	-	1 [Reference]	-	1 [Reference]	-
Prefrailty	1.79 (0.47-6.84)	.394	0.37 (0.10-1.36)	.134	2.77 (1.05-9.26)	.044*
Frailty	5.76 (1.20-27.6)	.029*	5.53 (1.64-18.7)	.006⁵	19.1 (3.73-98.0)	<.001

The analyses for cognitive decline and memory decline were adjusted for age, BMI, and medications.

significant differences in the prevalence of cognitive decline, memory decline, and sarcopenia (Table 1). In addition, the frailty group had significantly lower MMSE (F = 6.78, P = .001, Figure 1, a) and SPMT (F = 18.5, P < .001, Figure 1, b) than the nonfrailty and prefrailty groups, and lower SMI (F = 5.17, P = .006, Figure 1, c) than the nonfrailty group.

Eighteen participants (6.6%) had cognitive decline, 20 participants (7.3%) had memory decline, and 23 participants (8.4%) had sarcopenia. In the multivariate logistic regression analysis after adjustment for age, body mass index, and medications, by using nonfrailty group as the reference, the prefrailty group was significantly more likely to have sarcopenia (OR: 2.77, 95% CI: 1.05-9.26, P=.044) but not cognitive decline or memory decline (Table 2). The frailty group was significantly more likely to have cognitive decline (OR: 5.76, 95% CI: 1.20-27.6, P=.029), memory decline (OR: 5.53, 95% CI: 1.64-18.7, P=.006), and sarcopenia (OR: 19.1, 95% CI: 3.73-98.0, P<.001) (Table 2).

In the logistic regression analysis in which the frailty groups were the dependent variables and cognitive decline and sarcopenia were independent variables, cognitive decline was independently only associated with a frailty score of ≥ 3 (OR: 3.73, 95% CI: 1.23–11.4, P=.020), whereas sarcopenia was independently associated with both prefrailty (score ≥ 1 ; OR: 5.33, 95% CI: 1.22–23.3, P=.026) and frailty (score ≥ 3 ; OR: 13.1, 95% CI: 4.98–34.2, P<.001). These associations remained significant after adjustment for age and medications (Table 3).

Discussion

The results of this study showed that frailty (defined as frailty score \geq 3) was associated with cognitive decline, memory decline, and sarcopenia, and that prefrailty (frailty score =1 or 2) was associated with only sarcopenia. It is a new and interesting finding that there were differences in the association between physical frailty and cognitive decline, memory decline, and sarcopenia according to level of frailty.

In this study, we showed that frailty, but not prefrailty, was associated with cognitive decline and memory decline. Our results also showed that frailty and prefrailty were associated with sarcopenia, in contrast to cognitive and memory decline. In Japanese, multicenter, population-based studies, the prevalence of dementia was not high among those aged 65–74 years (less than 10%), but was higher among those aged 75 years and older.²⁴ The prevalence of sarcopenia exhibited the same tendency, with the prevalence rising among those aged 75 years and older.^{25,26} Thus, older adults (particularly those 75 and older) are prone to both cognitive impairment and sarcopenia. However, low physical performance, low physical strength, and the decrease of muscle mass, which overlap with both sarcopenia and frailty, can be found from middle age.^{27–29} Thus, as shown in the results of this study, it is possible that sarcopenia is associated with frailty at an earlier stage than is cognitive impairment, and that sarcopenia is affected more by frailty than is cognitive impairment.

A recent study investigated the association of physical frailty and pre-frailty with dementia and cognitive impairment.³⁰ In that study, physically frail older adults were over 4 times more likely to have AD, and 8 times more likely to have cognitive impairment than robust older adults were. Prefrail older adults showed an increased risk for dementia in the aforementioned study, but some estimates were not statistically significant in the fully adjusted models.³⁰ The results of that study were consistent with our study. Previous studies indicated that frailty is associated with AD pathology¹³ and biological mechanisms, ¹⁴ such as diffuse neuritic plaques, oxidative stress, and inflammation. It is also possible that frailty and AD share common lifestyle risk factors, such as physical inactivity and smoking, that lead to their pathophysiology, which contributes simultaneously to physical frailty and AD. 13 On the other hand, it has been indicated that comorbidities caused by cognitive impairment were also associated with frailty in patients with AD or mild cognitive impairment.³¹ Thus, it is likely that these associations interact with one another, leaving the causal association between physical frailty and cognitive decline unclear. Further studies are required to understand these associations.

Definitions of frailty and sarcopenia overlap, and sarcopenia is considered one of the core symptoms of physical frailty. ^{5,6} The causal mechanisms underlying sarcopenia can be oxidative stress, dysregulation of inflammatory cytokines and hormones, malnutrition,

Table 3Independent Relationship Between Each Level of Frailty and Cognitive Decline or Sarcopenia

Domains	Univariate Analys	sis					Multivariate Anal	ysis				
	Frailty Score						Frailty Score			~		
	<u>≤1</u>		≤2		≤3		≤1		≤2		≤3	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Cognitive decline	1.76 (0.56-5.51)	.331	1.43 (0.54-3.84)	.473	3.73 (1.23-11.4)	.020*	2.48 (0.68-9.07)	.168	1.63 (0.56-4.72)	.371	4.61 (1.27–16.8)	.020*
Sarcopenia	5.33 (1.22-23.3)	.026*	9.07 (3.22-25.5)	<.001	13.1 (4.98-34.2)	<.001	5.47 (1.21-24.6)	.027*	8.75 (3.00-25.5)	<.001	10.0 (3.40-29.6)	<.001

The multivariate analyses were adjusted for age and medications.

The analysis for sarcopenia was adjusted for age and medications.

 $^{^*}P < .05.$ $^\dagger P < .01.$

^{*}P < .05.

 $^{^{\}dagger}P < .01.$

physical inactivity, and muscle apoptosis, all of which have been hypothesized to contribute to frailty through interactive pathways. 32,33 Recently, the definition of sarcopenia has been the coexistence of low muscle mass and low physical performance, 5,20,34 which are contained in frailty domains. Thus, the association of sarcopenia with even prefrailty seems reasonable. Overlapping intervention strategies (eg, nutritional supplementation and exercise) may be required to prevent both frailty and sarcopenia.

During recent years, the definition of frailty has been changing. Frailty has been considered to include other aspects, for instance social aspects and comorbidities. ¹⁵ In addition to these aspects, poor cognition needs to be included in the definition of frailty, as shown in previous studies ^{4,8} and by this study. Furthermore, this study indicated that poor cognition was associated with frailty and that sarcopenia was associated even with prefrailty. The results indicate that we need to understand the consecutive mechanism as well as the association of prefrailty and frailty with cognitive decline, sarcopenia, and other adverse health outcomes. Interventions may need to be tailored to the level of frailty to effectively prevent various functional declines. Future studies should investigate these intervention strategies.

There were several limitations to this study. First, the cross-sectional design prevented us from establishing causal associations between frailty and cognitive decline or sarcopenia. Second, the findings in this study should be considered preliminary owing to the relatively small sample size, which may introduce some error of inference, reduce the power of analysis, and limit generalization. Third, the design of this study was not a population sampling, and participants in this study were independent in activities of daily living. This may lead to an underestimation of the prevalence of frailty, cognitive decline, and sarcopenia, as the participants were relatively healthy elderly persons.

In conclusion, our results indicate that there were differences in the association between physical frailty and cognitive decline, memory decline, and sarcopenia according to the level of frailty. Cognitive decline and memory decline were associated with frailty. Sarcopenia was associated with prefrailty and frailty. Further studies are required to understand these associations including biological mechanisms.

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Research paper

Ethnic and geographic variations in muscle mass, muscle strength and physical performance measures



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ABSTRACT

Purpose: While a universal definition of sarcopenia is desirable, ethnic diversity affects anthropometric measures, which in turn may affect the parameters used for the definition of sarcopenia. Other than Caucasian Asian differences, there may be diversity within different Asian populations. It is important to examine differences, if any, in the field of sarcopenia research. We compared available data (mean body mass index, muscle mass, grip strength, walking speed and chair stand times) for community living older people from different Asian locations and ethnicity to explore the extent of variation, and compared similar data from a Caucasian population.

Subjects and methods: Recent community studies which contain anthropometric and physical performance variables for men and women in the three age groups (65–74, 75–84, 85+) were identified from participants of the Asian Working Group on Sarcopenia and from other known longitudinal studies in the region. Caucasian values from the UK Hertfordshire Cohort Study were also used for comparison. Results: There was considerable variation in mean values in body mass index, appendicular skeletal mass index (ASM/ht²), grip strength, walking speed between different Asian ethnic groups, and also between same ethnic groups living in different geographic locations. Differences in mean values were greater between the Asian groups compared with Caucasians. Comparison of ASM/ht² between Asian groups was limited by the use of different instruments.

Conclusion: A universal definition of sarcopenia that depends on absolute measurements may not be applicable to all ethnic groups and different geographic locations.

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1. Introduction

In the past two decades, sarcopenia has come to be recognized as an important geriatric syndrome, becoming a major focus of research covering from basic science to clinical management perspectives [1]. A universally accepted definition is thus of great importance, to facilitate the conduct of clinical trials of a preventive or interventional nature. In particular, clinical trials involving pharmaceutical agents would need to fulfil regulatory requirements [2]. There is current consensus worldwide that the working definition has evolved from the original one covering muscle mass only [3] to including measures of muscle strength as

well as physical performance measures [4,5]. Three consensus groups have met and essentially arrived at the same conclusions, although there are minor variations. These are the International Working Group on Sarcopenia (IWGS) which has a predominantly North American input [6], the European Working Group on Sarcopenia in Older People (EWSOP) [7], and the Asian Working Group for Sarcopenia (AWGS) [8]. While there is broad consensus on the choice of measurement of each of these parameters (appendicular muscle mass divided by height², grip strength and walking speed), the classification of what values are normal so that cut-off values may be determined is unclear, there being variations between studies [6]. Among Caucasians, consensus cut-off values appear to have been accepted. Proposed cut-off values are not necessarily based on population studies, which have been limited. However, since all these measures are likely dependent on body

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size and shape, and to a certain extent lifestyle habits [9–11], it is not surprising that studies among Asian populations yield different values. The AWGS agreed on a consensus regarding the cut-off values appropriate for Asians, based on available published studies [8].

However there is ethnic diversity even within Asia with respect to anthropometry and lifestyle, factors which may affect the parameters used for the definition of sarcopenia. Existing data are sparse; yet a comparison of available age group and sex specific mean values used for sarcopenia definition between different Asian populations may begin to address this question. In this study we compared available data (mean body mass index, muscle mass, grip strength, walking speed and chair stand times) for community living elderly people aged 65–74, 75–84, and 85+ for Chinese in Beijing, Hong Kong, Singapore, Japanese, and Malays and Indians in Singapore, to explore the extent of variation. Similar data from a Caucasian population [12] are listed for comparison.

2. Subjects and methods

Recent community studies which contain anthropometric and physical performance variables for men and women in the three age groups (65-74, 75-84, 85+) were identified from participants of the Asian Working Group on Sarcopenia, consisting of researchers from Taipei, Beijing, Hong Kong, Japan, Malaysia, Thailand, Korea; and from other known longitudinal studies in the region (Singapore Longitudinal Aging Study [SLA]). The SLA consists of predominantly Chinese, but also smaller numbers of Malays and Indians [13]. Participants from each country and the Principal Investigator of the SLA were contacted to see if they can provide data for comparison. Data from Japan, China (mainland), China (Hong Kong), and Singapore (Chinese, Malays and Indians) were available, although not all parameters were available from all cohorts. Caucasian values from the UK Hertfordshire Sarcopenia Study (HSS), a sub-study of the Hertfordshire Cohort Study (HCS) were also used to compare Asian Caucasian differences [12].

The Hong Kong cohort was the Mr. and Ms Os dataset collected between 2001–2003 as part of a bone health survey, and consisted of two thousand community-dwelling Chinese men and women aged 65 and older recruited by placing recruitment notices in community centers for older adults and housing estates. Participants were volunteers, and excluded those who were unable to walk independently, had had bilateral hip replacement, and not competent to give informed consent [14].

Appendicular muscle mass was measured by DEXA using a Hologic Delphi W4500 densitometer (Hologic Delphi, auto whole body version 12.4, Hologic Inc, Bedford, Massachusetts, USA). ASM was calculated as the sum of appendicular lean mass minus bone mineral content of arms and legs. ASM index (ASMI) was calculated as ASM divided by height in meters squared (ASM/ht2). Grip strength was measured using a dynamometer (JAMAR Hand Dynamometer 5030JO, Sammons Preston Inc, Bolingbrook, IL, USA). Two readings were taken from each side, and the average value between right and left was used for analysis. Gait speed was measured using the average time in seconds to complete a walk along a straight-line 6 meters long. A warm up period of < 5 minutes was followed by two walks, and the average time recorded. Chair stand was measured by asking the participant to rise from a chair (seat height 54 cm) with arms folded across the chest, five times as quickly as possible. The time taken was recorded on a stopwatch.

The Japanese cohort consisted of community-dwelling older people living in both rural and urban areas [15]. Exclusion criteria

were classification as frail according to the long term care insurance certification in Japan: artificial implants such as cardiac pacemakers or joints which precluded the use of bioimpedance for measurement of muscle mass; severe cognitive impairments; severe cardiac, pulmonary or musculoskeletal disorders; comorbidities associated with greater risk of falls such as Parkinson's disease or stroke. Appendicular muscle mass was measured using bioimpedance [Inbody 720, Biospace Co. Ltd, Seoul, South Korea]. Participants stood on two metallic electrodes and held metallic grip electrodes. Grip strength was measured using a hand held dynamometer with the arm by the side of the body. Participants were instructed to squeeze as hard as they can use the dominant hand. The better of two performances was used. Walking speed was measured as the best time taken to walk 15 metres at a comfortable pace. The time required to reach the 10 m point (marked in the course) was recorded using a stopwatch. For the chair stand, participants were asked to stand up and sit down five times as quickly as possible, and the time taken from the initial sitting position to the final standing position at the end of the fifth stand was recorded. The better performance of two trials was taken.

The China (mainland) cohorts consist of volunteers ≥ 65 years, being part of a nation-wide survey of the health status of older people carried out from 2010–2013 in different regions of China. Some parameters were only available from the Beijing urban and rural cohorts, which consisted of retired teachers, workers and farmers [unpublished data]. Appendicular muscle mass was not available from this cohort. Grip strength was measured using a hand dynamometer (WCS-II, Beijing), with the highest of two readings for each hand being chosen; walking speed was measured over 6 m.

The Singapore data were from the Singapore Longitudinal Ageing Study [13], which consists of whole population samples from several contiguous small areas in the South East and South West Region of Singapore, covering Singapore citizens and permanent residents who were aged 55 years and above, not physically or mentally incapacitated, able to provide informed consent, participate in face-to-face interviews and carry out physical performance tests. The response rate was 75%. Muscle strength was assessed as knee extension strength. This was measured isometrically in the dominant leg, with the angles of the hip and knee at 90 degrees with the participant seated, using Lord's strap and strain gauge assembly component of the Physiological Profile Assessment (PPA). The best of three trials was recorded in kg [16]. The 6-meter fast gait speed test used the average of two measurements of the participants walking across a distance of 6 m as fast as possible [17]. Single timed chair rise was measured as the time in seconds taken for the participant to complete 5 stands from a seated position on a hard back chair with arms folded [18].

For the Hertfordshire cohort, only data for men were available. Body composition was assessed by anthropometry in all participants and validated using DEXA (Hologic Discovery, software version 12.5) in a sub-set; the walking speed measured as the customary paced walk over 3-m; chair rise time as the time to move from a seated position to fully standing five times unaided, and grip strength measured using a Jamar dynamometer with the maximum value attained from three attempts in both the right and left hands derived as the best grip strength (Promedics, Blackburn, UK) [19].

For each parameter, the mean (SD) values and the lowest 20th percentile values with the exception of chair stand time were listed according to the three age groups for men and women separately. Linear trend ANOVA test was used to examine changes with age within each cohort, and Student's unpaired *t*-test to examine between cohort differences by age and gender, using HK Chinese as a reference group.

 Table 1a

 Descriptive statistics and comparison by populations on body mass index (BMI).

Ethnic groups	Male							Fema	le					
	n	65-74	n	75-84	n	≥85	<i>P</i> -value ^c	n	65-74	n	75-84	n	≥85	<i>P</i> -value ^c
Mean (±SD), lowest 20th percentile Chinese (Hong Kong) ^d	1295	23.62 (±3.06), 21.25	543	23.08 (± 3.23), 20.2	42	21.98 (± 3.02), 18.91	< 0.001	1292	24.19 (± 3.42), 21.37	583	23.53 (±3.44), 20.68	57	22.5 (± 3.71), 18.71	< 0.001
Chinese (Beijing) ^d	1759	24.1° (±3.1), 21.5	1581	24^{f} (\pm 3.2), 21.2	347	$23.7^{\rm g}$ (± 3.2), 21	0.002	1950	24.3 (±3.5), 21.5	1193	23.8 (±3.6), 20.8	177	23.1 (±3.6), 20	< 0.001
Chinese (Singapore) ^d	353	23.6 (\pm 3.55), 20.6	148	23 (± 3.68), 19.8	165	22.9 (±3.76), 19.5	0.043	541	24.2 (±3.99), 20.9	178	23.8 (\pm 4), 20.4	204	23.6 (±3.98), 20.3	0.062
Japanese ^d	266	23.2^{e} (± 3.2), 20.7	254	23.1 (±2.5), 21	48	21.9 (± 3.6), 19.3	< 0.001	650	23^{h} (± 3.4), 20.3	594	22.7 ⁱ (±3.11), 20.3	70	22 (\pm 2.3), 20.5	< 0.001
Malays and Indians (Singapore) ^d	41	$25^{\rm e}$ (\pm 3.57), 21.3	27	23.2 (±2.38), 21	29	23.2 (\pm 2.4), 20.5	0.016	67	28 ^h (±4.25), 24.9	14	24.9 (±5.17), 18.7	15	25^{j} (± 4.99), 18.9	0.009
UK – HSS ^{a,d}	81	27.1° (±3.8), 24.0	24	27.6^{f} (\pm 2.6), 26.1	b			b		b		b		

- ^a Hertfordshire Sarcopenia Study (HSS) cohort is only comprised of male participants, and is classified into 2 age groups: 68.3 years –74.9 years and 75.0 years –77.4 years, respectively.
- ^b Figures not available.
- c ANOVA test for linear trend was used to examine any significant difference by age group.
- d Independent 2-sample t-test (2-tailed) was used to examine age-specific difference in mean values, with Chinese (Hong Kong) as reference. Only significant difference (P-value < 0.05) is reported.
- e Significantly different from Chinese (Hong Kong) Chinese (Beijing) (mean difference 0.48, P < 0.001), Japanese (mean difference –0.42, P = 0.042), Malays and Indians (Singapore) (mean difference 1.38, P = 0.005), and UK Caucasian (mean difference 3.68, P < 0.001).
- f Significantly different from Chinese (Hong Kong) Chinese (Beijing) (mean difference 0.92, P < 0.001), and UK Caucasian (mean difference 4.12, P < 0.001).
- g Significantly different from Chinese (Hong Kong) Chinese (Beijing) (mean difference 1.72, P=0.001).
- h Significantly different from Chinese (Hong Kong) Japanese (mean difference –1.19, P < 0.001), and Malays and Indians (Singapore) (mean difference 3.81, P < 0.001).
- ⁱ Significantly different from Chinese (Hong Kong) Japanese (mean difference -0.83, P < 0.001).
- Significantly different from Chinese (Hong Kong) Malays and Indians (Singapore) (mean difference 2.5, P=0.035).

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Table 1bDescriptive statistics and comparison by populations on appendicular skeletal mass index (ASM)/height² (kg/m²).

Ethnic groups	Male							Female	2					
	n	65-74	n	75-84	n	≥85	P-value ^c	n	65-74	n	75-84	n	≥85	P-value ^c
Mean (±SD), lowest 20th percentile Chinese (Hong Kong)	1295	7.3 (± 0.8), 6.66	543	7.01 (± 0.82), 6.31	42	6.64 (± 0.79), 5.93	< 0.001	1292	6.13 (± 0.74), 5.51	583	5.94 (±0.68), 5.35	57	5.89 (±0.77), 5.3	< 0.001
Chinese (Beijing) ^d	b		b		b			b		b		ь		
Chinese (Singapore) ^d	b		b		b			b		b		b		
Japanese ^d	266	$6.99^{e} (\pm 1.1), 6.22$	254	6.73 ^f (± 1.08), 5.57	48	6.28 (± 1.71), 4.93	< 0.001	650	$5.57^{g} \ (\pm 1.03), 4.6$	594	$5.17^{\rm h}$ (\pm 1.01), 4.12	70	$4.64^{i}\ (\pm0.86)$, 3.77	< 0.001
Malays and Indians (Singapore) ^d	b		b		b			b		b		b		
UK – HSS ^{a,d}	81	7.99° (±0.91), 7.30	24	$7.89^{f} (\pm 0.74), 7.18$	ь			b		ь		b		

- ^a Hertfordshire Sarcopenia Study (HSS) cohort is only comprised of male participants, and is classified into 2 age groups: 68.3 years-74.9 years and 75.0 years-77.4 years, respectively.
- b Figures not available.
- ^c ANOVA test for linear trend was used to examine any significant difference by age group.
- d Independent 2-sample t-test (2-tailed) was used to examine age-specific difference in mean values, with Chinese (Hong Kong) as reference. Only significant difference (P-value < 0.05) is reported.
- ^e Significantly different from Chinese (Hong Kong) Japanese (mean difference –0.31, P < 0.001), and UK Caucasian (mean difference 0.7, P < 0.001).
- Significantly different from Chinese (Hong Kong) Japanese (mean difference –0.28, P < 0.001), and UK Caucasian (mean difference 0.89, P < 0.001).
- g Significantly different from Chinese (Hong Kong) Japanese (mean difference -0.56, P < 0.001).
- ^h Significantly different from Chinese (Hong Kong) Japanese (mean difference -0.77, P < 0.001).
- ⁱ Significantly different from Chinese (Hong Kong) Japanese (mean difference -1.25, P < 0.001).

Table 1cDescriptive statistics and comparison by populations on appendicular skeletal mass index (ASM)/weight.

Ethnic groups	Male							Female						
	n	65-74	n	75-84	n	≥ 85	P-value ^c	n	65-74	n	75-84	n	≥ 85	P-value ^c
Mean (±SD), lowest 20th percentile Chinese (Hong Kong) ^d	1295	0.31 (±0.02), 0.29	543	0.31 (±0.03), 0.28	42	0.3 (± 0.03), 0.28	< 0.001	1292	0.25 (± 0.02), 0.24	583	0.26 (± 0.03), 0.23	57	0.27 (±0.03), 0.24	< 0.001
Chinese (Beijing) ^d	b		ь		b			b		b		b		
Chinese (Singapore) ^d	b		b		b			b		b		ь		
Japanese ^d	266	$0.3^{\rm e}~(\pm0.04)$, 0.27	254	$0.29^{\rm f}~(\pm0.05)$, 0.24	48	$0.28^{\rm g}~(\pm0.05), \ 0.23$	< 0.001	650	$0.24^{\rm h}~(\pm0.04)$, 0.19	594	$0.22^{i} \ (\pm 0.04), \ 0.18$	70	$0.21^{j} \ (\pm 0.04), \ 0.17$	< 0.001
Malays and Indians (Singapore) ^d	b		ь		b			b		b		b		
UK – HSS ^{a,d}	81	$0.30^{\rm e}~(\pm0.03)$, 0.28	24	$0.29^{\rm f}~(\pm0.02)$, 0.26	ь			b		ь		b		

^a Hertfordshire Sarcopenia Study (HSS) cohort is only comprised of male participants, and is classified into 2 age groups: 68.3 years-74.9 years and 75.0 years-77.4 years, respectively.

b Figures not available.

c ANOVA test for linear trend was used to examine any significant difference by age group.

Independent 2-sample t-test (2-tailed) was used to examine age-specific difference in mean values, with Chinese (Hong Kong) as reference. Only significant difference (P-value < 0.05) is reported.

e Significantly different from Chinese (Hong Kong) – Japanese (mean difference –0.01, P < 0.001), and UK Caucasian (mean difference –0.02, P < 0.001).

Significantly different from Chinese (Hong Kong) – Japanese (mean difference –0.02, P < 0.001), and UK Caucasian (mean difference –0.02, P < 0.001).

^g Significantly different from Chinese (Hong Kong) – Japanese (mean difference -0.05, P < 0.001).

h Significantly different from Chinese (Hong Kong) – Japanese (mean difference -0.01, P < 0.001).

i Significantly different from Chinese (Hong Kong) – Japanese (mean difference -0.04, P < 0.001).

^j Significantly different from Chinese (Hong Kong) – Japanese (mean difference -0.06, P < 0.001).

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Table 1dDescriptive statistics and comparison by populations on average grip strength (kg).

Ethnic groups	Male							Femal	e					
	n	65-74	n	75-84	n	≥85	P-value ^e	n	65-74	n	75-84	n	≥85	P-value ^e
Mean (±SD), lowest 20th percentile Chinese (Hong Kong) ^f	1295	32.7 (± 6.05), 27.5	543	28.64 (±6.21), 24	42	25.06 (±6.74), 19.3	< 0.001	1292	21.09 (±4.18), 17.5	583	18.77 (±3.78), 15.5	57	17.86 (±3.73), 14.5	< 0.001
Chinese (Beijing) ^f	85	$34 \ (\pm 8.6)$, 27.2	77	$30.6^{h}~(\pm7.5)$, 23	10	27.4 (\pm 5.6), 20	< 0.001	197	22.1^{j} (± 5.3), 17.5	96	20.9^{k} (\pm 6.1), 15.5	3	16.2 (\pm 3.3), $^{\rm c}$	< 0.001
Chinese (Singapore) ^{a,f}	353	20.6^{g} (± 6.75), 14	148	17.8 ^h (±6.53), 12.6	165	$17.8^{i} (\pm 6.47), 12.7$	< 0.001	541	14.2^{j} (± 4.31), 10.7	178	$12^k \ (\pm 3.74), \ 9$	204	$12^{1} (\pm 3.66), 9$	< 0.001
Japanese ^f	266	$35^{\rm g}$ (± 6.1), 31	254	$29.6^{\rm h}~(\pm6.4)$, 25	48	22.9 (\pm 5.7), 18	< 0.001	650	23.1^{j} (± 5.1), 19	594	19.8^{k} (± 4.4), 16	70	17.3 (±4.2), 15	< 0.001
Malays and Indians (Singapore) ^{a,f}	41	18g (±5.73), 13.5	27	$15.6^{\rm h}$ (± 7.04), 10.1	29	15.7^{i} (± 6.82), 10.3	0.155	67	13.4^{j} (± 5.05), 9.1	14	10.6^k (± 3.7), 8	15	$10.7^{i} \ (\pm 3.58), \ 8$	0.023
UK – HSS ^{b,f}	81	40.4g (±8.2), 34.0	24	33.0 ^h (±6.5), 28.0	d			d		d		d		

- ^a Lower limb strength was used in Singapore data, measured by average knee extension (kg).
- b Hertfordshire Sarcopenia Study (HSS) cohort is only comprised of male participants, and is classified into 2 age groups: 68.3 years-74.9 years and 75.0 years-77.4 years, respectively.
- ^c Corresponding statistics not available.
- d Figures not available.
- e ANOVA test for linear trend was used to examine any significant difference by age group.
- Independent 2-sample t-test (2-tailed) was used to examine age-specific difference in mean values, with Chinese (Hong Kong) as reference. Only significant difference (P-value < 0.05) is reported.
- g Significantly different from Chinese (Hong Kong) Chinese (Singapore) (mean difference −12.1, P < 0.001), Japanese (mean difference 2.3, P < 0.001), Malays and Indians (Singapore) (mean difference −14.7, P < 0.001), and UK Caucasian (mean difference 7.9, P < 0.001).
- h Significantly different from Chinese (Hong Kong) Chinese (Beijing) (mean difference 1.96, P = 0.011), Chinese (Singapore) (mean difference -10.84, P < 0.001), Japanese (mean difference 0.96, P = 0.044), Malays and Indians (Singapore) (mean difference -13.04, P < 0.001), and UK Caucasian (mean difference 5.56, P < 0.001).
- i Significantly different from Chinese (Hong Kong) Chinese (Singapore) (mean difference -7.26, P < 0.001), and Malays and Indians (Singapore) (mean difference -9.36, P < 0.001).
- j Significantly different from Chinese (Hong Kong) Chinese (Beijing) (mean difference 1.01, P=0.002), Chinese (Singapore) (mean difference –6.89, P < 0.001), Japanese (mean difference 2.01, P < 0.001), and Malays and Indians (Singapore) (mean difference –7.69, P < 0.001).
- k Significantly different from Chinese (Hong Kong) Chinese (Beijing) (mean difference 2.13, P < 0.001), Chinese (Singapore) (mean difference –6.77, P < 0.001), Japanese (mean difference 1.03, P < 0.001), and Malays and Indians (Singapore) (mean difference –8.17, P < 0.001).
- Significantly different from Chinese (Hong Kong) Chinese (Singapore) (mean difference -5.86, P < 0.001), and Malays and Indians (Singapore) (mean difference -7.16, P = 0.035).

Table 1eDescriptive statistics and comparison by populations on walking speed using best time (m/s).

Ethnic groups	Male							Female						
	n	65-74	n	75–84	n	≥85	P-value ^c	n	65-74	n	75–84	n	≥ 85	P-value ^c
Mean (±SD), lowest 20th percentile Chinese (Hong Kong)	1295	1.12 (± 0.22), 0.94	543	1 (±0.22), 0.81	42	0.87 (±0.17), 0.73	< 0.001	1292	1 (±0.2), 0.84	583	0.88 (± 0.22), 0.71	57	0.81 (± 0.22), 0.58	< 0.001
Chinese (Beijing) ^d	862	$1.092^{e}\ (\pm0.334)$, 0.853	533	$1.007~(\pm0.335)$, 0.711	45	$0.781~(\pm0.288), \ 0.534$	< 0.001	1026	$0.997~(\pm0.307)$, 0.736	498	$0.936^{i} \ (\pm 0.335), \ 0.647$	43	$0.753~(\pm 0.254), \ 0.516$	< 0.001
Chinese (Singapore) ^d	353	$1.4^{\rm e}~(\pm0.37)$, 1.11	148	$1.3^{\circ} (\pm 0.37),$ 0.97	165	$1.2^{ m g}~(\pm0.38), \ 0.94$	< 0.001	541	$1.3^{\rm h}~(\pm0.32)$,	178	$1.1^{i} (\pm 0.32)$, 0.78	204	1^{j} (± 0.33), 0.74	< 0.001
Japanese ^d	266	$1.38^{\circ} \ (\pm 0.24),$ 1.22	254	$1.23^{\rm f}$ (± 0.25),	48	$1.06^{\rm g}~(\pm0.26)$, 0.83	< 0.001	650	$1.37^{h} (\pm 0.25),$ 1.22	594	$1.21^{i} (\pm 0.25),$	70	1.03^{j} (± 0.25), 0.8	< 0.001
Malays and Indians (Singapore) ^d	41	$1.4^{\rm e}~(\pm0.36), \ 0.99$	27	$1.1^{\rm f}$ (± 0.39), 0.71	29	$1.1^{\mathrm{g}} \ (\pm 0.39)$, 0.7	0.002	67	$1.1^{\rm h}~(\pm0.27), \ 0.82$	14	0.9 (± 0.36), 0.62	15	0.9 (± 0.35), 0.64	0.008
UK – HSS ^{a,d}	81	1.11 (±0.19), 0.95	24	$1.09^{\rm f}$ (\pm 0.22), 0.86	b			b		b		b		

^a Hertfordshire Sarcopenia Study (HSS) cohort is only comprised of male participants, and is classified into 2 age groups: 68.3 years -74.9 years and 75.0 years -77.4 years, respectively. Two values were missing.

b Figures not available.

^c ANOVA test for linear trend was used to examine any significant difference by age group.

d Independent 2-sample t-test (2-tailed) was used to examine age-specific difference in mean values, with Chinese (Hong Kong) as reference. Only significant difference (P-value < 0.05) is reported.

e Significantly different from Chinese (Hong Kong) – Chinese (Beijing) (mean difference 0.028, P = 0.019), Chinese (Singapore) (mean difference 0.28, P < 0.001), Japanese (mean difference 0.26, P < 0.001), and Malays and Indians (Singapore) (mean difference 0.28, P < 0.001).

f Significantly different from Chinese (Hong Kong) – Chinese (Singapore) (mean difference 0.3, P < 0.001), Japanese (mean difference 0.23, P < 0.001), Malays and Indians (Singapore) (mean difference 0.1, P = 0.028), and UK Caucasian (mean difference 0.1, P = 0.014).

g Significantly different from Chinese (Hong Kong) - Chinese (Singapore) (mean difference 0.33, P < 0.001), Japanese (mean difference 0.19, P < 0.001), and Malays and Indians (Singapore) (mean difference 0.23, P < 0.001).

h Significantly different from Chinese (Hong Kong) – Chinese (Singapore) (mean difference 0.3, P < 0.001), and Japanese (mean difference 0.37, P < 0.001), and Malays and Indians (Singapore) (mean difference 0.1, P < 0.001).

Significantly different from Chinese (Hong Kong) - Chinese (Beijing) (mean difference 0.056, P=0.001), Chinese (Singapore) (mean difference 0.22, P<0.001), and Japanese (mean difference 0.33, P<0.001).

^j Significantly different from Chinese (Hong Kong) – Chinese (Singapore) (mean difference 0.19, P < 0.001), and Japanese (mean difference 0.22, P < 0.001).

Table 1fDescriptive statistics and comparison by populations on time to complete 5 stands (second).

Ethnic groups	Male							Female	2					
	n	65-74	n	75-84	n	≥85	P-value ^d	n	65-74	n	75-84	n	≥85	P-value ^d
Mean (±SD) Chinese (Hong Kong)	1293	12.18 (± 3.66)	536	13.31 (±3.81)	41	15 (±5.7)	< 0.001	1271	12.79 (± 4.3)	574	14.69 (± 6.33)	56	13.63 (±3.61)	0.003
Chinese (Beijing) ^e	55	11.2 (±3.5)	26	$11.1^{\rm g}~(\pm2.8)$	1	17 ^b	< 0.001	95	$10.3^{i} (\pm 3.7)$	40	$14.2~(\pm12.8)$	1	12.7 ^b	0.135
Chinese (Singapore) ^e	353	$10.7^{\rm f}~(\pm3.16)$	148	12.7 (\pm 5.21),	165	$12.9^{\rm h}~(\pm5.35)$	< 0.001	541	$11.4^{i} (\pm 3.65)$	178	$13.1^{j} (\pm 4.79)$	204	$14 \ (\pm 9.03)$	< 0.001
Japanese ^e	216	$8^{f}(\pm 1.9)$	160	$8.5^g\ (\pm2)$	12	$8^{h} (\pm 1.9)$	1	422	$7.9^{i}~(\pm2.5)$	270	$8.5^{j}~(\pm2.6)$	6	$6.87^k\ (\pm1.4)$	< 0.001
Malays and Indians (Singapore) ^{a,e}	41	11.5 (±3.29)	27	$14.6~(\pm 6.39)$	29	14.5 (\pm 6.22)	0.023	67	$14.1^i\ (\pm6.24)$	14	$17~(\pm7.65)$	15	$16.5^k\ (\pm7.62)$	0.154
UK – HSS ^{a,e}	81	$17.1^{f} (\pm 4.3)$	24	$17.6^{g} (\pm 4.0)$	c			c		c		c		

^a Hertfordshire Sarcopenia Study (HSS) cohort is only comprised of male participants, and is classified into 2 age groups: 68.3 years-74.9 years and 75.0 years-77.4 years, respectively. Three values were missing.

^b Corresponding statistics not available.

c Figures not available.

d ANOVA test for linear trend was used to examine any significant difference by age group.

e Independent 2-sample t-test (2-tailed) was used to examine age-specific difference in mean values, with Chinese (Hong Kong) as reference. Only significant difference (P-value < 0.05) is reported.

^f Significantly different from Chinese (Hong Kong) – Chinese (Singapore) (mean difference –1.48, P < 0.001), Japanese (mean difference –4.18, P < 0.001), and UK Caucasian (mean difference 4.92, P < 0.001).

^g Significantly different from Chinese (Hong Kong) – Chinese (Beijing) (mean difference –2.21, P=0.004), Japanese (mean difference –4.81, P<0.001), and UK Caucasian (mean difference 4.09, P<0.001).

h Significantly different from Chinese (Hong Kong) – Chinese (Singapore) (mean difference –2.1, P=0.028), and Japanese (mean difference –7, P<0.001).

i Significantly different from Chinese (Hong Kong) – Chinese (Beijing) (mean difference –2.49, P < 0.001), Chinese (Singapore) (mean difference –1.39, P < 0.001), Japanese (mean difference –4.89, P < 0.001), and Malays and Indians (Singapore) (mean difference 1.31, P = 0.018).

^j Significantly different from Chinese (Hong Kong) – Chinese (Singapore) (mean difference –1.59, P=0.002), and Japanese (mean difference –6.19, P<0.001).

k Significantly different from Chinese (Hong Kong) - Japanese (mean difference -6.76, P < 0.001), and Malays and Indians (Singapore) (mean difference 2.87, P=0.04).

3. Results

The mean body mass index (BMI) for men aged 65–74 and the 20th percentile value for all Asian cohorts were similar. However with increasing age, these values appeared to decline to different degrees among the cohorts, with the Beijing Chinese, Singapore Chinese, Malays and Indians having the least decline, whilst Hong Kong Chinese and Japanese showed a more marked decline in the age 85+ group (Table 1a).

For women, more variations were observed in mean and lowest 20th percentile values for all age groups, with a declining trend with age, the lowest values for the 85+ age group occurring in the Hong Kong Chinese, Malays and Indians. The trend for Singapore Chinese was marginally non-significant. The mean values for UK Caucasian older people were higher than all the Asian values.

Appendicular mass index also showed a declining trend with age in Chinese and Japanese men and women, all values being slightly lower among the Japanese (Table 1b). Mean Caucasian values were higher than all Asian values. However if muscle mass was expressed as a percentage of weight, then Chinese and Japanese values were very similar, and also similar to Caucasian values (Table 1c), although a significant age-related decline was still observed.

For all age and ethnic groups, muscle strength was higher among men compared with women, and showed a decline with age. Excluding the Singapore cohort data, there were variations between Chinese and Japanese, as well as Chinese in different locations (Table 1d). All Asian values were lower than Caucasians. Similarly, walking speed differed between the cohorts, irrespective of ethnicity; Singaporean and Japanese cohorts had faster walking speeds than Chinese in Hong Kong and Beijing (Table 1e). All cohorts showed age-related decline, but the decline in mean values varied between cohorts. Overall walking speed values for Asians and Caucasians were similar. With respect to time for the chair stand, the best performance was observed in the Japanese cohort, while the Hong Kong Chinese and Malays and Indians showed the greatest decline in performance with age (Table 1f). No significant decline with age was observed among Beijing Chinese, Singapore Indian and Malaysian women. Performance for Caucasians was the poorest.

4. Discussion

This descriptive comparison of parameters used for the definition of sarcopenia shows considerable variations within Asian populations that do not fall into any particular pattern according to ethnicity (body size and shape presumably being underlying factors for ethnic difference), or geographic location. Furthermore, while many parameters show age-related decline, some cohorts exhibit greater decline than others, the extent again not following any pattern according to ethnicity or geographic location. These findings would be compatible with within Asian variations being explained by different body size and shape; lifestyle habits (nutrition and pattern of physical activity); cultural traditions such as sleeping and sitting on the floor or low lying furniture among Japanese, etc.; and differing prevalence of frailty with ageing populations. A further complication is that in considering cut-off values for ASM, a value less than 2SD from young adult mean values may be employed, and young adult mean values may also be influenced by lifestyle or early life course factors, such that lower young adult mean values may give rise to lower prevalence of sarcopenia in older adults if muscle mass is considered, as has been pointed out by Lau et al. [10].

The diversity of mean values, approach to diagnosis, and methods used in measurement is highlighted further in a group of

papers on research on sarcopenia in Asia published recently as a supplement in *Geriatrics and Gerontology International* (2014, volume 14, supplement 1).

Nevertheless, Asian values for BMI, ASM/height², and grip strength were much lower compared with those for Caucasian populations reported in the UK HCS study. Similarly, the mean (SD) BMI for older Italians aged 60-69 was 27.0(3) for men and 26.6(3.8) for women, and for those aged 70–80, 27.1(3.4) for men and 25.6(3.7) for women [20]. The values for ASM/height² for the Italian cohort aged 60-69 were also higher, being 8.6(0.9) for men and 6.7(0.9) for women; and for age group 70–80, 8.5(0.9) for men and 6.4(0.8) for women. However, Asian values for walking speed are very similar to those for Caucasians: 0.9(0.1) for men and 0.9(0.2) for women in the UK cohort. On the other hand, physical performance measure as assessed using chair stand was the worst among Caucasian older people. It is uncertain whether the longer chair stand times may be related to the higher BMI for Caucasian older people or just reflect protocol differences between the studies. A point of note is that ASM/ht² significantly decline with age in both men and women after age 65 to the same extent. suggesting that achievement of a higher peak muscle mass may attenuate the impact of age-related muscle loss.

The implications for searching for a universal definition of sarcopenia that involves absolute measurements is that possibly one cut-off value for walking speed may be applicable to all ethnic groups and different geographic locations, while different cut-off values for muscle mass, strength and other physical performance measures may be needed. Cut-off values have been proposed recently by the AWGS consensus opinion [8]. The AWGS also recommends a cut-off value for walking speed of 0.8 m/sec. However the cut-off values for muscle mass and grip strength are lower: height-adjusted ASM being 7.0 kg/m² for men and 5.4 kg/m² for women using DEXA, and 7.0 kg/m² for men and 5.7 kg/m² for women using BIA; and for grip strength the cut-off values are 26 kg for men and 18 kg for women. The findings also raise the question of the use of ASM/weight being a more universally applicable measurement of muscle mass.

While cut-off values may be used for epidemiological comparisons of sarcopenia prevalence, the most important aspect is the relationship with incident lower extremity physical limitation. It could be argued that the definition should be based on outcomes from longitudinal studies, as had been proposed by Woo et al. with respect to ASM/height² [9]. Along similar lines, a new parameter has been proposed recently by the Foundation of the National Institutes of Health to define sarcopenia: the skeletal muscle function deficit which seeks to relate muscle mass, strength and function cut points to mobility limitation [21]. Exact values used may not be as important for intervention studies, since change in outcomes are being measured, so that the criteria would only be used for recruitment of participants for these trials.

It may be that walking speed alone may be used as a single indicator in future, which would be applicable to all population groups.

There are limitations in this descriptive study, since the characteristics of cohorts may be slightly different, although they are matched by gender and age groups. For example, the Japanese cohort excluded those with stroke, while the Hong Kong cohort did not. However, for the latter cohort the numbers with stroke were small, so that the mean values were not affected after participants with history of stroke were excluded. Furthermore, different instruments and protocols were used for measurement: the Japanese cohort used BIA while the Hong Kong Chinese cohort used DEXA. The grip strength instruments were different between cohorts, although this may improve in the future as a standardized approach to measurement has now been developed [22]. No standardizations were made. Only available data were used, and

these were few. Nevertheless, this descriptive comparison is of interest in highlighting ethnic and cultural variations for some, but not all the parameters used in the definition of sarcopenia, such that for research and clinical care, appropriate classification should be used. Moreover, future studies may explore the underlying basis for variations in these parameters, and the utility of using a single parameter (walking speed) as a universal method for identification of sarcopenia in relating the syndrome to future adverse outcomes.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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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

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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 χ^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; 1.2 and (ii) the frailty phenotype is identified to detect people who find themselves between the independent and the dependent life stages. 3

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

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Welfare that identifies vulnerable older adults as those who have a higher risk of becoming dependent^{4,5} based on the needs of the Japanese long-term care insurance (LTCI) system.⁶ 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%.⁷ 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.⁸

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

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.9 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.¹⁰ 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. 11,12

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 ± 6.41 years; Brazilian Japanese descendants n = 55, mean age 70.8 ± 8.38 years; and Japanese n = 84; mean age 73.2 ± 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.¹³

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.14 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.4

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,

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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	Brazilian Japanese descendants	Japanese	Р
	(n = 72)	(n = 55)	(n = 84)	
Age (years)	69.0 ± 6.41 [†]	70.8 ± 8.38	$73.2 \pm 4.21^{\dagger}$	< 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 \pm standard deviation and valid percentage (n); n = 211. Tukey's post-hoc: $^{\dagger}P < 0.001$.

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

Variables	Brazilian	Brazilian Japanese descendants	Japanese	P
	(n = 72)	(n = 55)	(n = 84)	
BMI (kg/m²)	28.1 ± 5.39 ^{†,‡}	$23.6 \pm 2.50^{\dagger}$	22.9 ± 2.84 [‡]	< 0.001
On medication	84.7 (61)	85.5 (47)	81.9 (68)	0.831
No. medications	$2.9 \pm 2.1^{\S}$	2.7 ± 2.4	$2.1 \pm 1.5^{\S}$	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 \pm standard deviation and valid percentage (n); n = 211. Tukey's post-hoc: $^{\dagger \pm}P < 0.001$; $^{\S}P = 0.027$.

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 $(n = 84)$	Р
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 \pm 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

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