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

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...
synthesis, suggesting it as a strategy to reverse sarcopenia 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 (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), body mass index (BMI) less than 22.0 kg/m^2 and knee extension strength less than 1.01 Nm/kg (n = 87), usual walking speed less than 1.22 m/s (n = 154), body mass index (BMI) less than 22.0 kg/m^2 and knee extension strength less than 1.01 Nm/kg (n = 325), usual walking speed less than 1.22 m/s (n = 154).

Baseline assessment

Community dwelling elderly women aged ≥75, n=1,377

Appendicular skeletal muscle mass by bioelectrical impedance analysis/height^2 (kg/m^2)

≤6.42 kg/m^2 n=287

Knee extension strength

≥1.01 Nm/kg n=68

> 1.01 Nm/kg n=219

BMI

>22.0 n=765

≤22.0 n=325

Usual walking speed

≤1.22 m/sec n=65

>1.22 m/sec n=154

Sarcopenic women 304/1,377 (22.1%)

149/304 (49.0%) excluded

Randomization =155 (51.0%)

Exercise + Amino acid group =38

Exercise group =39

Amino acid group =39

Health education group =39

Intervention for 3 months

4 did not complete study

3 did not complete study

2 did not complete study

2 did not complete study

34 included in post test and analysis data in July 2009

36 included in post test and analysis data in July 2009

37 included in post test and analysis data in July 2009

37 included in post test and analysis data in July 2009

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/m² 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/m²). 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 (\(\alpha = 0.05\), \(\beta = 0.80\)) with an effect size of 0.15 required a sample size of 28 participants. Estimating 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 = \(((\text{postintervention value–baseline value}) / \text{baseline value}) \times 100\). 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 + 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.2,5 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-analysis9 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>
<thead>
<tr>
<th>Characteristic</th>
<th>Exercise + AAS (n = 38)</th>
<th>Exercise (n = 39)</th>
<th>AAS (n = 39)</th>
<th>Health Education (n = 39)</th>
<th>F-Value*</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>79.5 ± 2.9</td>
<td>79.0 ± 2.9</td>
<td>79.2 ± 2.8</td>
<td>78.7 ± 2.8</td>
<td>0.577</td>
<td>.63</td>
</tr>
<tr>
<td>Height, cm, mean ± SD</td>
<td>147.1 ± 6.7</td>
<td>147.7 ± 4.4</td>
<td>145.8 ± 4.5</td>
<td>146.5 ± 4.9</td>
<td>0.860</td>
<td>.41</td>
</tr>
<tr>
<td>Body weight, kg, mean ± SD</td>
<td>39.5 ± 5.5</td>
<td>41.1 ± 4.7</td>
<td>40.1 ± 3.2</td>
<td>40.4 ± 3.9</td>
<td>0.874</td>
<td>.46</td>
</tr>
<tr>
<td>Body mass index, kg/m², mean ± SD</td>
<td>18.3 ± 2.5</td>
<td>18.9 ± 2.0</td>
<td>18.9 ± 1.6</td>
<td>18.8 ± 1.7</td>
<td>0.745</td>
<td>.53</td>
</tr>
<tr>
<td>Calf girth, cm, mean ± SD</td>
<td>18.3 ± 2.5</td>
<td>18.9 ± 2.0</td>
<td>18.9 ± 1.6</td>
<td>18.8 ± 1.7</td>
<td>0.745</td>
<td>.53</td>
</tr>
<tr>
<td>Lean body mass, kg, mean ± SD</td>
<td>29.1 ± 3.4</td>
<td>30.0 ± 2.6</td>
<td>28.8 ± 2.0</td>
<td>29.3 ± 2.4</td>
<td>1.505</td>
<td>.22</td>
</tr>
<tr>
<td>Muscle mass, kg, mean ± SD</td>
<td>26.9 ± 3.1</td>
<td>27.7 ± 2.3</td>
<td>26.5 ± 1.8</td>
<td>27.0 ± 2.2</td>
<td>1.538</td>
<td>.21</td>
</tr>
<tr>
<td>Appendicular muscle mass, kg, mean ± SD</td>
<td>13.3 ± 1.6</td>
<td>13.7 ± 1.3</td>
<td>13.1 ± 1.0</td>
<td>13.3 ± 1.2</td>
<td>1.502</td>
<td>.22</td>
</tr>
<tr>
<td>Legs muscle mass, kg, mean ± SD</td>
<td>9.8 ± 1.2</td>
<td>10.1 ± 1.0</td>
<td>9.7 ± 0.7</td>
<td>9.9 ± 0.9</td>
<td>1.570</td>
<td>.20</td>
</tr>
<tr>
<td>Usual walking speed, m/s, mean ± SD</td>
<td>1.26 ± 0.27</td>
<td>1.29 ± 0.28</td>
<td>1.29 ± 0.2</td>
<td>1.18 ± 0.22</td>
<td>1.701</td>
<td>.17</td>
</tr>
<tr>
<td>Maximal walking speed, m/s, mean ± SD</td>
<td>1.62 ± 0.37</td>
<td>1.67 ± 0.31</td>
<td>1.67 ± 0.27</td>
<td>1.55 ± 0.32</td>
<td>1.150</td>
<td>.33</td>
</tr>
<tr>
<td>Knee extension strength, Nm, mean ± SD</td>
<td>45.9 ± 11.3</td>
<td>46.6 ± 11.1</td>
<td>46.7 ± 7.8</td>
<td>47.4 ± 10.5</td>
<td>0.139</td>
<td>.94</td>
</tr>
<tr>
<td>Falls, %</td>
<td>21.1</td>
<td>17.9</td>
<td>15.4</td>
<td>20.5</td>
<td>0.519</td>
<td>.91</td>
</tr>
<tr>
<td>Exercise habit, %</td>
<td>26.3</td>
<td>25.6</td>
<td>38.5</td>
<td>33.3</td>
<td>2.029</td>
<td>.57</td>
</tr>
<tr>
<td>Urinary incontinence, %</td>
<td>44.7</td>
<td>38.5</td>
<td>41.0</td>
<td>25.6</td>
<td>3.414</td>
<td>.33</td>
</tr>
<tr>
<td>Osteoporosis history, %</td>
<td>36.8</td>
<td>43.6</td>
<td>48.7</td>
<td>30.8</td>
<td>2.987</td>
<td>.39</td>
</tr>
<tr>
<td>Heart disease history, %</td>
<td>10.5</td>
<td>15.4</td>
<td>12.8</td>
<td>17.9</td>
<td>0.977</td>
<td>.81</td>
</tr>
<tr>
<td>Diabetes mellitus history, %</td>
<td>7.9</td>
<td>5.1</td>
<td>5.1</td>
<td>12.8</td>
<td>2.156</td>
<td>.54</td>
</tr>
</tbody>
</table>

* One-way analysis of variance for continuous variables and chi-square test for categorical variables. AAS = amino acid supplementation; SD = standard deviation.
9% to 15% increases in strength and approximately 5% in thigh muscle volume. Also, many studies have shown that resistance training in elderly people must be conducted at high intensities and volumes to see improvements. 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

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Baseline</th>
<th>After 3-Month Intervention</th>
<th>Analysis of Variance (Group × Time), P-Value</th>
<th>Post Hoc Analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle mass, kg</td>
<td>Exercise + AAS</td>
<td>26.76 ± 2.77</td>
<td>27.26 ± 3.04</td>
<td>F = 1.076, .36</td>
<td>Exercise + AAS &gt; HE</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>28.09 ± 1.90</td>
<td>28.53 ± 2.39</td>
<td></td>
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<td></td>
<td>AAS</td>
<td>26.25 ± 1.81</td>
<td>26.53 ± 2.10</td>
<td></td>
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<tr>
<td></td>
<td>HE</td>
<td>27.48 ± 2.04</td>
<td>27.66 ± 2.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appendicular muscle mass, kg</td>
<td>Exercise + AAS</td>
<td>13.25 ± 1.35</td>
<td>13.59 ± 1.53</td>
<td>F = 1.354, .26</td>
<td>Exercise + AAS &gt; HE</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>13.90 ± 1.06</td>
<td>14.19 ± 1.33</td>
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<tr>
<td></td>
<td>AAS</td>
<td>12.86 ± 0.99</td>
<td>13.03 ± 1.10</td>
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<tr>
<td></td>
<td>HE</td>
<td>13.57 ± 1.16</td>
<td>13.67 ± 1.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legs muscle mass, kg</td>
<td>Exercise + AAS</td>
<td>9.76 ± 1.01</td>
<td>10.07 ± 1.13</td>
<td>F = 4.253, .007</td>
<td>Exercise + AAS &gt; HE</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>10.28 ± 0.81</td>
<td>10.53 ± 1.05</td>
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<tr>
<td></td>
<td>AAS</td>
<td>9.55 ± 0.73</td>
<td>9.65 ± 0.83</td>
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<tr>
<td></td>
<td>HE</td>
<td>10.14 ± 0.87</td>
<td>10.11 ± 0.81</td>
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<td></td>
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<tr>
<td>BMI, kg/m²</td>
<td>Exercise + AAS</td>
<td>18.30 ± 2.64</td>
<td>18.14 ± 2.68</td>
<td>F = 0.606, .61</td>
<td>Exercise + AAS &gt; HE</td>
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<tr>
<td></td>
<td>Exercise</td>
<td>18.80 ± 1.30</td>
<td>18.50 ± 1.41</td>
<td></td>
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<tr>
<td></td>
<td>AAS</td>
<td>18.84 ± 1.43</td>
<td>18.56 ± 1.62</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>HE</td>
<td>18.83 ± 1.75</td>
<td>18.77 ± 1.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual walking speed, m/s</td>
<td>Exercise + AAS</td>
<td>1.27 ± 0.25</td>
<td>1.43 ± 0.29</td>
<td>F = 4.213, .007</td>
<td>Exercise + AAS &gt; HE</td>
</tr>
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<td></td>
<td>Exercise</td>
<td>1.31 ± 0.24</td>
<td>1.50 ± 0.23</td>
<td></td>
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<tr>
<td></td>
<td>AAS</td>
<td>1.30 ± 0.18</td>
<td>1.36 ± 0.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HE</td>
<td>1.19 ± 0.21</td>
<td>1.22 ± 0.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum walking speed, m/s</td>
<td>Exercise + AAS</td>
<td>1.64 ± 0.34</td>
<td>1.92 ± 0.37</td>
<td>F = 9.374, .001</td>
<td>Exercise + AAS &gt; HE</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>1.72 ± 0.27</td>
<td>2.04 ± 0.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>AAS</td>
<td>1.71 ± 0.28</td>
<td>1.92 ± 0.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HE</td>
<td>1.57 ± 0.31</td>
<td>1.64 ± 0.31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee extension strength, Nm/kg</td>
<td>Exercise + AAS</td>
<td>1.15 ± 0.27</td>
<td>1.23 ± 0.29</td>
<td>F = 3.558, .02</td>
<td>Exercise + AAS &gt; HE</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>1.12 ± 0.30</td>
<td>1.14 ± 0.26</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>AAS</td>
<td>1.15 ± 0.25</td>
<td>1.14 ± 0.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HE</td>
<td>1.14 ± 0.26</td>
<td>1.00 ± 0.26</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* A post hoc analysis was performed using the Scheffe method.

AAS = amino acid supplementation; HE = health education; BMI = body mass index.

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

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

Reference: health education.

* 1 = improve, 0 = no change or decrease.

AAS = amino acid supplementation.
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. 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. 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. 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. 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, 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. 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 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. 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. 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 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.

**Sponsor's Role:** The sponsors had no role in the design of this study, subject recruitment, baseline and post survey, development of the intervention program, data analysis, or preparation of the manuscript.

**REFERENCES**