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Authors' contributions
HS and MS were responsible for the study concept and design. HS was responsible for the draft of the manuscript. MI, TI, KH, and TS were responsible for the critical revision of the manuscript for important intellectual content. KK was responsible for the coordination of acquisition of data. All authors were responsible for the final approval of the manuscript.

Competing interests
The authors declare that they have no competing interests.

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Effects of Exercise and Amino Acid Supplementation on Body Composition and Physical Function in Community-Dwelling Elderly Japanese Sarcopenic Women: A Randomized Controlled Trial

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OBJECTIVES: To evaluate the effectiveness of exercise and amino acid supplementation in enhancing muscle mass and strength in community-dwelling elderly sarcopenic women.

DESIGN: Randomized controlled trial.

SETTING: Urban community in Tokyo, Japan.

PARTICIPANTS: One hundred fifty-five women aged 75 and older were defined as sarcopenic and randomly assigned to one of four groups: exercise and amino acid supplementation (exercise + AAS; n = 38), exercise (n = 39), amino acid supplementation (AAS; n = 39), or health education (HE; n = 39).

INTERVENTION: The exercise group attended a 60-minute comprehensive training program twice a week, and the AAS group ingested 3 g of a leucine-rich essential amino acid mixture twice a day for 3 months.

MEASUREMENTS: Body composition was determined using bioelectrical impedance analysis. Data from interviews and functional fitness parameters such as muscle strength and walking ability were collected at baseline and after the 3-month intervention.

RESULTS: A significant group × time interaction was seen in leg muscle mass ($P = .007$), usual walking speed ($P = .007$), and knee extension strength ($P = .017$). The within-group analysis showed that walking speed significantly increased in all three intervention groups, leg muscle mass in the exercise + AAS and exercise groups, and knee extension strength only in the exercise + AAS group (9.3% increase, $P = .01$). The odds ratio for leg muscle mass and knee extension strength improvement was more than four times as great in the exercise + AAS group (odds ratio = 4.89, 95% confidence interval = 1.89–11.27) as in the HE group.

CONCLUSION: The data suggest that exercise and AAS together may be effective in enhancing not only muscle strength, but also combined variables of muscle mass and walking speed and of muscle mass and strength in sarcopenic women. J Am Geriatr Soc 60:16–23, 2012.

Key words: sarcopenic women; exercise; amino acid supplementation; muscle mass; muscle strength

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Sarcopenia, defined as age-related involuntary loss of skeletal muscle mass and strength,[1,2] has been associated with physical disability, functional decline, falls, impaired mobility, and mortality in elderly people.[3,4] Therefore, treating or reversing sarcopenia is important in the maintenance of health and life expectancy in the elderly population. Although many factors, such as chronic disease, physical inactivity, and decreased muscle protein synthesis, may contribute to loss of muscle mass,[5–7] it has been suggested that only skeletal muscle disuse and undernutrition are potentially preventable or reversible with targeted interventions.[8]

Many studies have shown a strong relationship between resistance exercise and strength improvement, through which the efficacy of resistance exercise for the prevention and treatment of sarcopenia has been confirmed.[9] The previous studies have also shown that ingestion of essential amino acids can induce muscle protein anabolism in elderly adults.[10,11] One study showed that the combination of resistance exercise and essential amino acid supplementation (AAS) augmented muscle protein

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synthesis, suggesting it as a strategy to reverse sarcopenia[12] but in a small sample size. There are few randomized controlled trials (RCTs) on the effects of exercise and AAS on body composition and functional capacity.

The purpose of this study was to investigate the effects of exercise and AAS on muscle mass, strength, and walking ability in sarcopenic women.

METHODS

Subjects

A letter outlining the comprehensive geriatric health examination survey, describing its objective and the way that the personal data would be used, was mailed to the women randomly selected from the Basic Resident Register of 5,932 people aged 75 and older residing in the Itabashi ward of metropolitan Tokyo inviting them to participate in the study. Two thousand eighteen people responded to the mailed letters of invitation to participate in the study, with 1,670 people agreeing and 348 people declining to participate. The baseline assessment was conducted at the Tokyo Metropolitan Institute of Gerontology (TMIG) from October 12 to November 3, 2008. One thousand three hundred eighty-three women aged 75 and older were screened; 287 who originally agreed to participation were absent. Written informed consent was obtained for baseline screening; six people did not sign the informed consent form and were not included in this study.

Three hundred four of 1,377 women (22.1%) were operationally defined as sarcopenic (Figure 1), with selection based on categorization into one or more of the following inclusion criteria groups: appendicular skeletal muscle mass/height^2 less than 6.42 kg/m^2 and knee extension strength less than 1.01 Nm/kg[13,14] (n = 68), appendicular skeletal muscle mass/height^2 less than 6.42 kg/m^2 and usual walking speed less than 1.22 m/s (n = 65),[14] body mass index (BMI) less than 22.0 kg/m^2[14] and knee

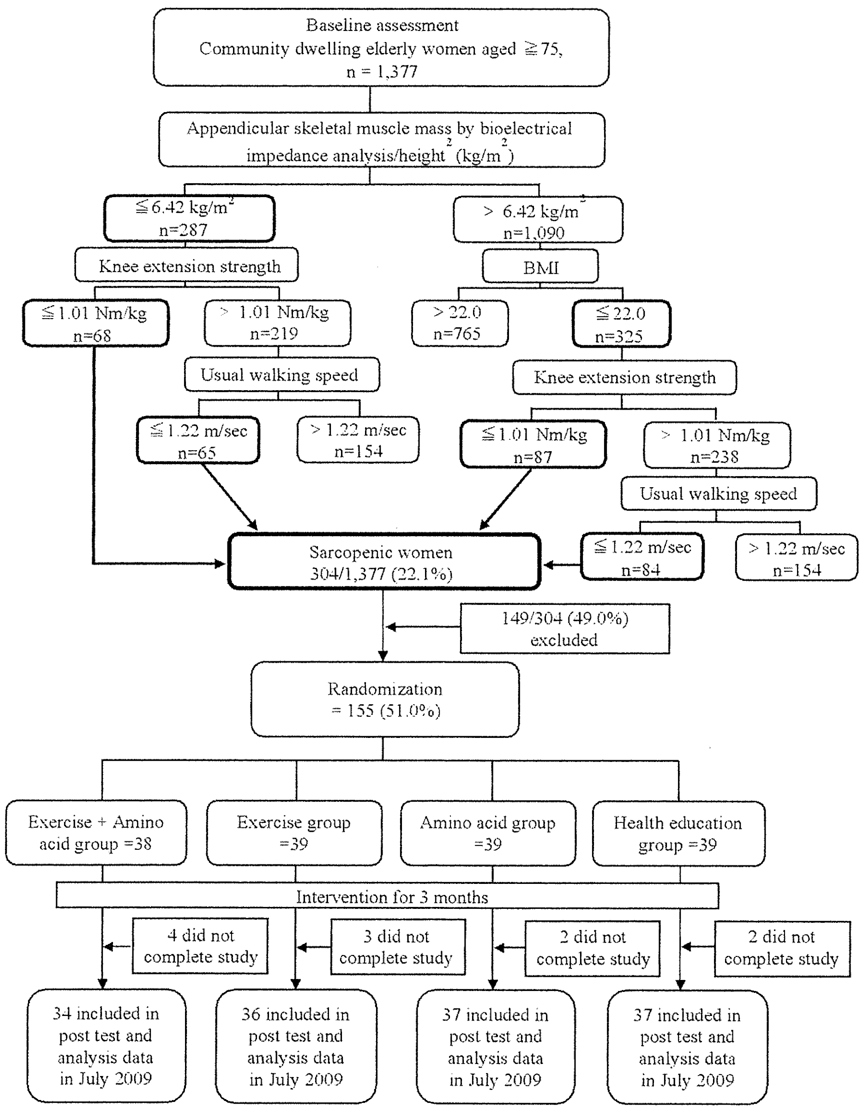

Figure 1. Algorithm for the selection of women who were operationally defined as sarcopenic and flowchart of participants in the randomized controlled trial of exercise and amino acid supplementation.

extension strength less than 1.01 Nm/kg (n = 87), and BMI less than 22.0 kg/m^2 and usual walking speed less than 1.22 m/s (n = 84). Exclusion criteria were severe knee or back pain; severely impaired mobility; impaired cognition (Mini-Mental State Examination (MMSE) score < 24);[16] missing baseline data; and unstable cardiac conditions such as ventricular dysrhythmias, pulmonary edema, or other musculoskeletal conditions. One hundred forty-nine (49.0%) of the potential sarcopenic participants were excluded because they were classified into one or more of the exclusion criteria or declined participation. The Clinical Research Ethics Committee of TMIG approved the study protocol. The intervention procedures were fully explained to all participants, and written informed consent was obtained (Figure 1).

Randomization

Randomization was performed after the baseline assessment; any variable that identified personal information was not included in the randomization process. Computer-generated random numbers were assigned to 155 participants who were then sorted and divided into four equal groups. The groups were randomly assigned to one of the four interventions groups: exercise + AAS (n = 38), exercise (n = 39), AAS (n = 39), or health education (HE; n = 39). All participants agreed to the group allocations that were mailed to them. There was no attempt to equalize the size of the groups based on their characteristics or to recruit subjects with specific characteristics. The co-investigators were blind to the randomization procedure and group allocations, separate physical therapy staff members who were also blind to the allocation of treatments collected data.

Outcome Measures

Outcome measures were evaluated according to data collected from interviews, body composition assessments using bioelectrical impedance analysis (BIA), and physical fitness tests at baseline and after the 3-month intervention.

Interview Survey

Face-to-face interviews were conducted to assess the individual's history of fractures and falls over the previous year, number of falls, cause of falls, urinary incontinence, exercise habits, smoking status, and MMSE score.

Body Composition Assessment

Measurements of height and weight were used to calculate BMI (kg/m^2). Body composition was measured using a segmental multifrequency BIA instrument that operated at frequencies of 5, 50, 250, and 550 kHz (Well-Scan 500, Elk Corp., Tokyo, Japan). Participants removed their socks, stood on two metallic electrodes on the floor scale barefoot, and held metallic grip electrodes placed in the palm of the hand with the fingers wrapped around the handrails. Using segmental body composition and muscle mass values of both legs, both arms, and the trunk, appendicular skeletal muscle mass and leg muscle mass values were obtained and used for analysis by summing the appropriate segmental muscle mass values.[13,17,18] Reliability of body composition measurements in all 155 participants in this study was not analyzed, although for the AAS group (n = 39), measurements were taken for a second time 1 week after baseline testing, and reliability was examined; the intraclass correlation coefficients (ICC) were: 0.98 for the right arm, 0.97 for the left arm, 0.97 for the right leg, 0.96 for the left leg, and 0.93 for the trunk.

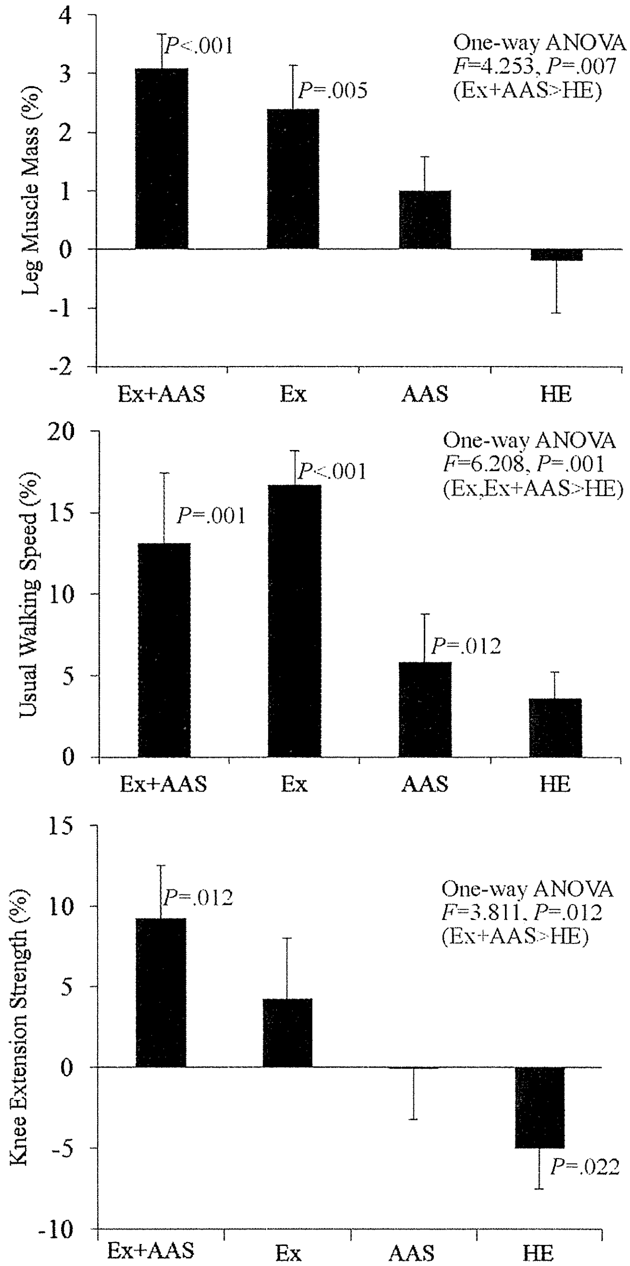

Figure 2. Mean percentage changes (standard errors) in leg muscle mass, usual walking speed, and knee extension strength after exercise (Ex), amino acid supplementation (AAS), both (Ex + AAS), or health education (HE). Bars indicate average changes from baseline to after the 3-month intervention. ANOVA = analysis of variance.

Functional Fitness Test

Calf girth and functional fitness variables including usual and maximum walking speeds and knee extension strength were measured. In measures of walking speed, participants were allowed to use assistive walking devices only if they expressed strong concerns about walking without a device or if there was any danger of falling. The knee extension strength measurement was taken twice, and the higher value divided by body weight (Nm/kg) were analyzed. The procedures for the functional fitness tests have been described in detail in previous reports.[19,20]

Intervention

Exercise

A comprehensive physical fitness and muscle mass enhancement training program of moderate intensity was provided for the participants in the exercise groups. The exercise intervention consisted of 60-minute exercise sessions held at the TMIG twice per week for 3 months. Each exercise intervention group was divided into two subgroups, with participants exercising together within their assigned group in one of four exercise sessions offered per day.

Each exercise session consisted of a 5-minute warm-up, 30 minutes of strengthening exercise, 20 minutes of balance and gait training, and 5 minutes of cool down. The strengthening exercises were performed in a progressive sequence from seated to standing positions. For each type of exercise, participants were instructed to complete up to eight repetitions of the movements. When the exercises were properly executed without significant fatigue or loss of proper execution, the resistance was increased. The progressive resistance was provided through the use of resistance bands or ankle weights. Intensity was maintained at approximately 12 to 14 on the Borg Rate of Perceived Exertion scale.[21] The principal investigator, along with the exercise instructor and assistant trainers, assessed each individual's ability to increase intensity.

Chair exercise: The chair-seated exercises were used in the early stages of the program because the participants were frail older adults and it provided a secure and stable position. Repetitions of toe raises, heel raises, knee lifts, knee extensions, and others were performed while seated on a chair. Hip flexions, lateral leg raises, and repetitions of other exercises were performed standing upright behind the chair and holding the back of the chair for stability.

Ankle-weight exercise: To strengthen lower extremities, a fixed weight was placed on the ankle while participants performed strengthening exercises. Weights of 0.50, 0.75, 1.00, and 1.50 kg were prepared and used in accordance with each participant's strength level as the resistance progressively increased. The exercises performed using these ankle weights included seated knee flexion and extension and standing knee flexion and extensions.

Exercises using a resistance band: Resistance bands were used to strengthen the upper and lower body. Lower body exercises included leg extension and hip flexion. Upper body exercises included double-arm pull downs and biceps curls.

Balance and gait training: The balance training was focused on improvement of static, dynamic, and lateral balancing ability. Exercises included standing on one leg, multidirectional weight shifts, tandem stand, and tandem walk. Participants practiced proper gait mechanics that focused on the maintenance of stability during walking and increasing stride length, toe elevation of the forward limb, heel elevation of the rear limb, frequency of stepping, and heel–floor angle. Exercises included raising the toes (dorsiflexion) during the forward swing of the leg, kicking off the floor with the ball of the foot, walking with directional changes, and gait pattern variations.

Amino Acid Supplementation

Essential AAS was provided for the participants in the AAS groups every 2 weeks. Packets of powdered amino acid supplements (42.0% leucine, 14.0% lysine, 10.5% valine, 10.5% isoleucine, 10.5% threonine, 7.0% phenylalanine, and 5.5% other) were provided for the participants to be taken with water or milk, and they were instructed to take the 3-g supplement two times a day (6 g daily) every day for 3 months.[22] To monitor their amino acid intake accurately, participants were given record sheets that were collected every 2 weeks on which they recorded what time of day they took the supplement and the amount of amino acid taken every day.

Health Education

Participants in the HE group took a class once a month for 3 months, a total of three times. The classes focused on cognitive function, osteoporosis, and oral hygiene. Participants were asked to continue their regular lifestyle habits, and no specific instructions on diet or physical activity were given.

Data Analysis

Sample size calculations using univariate one-factor repeated-measures analysis of variance (ANOVA) to examine significant differences in means at baseline and after the 3-month intervention ($\alpha = 0.05$, power $= 0.80$) with an effect size of 0.15 required a sample size of 28 participants. Esimating a potential attrition rate of 25%, 38 subjects per group were required.[23] One-way ANOVA was used to test any differences in baseline measures and percentage changes between groups, and chi-square tests were performed on categorical variables. Percentage changes in muscle mass and functional fitness after the intervention were calculated using the following formula: % change = ((postintervention value–baseline value)/(baseline value) × 100). Two-way repeated-measures ANOVA was used to evaluate the differences in the effect of the intervention on the outcome measures between groups, and a post hoc test was done on variables showing significant differences to determine which groups were different. Multiple logistic regressions were performed to compare the effects of the four intervention groups on each outcome variable after 3 months of intervention. All analyses were performed using SPSS version 15.0 of Windows (SPSS, Inc., Tokyo, Japan).

RESULTS

The baseline demographic, fitness, and interview variables of the participants in the four groups are summarized in Table 1. All of the baseline characteristics were similar between the groups.

The mean attendance rates during the 3-month intervention were 70.3% in the exercise + AAS group, 80.5% in the exercise group, 72.2% in the AAS group, and 71.8% in the HE group. Eleven participants (exercise + AAS = 4, exercise = 3, AAS = 2, HE = 2) were unable to complete the study after randomization because of spouse care (n = 3), admission to nursing home (n = 2), lack of motivation (n = 2), severe knee or back pain (n = 1), death (n = 1), falls and hip fracture (n = 1), and hospitalization (n = 1; Figure 2).

In comparing the pre- and postintervention changes in body composition and functional fitness of the groups (Table 2), there was a significant group × time interaction for leg muscle mass ($F = 4.253$, $P < .007$; exercise + AAS > HE), usual and maximum walking speeds (exercise and exercise + AAS > HE), and knee extension strength ($F = 3.558$, $P = .02$; exercise + AAS > HE).

The within-group analysis showed significant changes in leg muscle mass in the exercise + AAS ($P < .001$) and exercise ($P = .005$) groups and changes in usual walking speed in the exercise + AAS ($P = .001$), exercise ($P < .001$), and AAS groups ($P = .01$). Knee extension strength improved significantly only in the exercise + AAS group ($P = .01$), no improvement was seen in exercise or AAS, and a statistically significant decrease was observed in the HE group ($P = .02$; Figure 1).

Table 3 shows the effects of the type of intervention on changes in combined variables of muscle mass and physical function. Significant increases in leg muscle mass and knee extension strength (odds ratio (OR) = 4.89, 95% confidence interval (CI) = 1.89–11.27) and leg muscle mass and usual walking speed (OR = 4.11, 95% CI = 1.33–13.68) were observed in only the exercise + AAS group.

DISCUSSION

Although many definitions of sarcopenia have been reported,[1 3,24] there has recently been a focus not only on the loss of appendicular skeletal muscle mass, but also on functional decline.[25] In this study, sarcopenic women were operationally defined based on declines in muscle strength or walking ability that accompany the loss of skeletal muscle mass or low BMI. Because defining sarcopenia was beyond the scope of this study, the focus of the discussion will be on the effects of the intervention. To evaluate the intervention effects, the changes observed in the single variables as well as the combined variables will be discussed.

Many studies have focused on exercise or nutrition as interventions to reverse sarcopenia, but the results of these studies have not always been consistent.[8,9,12,26]

This study demonstrated that appendicular muscle mass and walking speed increased with the combination of exercise and essential amino acid ingestion, as well as with the separate exercise and amino acid interventions, but muscle strength improved only with the combination of exercise and amino acid ingestion.

A recently published meta-analysis[9] and a Cochrane review article also confirmed that resistance training two to three times a week can improve physical function and functional limitations and can reduce disability and muscle weakness in older people.[27] Previous studies have demonstrated that resistance training in elderly people produces

Table 1. Selected Variable Characteristics of Participants at Baseline According to Study Group

Characteristic	Exercise + AAS (n = 38)	Exercise (n = 39)	AAS (n = 39)	Health Education (n = 39)	F-Value*	P-Value*
Age, mean ± SD	79.5 ± 2.9	79.0 ± 2.9	79.2 ± 2.8	78.7 ± 2.8	0.577	.63
Height, cm, mean ± SD	147.1 ± 6.7	147.7 ± 4.4	145.8 ± 4.5	146.5 ± 4.9	0.960	.41
Body weight, kg, mean ± SD	39.5 ± 5.5	41.1 ± 4.7	40.1 ± 3.2	40.4 ± 3.9	0.874	.46
Body mass index, kg/m^2, mean ± SD	18.3 ± 2.5	18.9 ± 2.0	18.9 ± 1.6	18.8 ± 1.7	0.745	.53
Calf girth, cm, mean ± SD	18.3 ± 2.5	18.9 ± 2.0	18.9 ± 1.6	18.8 ± 1.7	0.745	.53
Lean body mass, kg, mean ± SD	29.1 ± 3.4	30.0 ± 2.6	28.8 ± 2.0	29.3 ± 2.4	1.505	.22
Muscle mass, kg, mean ± SD	26.9 ± 3.1	27.7 ± 2.3	26.5 ± 1.8	27.0 ± 2.2	1.538	.21
Appendicular muscle mass, kg, mean ± SD	13.3 ± 1.6	13.7 ± 1.3	13.1 ± 1.0	13.3 ± 1.2	1.502	.22
Legs muscle mass, kg, mean ± SD	9.8 ± 1.2	10.1 ± 1.0	9.7 ± 0.7	9.9 ± 0.9	1.570	.20
Usual walking speed, m/s, mean ± SD	1.26 ± 0.27	1.29 ± 0.28	1.29 ± 0.20	1.18 ± 0.22	1.701	.17
Maximal walking speed, m/s, mean ± SD	1.62 ± 0.37	1.67 ± 0.31	1.67 ± 0.27	1.55 ± 0.32	1.150	.33
Knee extension strength, Nm, mean ± SD	45.9 ± 11.3	46.6 ± 11.1	46.7 ± 7.8	47.4 ± 10.5	0.139	.94
Falls, %	21.1	17.9	15.4	20.5	0.519	.91
Exercise habit, %	26.3	25.6	38.5	33.3	2.029	.57
Urinary incontinence, %	44.7	38.5	41.0	25.6	3.414	.33
Osteoporosis history, %	36.8	43.6	48.7	30.8	2.987	.39
Heart disease history, %	10.5	15.4	12.8	17.9	0.977	.81
Diabetes mellitus history, %	7.9	5.1	5.1	12.8	2.156	.54

* One-way analysis of variance for continuous variables and chi-square test for categorical variables.

AAS = amino acid supplementation; SD = standard deviation.

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

Variable	Group	Mean ± Standard Deviation: Baseline	Mean ± Standard Deviation: After 3-Month Intervention	Analysis of Variance (Group × Time), *P*-Value	Post Hoc Analysis*
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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第 1 節　サルコペニアと老年症候群

Summary

- サルコペニアは，加齢に伴う筋肉量，筋力，身体機能の低下と定義づけられている．
- 老年症候群は，“加齢に伴う複数の臓器/器官の機能低下によって起こる多彩な症状/徴候”のことで，治療や管理が容易でなく，放っておくと QOL，ADL の低下につながる．
- サルコペニアがもとで，要介護状態の原因として重要な老年症候群の一つである転倒が起こる．
- 転倒の予測には Up & go テストなどの歩行機能検査の他，転倒スコアや介護予防健診の基本チェックリストが役立つ．
- 転倒予防教室や筋力訓練・バランス運動などの継続が転倒予防対策として有効である．

はじめに

サルコペニアは，高齢者が虚弱になる過程で生じる全身，特に四肢の筋肉が量的，質的に低下することを指し，これが原因で様々な老年症候群が生じる．本稿では，サルコペニアと老年症候群との関係について，特に高齢者の生活の質 (quality of life：QOL)，日常生活活動 (activities of daily living：ADL) を阻害する大きな要因である転倒との関係について説明する．

1．サルコペニア

サルコペニアは加齢に伴う筋肉量の減少および筋力の低下を指し，最近 The European Working Group on Sarcopenia in Older People から定義に関するコンセンサスが発表された[1]．同報告では，サルコペニアを筋肉量，筋力，身体機能の 3 つの観点から判断するよう推奨している．ちなみに，筋肉量は二重エネルギー X 線吸収法 (dual energy X-ray absorptiometry：DXA)，生体電気インピーダンス法 (bioelectrical impedance analysis：BIA)，CT，MRI などを用いて，筋力は握力，膝屈伸力，呼気流出速度で，身体機能は歩行速度，Up & go テスト，階段昇り時間などで測定することが紹介されている．

サルコペニアの発生原因はよくわかっていないが，図 1 に示すように，様々な要因が関わる

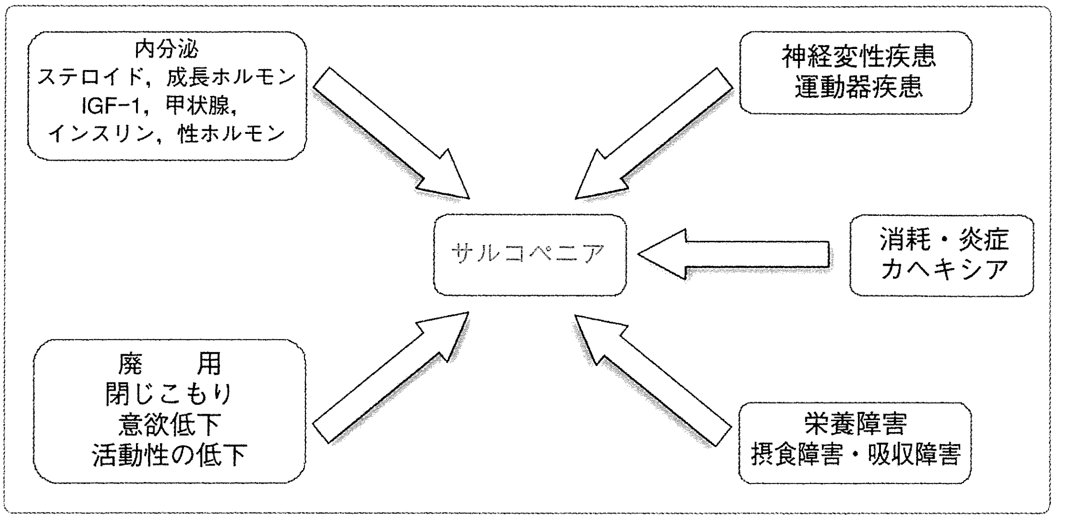

図1　サルコペニアの成因

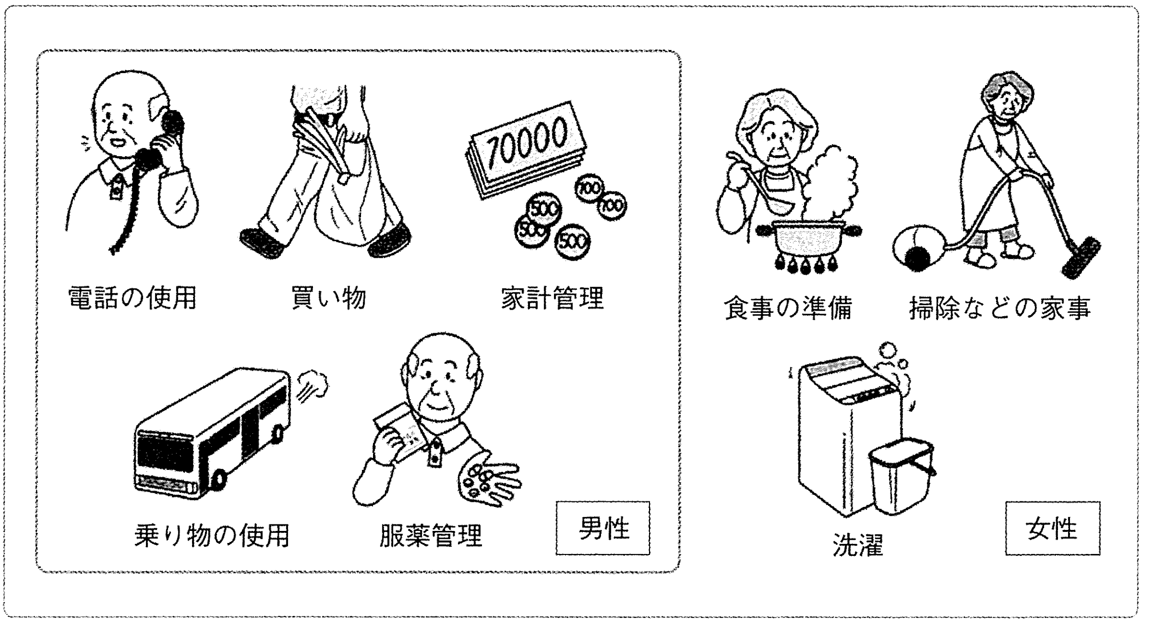

図2　IADL 尺度（Lawton & Brody）（手段的 ADL 評価法）

とされている．サルコペニアの評価方法，発生原因については他章を参照されたい．前述の報告の中には書かれていないが，身体能力として実生活上問題になるのは，手段的 ADL（IADL）の障害である．手段的 ADL は，図2に示すように，女性は8項目，男性は5項目で評価する．これらの項目に障害があると自立した生活が困難となり，要介護状態に陥る．この中でサルコペニアと特に関連が深いのは乗り物の利用である．外来通院者の場合，「乗り物を使って病院に来るのが大変になっていないか」，都市部に住む女性の場合，「比較的近傍のデパートに1人で買い物に行っているか」というような問いかけで聞き取ることができる．

2．老年症候群とサルコペニア

老年症候群とは，“加齢に伴う諸臓器/器官の

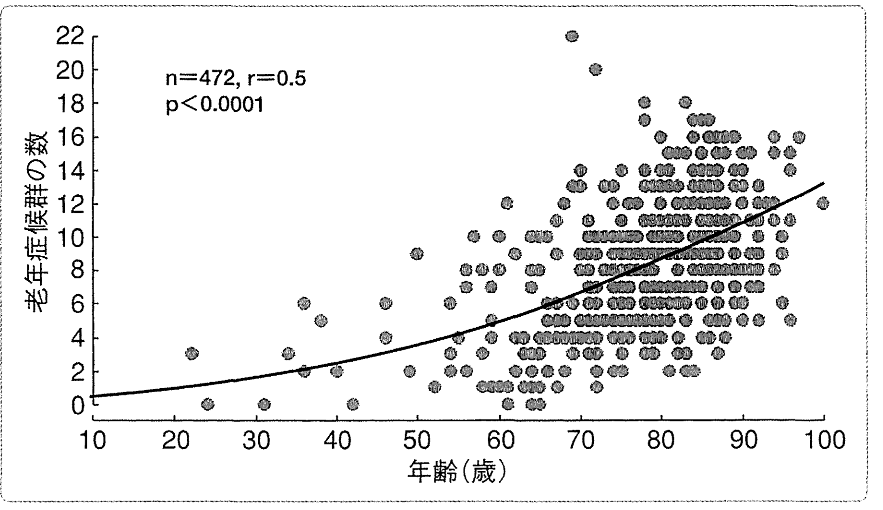

図3　加齢に伴う老年症候群の増加（文献4より引用）

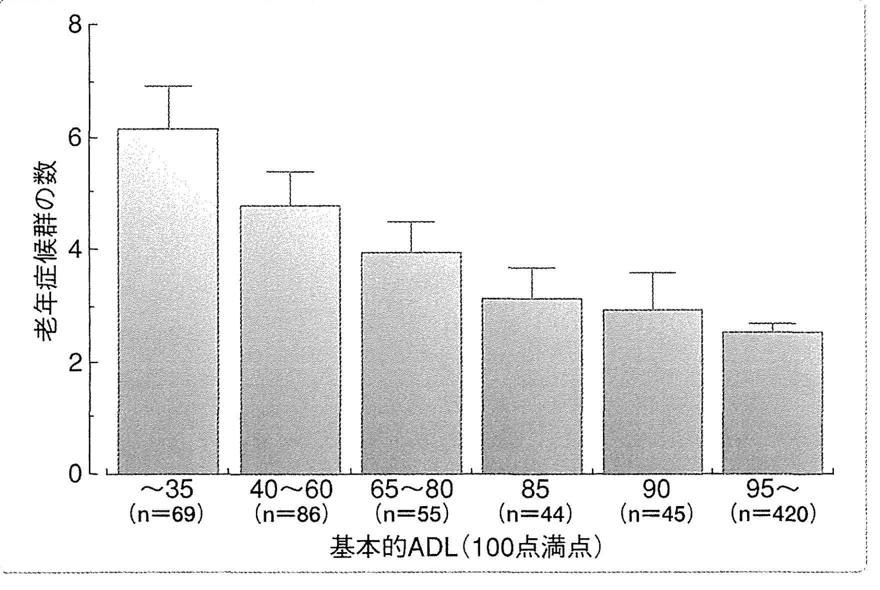

図4　基本的日常生活活動度と老年症候群

老年症候群の数が多いほど，基本的ADLは低い（基本的ADLの点数が低い）．

機能低下によって起こる多彩な症状/徴候"のことで，治療や管理が難しく，しかしながら放っておくとQOL，ADLの低下につながる．老年症候群の数は加齢とともに増加し（図3），その増加はADLの低下（図4），介護の必要性の増加につながり，結果的に，介護病床や介護老人保健施設（老健施設）での生活につながる（図5）．

老年症候群には図6に示すように様々な症候があるが，例えば歩行障害・転倒を例に挙げれば，その発生には筋力低下，バランス障害，めまい，視力低下，骨量減少，脊椎・関節の変形，脳機能の障害（認知機能障害，注意力障害，うつ，意欲低下，深部白質病変），末梢神経（表在知覚，深部知覚）障害，呼吸機能低下（慢性閉塞性肺疾患：COPDなど），循環機能低下（心不全など），転倒誘発薬物の服用など様々な要因が，複合して起こる．単一要因でなく，しか

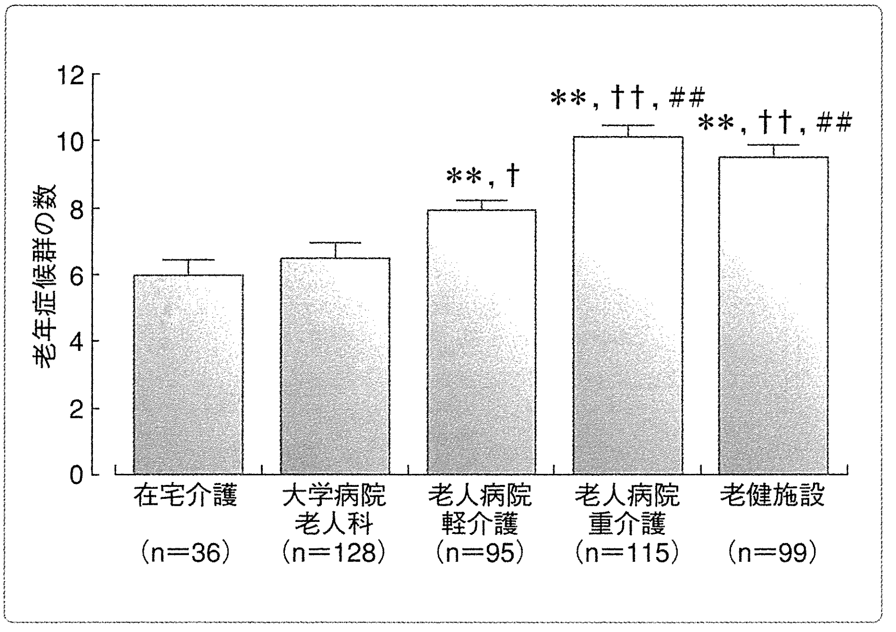

図５　施設別の老年症候群の数

＊＊：p＜0.01 vs 在宅介護．†，††：p＜0.05，0.01 vs 大学病院老人科．
##：p＜0.01 vs 老人病院軽介護．

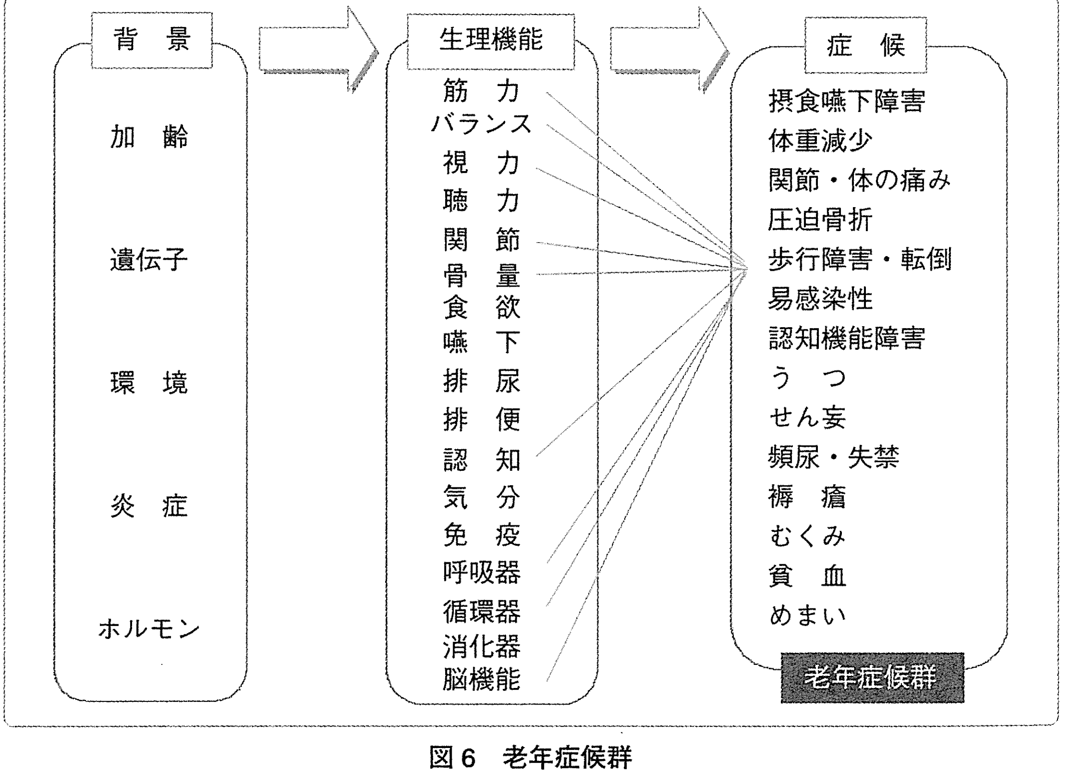

図６　老年症候群

加齢に伴って現れる様々な症候．原因は様々であり特定することは難しいが，放置すると QOL や ADL を阻害するため，早めに対処する必要がある．

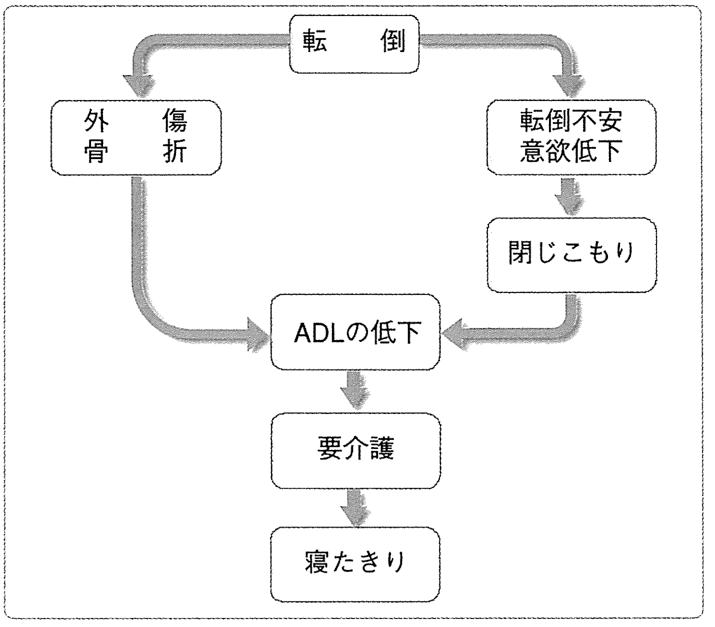

図7　転倒のもたらす影響（文献2より引用改変）

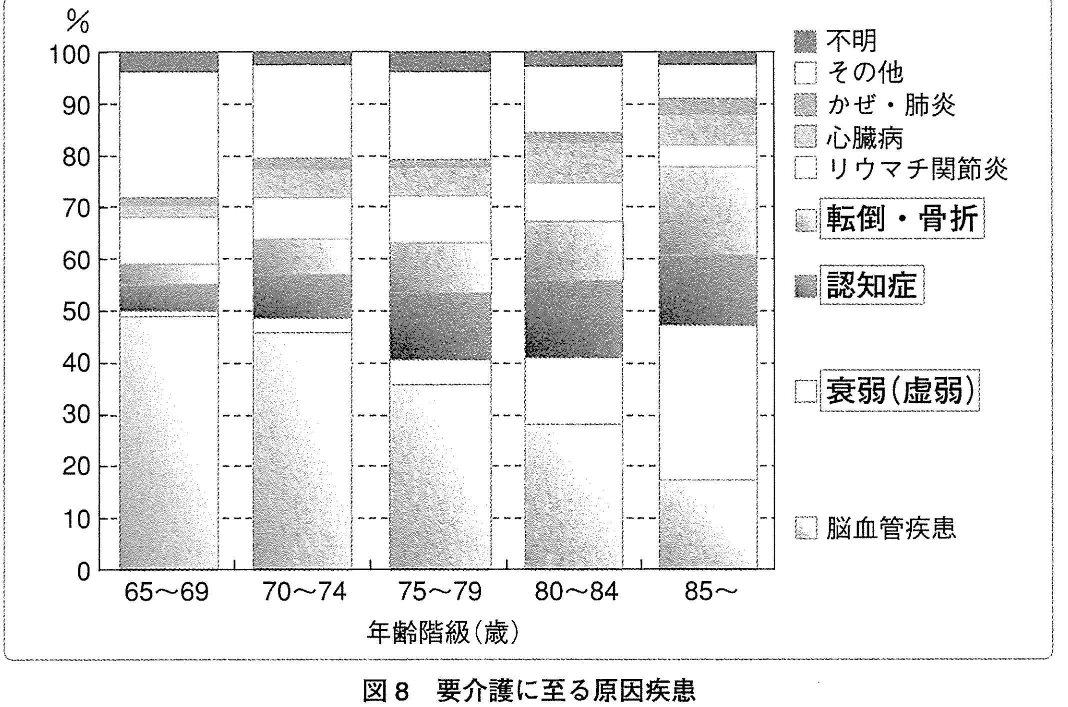

図8　要介護に至る原因疾患

も，どの要因が大きなウエイトを占めるのか判別が困難なため，介入策を講ずることが難しい．しかしながら，放っておけば歩行障害は確実に進行し，やがて転倒し，骨折もしくは閉じこもりのため寝たきりになる（図7）[2]．

老年症候群には，歩行障害・転倒以外に失禁，うつ，せん妄，摂食嚥下障害，めまい，褥瘡など様々な症候があり，それぞれが加齢に伴う複数の臓器・器官の機能の低下に起因する．病気に至らない程度の各種臓器・器官の機能低下はいわゆる虚弱と呼ばれ，その表現形が老年症候群と考えるとイメージしやすい（図6）．そして，

表1　転倒外来検査

問　診（転倒歴，ADL，環境要因，基礎疾患，服用薬物）	Up & go テスト
理学所見（神経学的検査を含む）	**転倒スコア**
身長，体重	重心動揺検査
下腿最大周囲径その他の身体計測	脊椎X線
血　圧	起立性血圧変動
握　力	視　力
下肢筋力	聴力・内耳機能
片足立ち時間（開眼，閉眼）	体脂肪率
継ぎ足歩行	骨密度測定
手伸ばし試験	頭部MRI

表2　転倒群と非転倒群の比較

	全体 (n=79)	転倒群 (n=29)	非転倒群 (n=50)	ノンパラメトリック検定
年　齢	78.1±5.9	78.3±5.0	78.0±6.4	NS
性　別	男 28，女 51	男 13，女 16	男 15，女 35	NS
転倒スコア	8.7±4.1	10.5±4.2	7.8±3.8	p=0.021
下腿最大周囲径	32.1±3.1	32.6±3.1	31.8±3.1	NS
利き手握力	14.1±6.5	14.3±7.7	14.0±5.8	NS
片足立ち持続時間	11.0±18.3	7.2±7.3	13.1±21.9	p=0.046
Up & go テスト	15.4±6.3	17.3±7.0	14.4±5.8	p=0.028
継足歩行	5.3±4.3	4.9±4.1	5.6±4.5	NS
Functional reach	24.2±6.2	22.7±6.5	25.1±5.9	p=0.026

$p<0.05$

虚弱，転倒・骨折は後期高齢者の要介護状態招来の大きな要因である（図8）.

一方，転倒以外でサルコペニアと関連する老年症候群として，摂食嚥下障害(原因として)，体重減少，関節・体の痛み，歩行障害，失禁，めまい（活動性の低下によってもたらされる）などを挙げることができる.

3．転倒の評価

以上のように転倒を起こす要因は様々あり，そのため，転倒リスクを評価することは重要である．杏林大学病院もの忘れセンターでは，転倒リスクが高いことで知られる高齢認知症患者の転倒リスクを評価するため，表1にあるような項目について外来で検査を行っている．このうち，骨密度測定（脂肪量，除脂肪量を同時に測定），体脂肪率は筋肉量の測定項目として，握力は筋力の測定項目として，Up & go テストは歩行機能として，前述の The European Working Group on Sarcopenia in Older People で推奨されている方法である.

筆者らは，もの忘れセンターを受診中の患者79名を対象に各種転倒関連検査を行い，その後1年間の転倒の有無を前向きに調査した．その結果，調査以前に転倒したことがない患者の

表３　転倒スコア

過去１年に転んだことがありますか？ 「はい」の場合，転倒回数（　　回/年）	（はい　いいえ）	
１．つまずくことがありますか？	（はい　いいえ）	身体機能
２．手すりを使わないと階段昇降ができませんか？	（はい　いいえ）	身体機能
３．歩く速度が遅くなってきましたか？	（はい　いいえ）	身体機能
４．横断歩道を青のうちに渡りきれますか？	（はい　いいえ）	身体機能
５．1 km くらい続けて歩けますか？	（はい　いいえ）	身体機能
６．片足で５秒くらい立つことができますか？	（はい　いいえ）	身体機能
７．杖を使ってますか？	（はい　いいえ）	身体機能
８．タオルはかたく絞れますか？	（はい　いいえ）	身体機能
９．めまい・ふらつきがありますか？	（はい　いいえ）	認知 感覚器 骨運動器
10．背中が丸くなってきましたか？	（はい　いいえ）	認知 感覚器 骨運動器
11．膝が痛みますか？	（はい　いいえ）	認知 感覚器 骨運動器
12．目が見えにくいですか？	（はい　いいえ）	認知 感覚器 骨運動器
13．耳が聞こえにくいですか？	（はい　いいえ）	認知 感覚器 骨運動器
14．もの忘れが気になりますか？	（はい　いいえ）	認知 感覚器 骨運動器
15．転ばないかと不安になりますか？	（はい　いいえ）	認知 感覚器 骨運動器
16．毎日，お薬を５種類以上飲んでいますか？	（はい　いいえ）	
17．家の中が暗く感じますか？	（はい　いいえ）	環境要因
18．家の中によけて通るものがありますか？	（はい　いいえ）	環境要因
19．家の中に段差がありますか？	（はい　いいえ）	環境要因
20．階段を使わなくてはなりませんか？	（はい　いいえ）	環境要因
21．生活上，急な坂道を歩きますか？	（はい　いいえ）	環境要因

表４　特定高齢者の選定基準

以下の５項目すべてに該当する場合

１．階段や手すりを壁をつたわらずに昇っていますか？
２．椅子に座った状態から何もつかまらずに立ち上がっていますか？
３．15 分くらい続けて歩いていますか？
４．この１年間に転んだことがありますか？
５．転倒に対する不安が大きいですか？

補助基準	基準値 男性	基準値 女性	配点
握力	＜29	＜19	2
開眼片足立ち時間（秒）	＜20	＜10	2
10 m 歩行速度（秒）	＞8.8	＞10.0	3
（5 m の場合）	（＞4.4	＞5.0）	

配点合計 0〜4 点…運動機能の著しい低下を認めない
5〜7 点…運動機能の著しい低下を認める

表５　転倒骨折予防事業の科学的成績（EBM）（文献６より引用）

予防事業の種類	研究数	対象数	危険度
家屋環境改善	1	530	0.64
筋力訓練・バランス訓練	3	566	0.80
太極拳	1	200	0.51
向精神薬中止	1	93	0.34
総合機能評価・個別指導	3	1,973	0.73
ヒッププロテクター	6	3,412	0.35

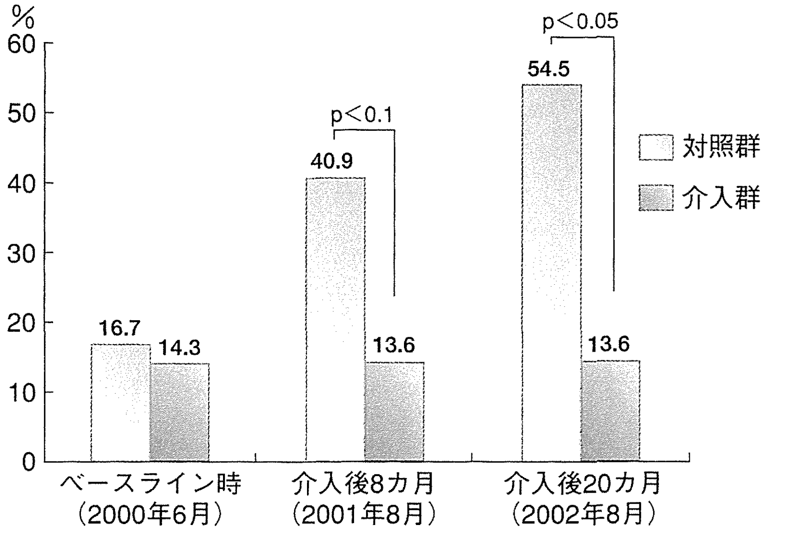

図９　トレーニングによる転倒抑制効果

その後１年間の転倒発生率が27％であったのに対して，調査以前に転倒したことのある患者のその後１年間の転倒率は47％と有意に高く，１度転倒した人は，再度，転倒しやすいことを示していた（転倒歴もサルコペニアの一つの基準と考えられる）．

その他，１年間で転倒した人としなかった人との間で，片足立ち時間（バランス保持能と筋力），Up & go テスト（起立と歩行ならびに方向転換能力），functional reach（柔軟性）において有意な差が認められた点で，転倒しやすい人の方が身体機能において sarcopenic であったことがわかる（表２）[3]．なお，筋肉量，筋力に関してはまだ十分な評価を行っていないので，今後，検討が必要である．

また，表１，２にある転倒スコア（自己記入式アンケート）は転倒予測に役立つことが示されており（表３）[4,5]，その中の質問項目1〜8は身体機能を調べるための項目になっている．また，介護予防のための特定高齢者健診基本チェックリストには，表４にあるような５つの質問項目と補助基準が設定されており，これによって転倒しやすいハイリスク高齢者を選び出す仕組みになっている．これも機能からみた sarcopenic な高齢者の選定方法である．

４．転倒予防

転倒を起こす要因は様々であり，一定の介入方法で十分な効果を上げることは難しい．それ

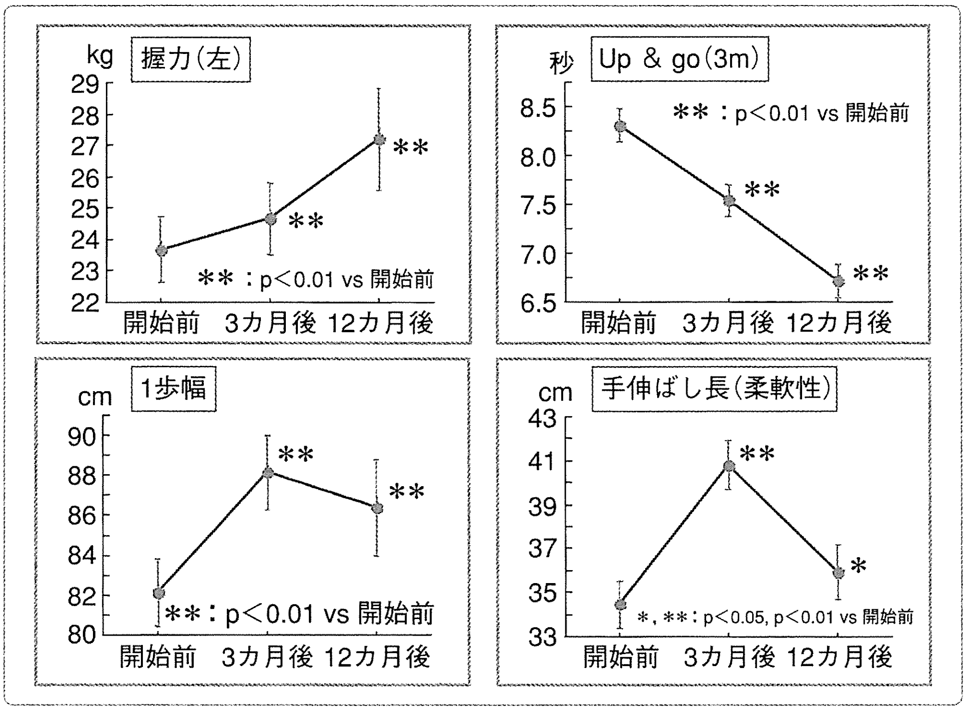

図 10　サルコペニアに対する介入の効果

でもエビデンスとして，表 5 のような方法によって，ある程度転倒の発生を減らすことができる[6]．このうち，筋力訓練・バランス運動や太極拳はサルコペニアに対する介入手段と考えてよいだろう．わが国では数少ない無作為割付け比較介入試験の一つとして，鈴木らが独歩可能な地域在住高齢女性（73〜90 歳）に対して，6 カ月間の転倒予防教室と在宅での継続的な運動によって，その後約 1.5 年間にわたって，転倒の発生を抑えることができたことを報告している（図 9）[7]．

筆者らも，長野県の地域在住高齢者に対して 3 カ月間，専属トレーナーが月 2 回各 30 分間運動を指導し，かつ在宅でも続けるよう指示した結果，握力，Up & go テスト，歩幅，柔軟性に改善が認められること，すなわち，サルコペニアの予防，改善につながる可能性を示す結果を得た（図 10）．

おわりに

本稿では，サルコペニアを老年症候群，中でも直接帰結する転倒との関係で考察した．サルコペニアの研究は老年医学研究の柱になるものであり，発生メカニズムの解明のほか，治療・介入によって，歩行機能，転倒をはじめとする老年症候群の発生に対してどれだけ改善・予防効果をもたらすのか，ひいては介護予防，寝たきり予防にどこまで貢献するのか，今後の研究の発展が期待される．

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認知症学 下
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III. 臨　床　編

認知症の重症化に伴う医学的諸問題　各論

老年症候群と高齢者総合機能評価

神崎恒一