

# Serum Albumin Levels as a Predictive Biomarker for Low-Load Resistance Training Programs' Effects on Muscle Thickness in the Community-Dwelling Elderly Japanese Population: Results From the Interventional Study

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## Research Article

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# Abstract

**Background** Resistance training has been recommended as an effective measure against age-related loss of muscle mass and muscle strength, called sarcopenia, even in older adults. However, despite subjecting each participant to the same training program, the training effect solely depended on the individual. This study aimed to evaluate whether certain blood parameters influenced the effect of a low-load resistance training program on muscle thickness in the community-dwelling elderly population.

**Methods** Sixty-nine community-dwelling Japanese (49 women and 20 men) subjects aged  $69.4 \pm 6.5$  years were included. Low-load resistance training was performed twice a week for 12 weeks. Muscle thickness at the anterior aspects of the thigh (AT) was measured using a B-mode ultrasound device, and 22 blood parameter levels were assessed before and after the program. We checked the first quartile value of each parameter to establish cutoff values, and participants were divided into low or normal groups for each parameter.

**Results** A low-load resistance training program significantly increased muscle thickness at the AT. The interaction between time and groups was examined at low ( $<4.1$  g/dL) versus normal ( $\geq 4.1$  g/dL) serum albumin (Alb) levels. Although there was no difference in muscle thickness at the AT before the training intervention, the hypertrophic effects were higher in the normal serum Alb level group than in the low serum Alb level group. The binomial logistic regression analysis showed that participants in the low serum Alb group had an odds ratio of 7.08 for decreased muscle thickness at the AT. The effect of a low-load resistance training program on lower limb muscle thickness appears to be limited in participants with low serum Alb levels before training interventions.

**Conclusions** Serum Alb level may act as a biomarker to predict the effects of low-load resistance training programs on muscle hypertrophy in elderly individuals.

**Trial registration** This study was retrospectively registered in UMIN-Clinical Trial Registry (CTR), ID: UMIN000042759. Date of registration: 14/12/2020.

## Background

Skeletal muscle plays an important role in physical functions related to the activities of daily living [1] and in systemic energy regulation controlled by glucose and lipid metabolism [2]. Despite playing a major role in systemic homeostasis, skeletal muscle size and strength both decrease with age [3, 4]. This age-related loss of muscle mass and muscle strength, called sarcopenia, is related to a wide range of chronic disorders [5–8], motor disorders [9, 10], and mortality [11]. Because of this, sarcopenia is a primary therapeutic target for improving the effects of aging in the elderly, and it has been reported that exercise intervention, especially involving resistance training, is a key approach for preventing and improving sarcopenia [12, 13].

Resistance training has been recommended as an effective method against the problems indicated above, even in older adults [14, 15]. Although high-load resistance training is the primary method to reduce the effects of aging, this type of training generally requires high external loads, which may be difficult for older adults to conduct safely. To identify an appropriate approach for older adults, we found that a low-load resistance training program could induce muscle hypertrophy in middle-aged and older adults [16]. However, despite subjecting each participant to the same training program, the training effect solely depended on the individual.

It is well known that blood parameters are effective screening tools for identifying the risk of metabolic syndromes, locomotive syndromes, and other multi-factorial diseases [17–19]. To diagnose diseases early, annual medical checkups that include complete blood counts and blood biochemistry panels have been conducted in Japan. The consultation rate of annual medical checkups was reported to be 63.7% [20], which indicates the percentage of Japanese citizens managing their health through annual checkups. From this viewpoint, we focused on blood parameters, including complete blood counts and blood biochemistry panels, and hypothesized that these blood parameters might affect skeletal muscle adaptation in response to a low-load resistance training program. To test this, we first comprehensively verified the blood parameters, including complete blood count and blood biochemistry, which entailed annual medical checkups conducted in Japan, before and after a low-load resistance training program.

This study aimed to evaluate whether the levels of some blood parameters influenced the effect of a low-load resistance training program on lower limb muscle thickness in community-dwelling middle-aged and elderly individuals.

## Methods

### Participants

Healthy, community-dwelling Japanese middle-aged and elderly individuals were recruited to participate in this study through printed advertisements in the public information magazine. They were informed about the methods, procedures, and risks and provided written informed consent before participating. We excluded individuals who did not follow our instructions or those with medical conditions that limited their ability to participate in the resistance training program. Sixty-nine participants aged  $69.4 \pm 6.5$  years (49 women and 20 men) volunteered for this study. Their heights, weights, muscle thicknesses, and blood parameters were evaluated before (pre) and after (post) the training period. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee for Human Experiments of Juntendo University, Chiba, Japan (Approval Number: 27–52). This study was registered in UMIN-Clinical Trial Registry (CTR) (ID: UMIN000042759, Date of registration: 14/12/2020).

### Training program

Participants were instructed to engage in a low-load resistance training program using their own body weight and an elastic band. They were also instructed to avoid changing their dietary patterns throughout the training period. The program was conducted twice a week for 12 weeks, and the total number of classes was 22 or 23. The program was composed of nine exercises: squats, split squats, push-ups, heel raises, crunches, hip lifts, seated rows, shoulder presses, and arm curls. The first six exercises involved the participant's own body weight, and the last three exercises required an elastic band (Thera-Band®; The Hygenic Corporation, Akron, OH, USA). In the first 2 weeks of the training period, the program was composed of only 4 exercises: squats, push-ups, crunches, and hip lifts, and the participants performed 3 sets of 8 repetitions with a 60-second rest between each set. In each repetition, they were instructed to spend 3 seconds in both the concentric and eccentric phases. After the first 2 weeks, the number of exercises per session, repetitions, sets per exercise, and exercise times were gradually increased, and the rest interval was gradually decreased every 2 weeks throughout the 12-week training period. This training program was conducted according to the protocol followed in a previous study, and the details are described by Ozaki et al. [16].

# Muscle thickness

Each participant's muscle thickness was measured with a B-mode ultrasound device using a 5 to 18-MHz scanning head (Noblus; Aloka, Tokyo, Japan). We evaluated the anterior aspects of the thigh (AT) at the midpoint between the greater trochanter and lateral condyle of the femur. The participants were required to rest in the sitting position for at least 30 minutes before the measurement and to be in a supine position during the measurement. This measurement was also conducted according to the method used in a previous study, and the details are described by Ozaki et al. [16].

## Blood parameters

Venous blood samples of approximately 13 mL were obtained following at least 2 hours of fasting before (pre) and after (post) the 12-week training program, and the levels of the following blood parameters were assessed: white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count (PLT), total protein (TP), albumin (Alb), aspartate aminotransferase (glutamic oxaloacetic transaminase; AST [GOT]), alanine aminotransferase (glutamic pyruvic transaminase; ALT [GPT]), alkaline phosphatase (ALP), leucine aminopeptidase (LAP), lactate dehydrogenase (LD [LDH]),  $\gamma$ -glutamyl transferase ( $\gamma$ -GTP), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), hemoglobin A1c (HbA1c), and fasting blood sugar (FBS). These items were monitored using the complete blood count and blood biochemistry tests, which are included in annual medical checkups conducted in Japan.

We checked each blood parameter's first quartile value to establish the following cutoff criteria for reduced levels: WBC = 4400/ $\mu$ L, RBC =  $414 \times 10^4$ / $\mu$ L, Hb = 12.6 g/dL, Ht = 37.9%, MCV = 87.7 fL, MCH = 29.2 pg, MCHC = 32.8%, PLT =  $18.8 \times 10^4$ / $\mu$ L, TP = 7 g/dL, Alb = 4.1 g/dL, AST(GOT) = 18 U/L, ALT(GPT) = 14 U/L, ALP = 178 U/L, LAP = 45 U/L, LD(LDH) = 169 U/L,  $\gamma$ -GTP = 14 U/L, TC = 181 mg/dL, HDL-C = 52 mg/dL, TG = 85 mg/dL, LDL-C = 102 mg/dL, HbA1c = 5.3%, and FBS = 95 mg/dL. Using criteria for each blood parameter, participants were divided into the first quartile group, which is the lowest quartile group, as participants in this group have relatively low blood parameter values, or into the combined second, third, and fourth quartile groups with participants having normal blood parameter values.

## Statistical analyses

To verify the training effect on muscle thickness at the AT, we analyzed the parameters before (pre) and after (post) the training program. Data were analyzed using the paired t-tests, two-way analysis of variance, analysis of covariance, and binomial logistic regression analysis. If there was a significant interaction in the two-way analysis of variance between time and group, the simple main effects analysis was conducted. In the binomial logistic regression analysis and the multiple regression analysis, the variable selection was conducted using a stepwise method with  $p = 0.20$ . A  $p$  value less than 0.05 was considered statistically significant. Results were expressed as means and standard deviations, and the odds ratio was represented by means and 95% confidence intervals. Statistical analyses were performed using BellCurve for Excel (Social Survey Research Information Co., Ltd., Japan).

## Results

The participants' average height was 156.8±7.6 cm, and the average weight was 59.1±10.3 kg. The average participation rate of the classes was 87.4% (range: 63.6%–100.0%).

The average muscle thickness at the AT of all participants was 26.65±5.12 mm before the training intervention, which significantly increased to 29.48±5.38 mm after undergoing the biweekly low-load resistance training program for 12 weeks ( $p<0.001$ , Figure 1A). The average serum Alb concentration at the AT of all participants was 4.25±0.25 g/dL before the training intervention, which significantly increased to 4.32±0.26 g/dL after the training program ( $p<0.001$ , Figure 1B).

**Table 1.** The first quartile value of each blood parameter

|          | Unit                 | Mean<br>Value | Minimum<br>Value | Maximum<br>Value | 1 <sup>st</sup> Quartile Value |
|----------|----------------------|---------------|------------------|------------------|--------------------------------|
| WBC      | /μL                  | 5369.6        | 2800             | 8400             | 4400                           |
| RBC      | ×10 <sup>4</sup> /μL | 439.7         | 366              | 552              | 414                            |
| Hb       | g/dL                 | 13.2          | 10.3             | 16.2             | 12.6                           |
| Ht       | %                    | 39.64         | 32.8             | 48               | 37.9                           |
| MCV      | fL                   | 90.35         | 77.5             | 101              | 87.7                           |
| MCH      | pg                   | 30.09         | 25.5             | 33.5             | 29.2                           |
| MCHC     | %                    | 33.3          | 30.9             | 34.7             | 32.8                           |
| PLT      | ×10 <sup>4</sup> /μL | 22.78         | 13.2             | 47.1             | 18.8                           |
| TP       | g/dL                 | 7.23          | 6.6              | 8                | 7                              |
| Alb      | g/dL                 | 4.25          | 3.7              | 4.9              | 4.1                            |
| AST(GOT) | U/L                  | 21.6          | 12               | 41               | 18                             |
| ALT(GPT) | U/L                  | 19.4          | 7                | 63               | 14                             |
| ALP      | U/L                  | 216.7         | 74               | 387              | 178                            |
| LAP      | U/L                  | 48.2          | 32               | 83               | 45                             |
| LD(LDH)  | U/L                  | 190.9         | 135              | 276              | 169                            |
| γ-GTP    | U/L                  | 23.4          | 10               | 107              | 14                             |
| TG       | mg/dL                | 140.7         | 46               | 393              | 85                             |
| TC       | mg/dL                | 209.7         | 148              | 307              | 181                            |
| HDL-C    | mg/dL                | 62.2          | 29               | 101              | 52                             |
| LDL-C    | mg/dL                | 121.2         | 64               | 211              | 102                            |
| HbA1c    | %                    | 5.57          | 4.7              | 7.3              | 5.3                            |
| FBS      | mg/dL                | 106.6         | 72               | 191              | 95                             |

WBC, white blood cell count; RBC, red blood cell count; Hb, hemoglobin; Ht, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet count; TP, total protein; Alb, albumin; AST(GOT), aspartate aminotransferase (glutamic oxaloacetic transaminase); ALT(GPT), alanine aminotransferase (glutamic pyruvic transaminase); ALP, alkaline phosphatase; LAP, leucine aminopeptidase; LD(LDH), lactate dehydrogenase;  $\gamma$ -GTP,  $\gamma$ -glutamyltransferase; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, hemoglobin A1c; FBS, fasting blood sugar.

Using the blood parameter criteria, we checked the first quartile value of each blood parameter to establish the cutoff criteria for reduced levels (Table 1). When the two-way analysis of variance was conducted, the effects were significant for time, but not for group, and the time  $\times$  group interactions were significant for low (<32.8%) versus normal ( $\geq$ 32.8%) MCHC levels, low (<4.1 g/dL) versus normal ( $\geq$ 4.1 g/dL) serum Alb levels, and low (<102 mg/dL) versus normal ( $\geq$ 102 mg/dL) serum LDL-C levels ( $p < 0.05$ ; Table 2). The time  $\times$  group interactions were detected in the serum Alb levels. When comparing the low and normal serum Alb level groups using the simple main effects analysis, there was no difference in muscle thickness at the AT before the training intervention; however, participants in the normal serum Alb level group had greater muscle thickness after the training intervention than those in the low serum Alb level group ( $30.26 \pm 5.31$  mm,  $26.45 \pm 4.68$  mm,  $p < 0.001$ ; Figure 2A). To verify the effect of participation rate of the classes, an analysis of covariance was conducted. Although regression parallelism was confirmed, the regression was not significant. Time  $\times$  group interactions were also detected in the MCHC and serum LDL-C levels ( $p < 0.001$ ; Table 2), but no differences in muscle thickness at the AT either before or after the training intervention were observed between the low and normal groups, using the simple main effects analysis (Figure 2B, 2C).

**Table 2.** Summarized the results of the two-way analysis of variance

|          | n   |        | muscle thickness(mm) |          |          |          | time              | group         | interaction   |
|----------|-----|--------|----------------------|----------|----------|----------|-------------------|---------------|---------------|
|          | pre |        | pre                  |          | post     |          |                   |               |               |
|          | low | normal | low                  | normal   | low      | normal   | p value           |               |               |
| WBC      | 17  | 52     | 23.9±4.6             | 27.6±5.0 | 27.7±5.3 | 30.1±5.3 | <<br><b>0.001</b> | <b>0.0306</b> | 0.082         |
| RBC      | 17  | 52     | 24.5±4.6             | 27.3±5.1 | 27.4±5.2 | 30.2±5.3 | <<br><b>0.001</b> | <b>0.0461</b> | 0.9887        |
| Hb       | 16  | 53     | 23.8±3.1             | 27.5±5.3 | 26.8±3.9 | 30.3±5.5 | <<br><b>0.001</b> | <b>0.0118</b> | 0.8063        |
| Ht       | 17  | 52     | 25.2±4.4             | 27.1±5.3 | 27.7±5.2 | 30.1±5.4 | <<br><b>0.001</b> | 0.1295        | 0.5764        |
| MCV      | 17  | 52     | 26.7±5.0             | 26.6±5.2 | 29.1±4.7 | 29.6±5.6 | <<br><b>0.001</b> | 0.8868        | 0.5129        |
| MCH      | 17  | 52     | 25.2±4.6             | 27.1±5.2 | 28.7±4.8 | 29.8±5.6 | <<br><b>0.001</b> | 0.297         | 0.2858        |
| MCHC     | 13  | 56     | 25.0±5.8             | 27.0±4.9 | 29.5±4.8 | 29.5±5.5 | <<br><b>0.001</b> | 0.5249        | <b>0.0146</b> |
| PLT      | 17  | 52     | 27.1±5.1             | 26.5±5.2 | 29.5±4.4 | 29.5±5.7 | <<br><b>0.001</b> | 0.8204        | 0.4596        |
| TP       | 17  | 52     | 23.4±3.6             | 27.7±5.1 | 26.9±4.9 | 30.3±5.3 | <<br><b>0.001</b> | <b>0.0057</b> | 0.2622        |
| Alb      | 14  | 55     | 25.4±5.1             | 27.0±5.1 | 26.5±4.7 | 30.3±5.3 | <<br><b>0.001</b> | 0.0791        | <b>0.003</b>  |
| AST(GOT) | 16  | 53     | 27.1±4.4             | 26.5±5.4 | 30.4±4.7 | 29.2±5.6 | <<br><b>0.001</b> | 0.5378        | 0.4372        |
| ALT(GPT) | 15  | 54     | 24.6±3.2             | 27.2±5.4 | 27.6±4.0 | 30.0±5.6 | <<br><b>0.001</b> | 0.0902        | 0.8594        |
| ALP      | 15  | 54     | 27.3±5.4             | 26.5±5.1 | 30.0±5.7 | 29.3±5.3 | <<br><b>0.001</b> | 0.6309        | 0.8943        |
| LAP      | 16  | 53     | 24.8±3.9             | 27.2±5.4 | 27.9±4.0 | 30.0±5.7 | <<br><b>0.001</b> | 0.1252        | 0.6677        |
| LD(LDH)  | 17  | 52     | 28.7±4.6             | 26.0±5.1 | 31.3±5.0 | 28.9±5.4 | <<br><b>0.001</b> | 0.068         | 0.5984        |
| γ-GTP    | 14  | 55     | 23.8±3.6             | 27.4±5.2 | 26.2±3.6 | 30.3±5.5 | <<br><b>0.001</b> | <b>0.0105</b> | 0.4903        |
| TG       | 17  | 52     | 23.6±3.3             | 27.6±5.2 | 26.4±4.3 | 30.5±5.4 | <<br><b>0.001</b> | <b>0.0038</b> | 0.9606        |
| TC       | 17  | 52     | 27.4±4.8             | 26.4±5.3 | 29.3±5.7 | 29.5±5.3 | <<br><b>0.001</b> | 0.7951        | 0.1247        |
| HDL-C    | 17  | 52     | 28.7±4.7             | 26.0±5.1 | 32.0±4.1 | 28.7±5.5 | <<br><b>0.001</b> | <b>0.0326</b> | 0.4299        |

|       |    |    |          |          |          |          |                   |        |               |
|-------|----|----|----------|----------|----------|----------|-------------------|--------|---------------|
| LDL-C | 17 | 52 | 27.2±5.8 | 26.5±4.9 | 28.7±5.6 | 29.7±5.3 | <<br><b>0.001</b> | 0.9126 | <b>0.0105</b> |
| HbA1c | 15 | 54 | 28.1±4.8 | 26.3±5.2 | 31.1±4.2 | 29.0±5.6 | <<br><b>0.001</b> | 0.1987 | 0.7482        |
| FBS   | 16 | 53 | 27.0±5.7 | 26.6±5.0 | 30.7±5.5 | 29.1±5.3 | <<br><b>0.001</b> | 0.4946 | 0.102         |

Data of muscle thickness are presented as mean±SD.

WBC, white blood cell count; RBC, red blood cell count; Hb, hemoglobin; Ht, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet count; TP, total protein; Alb, albumin; AST(GOT), aspartate aminotransferase (glutamic oxaloacetic transaminase); ALT(GPT), alanine aminotransferase (glutamic pyruvic transaminase); ALP, alkaline phosphatase; LAP, leucine aminopeptidase; LD(LDH), lactate dehydrogenase;  $\gamma$ -GTP,  $\gamma$ -glutamyltransferase; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, hemoglobin A1c; FBS, fasting blood sugar.

To verify the influence that serum Alb concentration and serum Alb levels (<4.1 g/dL or not) had on the change in muscle thickness at the AT, binomial logistic regression analysis was performed with muscle thickness at the AT (increased as 0, decreased as 1) as a target variable and with the serum Alb concentration and serum Alb level ( $\geq$ 4.1 g/dL as 0, <4.1 g/dL as 1) as explanatory variables. The serum Alb level was selected as a significant variable ( $p=0.0102$ ), and the odds ratio for decreasing muscle thickness at the AT was 7.08, while the 95% confidence interval was 1.59–31.54.

## Discussion

This study revealed that a low-load resistance training program using a participant's own body weight and elastic bands, even when performed only twice a week, induced muscle hypertrophy after 12 weeks of training intervention in community-dwelling elderly Japanese participants. The average muscle thickness at the AT increased about 10% over the 12 weeks of the low-load resistance training program. However, there were individual differences in the training effect on muscle thickness at the AT. For example, the increase was restricted in individuals with a relatively lower serum Alb before the training intervention. Our data suggested that low serum albumin levels may predict decreased efficacy of a resistance training intervention on muscle thickness in community-dwelling elderly Japanese participants.

It is common to divide participants using quartile values of blood parameters or based on physical performance tests [21, 22]; here, we compared the lowest quartile with the three higher quartiles combined as reported in a previous study [23]. When we divided the participants into two groups using each blood parameter's quartile criteria (Table 1), an interaction between time and group was detected for MCHC levels, serum Alb levels, and serum LDL-C levels (Table 2). The training effect on muscle thickness at the AT was limited in the low serum Alb group compared with that in the normal serum Alb group (Fig. 2A). From the results of the analysis of covariance, this was not affected by the participation rate of the classes. The results of the binomial logistic regression analysis showed that classification in the low serum Alb group had an odds ratio of 7.08 for decreasing muscle thickness at the AT, which supports the above-mentioned limitation. Although this criterion was much higher than that of clinical malnutrition (< 3.5 g/dL), the patients with relatively low serum Alb had inhibited training effects.

This influence was not seen in participants with lower levels of the other blood parameters, including MCHC and LDL-C (Table 2, Fig. 2B, Fig. 2C). Our data demonstrated that the effect of a low-load resistance training program on lower limb muscle thickness appears to be limited in participants, depending on their serum Alb levels before the training intervention. Serum Alb is a clinical indicator of energy and protein deficiency; therefore, our data suggest that participants with lower serum Alb before a training intervention ought to improve their nutritional status to obtain the most optimal training effects on their muscle mass. The relatively lower serum Alb level (3.9–4.2 g/dL) was also reported to be related to cognitive decline or dementia [24–26]. Some other previous longitudinal observational studies reported that relatively lower serum Alb levels were associated with loss of muscle mass and muscle strength [22, 27, 28]. It was also reported that a relatively lower serum Alb level combined with sarcopenia would increase disability risk in older adults [29]. As these studies and our data showed, even though the serum Alb level is much higher than that of clinical malnutrition (< 3.5 g/dL), relatively lower serum Alb level might be an indicator for our healthy aging.

Measuring muscle thickness via a B-mode ultrasound device is a non-invasive method to assess the muscle mass, which can also be assessed in individual parts. The training effects are known to appear in a site-specific manner, making this a superior method to assess the training effects on muscle mass. Some RCT studies have revealed that exercise intervention improved muscle strength, physical function, or muscle mass in older adults. Binder et al. provided information on an exercise intervention program implemented 3 times a week, including low- to moderate-intensity resistance training for community-dwelling elderly and frail men and women for 9 months; they revealed that such a training intervention induced greater increments in whole-body fat-free mass assessed by dual energy X-ray absorptiometry [30]. Kim et al. discussed the benefits of an intervention program provided for 60 minutes twice a week, including low- to moderate-intensity resistance training using the participants' own body weight, ankle weight, and resistance bands for community-dwelling sarcopenic elderly women for 3 months; they revealed that the training intervention induced increased leg muscle mass assessed by segmental multifrequency bioelectrical impedance analysis [31]. However, these studies targeted frail or sarcopenic older adults and did not adequately verify if exercise intervention could improve muscle mass in community-dwelling healthy older adults. Our data is therefore important, as it reveals that a low-load resistance training program is effective at increasing the site-specific muscle mass of community-dwelling middle-aged and older adults.

Our study had some limitations. First, there was no control group when we verified the effects of the 12-week training intervention. Second, even though it has been reported that a combination of exercise and a nutritional approach is the most effective method to improve sarcopenia, we did not control the participants' nutrient intake during the training period. Third, we cannot verify the sex difference when examining the association between serum Alb levels and the low-load resistance training effects. To minimize these limitations, further studies must be conducted in the future.

## Conclusions

In conclusion, serum Alb levels may be a predictive biomarker for the effect of a low-load resistance training program on muscle hypertrophy in community-dwelling elderly individuals.

## List Of Abbreviations

AT

the anterior aspects of the thigh; WBC:white blood cell count; RBC:red blood cell count; Hb:hemoglobin; Ht:hematocrit; MCV:mean corpuscular volume; MCH:mean corpuscular hemoglobin; MCHC:mean corpuscular hemoglobin concentration; PLT:platelet count; TP:total protein; Alb:albumin; AST(GOT):aspartate aminotransferase (glutamic oxaloacetic transaminase); ALT(GPT):alanine aminotransferase (glutamic pyruvic transaminase); ALP:alkaline phosphatase; LAP:leucine aminopeptidase; LD(LDH):lactate dehydrogenase;  $\gamma$ -GTP: $\gamma$ -glutamyltransferase; TG:triglyceride; TC:total cholesterol; HDL-C:high-density lipoprotein cholesterol; LDL-C:low-density lipoprotein cholesterol; HbA1c:hemoglobin A1c; FBS:fasting blood sugar.

## Declarations

### Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee for Human Experiments of Juntendo University, Chiba, Japan (Approval Number: 27-52). Written informed consent was obtained from all study participants.

### Consent for publication

Not applicable.

### Availability of data and materials

The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interests.

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### Authors' contributions

S.S. designed and performed experiments, analyzed and interpreted data, and prepared the manuscript. H.O., T.N., D.N., P.D. T.Y., and T.O. performed experiments. H.K. was responsible for medical examination of the participants. S.M. and H.N. contributed to the manuscript preparation and to the discussion, and they are the guarantors of this work. All the authors reviewed and approved the final manuscript.

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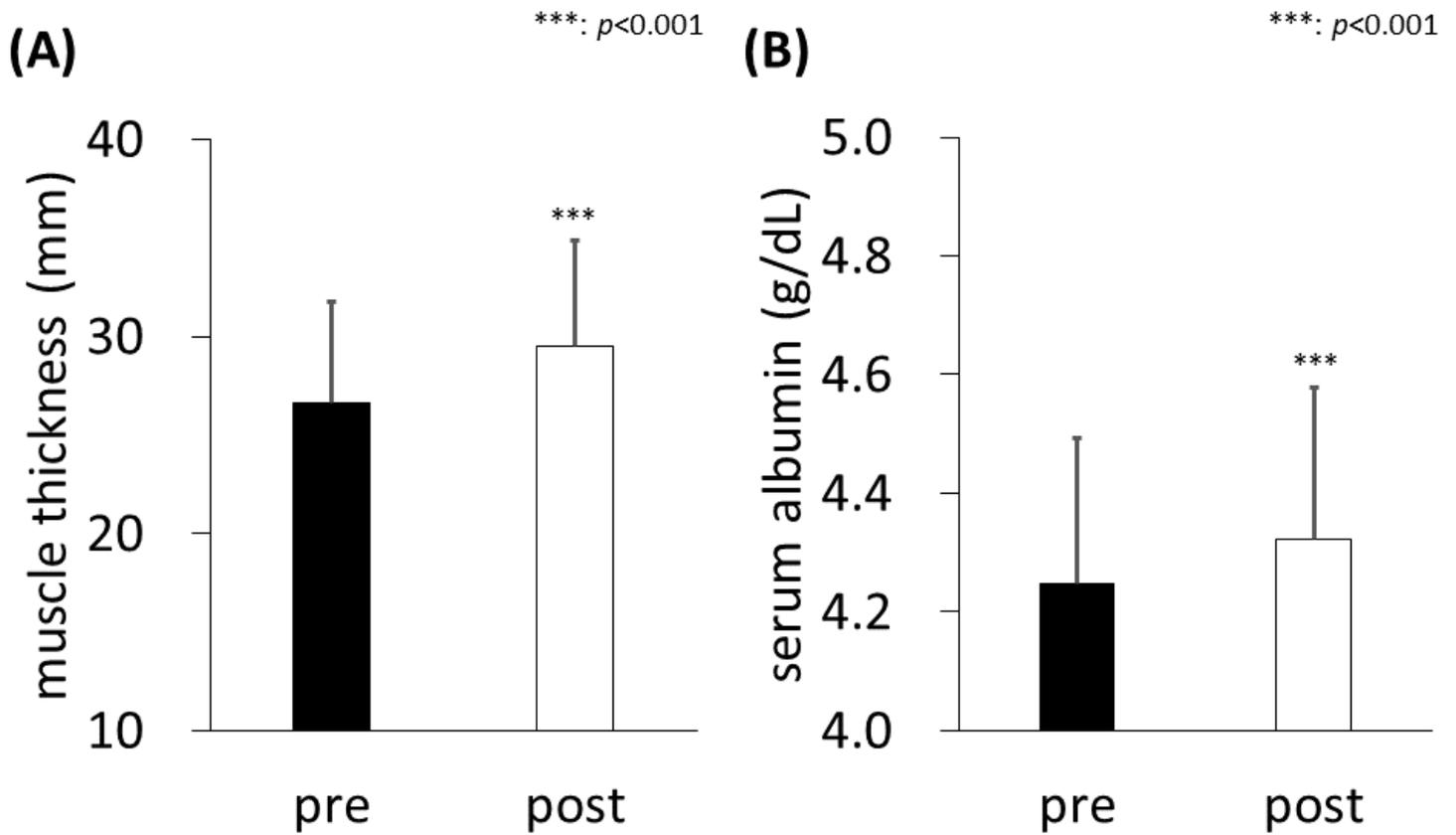
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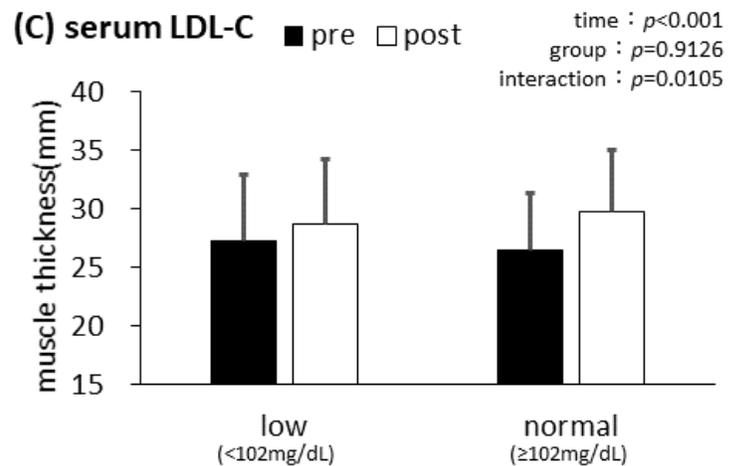
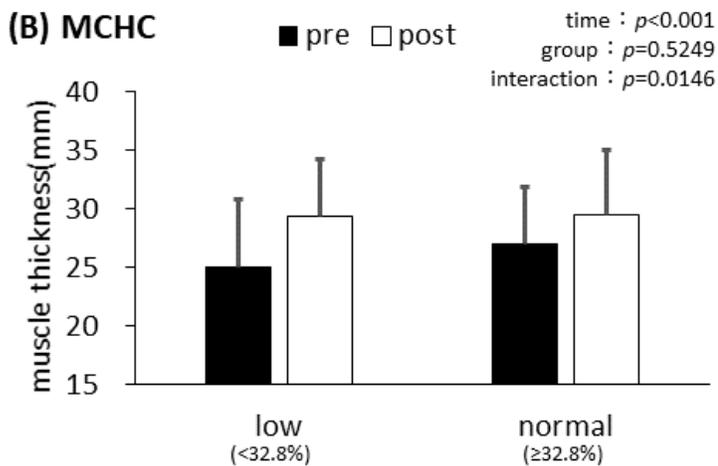
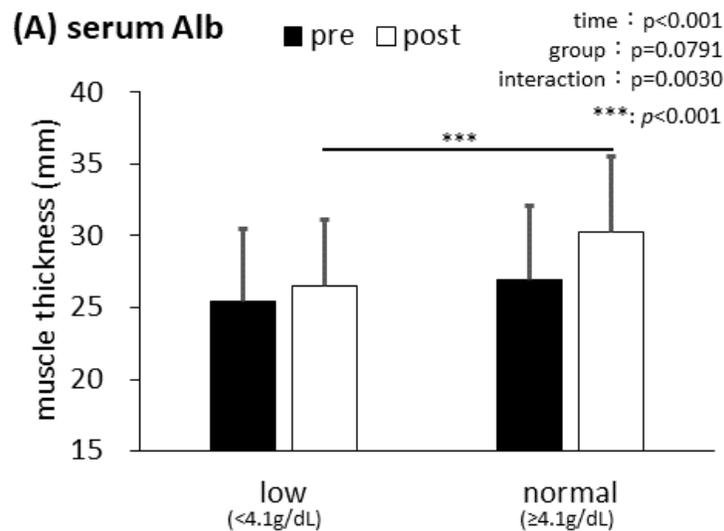
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## Figures



**Figure 1**

Effect of a low-load resistance training program on (A) muscle thickness, and (B) serum albumin levels. Data are presented as mean ± SD. N=69.



**Figure 2**

Comparison of changes in muscle thickness for (A) low serum Alb and normal serum Alb levels, (B) low MCHC and normal MCHC levels, and (C) low serum LDL-C and normal LDL-C levels. Data were analyzed using two-way analysis of variance; the main effects on time, but not on group, and the time  $\times$  group interactions were significant for all three measurements. Although the time  $\times$  group interactions were detected in all three measurements, a significant difference after training intervention was only detected in serum Alb levels compared with the low and normal groups using Tukey's multiple comparison test as a post-hoc analysis. Data are presented as mean  $\pm$  SD. N=69.