Table 2. Comparison of Muscle Mass and Functional Fitness Variables Between Groups After 3-Month Intervention

Variable	Group	Mean ± Standard Deviation		Analysis of Variance (Group × Time), *P*-Value	Post Hoc Analysis*
		Baseline	After 3-Month Intervention		
Muscle mass, kg	Exercise + AAS	26.76 ± 2.77	27.26 ± 3.04	*F* = 1.076, .36	
	Exercise	28.09 ± 1.90	28.51 ± 2.39		
	AAS	26.25 ± 1.81	26.53 ± 2.10		
	HE	27.48 ± 2.04	27.66 ± 2.23		
Appendicular muscle mass, kg	Exercise + AAS	13.25 ± 1.35	13.59 ± 1.53	*F* = 1.354, .26	
	Exercise	13.90 ± 1.06	14.19 ± 1.33		
	AAS	12.86 ± 0.99	13.03 ± 1.10		
	HE	13.57 ± 1.16	13.67 ± 1.05		
Legs muscle mass, kg	Exercise + AAS	9.76 ± 1.01	10.07 ± 1.13	*F* = 4.253, .007	Exercise + AAS > HE
	Exercise	10.28 ± 0.81	10.53 ± 1.05		
	AAS	9.55 ± 0.73	9.65 ± 0.83		
	HE	10.14 ± 0.87	10.11 ± 0.81		
BMI, kg/m^2	Exercise + AAS	18.30 ± 2.64	18.14 ± 2.68	*F* = 0.606, .61	
	Exercise	18.80 ± 1.30	18.50 ± 1.41		
	AAS	18.84 ± 1.43	18.56 ± 1.62		
	HE	18.83 ± 1.75	18.77 ± 1.67		
Usual walking speed, m/s	Exercise + AAS	1.27 ± 0.25	1.43 ± 0.29	*F* = 4.213, .007	Exercise and Exercise + AAS > HE
	Exercise	1.31 ± 0.24	1.50 ± 0.23		
	AAS	1.30 ± 0.18	1.36 ± 0.18		
	HE	1.19 ± 0.21	1.22 ± 0.23		
Maximum walking speed, m/s	Exercise + AAS	1.64 ± 0.34	1.92 ± 0.37	*F* = 9.374, <.001	Exercise and Exercise + AAS > HE
	Exercise	1.72 ± 0.27	2.04 ± 0.27		
	AAS	1.71 ± 0.28	1.92 ± 0.27		
	HE	1.57 ± 0.31	1.64 ± 0.31		
Knee extension strength, Nm/kg	Exercise + AAS	1.15 ± 0.27	1.23 ± 0.29	*F* = 3.558, .02	Exercise + AAS > HE
	Exercise	1.12 ± 0.30	1.14 ± 0.26		
	AAS	1.15 ± 0.25	1.14 ± 0.25		
	HE	1.14 ± 0.26	1.00 ± 0.26		

* A post hoc analysis was performed using the Scheffe method.
AAS = amino acid supplementation; HE = health education; BMI = body mass index.

Table 3. Change in Leg Muscle Mass and Functional Fitness After Intervention According to Study Group

Dependent Variable*	Adjusted Odds Ratio (95% Confidence Interval)		
	AAS	Exercise	Exercise + AAS
Change in leg muscle mass and knee extension strength	1.99 (0.72–5.65)	2.61 (0.88–8.05)	4.89 (1.89–11.27)
Change in leg muscle mass and usual walking speed	1.35 (0.45–4.08)	2.41 (0.79–7.58)	4.11 (1.33–13.68)

Reference: health education.
* 1 = improve, 0 = no change or decrease.
AAS = amino acid supplementation.

9% to 15% increases in strength and approximately 5% in thigh muscle volume.[28,29] Also, many studies have shown that resistance training in elderly people must be conducted at high intensities and volumes to see improvements.[9,27] In contrast, less-intense resistance exercise programs have produced little or no strength gains.

The data in this study show improvements of 2.4% in leg muscle mass, 2.0% in appendicular muscle mass, and 4.3% in leg strength in the exercise group. The moderate-intensity exercise provided in this trial produced strength gains that were smaller than those seen in previous studies, but the combination of moderate intensity exercise and AAS increased muscle mass 3.1% and muscle strength 9.3%, gains that are comparable with those observed in previous studies of high-intensity exercise.[28]

The results of the current study showed that total muscle mass, appendicular muscle mass, and walking speed significantly increased in the exercise group, suggesting that exercise is effective in the improvement of muscle mass and functional fitness, but increases in muscle

strength were not observed. These results indicate that exercise alone is insufficient for recovery in sarcopenic elderly women.

Previous studies have indicated that declines in muscle mass are related to declines in muscle protein synthesis rates in older adults and that leucine-enriched essential amino acid mixtures are primarily responsible for the amino acid-induced muscle protein anabolism in elderly people.[11,22] These studies investigated the effects of different amino acid dosages (from 6.7 to 20.0 g/d) on protein synthesis, and the 6.0-g/d dosage provided in this study is lower than in previous studies, but the mean weights of the subjects in such studies were from 71.0 to 81.3 kg, making the dosage of amino acid between 0.090 and 0.246 g/kg of body weight. The amino acid dosage in the current study was 0.151 g/kg, which is comparable with the amounts found in the literature.[11,22,26] The results of the current study showed that muscle mass, appendicular muscle mass, and leg muscle mass significantly increased in the AAS group, which is consistent with previous findings.

Many studies have demonstrated an increase in muscle mass from nutritional supplementation, but an increase in muscle strength does not always accompany an increase in muscle mass. A recent study concluded that essential AAS alone was not sufficient to increase muscle strength.[26] Similarly, although the results of the current study showed that AAS alone increased muscle mass, improvement in muscle strength was not observed. The results of the present study showed that muscle mass increased significantly with exercise or essential AAS, although muscle strength, measured according to knee extension strength, improved significantly only in the exercise + AAS group.

Next, the discussion will focus on the changes in the combined variables. One study that investigated the effects of resistance exercise and nutritional supplementation on muscle mass and strength in older adults concluded that high-intensity resistance exercise was beneficial in increasing muscle mass and muscle strength, but the nutritional supplementation, which contained only a small percentage of a soy-based protein within a mixture of mainly carbohydrates, did not contribute to those gains.[8] As illustrated in Figure 2, exercise alone was effective in enhancing single variables such as leg muscle mass or usual walking speed. Similarly, the AAS group improved usual walking speed, but rationally, to treat sarcopenia, improvements in single variables are not sufficient. Improvements observed in the combined variables would presumably lead to the most-efficient reversal of sarcopenia. Significant improvements in the combinations of leg muscle mass, knee extension strength, and walking speed were seen only in the exercise + AAS group. Although whether exercise + AAS was better than either intervention alone remains inconclusive, these results suggest that exercise + AAS may be necessary for benefits in muscle mass and strength.

This study has several limitations. First is the measurement of body composition estimated using BIA. Although magnetic resonance imaging (MRI), computed tomography, and dual-energy X-ray absorptiometry are common, accurate clinical methods of measuring muscle mass,[30,31] they are cost ineffective and are not always appropriate for field studies. BIA is simple, noninvasive, and inexpensive and has been widely used in field studies. The comparison of MRI and BIA measurements has revealed a strong correlation between the two, confirming the validity of the BIA method for muscle mass measurement in older adults.[13,17,18] Therefore, the validity of the data collected using BIA has little influence on the interpretation of the results of this study. Second, it has been reported that AAS enhances muscle protein synthesis,[11,22,32] but the mechanism of the increase in muscle mass from AAS was not explored in the current investigation. Therefore, the results of this study were interpreted based on the assumption that muscle protein synthesis had been enhanced. Third, the effects of the exercise + AAS should have been determined with the use of placebos, but placebo treatments were not provided in this study, so future research should include placebos to observe the effects of exercise and AAS on physical function and muscle strength. Fourth, the total number of dropouts in this study was 11 people, and they were not included in the data analysis. Many studies have used intention-to-treat (ITT) analyses to determine the effects of RCTs, and the use of ITT analyses are increasing, although one previous study found that only approximately 35% of 274 RCTs used ITT analyses.[33] The current study was not an ITT analysis because it confirmed that there were no significant differences between the dropouts and the participants who completed the study, and the exclusion of the 11 dropouts from the analysis did not affect the integrity of the baseline randomization. Finally, previous research has shown that milk contains essential amino acids.[34,35] Because some of the participants took the AAS with milk, the exact essential amino acid dosage in this study could not be determined, and the effect of drinking milk on the results of this study was not confirmed. Future research should avoid the intake of milk with amino acids when investigating the effects of amino acids on muscle strength and mass and physical function.

This study demonstrated that exercise and nutrition may be necessary for the basic treatment of increasing muscle mass and strength to reverse the effects of sarcopenia in community-dwelling sarcopenic women. Exercise and AAS together have significant effects on enhancing not only muscle strength, but also the combined variables of muscle mass and walking speed and of muscle mass and strength in this study population, but further follow-up studies on larger populations are required to confirm these results.

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Author Contributions: H. Kim developed the study concept and design, recruited subjects, developed the intervention program, analyzed and interpreted the data, and prepared the manuscript. S. Takao interpreted the data and reviewed the manuscript for accuracy. K. Saito assisted in AAS and supervised the interview survey. Y. Hideyo assisted in subject recruitment, supervised the

interviewers, and interpreted the data. M. Kobayashi assisted in AAS and subject recruitment and interpreted the data. H. Kato assisted in assisted AAS and body composition assessment. M. Katayama assisted in AAS and interview survey.

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Vitamin D Deficiency in Elderly Women in Nursing Homes: Investigation with Consideration of Decreased Activation Function from the Kidneys

Yasuhito Terabe, MD,[*] *Atsushi Harada, MD, PhD,*[†] *Haruhiko Tokuda, MD, PhD,*[‡] *Hiroyasu Okuizumi, MD, PhD,*[§‖] *Masahiro Nagaya, MD, PhD,*[#] *and Hiroshi Shimokata, MD, PhD*[§]

OBJECTIVES: To determine the approximate percentage of women in nursing homes who have vitamin D deficiency and to investigate whether, in assessing vitamin D status in elderly women, there are problems with measuring only 25 hydroxy-vitamin D_3 ($25(OH)D_3$) and whether decreased vitamin D activation as a result of poor renal function needs to be considered.

DESIGN: Cross-sectional study.

SETTING: Forty-eight nursing homes in Japan.

PARTICIPANTS: Four hundred three women with a mean age of 86.5 living in nursing homes who had participated in a clinical trial for hip protectors and were not bedridden.

MEASUREMENTS: At the start of the trial, in addition to general biochemical data, $25(OH)D_3$, 1,25-dihydroxy-vitamin D_3 ($1,25(OH)_2D_3$), intact parathyroid hormone (intact PTH), calcium (Ca), phosphorus (P), bone alkaline phosphate (BAP), cross-linked *N*-telopeptide of type I collagen (NTx), and osteocalcin were measured in participants' blood, and statistical analysis was performed.

RESULTS: $25(OH)D_3$, which is thought to reflect vitamin D status in the body, was surveyed and found to have a mean value of 16.7 ng/mL. $25(OH)D_3$ was less than 16 ng/mL in 49.1% of all participants. Creatinine clearance (CCr) was less than 30 mL/min in 20.1% of participants. Participants with serum $25(OH)D_3$ less than 16 ng/mL and CCr less than 30 mL/min had significantly higher levels of intact PTH and serum NTx. Participants with a CCr less than 30 mL/min had significantly lower levels of $1,25(OH)_2D_3$.

CONCLUSION: Frail elderly adults living in nursing homes with poor renal function had lower $1,25(OH)_2D_3$ and higher intact PTH levels and were thus thought to have poorer vitamin D activating capacity. Supplementation with cholecalciferol may be insufficient in people who have poor renal function. J **Am Geriatr Soc 60:251–255, 2012.**

Key words: 25-hydroxy-vitamin D_3; 1,25-dihydroxy-vitamin D_3; nursing homes

The importance of vitamin D for bones has been indicated in previous studies.[1,2] Frail elderly adults with limited ability to perform activities of daily living (ADL) who enter a nursing home are at high risk for low vitamin D as a result of poor nutrition and lack of sunlight. Vitamin D deficiency is an important risk factor for osteoporosis and fractures from falls in elderly adults.[3–5] When assessing serum 25 hydroxy-vitamin D_3 ($25(OH)D_3$) levels to define vitamin D deficiency, many reports have adopted a cutoff of 20 ng/mL.[6–8] It has also been reported that individuals with hip fracture or those with a history of falls have low $25(OH)D_3$ levels.[9,10] Secondary hyperparathyroidism from poor renal function in elderly adults must also not be overlooked.[11] The group that is probably at the highest risk of falls and fractures is elderly women living in nursing homes who are not completely bedridden but have a mobility level of at least being able to move about in a wheelchair with assistance. The participants in this study were such a group of people, who had previously participated in a fracture prevention trial using hip protectors.[12] Vitamin D levels, renal function, and the relationship between the two were investigated in these women, and the approximate percentage of these nursing home residents who needed supplemental vitamin D was considered.

From the Departments of [*]Orthopedic Surgery, [†]Advanced Medicine, [‡]Clinical Laboratory, [§]Center for Development of Advanced Medicine for Dementia, National Center for Geriatrics and Gerontology, Obu City, Aichi, Japan; [‖]Mimaki Onsen Clinic, Tomi City, Nagano, Japan; and [#]Geriatric Health Services Facility, Luminous Obu, Obu City, Aichi, Japan.

Address correspondence to Yasuhito Terabe, Department of Orthopaedic Surgery, National Center for Geriatrics and Gerontology, Gengo 35, Morioka-cho, Obu, Aichi, Japan. E-mail: yst-trb@ncgg.go.jp

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METHODS

Participants were 403 women aged 70 and older (range: 70–103) who lived in 48 nursing homes from whom consent was obtained for participation in a fracture prevention trial using hip protectors.[12] They had a mobility level of at least being able to move about in a wheelchair with assistance. A history of bilateral hip fracture was a condition for exclusion. Written informed consent was obtained from all participants. The Ethics Committee of the National Center for Geriatrics and Gerontology approved the study. Blood was collected from participants as the 48 nursing homes in the southern part of central Japan were visited in turn between January 2005 and May 2008. At the start of the trial, in addition to general biochemical data, $25(OH)D_3$, 1,25-dihydroxy-vitamin D_3 ($1,25(OH)_2D_3$), intact parathyroid hormone (PTH), calcium (Ca), phosphorus (P), bone alkaline phosphate (BAP), cross-linked *N*-telopeptide of type I collagen (NTx), and osteocalcin were measured using participants' blood, and statistical analysis was performed. $25(OH)D_3$ was measured using the radioimmunoassay double antibody method. Frail elderly adults have little muscle, and even if creatinine (Cr) is in the normal range, it cannot be concluded that renal function is normal. For a simpler assessment of renal function, we estimated Cr clearance (CCr) with adjustments for age and body weight using the widely adopted Cockcroft-Gault formula.[13]

Statistical Analyses

SPSS (version 17.0, SPSS, Inc., Chicago, IL) was used in the statistical analysis. Adjustment was made for age as a control variable in partial correlation. Two-tailed significance probability <.05 was taken to be significant. The Student *t*-test was used to test for differences between the mean values of the two groups, with $P < .05$ taken to indicate significance. The Bonferroni test was used to compare the mean values in the groups, using a general linear model adjusted for age. $P < .05$ was taken to indicate a significant difference.

RESULTS

Participants were aged 70 were to 103 (mean 86.5). Mean $25(OH)D_3$ level, which is an indicator of vitamin D level, was low (16.7 ng/mL). The mean values for the following tests were: $1,25(OH)_2D_3$, 44.4 ± 17.5 pg/mL; intact PTH, 57.4 ± 38.7 pg/mL; BAP, 32.4 ± 13.2 U/L; osteocalcin, 7.8 ± 3.8 ng/mL; and NTx, 17.6 ± 9.7 nmol bone collagen equivalent/L. The percentile distribution in the $25(OH)D_3$ distribution is shown in Figure 1. When $25(OH)D_3$ concentration of less than 20 ng/mL was taken to indicate vitamin D deficiency, 78.1% of participants were found to be vitamin D deficient.

To further investigate $25(OH)D_3$, the partial correlation was first examined adjusted for age. There were significant positive correlations between $25(OH)D_3$ and $1,25(OH)_2D_3$ (correlation coefficient (r) = 0.149, $P = .003$), albumin ($r = 0.185$, $P < .001$), total cholesterol ($r = 0.165$, $P = .001$), blood urea nitrogen ($r = 0.116$, $P = .02$), Ca ($r = 0.153$, $P = .002$), and P ($r = 0.100$, $P = .04$). Significant negative correlations were shown with serum NTx ($r = -0.153$, $P = .002$) and intact PTH ($r = -0.178$, $P < .001$). It was then decided to further investigate intact PTH, which had shown a high correlation. Mean intact PTH levels in the group with a serum $25(OH)D_3$ concentration less than 12.0 ng/mL, 12.0 to 15.9 ng/mL, and 16.0 ng/mL or higher were 72.3 pg/mL, 60.4 pg/mL, and 51.1 pg/mL, respectively. Mean intact PTH level was significantly higher in participants with a serum $25(OH)D_3$ concentration less than 12.0 ng/mL ($P < .001$) and 12.0 to 15.9 ng/mL ($P = .02$) than in those with a concentration of 16.0 ng/mL or higher. Participants younger than 85 were then compared with those aged 85 and older to determine whether the various data differed depending on age (Table 1). Significant differences were seen in $25(OH)D_3$, $1,25(OH)_2D_3$, and intact PTH. Because $1,25(OH)_2D_3$, a form of activated vitamin D, also decreases with age, it was decided to investigate $1,25(OH)_2D_3$. First, in the age-adjusted partial correlation, $1,25(OH)_2D_3$ showed the strongest negative correlation with Cr ($r = -0.323$, $P < .001$). This finding suggests that renal function strongly affects $1,25(OH)_2D_3$. The relationship between $1,25(OH)_2D_3$ concentration and estimated CCr is shown in Table 2. $1,25(OH)_2D_3$ concentration was significantly lower in participants with CCr less than 30 mL/min. Similarly, intact PTH concentration was significantly higher in participants with CCr less than 30 mL/min, in whom $1,25(OH)_2D_3$ concentration was significantly lower (Table 2). A tendency was seen for $25(OH)D_3$ levels to be higher with lower CCr, and a significant difference was seen between groups with CCr of less than 30 and 45 mL/min or greater ($P < .05$, general linear model Bonferroni test). To improve understanding of how participants were distributed according to $25(OH)D_3$ concentration and CCr value, they were divided into four groups with $25(OH)D_3$ concentrations of less than 16 and 16 ng/mL and greater and CCr of less than 30 and 30 mL/min and greater. Concentrations of $1,25(OH)_2D_3$, intact PTH, and serum NTx of the groups were then compared (Table 3). Of 198 participants with $25(OH)D_3$ concentrations of less than 16 ng/mL, 36 (18.4%) had poor renal function (CCr < 30 mL/min), and of 205 participants with

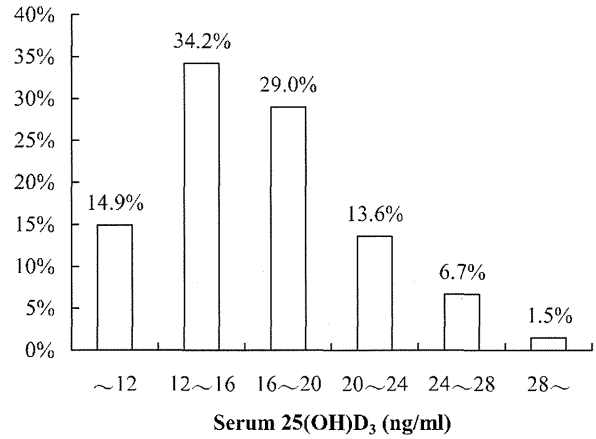

Figure 1. Percentile distribution of serum 25 hydroxy-vitamin D_3 ($25(OH)D_3$) concentrations. $25(OH)D_3$ level was < 20 ng/mL in 78.1% and < 16 ng/mL in approximately half.

Table 1. Comparison of Mean Data Values According to Age

Characteristic	Normal Range	Mean ± Standard Deviation <85 (n = 139)	Mean ± Standard Deviation ≥85 (n = 264)	*P*-Value
Age	—	79.1 ± 3.8	90.4 ± 3.7	<.001
Height, cm	—	145.2 ± 7.5	142.8 ± 7.2	.003
Weight, kg	—	44.1 ± 8.3	41.6 ± 7.5	.003
Body mass index, kg/m^2	—	20.7 ± 4.4	20.0 ± 3.3	.28
25 hydroxy-vitamin D_3, ng/mL	—	17.5 ± 4.9	16.3 ± 4.7	.01
1,25-dihydroxy-vitamin D_3, pg/mL	20–60	47.5 ± 18.1	42.7 ± 16.9	.008
Intact parathyroid hormone, pg/mL	10–65	51.6 ± 27.4	60.4 ± 43.2	.03
Albumin, g/dL	3.9–4.9	3.9 ± 0.3	3.9 ± 0.4	.01
Total protein, g/dL	6.5–8.2	6.9 ± 0.5	6.9 ± 0.5	.26
Total cholesterol, mg/dL	120–220	207.6 ± 38.0	195.9 ± 36.3	.003
Blood urea nitrogen, mg/dL	8–20	17.8 ± 6.5	18.7 ± 7.7	.25
Creatinine, mg/dL	0.5–0.8	0.66 ± 0.3	0.72 ± 0.4	.13
Creatinine clearance (Cockcroft-Gault formula), mL/min	—	55.2 ± 18.6	38.9 ± 12.7	<.001
Glomerular filtration rate (modified diet in renal disease formula), mL/min	—	73.9 ± 25.0	65.4 ± 22.1	.001
Calcium, mg/dL	8.7–10.1	8.8 ± 0.4	8.8 ± 0.5	.25
Phosphorus, mg/dL	2.5–4.5	3.6 ± 0.4	3.6 ± 0.5	.21
Aspartate aminotransferase, U/L	10–40	19.2 ± 6.2	19.7 ± 6.2	.39
Alanine aminotransferase, U/L	5–45	13.2 ± 7.5	11.5 ± 6.0	.02

Table 2. Comparison of 1,25-Dihydroxy-Vitamin D_3 ($1,25(OH)_2D_3$), Intact Parathyroid Hormone (PTH), and 25 Hydroxy-Vitamin D_3 ($25(OH)D_3$) Concentrations According to Creatinine Clearance (CCr)

CCr, mL/min	Mean (Standard Error) $1,25(OH)_2D_3$, pg/mL	Intact PTH, pg/mL	25 Hydroxy-Vitamin D_3, ng/mL
<30.0 (n = 82)	33.0 (1.9)*	80.1 (4.3)*	17.9 (5.2)
30.0–44.9 (n = 160)	45.8 (1.3)	52.7 (3.0)	17.0 (4.9)
≥45 (n = 161)	48.8 (1.4)	50.5 (3.2)	15.9 (4.4)

* $P < .05$, general linear model Bonferroni test.

Table 3. Comparison of 1,25-Dihydroxy-Vitamin D_3 ($1,25(OH)_2D_3$), Intact Parathyroid Hormone (PTH), and Cross-Linked *N*-Telopeptide of Type I Collagen (NTx) Concentrations According to Creatinine Clearance (CCr) and 25 Hydroxy-Vitamin D_3 ($25(OH)D_3$) Concentration

CCr, mL/min	Mean (Standard Error) $25(OH)D_3$, ng/mL <16	$25(OH)D_3$, ng/mL ≥16
<30		
$1,25(OH)_2D_3$), pg/mL	29.0 (2.7)*	36.3 (2.5)*
Intact PTH, pg/mL	104.8 (6.1)*	60.7 (5.4)
NTx, nmolBCE/L	28.3 (1.6)*	18.9 (1.4)
≥30		
$1,25(OH)_2D_3$, pg/mL	45.2 (1.2)	49.3 (1.3)
Intact PTH, pg/mL	55.1 (2.8)	48.1 (2.9)
NTx, nmolBCE/L	17.1 (0.7)	15.3 (0.7)

$1,25(OH)_2D_3$ levels were significantly lower in participants with CCr lower than 30 mL/min than those with CCr of 30 mL/min and higher. Mean intact PTH and NTx concentrations in participants with CCr lower than 30 mL/min and $25(OH)D_3$ of less than 16 ng/mL were significantly higher than in the other participants.

* $P < .05$, general linear Bonferroni test.

$25(OH)D_3$ concentrations of 16 ng/mL and higher, 45 (22.0%) had poor renal function. These percentages were approximately the same, but concentrations of intact PTH and NTx were significantly higher in the group with $25(OH)D_3$ of less than 16 ng/mL and CCr of less than 30 mL/min. In addition, in the group with CCr of less than 30 mL/min, $1,25(OH)_2D_3$ concentration was significantly lower than in the group with CCr of 30 mL/min and higher, regardless of $25(OH)D_3$ concentration.

DISCUSSION

Table 4 summarizes the reports on $25(OH)D_3$ concentration in elderly cohorts.[14–20] A comparison of reports in which participants were living in institutions and reports in which participants were living independently revealed lower levels of $25(OH)D_3$ in residents of institutions, who are thought to have greater difficulty with activities of daily living. Experts have proposed that $25(HO)D_3$ concentrations of 20 to 32 ng/mL, or roughly 30 ng/mL, are the minimum necessary concentration to prevent fractures.[21] A recent meta-analysis also reported that concentrations of 75 to 100 nmol/L balanced the benefits and risks of the health of elderly people.[22] Many studies take PTH to be an indicator of the cutoff value for $25(OH)D_3$ concentration.[6–8] When PTH is taken as an indicator, a $25(OH)D_3$ concentration of 20 ng/mL is taken as the cutoff

Table 4. Past Reports of 25 Hydroxy-Vitamin D_3 (25 $(OH)D_3$) Levels in Elderly Cohorts

Study Participants	n	Age, Mean	25$(OH)D_3$, ng/mL, Mean	References
Nursing home (Japan)	133	84.6	11.9	14
Nursing home or housebound (United States)	116	81	12.6	15
Nursing home (this study, Japan)	425	86.4	16.8	—
Nursing home (United States)	35	74	17.4	16
Independent women (Canada)	186	73	15.6	17
Independent women (France)	440	80	17.0	18
Community-dwelling elderly women (Japan)	2,007	75.4	24.2	19
Independent women (United States)	500	71	29.6	20

in many reports.[6–8] In the participants in this study, 78.1% had 25$(OH)D_3$ levels less than 20 ng/mL. Another study reported that 25$(OH)D_3$ of 20 ng/mL and greater is needed when intact PTH is taken as the indicator and that 28 ng/mL and greater is needed when bone density in the femoral neck is taken as the indicator.[6] From the present results, the cutoff value for 25$(OH)D_3$ as an indicator of intact PTH was thought to be 16 ng/mL; 49.1% of participants had 25$(OH)D_3$ of less than 16 ng/mL (Figure 1). In general, people with poor renal function have lower levels of 1,25$(OH)_2D_3$, an activated form of vitamin D, as a result of poor vitamin D activating capacity. Moreover, secondary hyperparathyroidism from poor renal function is not unusual in elderly people.[11] In the present results as well, there was a strong negative correlation between 1,25 $(OH)_2D_3$ and CCr ($r = -0.323$, $P < .001$), which suggests that renal function strongly affects 1,25$(OH)_2D_3$. As shown in Table 2, intact PTH levels were significantly higher and 1,25$(OH)_2D_3$ significantly lower with a CCr of less than 30 mL/min. From this it can be conjectured that vitamin D activation in the kidneys may decrease in cases of secondary hyperparathyroidism from poor renal function. In addition, as shown in Table 3, the percentage of people with poor renal function (CCr < 30 mL/min) was nearly the same in participants with 25$(OH)D_3$ levels greater and less than 16 ng/mL. Women with such vitamin D activating capacity made up 20.1% of all participants, although according to guidelines published in the United States in 2003[23] for bone metabolism disorders in individuals with chronic kidney disease, if PTH is measured and found to be high in people undergoing dialysis and those with chronic renal failure with less than 60% renal function, it is recommended that serum 25$(OH)D_3$ be measured and vitamin D_2 be administered if it is less than 30 ng/mL. Considering these guidelines, a greater number of people would probably be judged to have poor renal function, although there are limitations to this investigation. All CCr values were derived through calculation, not from actual measurements of CCr or glomerular filtration rate (GFR). Cystatin C was not measured either. The Cockcroft-Gault formula was first used to calculate CCr, but the Modification of Diet in Renal Disease (MDRD) formula[24] was also used to investigate CCr. The correlation between CCr calculated using the Cockcroft-Gault formula and GFR calculated using the MDRD formula was high ($r = 0.769$, $P < .001$). Moreover, in the group with GFR of less than 50 mL/min (n = 84, 20.8%), a significant difference, similar to that in the results obtained with the Cockcroft-Gaults formula, was seen. Thus, although CCr obtained from calculations is not ideal, it seems to be reliable. In addition, intact PTH level may be a useful indicator in establishing a cutoff value for 25(OH) D_3 in frail elderly adults such as the present participants. Moreover, because plainly higher intact PTH levels were shown in participants with poor vitamin D activation in the kidneys, intact PTH may have an important role in considering vitamin D supplementation in frail elderly adults. Many experts recommend vitamin D supplementation with cholecalciferol when 25$(OH)D_3$ level drops below 30 to 32 ng/mL. A recent Institute of Medicine report[25] recommends supplementation when 25$(OH)D_3$ is less than 20 ng/mL, but it does not specifically address frail elderly adults. Vitamin D is not activated efficiently even with cholecalciferol supplementation in frail elderly adults, such as the present participants, who seem to have poor activation of vitamin D. Theoretically, therefore, it would seem that supplementation with a form of activated vitamin D such as paricalcitol or alfacalcidol may be beneficial in the case of frail elderly adults with poor renal function.

CONCLUSION

In this study, 25$(OH)D_3$ levels were found to be low in women living in nursing homes who were at least able to move about in a wheelchair with assistance. Approximately 50% to 80% of participants were thought to be vitamin D deficient, although this depends somewhat on the cutoff value used for 25$(OH)D_3$. In addition, approximately 20% of all participants were thought to have decreased vitamin D activating capacity in the kidneys. Such poor vitamin D activation capacity in the kidneys was present in a similar 20% of people whose 25$(OH)D_3$ level was above the cutoff level (16 ng/mL). An unexpectedly large number of women in nursing homes thus had poor vitamin D activation secondary to poor renal function. For vitamin D supplementation, therefore, it may be necessary to make a comprehensive judgment with measurements of intact PTH and CCr or GFR and 1,25 $(OH)_2D_3$ rather than cholecalciferol supplementation based simply on 25$(OH)_3$ level.

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Leisure activities and cognitive function in elderly community-dwelling individuals in Japan: A 5-year prospective cohort study

Hajime Iwasa [a,b,*], Yuko Yoshida [b], Ichiro Kai [a], Takao Suzuki [c], Hunkyung Kim [b], Hideyo Yoshida [b]

[a] School of Public Health, The Graduate School of Medicine, The University of Tokyo, Japan
[b] Tokyo Metropolitan Institute of Gerontology, Japan
[c] National Center for Geriatrics and Gerontology, Japan

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ABSTRACT

Objective: This study aimed to clarify the longitudinal relationship between leisure activities and cognitive decline among Japanese community-dwelling older adults, using a 5-year prospective cohort study design.
Methods: A total of 567 men and women, aged 70 years and over, participated in the study. The Mini-Mental State Examination was used in baseline and follow-up surveys to assess cognitive function. The change in cognitive function from baseline to follow-up was determined, and cognitive decline over 5 years was used as the outcome variable. Leisure activities (hobby, social activity, and physical activity) were assessed at baseline and used as independent variables. Age, gender, number of years of education, presence of chronic diseases, instrumental activities of daily living, depressive symptoms, smoking, hearing deficits, and level of cognitive function at baseline were used as covariates.
Results: Multivariate logistic regression analysis, adjusted for potential confounders, showed that non-participation in a hobby was significantly and independently associated with cognitive decline (odds ratio: 1.87, 95% confidence interval: 1.16–3.02, $p<0.01$). There were no significant relationships between social activity, physical activity and cognitive decline.
Conclusions: Our study found a longitudinal inverse relationship between hobby participation and cognitive decline among elderly Japanese community-dwelling individuals, suggesting that engaging in a hobby in later life can contribute to preserving cognitive function.

Introduction

Along with the aging of populations worldwide, the prevalence of dementia in later life will increase rapidly. In Japan, it has been estimated that the number of people with dementia will peak in 2036 at around 3,550,000 people, that is, 10.8% of subjects aged 65 years and older [1]. These predicted changes offer complex and intriguing challenges for geriatricians and gerontologists who endeavor to prevent older people from developing dementia and becoming bedridden.

It has been reported that frequently engaging in leisure activities is associated with a lower risk of dementia and deterioration in cognitive function among community-dwelling older adults [2–4]. The Japan Ministry of Health, Labour and Welfare has introduced a Dementia Prevention Program [5], which encourages community-dwelling elderly subjects to engage in various leisure activities that help to stimulate their cognitive function in daily life (e.g., reading books, watching TV shows, gardening, playing challenging board games such as go or shogi, walking, and light exercise). We focus on the Dementia Prevention Program developed by the Japan Ministry of Health, Labour and Welfare because it is appropriate for the very elderly living in a community setting, who have various everyday physical impediments and whose physical function gradually deteriorates.

The Dementia Prevention Program was developed on the basis of findings from European and American longitudinal studies [2–4], which found an association between participation in leisure activities and a reduction in the incidence of dementia. However, since lifestyles and preferred activities among elderly individuals in Western countries may be different from those of elderly Japanese, it is questionable whether the findings from Western countries are applicable to dementia prevention strategies for older Japanese adults. The Cabinet Office of the Japanese Government reported that elderly individuals in Japan frequently engaged in various leisure activities, including gardening (34.3%), watching TV (31.4%), traveling (27.9%), walking (20.8%), knitting or Japanese-style pursuits (tea ceremonies, Japanese dancing, flower arrangement) (17.5%), reading books (16.4%), drawing (15.9%), sports (14.8%), Karaoke (10.5%), theater (6.8%), and playing challenging board games such as go or shogi (4.7%) [6]. Some of these activities were particular to Japan, thus the association between leisure

* Corresponding author at: School of Public Health, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, Japan (zip 113-0033). Tel.: +81 3 5841 3514; fax: +81 3 5684 6083.
E-mail address: hajimei-tky@umin.ac.jp (H. Iwasa).

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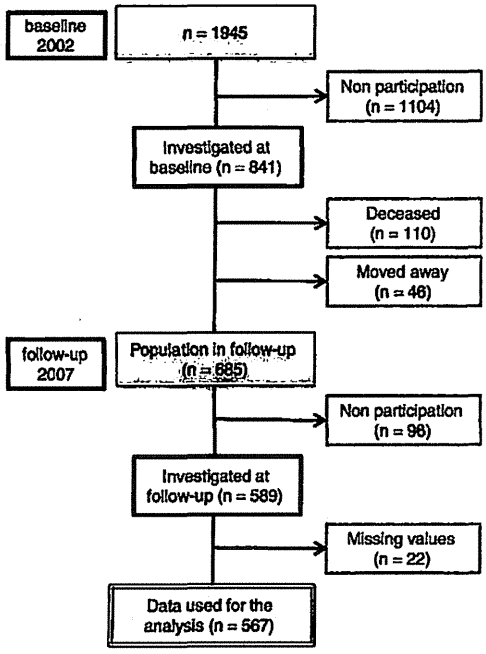

Fig. 1. Study sample in the analysis.

activity and cognitive decline should be re-examined among elderly Japanese subjects.

This study aimed to clarify a longitudinal relationship between leisure activities and cognitive decline among community-dwelling elderly Japanese, using a 5-year prospective cohort study design. Confirmation of a longitudinal relationship between leisure activities and cognitive decline could facilitate the development of specific strategies to prevent cognitive decline and dementia in older adults in Japan.

Methods

Participants

The data for the present study was acquired from the mass health checkups for community-dwelling older adults ("Otasha-Kenshin") [7,8], conducted by the Tokyo Metropolitan Institute of Gerontology. "Otasha-Kenshin" means "health checkups for accomplishing successful aging" in Japanese. The study was administered in Itabashi ward in northern Tokyo, and we were granted access to the municipal resident registration files by the Itabashi ward authorities. Participants took part in a face-to-face interview at baseline and at 5-year follow-up with trained research assistants. The study was approved by the Ethics Committee of the Tokyo Metropolitan Institute of Gerontology. The study was explained to all participants, who were advised that: 1) their participation would be entirely voluntary; 2) they could withdraw from the study at any time; and 3) if they chose not to participate or to withdraw, then they would not be disadvantaged in any way. As of 2002, a sample of 1945 residents (aged 70–84 years) was obtained systematically from the municipal resident registration files. We acquired 841 completed sets of data (43.2% participation) in the baseline survey.

Of those who participated in the baseline survey, 589 participated in the follow-up survey 5 years later in 2007. Of the remaining 252 subjects, 110 had died during the 5-year follow-up period, 46 had moved to a different part of Japan, and 96 declined to participate. Of the 589 people who did participate in the follow-up survey, 22 were excluded from the analysis because they had missing cognitive performance data. In total, 567 participants (285 male, 282 female; mean age: 75.8 ± 3.5, age range: 70–84 at baseline) with a complete set of data were included in this analysis (see Fig. 1).

Those subjects who died or moved away during the follow-up period had a lower proportion of women (30.8% vs. 49.7%, $p<0.01$), were older (77.1 vs. 75.8 years, $p<0.01$) and had a similar number of years of education (10.8 vs. 10.7 years, $p=0.83$), an identical rate of depression (3.2% vs. 1.6%, $p=0.19$), a higher rate of chronic disease (48.7% vs. 35.9%, $p<0.01$), an identical rate of hearing deficits (9.6% vs. 7.8%, $p=0.45$), an identical rate of smoking (21.9% vs. 16.9%, $p=0.15$), lower instrumental activities of daily living score (IADL) [9], measured according to the Tokyo Metropolitan Institute of Gerontology Index of Competence (4.6 vs. 4.8 points, $p<0.01$), lower Mini-Mental State Examination [10] (MMSE) score (26.9 vs. 28.3 points, $p<0.01$) at baseline, exhibited a lower rate of engaging in hobbies (34.6 vs. 45.7, $p<0.01$), and similar rates of engagement in social activity (30.1 vs. 37.2, $p=0.11$) and physical activity (69.9 vs. 69.7, $p=0.96$) compared with subjects used in the analysis (Table 1).

Those subjects who were excluded or declined to participate in the follow-up survey had an almost identical proportion of women (47.5 vs. 49.7, $p=0.65$), similar age (76.4 vs. 75.8 years, $p=0.15$), fewer years of education (10.1 vs. 10.7 years, $p<0.05$), a higher rate of depression (5.1% vs. 1.6%, $p<0.05$), an identical rate of chronic disease (37.3% vs. 35.9%, $p=0.79$), an identical rate of hearing deficits (11.9% vs. 7.8%, $p=0.15$), an identical rate of smoking (22.0% vs. 16.9%, $p=0.19$), a lower IADL score (4.6 vs. 4.8 points, $p<0.01$), a lower MMSE score (27.3 vs. 28.3 points, $p<0.01$) at baseline, exhibited a lower rate of engaging in hobbies (33.1 vs. 45.7, $p<0.01$), and

Table 1
Characteristics of subjects.

	Participants ($n=576$)	Deceased/moved away ($n=156$)	Non-participants at follow-up ($n=118$)	Participants vs. deceased/moved away	Participants vs. non-participants
Gender (% women)	282 (49.7)	48 (30.8)	56 (47.5)	<0.01	0.65
Age (year)	75.8 ± 3.5	77.1 ± 3.7	76.4 ± 3.9	<0.01	0.15
Education (year)	10.7 ± 3.0	10.8 ± 3.5	10.1 ± 2.9	0.83	0.04
Depression (%)	9 (1.6)	5 (3.2)	6 (5.1)	0.19	0.02
Chronic disease (%)	204 (35.9)	76 (48.7)	44 (37.3)	<0.01	0.79
Hearing deficit (%)	44 (7.8)	15 (9.6)	14 (11.9)	0.45	0.15
Smoking (%)	96 (16.9)	34 (21.9)	26 (22.0)	0.15	0.19
IADL (points)	4.8 ± 0.6	4.6 ± 0.93	4.6 ± 0.9	<0.01	<0.01
MMSE (points)	28.3 ± 2.1	26.9 ± 3.2	27.3 ± 2.7	<0.01	<0.01
Hobby (yes %)	259 (45.7)	54 (34.6)	39 (33.1)	0.01	0.01
Social activity (yes %)	211 (37.2)	47 (30.1)	44 (37.3)	0.11	0.99
Physical activity (yes %)	395 (69.7)	109 (69.9)	74 (62.7)	0.96	0.14

Note: t tests for continuous measures and chi-square tests for categorical measures were used to clarify the significance of differences in these characteristics between the two groups (participants vs. deceased/moving away, participants vs. non-participants).

exhibited almost the same rates of engagement in social activity (37.3 vs. 37.2, $p=0.99$) and physical activity (62.7 vs. 69.7, $p=0.14$) compared with subjects used in the analysis (Table 1).

Outcome measure

MMSE was used to assess cognitive function at baseline and follow-up. The change in cognitive function during the 5 years (calculated by subtracting baseline MMSE score from follow-up MMSE score: a negative value signifying a decrease in MMSE score) was an outcome variable. In addition, we used a cutoff score of −3 (meaning that scores of −3 and below were classified as "cognitive decline") to judge whether participants had meaningful deteriorations in cognitive function over 5 years. Previous studies have pointed out that a change in MMSE score may reflect not only true improvement or decline with aging, but also may be a result of measurement error, regression to the mean, and a practice effect of the test [11,12], and showed that a change in MMSE score of at least 2 to 4 points was necessary to reliably measure a change in scores [12,13].

Independent variables (leisure activities)

Data collected at baseline were used as independent variables. Participants were interviewed regarding leisure activities: hobby, social activity, and physical activity. Subjects were asked whether they engaged in any hobbies (e.g., gardening, watching TV, traveling, knitting, reading books, Karaoke, and playing board games such as go or shogi) "never", "occasionally", or "frequently". In the analysis, these responses were dichotomized into two categories: "never/occasionally" and "frequently", the former being defined as "no" and the latter as "yes". Question regarding engagement in social activities (e.g., volunteering and group activities for the elderly) was answered "yes" or "no". The question regarding regular physical activities (e.g., jogging, walking, Japanese croquet, hiking, dance, swimming, and gymnastics) was answered with a "yes" or "no" response.

Covariates

Data collected at baseline were used as covariates in the analysis of an independent association between leisure activities and cognitive decline. Data for age, gender, number of years of education, presence of chronic diseases, IADL, depressive symptoms (measured according to Mini-International Psychiatric Interview (MINI) [14]), smoking, hearing deficit, and baseline MMSE score, were included. The presence of chronic diseases was defined as at least one disease among diabetes, heart disease, and stroke.

Statistical analyses

Chi-square tests were performed to test the univariate associations between leisure activities and cognitive decline according to each leisure activity (i.e., hobby, social activity, and physical activity). Logistic regression analyses were performed to test the multivariate associations between leisure activities and cognitive decline according to each leisure activity. Adjusted odds ratio estimates and confidence intervals for engagement in the leisure activities, controlled for the above-mentioned covariates, were calculated. All statistical procedures were performed using SAS version 9.1 software (SAS Institute Inc., Cary, NC, USA).

Results

Fig. 2 shows distributions of change in MMSE score between the baseline and follow-up survey. The mean change in MMSE score was -0.94 ± 2.61 (range: −16 to 7). The number (proportion) of participants with cognitive decline was 109 (19.2%).

Table 2 shows the associations between leisure activities and cognitive decline, as assessed by chi-square tests. Those who did not engage in a hobby were more likely to experience cognitive decline over 5 years, compared with participants who did (23.4% vs. 14.3%, $p<0.01$). Those who did not engage in social activities and physical activities had an almost identical proportion experiencing cognitive decline, compared with participants who did (20.5% vs. 17.1%, $p=0.31$; 19.8% vs. 18.9%, $p=0.83$, respectively).

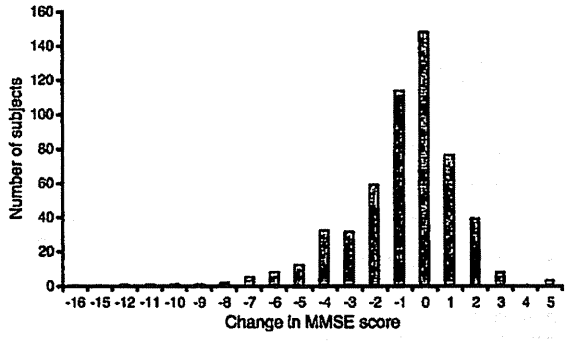

Fig. 2. Change in MMSE score over 5 years ($n=567$). Note: Change in cognitive function was calculated by subtracting baseline MMSE score from follow-up MMSE score: a negative value means a decrease in MMSE score during the 5-year period.

Multiple logistic regression analyses were carried out to examine the independent relationships between participation in leisure activities and cognitive decline. There was a significant relationship between lack of participation in a hobby and cognitive decline (odds ratio: 1.87, 95% confidence interval: 1.16–3.02, $p<0.01$) during the 5-year period. There were no significant relationships between participation in social and physical activities and cognitive decline (Table 3).

To examine whether the relationships between participation in leisure activities and cognitive decline were affected by cognitive impairment at baseline, we repeatedly performed the above analysis in subjects with no cognitive impairment according to MMSE scores at baseline. We used a cutoff MMSE score of 24, meaning that scores of 24 and above were classified as no cognitive impairment [15] ($n=541$). The results revealed that, in participants with a score of 24 or above, the association between hobby engagement and cognitive decline remained significant (odds ratio: 1.65, 95% confidence interval: 1.02–2.68, $p<0.05$), while the associations between social and physical activity and cognitive decline remained non-significant.

Discussion

This study aimed to clarify the longitudinal relationship between leisure activities (hobby, social activity, and physical activity) and cognitive decline among Japanese community-dwelling older adults, and found a significant and independent inverse relationship between hobby participation and cognitive decline, even when adjusting for potential confounding factors such as age, gender, number of years of education, presence of chronic diseases, IADL, depressive symptoms, smoking, hearing deficit, and level of cognitive function at baseline, indicating that older individuals who did not enjoy hobbies were more likely to experience cognitive decline during the 5-year period, compared to those who did. There were no significant

Table 2
The number (rate) of participants with cognitive decline over 5 years corresponding to engaging in leisure activities ($n=567$).

	Change in cognitive function		p^a
	Decline	Stable/improved	
Hobby			
Yes	37 (14.3)	222 (85.7)	<0.01
No	72 (23.4)	236 (76.6)	
Social activity			
Yes	36 (17.1)	175 (82.9)	0.31
No	73 (20.5)	283 (79.5)	
Physical activity			
Yes	75 (18.9)	320 (81.1)	0.83
No	34 (19.8)	138 (80.2)	

[a] Chi-square test. A cut-off score of −3 (meaning that scores of −3 and below were classified as "cognitive decline") was used to judge whether participants had significant deterioration over 5 years with respect to cognitive function.

Table 3
Longitudinal relationship between leisure activity and cognitive decline ($n = 567$).

	Odds ratio	95% Confidence interval	p^a
Hobby (no participation)	1.87	1.16–3.02	<0.01
Social activity (no participation)	1.45	0.89–2.34	0.14
Physical activity (no participation)	1.06	0.65–1.74	0.81

[a] Multiple logistic regression analyses adjusted for age, gender, number of years of education, presence of chronic disease, IADL (measured according to the Tokyo Metropolitan Institute of Gerontology Index of Competence [9]), depressive symptoms (measured according to MINI [14]), smoking, hearing deficit, and baseline MMSE score.

relationships between participation in social activities and cognitive decline, nor participation in physical activities and cognitive decline.

Our findings were similar to the results of previous studies. Wilson [2] reported that regular engagement in cognitive-stimulating activities (including viewing television, listening to radio, reading newspapers, reading magazines, reading books, playing games such as cards, checkers, crosswords, or other puzzles, and going to museums) was associated with a reduced risk of Alzheimer disease (AD) during a mean follow-up of 4.5 years. Verghese [4] found that regular engagement in cognitive activities (including reading books or newspapers, writing for pleasure, doing crossword puzzles, playing board games or cards, participating in organized group discussions, and playing musical instruments) was associated with a reduced risk of dementia during a mean follow-up of 5.1 years. The previous studies suggested that engaging in activities that demand relatively substantive cognitive resources may be effective in preserving cognitive function in the elderly. The previous studies also showed a significant relationship only between cognitive activities and incidence of dementia, but not a significant relationship between physical activity and incidence of dementia [2,4]. Thus, previous studies and ours suggest that enjoying a hobby (which is a cognitive stimulating activity) may have a protective effect in helping to preserve cognitive function in later life.

Meanwhile, the longitudinal relationship could be explained by "reverse causality", with which a loss of hobby participation would occur after an early stage of cognitive deficit developed owing to preclinical dementia. Quitting a hobby may constitute an early sign of dementia incidence [4], and such potential dementia cases are more likely to experience cognitive decline eventually. Because the current study did not conduct dementia discrimination at baseline, we cannot exclude the possibility that such potential dementia cases may have been included into the study cohort. However, the likelihood of this possibility occurring in the current study may be weakened, for two reasons. First, the multivariate analysis controlled for baseline cognitive function levels. Second, the association between hobby participation and cognitive decline remained significant when the analysis was restricted to subjects with no cognitive impairment [15] (defined by a cutoff MMSE score of 24 or above). Because, in the present findings, it is difficult to decide whether the longitudinal relationship ought to be explained by the protective effect or by reverse causality, further investigations with longer follow-up periods are needed in the future.

We speculate that there could be three mechanisms underlying the relationship between hobby participation and cognitive decline in the elderly. The first pathway may be related to the "use it or lose it" hypothesis [16], from a famous saying in English. Older individuals tend to experience deterioration in their cognitive and physical function if they physically and mentally receive little stimulus in everyday life (i.e., "disuse syndrome") [17]. Thus, since some hobbies demand use of cognitive resources and stimulate cognitive function, engagement in a hobby may have a beneficial effect in preventing older individuals from failing into the disuse syndrome, and consequently reduce the deterioration in cognitive function.

The second pathway underlying the relationship between hobby participation and cognitive decline may be related to the "cognitive reserve hypothesis" [18–20]. Previous studies have suggested that there are individual differences in tolerance to dementia pathology. Price [21] examined a relationship between neuropathological diagnosis at autopsy and clinical diagnosis of AD before death, and demonstrated that around 40% of non-demented individuals met at least some level of criteria for neuropathological AD, suggesting that there may be a lag between neuropathological states and manifestation of dementia symptoms (e.g., behavior disorders and cognitive decline), and that some non-demented older individuals may also have the potential for progression of cognitive dysfunction. Similarly, according to the Nun study [22], the lag may vary among individuals. The study found that those who showed a neuropathological state of AD at autopsy included not only individuals with dementia clinically manifest before death but also cognitively intact individuals. The findings indicate that there may be individual differences in cognitive reserve, which is an ability to tolerate dementia pathology. Previous studies assumed that cognitive reserve varied according to characteristics such as education and occupational attainment. Hence, those with higher education and career progression in earlier life are likely to have enhanced cognitive reserve in later life [18,19]. Previous studies demonstrated that older adults with higher education [23,24] and occupation attainment [23] were less likely to develop dementia. The results might be related to frequent engagement in cognitively challenging activities and consequent enhanced cognitive reserve. Thus, regularly engaging in a hobby may have a beneficial effect in preventing cognitive decline in later life by enhancing cognitive reserve.

The third pathway underlying the relationship between hobby participation and cognitive decline may be related to "the positive affect hypothesis". Engaging in a hobby brings a "positive affect" (including happiness, joy, enthusiasm, contentment, subjective well-being, self-esteem, and congenial mood) to older adults. A previous study [25] reviewed the relationships between these positive affects and health outcomes, including mortality, morbidity, physical functioning, and others (cardiovascular, endocrine, and immunological diseases), and suggested that a positive affect regulated the central nervous system and hypothalamic–pituitary–adrenal axis activity. Hyperactivity in the axis may be detrimental to health because it causes a loss of hippocampal neurons and hippocampus atrophy [3,26–28], and an increase in cardiovascular risk factors (e.g., elevated blood pressure, cardiac dysrhythmia, and elevated platelet activation) [3,25,29], which increase the risk of dementia. Hence, engaging in a hobby may preserve cognitive function by providing a positive affect.

The relationship between hobby participation and cognitive decline may be confounded by depressive symptoms. It is well known that quitting a hobby is an early sign of depressive symptoms. In fact, the Geriatric Depression Scale, which is widely used to assess depressive symptoms among older individuals, includes an item related to having quit their hobby (i.e., "Have you dropped many of your activities and interests?" [30]). Also, a previous study reported that older individuals with depressive symptoms tend to experience cognitive decline [31]. Thus, the presence of depressive symptoms can be a confounding factor that affects the association between engaging in hobbies and cognitive decline. Nevertheless, our study controlled for the confounding effect of depressive symptoms (assessed by the MINI [14]) and found an independent inverse relationship between participation in a hobby and cognitive decline.

Our findings were inconsistent with the results of previous studies, which showed a longitudinal relationship between social engagement and preserving cognitive function among older adults [32,33]. Wang [32] found a relationship between participation in social activities (including traveling, playing card games, group activities, and volunteer activities) and reduced risk of dementia. Ertel [33] found a relationship between participation in social activities (including marital status, volunteering, frequency of contact with children, parents, and neighbors) and preservation of cognitive function using a

large, representative sample of American citizens. Meanwhile, Fabrigoule [34] did not find a significant association between participation in golden age clubs, which is one of the social activities of the elderly, and incidence of dementia, using a 3-year longitudinal study design in older individuals dwelling in Gironde (France). Further detailed explorations of the relationship are required to resolve the contradictions.

Our findings were inconsistent with the results of previous studies, which showed a longitudinal relationship between regular physical activity and preservation of cognitive function among older adults by observational study [35,36,37]. Larson [35] reported that older individuals who engaged in regular exercise (three or more times per week) were less likely to develop dementia during a mean follow-up of 6.2 years. Lindsay [37] reported that regular exercise ("regular" was not explicitly defined in the study) was associated with a reduced risk of AD in a 5-year prospective cohort study. According to the previous studies, regular physical activity brings biological benefits related to improved cerebral blood circulation [38] and oxygen delivery to regions of the brain [39], thus preserving cognitive function in later life. However, Wang [32] did not find any significant associations between physical activity (including swimming, walking, and gymnastics) and risk of dementia, in a 6.4-year longitudinal study among very old individuals living in Stockholm, Sweden. Wilson [2] also conducted a 4.5-year longitudinal study among older Catholic clergy in the USA and did not find a significant association. Further detailed examinations of the relationship are needed to resolve the contradictory results.

Generalization of our findings is limited in two ways. First, we did not assess which kinds of activities the participants engaged in as a hobby because of restricted procedures in this survey. Various kinds of activities are included in the hobbies that Japanese older individuals enjoy [6], and the extent of effectiveness of hobbies in preserving cognitive function, may vary with type of hobby. For example, hobbies such as the board games of go and shogi would demand relatively more cognitive resources than watching TV. Fishing and sports may demand few cognitive resources because these activities mostly use physical resources (e.g., physical fitness). Thus, which kinds of activities are most effective in preserving cognitive function should be examined in future studies. Second, the representativeness of the sample in this study may have been restricted. The participation rate at baseline was relatively low (43.2% participation) because we acquired the data by administering mass health checkups. In addition, those who were deceased/moved away differed in terms of the proportion of women, age, rate of chronic disease, IADL, cognitive functioning, and rate of engaging in hobbies compared with participants whose data were used in this study (Table 1). Also, those without follow-up data differed in terms of years of education, rate of depression, IADL, cognitive functioning, and rate of engaging in hobbies, compared with participants whose data were used in this study (Table 1), suggesting that a selection bias may have occurred. Therefore, we cannot exclude the possibility that the extent to which our findings are generalized may be limited because of the two reasons.

In conclusion, this study found an independent inverse relationship between hobby participation and longitudinal decline in cognitive function among community-dwelling older adults in Japan, suggesting that engaging in hobbies in later life can contribute to preserving cognitive function. Our results may help to facilitate the development of efficient strategies to prevent cognitive decline and reduce the incidence of dementia in older individuals in Japan.

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Estimation of appendicular muscle mass and fat mass by near infrared spectroscopy in older persons

Daisuke Yoshida,[1] Hiroyuki Shimada,[1] Atsushi Harada,[2] Yasumoto Matsui,[2] Yoshihito Sakai[2] and Takao Suzuki[3]

[1]Section for Health Promotion, Department of Health and Medical Care, Center for Development of Advanced Medicine for Dementia, [2]Department of Orthopedic Surgery, National Hospital for Geriatric Medicine, and [3]Research Institute, National Center for Geriatrics and Gerontology, Obu, Aichi, Japan

Aim: Near infrared spectroscopy has been reported to have a high reliability and accuracy in assessing the percentage of body fat. However, whether muscle mass can be accurately estimated using this method has not been established. This study examined whether a near infrared spectroscopy method could estimate appendicular muscle mass and fat mass, with dual-energy X-ray absorptiometry as the standard method for comparison.

Methods: A total of 20 orthopedic inpatients (mean age 73.2 ± 6.8 years) were recruited for this study. Their body composition was assessed using near infrared spectroscopy and dual-energy X-ray absorptiometry. Appendicular muscle mass and fat mass were estimated from height, weight and optical densities.

Results: The optical densities for the upper arm (biceps, triceps) and forearm (flexor carpi radialis) were significantly correlated with appendicular muscle mass ($r = 0.534$ to 0.623) or fat mass ($r = -0.483$ to -0.827). Estimated appendicular muscle mass and fat mass explained 89% and 80% of the variance in the dual-energy X-ray absorptiometry-derived muscle mass and fat mass estimates using height, weight and optical density values of the proximal flexor carpi radialis.

Conclusions: Near infrared spectroscopy is a useful method to assess not only fat mass, but also muscle mass in older adults. **Geriatr Gerontol Int 2012; 12: 652–658.**

Keywords: aged, body composition, body fat, sarcopenia, skeletal muscles.

Introduction

Age-related loss of muscle mass (so-called sarcopenia) can lead to functional decline in older persons.[1–5] Two published Health, Aging and Body Composition reports showed that sarcopenia, as determined by computed tomography (CT) in the mid-thigh, was a weak to modest predictor of loss of physical function over the following 2 to 3 years.[6,7] Furthermore, one study reported that older sarcopenic patients were twice as likely to contract infection during a hospital stay compared with older patients with a normal muscle mass.[8] This suggested that sarcopenic individuals might have decreased immunity, which might provide a mechanistic link between sarcopenia and mortality risk. In addition, reduced arm muscle area was reported to be an independent predictor of long-term mortality in community-dwelling older adults.[9] According to the

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Correspondence: Dr Daisuke Yoshida PhD, Section for Health Promotion, Department of Health and Medical Care, Center for Development of Advanced Medicine for Dementia, National Center for Geriatrics and Gerontology, 35 Gengo, Morioka-machi, Obu, Aichi 474-8511, Japan.
Email: yoshida@ncgg.go.jp

New Mexico Elder Health Survey, the prevalence of sarcopenia increased from 13 to 24% in persons aged under 70 years to >50% in persons aged over 80 years.[1] To achieve successful aging, it is important to preserve muscle mass to maintain function.

Recently, some researchers reported that sarcopenic patients who were obese were at particularly high risk of functional impairment and physical disability.[10–13] The condition was termed sarcopenic obesity, and it was suggested that approximately 15% of those with sarcopenia were also obese.[10] This suggests that it is necessary to assess not only muscle mass, but also fat mass accurately in the elderly.

There are various methods for measurement of body composition. Total body and regional skeletal muscle mass can now be accurately quantified using imaging methods, including CT and magnetic resonance imaging (MRI).[14] However, CT and MRI are costly methods and access to the equipment can be limited. Dual-energy X-ray absorptiometry (DXA) has been widely used in clinical practice, not only for osteoporosis screening and diagnosis, but also for assessment of body composition, such as skeletal muscle mass and fat mass. DXA is less expensive and less invasive compared with MRI and CT. Previous studies have shown good correlations between DXA-derived lean soft tissue mass and skeletal muscle mass in the lower limb region when CT and MRI were used as the standards for comparison.[15,16] However, DXA methods take more time, although whole-body scanning by this method exposes the patient to minimal radiation.

Bioelectrical impedance analysis (BIA) is a non-invasive, portable, quick and inexpensive method for measuring body composition.[17] Previous studies have shown that there is a strong correlation between BIA resistance and skeletal muscle measurements in the arms[18] and legs.[19] In addition, one report suggested that BIA could provide rapid and accurate estimates of whole body skeletal muscle mass in adults.[20] There are some disadvantages with the BIA method. First, fat tissue also holds water, although the proportion is small.[21] Second, the volume of muscle derived by BIA might overestimate the actual volume. Third, there are a large proportion of older adults who have a changed distribution of body water, such as edema. One report showed that the expansion of extracellular water relative to intracellular water and to regional lean volume masks actual muscle cell atrophy during aging.[22] This suggested that it might be difficult to accurately assess body composition in older adults.

Another development that might have potential for use in older adults is near infrared spectroscopy (NIRS). NIRS is also a non-invasive, simple and rapid method of assessing the percentage of body fat. There are some reports that the NIRS method has a high reliability and accuracy in determination of the percentage of body fat.[23–25] In contrast, it has not been established whether muscle mass can be estimated accurately by NIRS.

The present study investigated whether a NIRS method could provide an accurate estimate of appendicular muscle mass (AMM) and appendicular fat mass (AFM) using DXA as the standard method for comparison.

Methods

Participants

A total of 20 orthopedic patients who were admitted to the National Hospital for Geriatric Medicine and who were aged 60 years or older were recruited for the present study. Patients with dementia or who had major laterality of muscle mass in the arms and legs, or who had surgery just before the study were excluded. All participants had their height (to the nearest 0.1 cm) and weight (to the nearest 0.1 kg) measured after admission. The details of the study were explained in advance and written consent was obtained from each participant. In addition, the present study was approved by the ethics committee of the National Center for Geriatrics and Gerontology.

Measurement of body composition

Whole and regional body composition was measured using DXA (Lunar DPX, Madison, WI, USA). This system provided the mass of lean soft tissue, fat and bone mineral for both the whole body and specific regions. Appendages were isolated from the trunk and head by using a DXA regional computer-generated default line. AMM or AFM was derived as the sum of the fat-free soft tissues or fat tissue of the arms and legs. A previous study reported that total body skeletal muscle mass can be accurately predicted from DXA-estimated appendicular lean soft tissue mass.[26,27]

NIRS

The NIRS measurements were carried out with the Fitness Analyzer BFT-3000 (Kett Electrical Laboratory, Tokyo, Japan, Fig. 1), the Japanese version of the Futrex 5000 (Futrex, Gaithersburg, MD, USA; 1988), which has potential for estimating body composition.[22,28] This device uses optical densities (OD) at two wavelengths (OD1 = 937 nm, OD2 = 947 nm) measured at each site. The NIRS instrument was tested immediately before taking measurements on each patients by using an optical standard, which was provided with the instrument and situated in a flexible light shield, to ensure that its performance was consistent throughout the study.

OD values were obtained at six sites: distal biceps (5 cm from the olecranon), distal triceps (5 cm from the

Figure 1 The near infrared spectroscopy instrument (Fitness Analyzer BFT-3000).

Figure 2 Method of measurement.

olecranon), proximal flexor carpi radialis (5 cm from the olecranon), distal quadriceps (5 cm from the upper edge of patella), proximal tibialis anterior (5 cm from the caput fibulae) and proximal calf (5 cm from the caput fibulae). The reliability was confirmed by test–retest. The test–retest reproducibility was excellent (intraclass correlation coefficient = 0.95–0.97, $P < 0.01$). Patients were required to maintain a seated position, with their arms relaxed at their sides (Fig. 2). NIRS measurements were carried out by a single trained physical therapist, and completed within a few minutes.

Statistical analysis

Pearson's correlation coefficient was used to determine the relationship between AMM or AFM and each OD value. Equations for estimation of AMM and AFM were developed with the use of multiple linear regression analysis. Potential explanatory variables included OD value, height and weight. DXA-measured AMM and AFM were set as the objective variable. The coefficient of determination (R^2) values were used to quantify the accuracy of model fit. The mean difference between DXA-measured AMM (AFM) and estimated AMM (AFM) was tested using the paired Student's *t*-test. Statistical analyses were carried out using PASW Statistics 18 for Windows (SPSS, Chicago, IL, USA) and the significance level was less than 5%.

Results

The characteristics of the patients are shown in Table 1. Mean age was 73.2 ± 6.8 years (range 62–84 years) and 70% were female. The subjects were diagnosed with the following: spinal canal stenosis ($n = 11$), disc herniation ($n = 1$), spinal tumor ($n = 2$), knee osteoarthritis ($n = 2$), compression fracture ($n = 1$), femoral neck fracture ($n = 1$) and others ($n = 2$).

The correlation coefficients between AMM or AFM and each OD value are listed in Table 2. AMM was significantly correlated with OD values at the distal triceps (OD1: $r = 0.623$; OD2: $r = 0.534$). AFM was significantly correlated with OD values at the distal biceps (OD1 $r = -0.570$; OD2 $r = -0.551$), distal triceps (OD1 $r = -0.483$; OD2 $r = -0.494$) and proximal flexor carpi radialis (OD1 $r = -0.827$; OD2 $r = -0.821$). In the correlation analysis between muscle mass or fat mass and the OD value, correlation coefficients were mostly higher with OD1 than with OD2. Thus, OD1 was used as the representative value of NIRS data for the estimation equation.

The results from linear regression analyses for the multivariate models are presented in Table 3. The multiple regression equations incorporated height, weight and OD1. Using anthropometric data (height and weight) as the explanatory variables, the R^2 value of AMM and AFM were 0.81 (standard error of the estimate [SEE] = 1.67 kg) and 0.50 (SEE = 1.77 kg), respectively (model 1). When OD1 was added to the explanatory variables, the R^2 values of AMM and AFM ranged from 0.85 to 0.89, and 0.58 to 0.80, respectively (models 2–5). The highest R^2 values of AMM and AFM were 0.89 (SEE = 1.33 kg) and 0.80 (SEE = 1.16 kg), respectively, when OD1 at the proximal flexor carpi radialis was added to the explanatory variables. For separate estimation equations (upper and lower limb), the accuracy of model fit was slightly less (muscle mass $R^2 = 0.82$–0.87, fat mass $R^2 = 0.53$–0.55). There were no significant differences between DXA-measured AMM and estimated AMM (mean difference 0.01, 95% confidence interval −0.56 to 0.58), or between DXA-measured AFM and estimated AFM (mean difference −0.25, 95% confidence interval −0.75 to 0.25).

Table 1 Physical characteristics of the study participants

Variables	All subjects ($n = 20$)	Men ($n = 6$)	Women ($n = 14$)
Age (years)	73.2 ± 6.8	67.8 ± 8.1	75.5 ± 4.9
Height (cm)	153.2 ± 9.5	166.1 ± 3.2	147.8 ± 4.3
Weight (kg)	53.9 ± 10.3	64.3 ± 6.8	49.4 ± 8.2
BMI (kg/m^2)	22.8 ± 2.9	23.3 ± 2.1	22.6 ± 3.2
AMM (kg)	15.7 ± 3.7	20.5 ± 1.2	13.6 ± 2.0
AFM (kg)	4.8 ± 2.4	4.1 ± 2.2	5.1 ± 2.4
Diagnosis *n* (%)			
Spinal canal stenosis	11 (55%)		
Disc herniation	1 (5%)		
Spinal tumor	2 (10%)		
Knee osteoarthritis	2 (10%)		
Compression fracture	1 (5%)		
Femoral neck fracture	1 (5%)		
Others	2 (10%)		

Values are mean ± standard deviation or *n* (%).
AFM, dual-energy X-ray absorptiometry-derived appendicular fat mass; AMM, dual-energy X-ray absorptiometry-derived appendicular muscle mass; BMI, body mass index.

Table 2 Correlation coefficients between limb muscle mass or fat mass and each optical densities value

	Biceps		Triceps		Flexor carpi radialis	
	OD1	OD2	OD1	OD2	OD1	OD2
Upper limb muscle mass						
Four limbs	0.369	0.350	0.623**	0.534*	0.343	0.324
Upper limb	0.292	0.286	0.572**	0.462*	0.279	0.267
Upper limb fat mass						
Four limbs	−0.570**	−0.551*	−0.483*	−0.494*	−0.827**	−0.821**
Upper limb	−0.423	−0.394	−0.403	−0.411	−0.723**	−0.705**
	Quadriceps		Tibialis anterior		Calf	
	OD1	OD2	OD1	OD2	OD1	OD2
Lower limb muscle mass						
Four limbs	0.332	0.190	0.139	0.118	0.297	0.327
Lower limb	0.383	0.248	0.138	0.125	0.346	0.373
Lower limb fat mass						
Four limbs	−0.348	−0.220	−0.421	−0.388	−0.426	−0.443
Lower limb	−0.333	−0.218	−0.434	−0.401	−0.458*	−0.472*

*$P < 0.05$; **$P < 0.01$. Optical density (OD)1 = 937 nm, OD2 = 947 nm.

Discussion

Recently, Sanada *et al.* reported prediction models for skeletal muscle index using body mass index (BMI) in Japanese adults.[29] The results showed that the R^2 values for the skeletal muscle index were 0.56 in men and 0.45 in women. Similarly, Gallagher *et al.* reported that height and weight accounted for 64% and 67% of the total variance of the appendicular skeletal muscle mass in African-American and Caucasian women, respectively, and 63% and 39% of the total variance in African-American and Caucasian men, respectively.[30] These results showed the difficulty in estimating the AMM accurately using only anthropometric measurements, and the need for an objective method for accurate measurement of body composition.

To address this problem, we investigated whether AMM and AFM could be estimated by a combination of height, weight and NIRS data (OD values). The present results showed that OD1 of the proximal flexor carpi

Table 3 Regression equation for estimating appendicular muscle mass and fat mass

Model	Equation	R^2	SEE
Appendicular muscle mass			
1	$y = 0.23 \times$ (height) + $0.13 \times$ (weight) − 26.35	0.81	1.67
2	$y = 0.17 \times$ (height) + $0.17 \times$ (weight) + $8.45 \times$ [OD1 [biceps]) − 28.97	0.89	1.34
3	$y = 0.13 \times$ (height) + $0.18 \times$ (weight) + $10.49 \times$ (OD1 [triceps]) − 23.19	0.85	1.55
4	$y = 0.10 \times$ (height) + $0.24 \times$ (weight) + $7.82 \times$ (OD1 [flexor carpi radialis]) − 21.42	0.89	1.33
5	$y = 0.20 \times$ (height) + $0.15 \times$ (weight) + $6.12 \times$ (OD1 [calf]) − 29.44	0.85	1.57
Appendicular fat mass			
1	$y = -0.22 \times$ (height) + $0.25 \times$ (weight) + 25.39	0.50	1.77
2	$y = -0.17 \times$ (height) + $0.21 \times$ (weight) − $7.89 \times$ (OD1 [biceps]) + 27.84	0.65	1.52
3	$y = -0.10 \times$ (height) + $0.20 \times$ (weight) − $12.11 \times$ (OD1 [triceps]) + 21.73	0.61	1.60
4	$y = -0.06 \times$ (height) + $0.12 \times$ (weight) − $10.01 \times$ (OD1 [flexor carpi radialis]) + 19.08	0.80	1.16
5	$y = -0.19 \times$ (height) + $0.23 \times$ (weight) − $6.55 \times$ (OD1 [calf]) + 28.70	0.58	1.66

R^2, coefficient of determination; SEE, standard error of the estimate.

radialis, in association with anthropometric data, can provide accurate estimates of both AMM and AFM in older adults, although the NIRS data alone did not reflect muscle mass except at the distal triceps. Furthermore, compared with the estimation equation that included only anthropometric data, the estimation equation that included both anthropometric and NIRS data had a higher coefficient of determination.

In the present study, the NIRS data were obtained at six sites to determine the best location for estimating AMM and AFM. As a result, OD values measured at the distal triceps and proximal flexor carpi radialis showed a good correlation coefficient with limb muscle mass and fat mass, respectively. Yasukawa *et al.* reported that the NIRS data (OD values) measured by BFT-2000 (old model of BFT-3000) had higher correlations with percentage fat at the thinner adipose sites than thicker adipose sites,[31] and similar results were observed by Futrex 5000 in another report.[25] Inconsistent strengths of the association of OD values with total body fat at the various sites might simply be a result of differences in the depth of penetration of the infrared radiation. These results suggested that it might be preferable to carry out measurements at sites where there is little subcutaneous fat, such as the flexor carpi radialis.

There are several reports of NIRS being a valid method to assess the percentage of fat or fat mass. For example, Sawai *et al.* reported that the correlation coefficient between percentage body fat as predicted by the NIRS method and as predicted by the hydrostatic weighing technique was 0.88 ($P < 0.001$, SEE = 3.2).[24] Fuller *et al.* also suggested that NIRS methods using Futrex 5000 have the potential to replace skinfold thickness (SFT) for estimation of body composition.[25] The BFT-3000 used in the present study was developed for Japanese patients, and the principle of measurement was the same as for Futrex 5000. Our findings that NIRS data could accurately reflect fat mass are consistent with a previous study.[25] These results suggest that NIRS is a valid method for the estimation of AFM.

Other reports (by Futrex 5000) showed that NIRS might have little or no advantage over SFT in determining body composition.[32,33] One of the reasons for this controversy is that the degree of obesity differs in each patient. Elia *et al.* concluded that NIRS might underestimate body fat in very obese patients.[32] In the present study, the mean BMI of the patients was 23.3 ± 2.1 kg/m^2 in men and 22.6 ± 3.2 kg/m^2 in women, and there was no patient whose BMI was over 30 kg/m^2. Previous studies of older Japanese patients also reported a BMI ranging from 19.9 to 23.3 kg/m^2.[21,22] These results imply that NIRS data might be less affected by subcutaneous fat in older Japanese patients, and that NIRS is a valid method to assess their percentage fat and fat mass.

In contrast, NIRS data were not correlated significantly with whole and regional muscle mass except in the distal triceps. It is possible that quantitative assessment of skeletal muscle mass might be difficult using only NIRS data, because near infrared light might not reach the deeper muscle layer. However, when bodyweight is divided into fat mass and fat-free mass, skeletal muscle constitutes the largest fraction of appendicular fat-free mass. Previous investigators also proposed several models for predicting skeletal muscle mass with DXA. Lean body mass consists mostly of skeletal muscle. If we obtain an accurate bodyweight and the fat mass, the lean body weight (i.e. skeletal muscle mass) can be calculated automatically. The results in the present study suggest that AMM might be estimated indirectly by using NIRS data and bodyweight.

The present study is limited by the small sample size and orthopedic patients who were mostly women. The estimation equations of AMM and AFM developed in

the present study might have high specificity. In addition, we did not confirm the validity of these estimation equations. Thus, further studies are required to check the validity of these equations in other older adults (cross-validity) and longitudinally monitored populations (predictive validity) in the future. Furthermore, these equations will be developed for each sex using larger samples. Finally, to our knowledge, it is unclear whether the OD value (wavelength 937–947 nm) is influenced by blood flow and oxygen saturation. In the previous study, investigators did not mention this point. However, all patients were maintained in a resting position before and during the measurement in the present study. We think that the influence of blood flow and oxygen saturation is not likely to be marked, but this should be considered in a future study.

In conclusion, NIRS data can provide reliable and accurate estimates of AMM and AFM in older adults with the use of anthropometric data (height and weight). The estimation equations of AMM and AFM suggest the possibility that NIRS is a convenient method to assess body composition and to screen sarcopenic (or sarcopenic-obesity) patients. For further adjustment of this equation, it might be expected that sarcopenia or sarcopenic-obesity patients can be screened easily.

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Disclosure statement

The authors have no financial disclosures or other conflicts of interest to report.

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