J Nutr Health Aging. 2019;23(6):564-570

TWENTY-FOUR MONTHS' RESISTANCE AND ENDURANCE TRAINING IMPROVES MUSCLE SIZE AND PHYSICAL FUNCTIONS BUT NOT MUSCLE QUALITY IN OLDER ADULTS REQUIRING LONG-TERM CARE

A. YOSHIKO[1,2], T. KAJI[3], H. SUGIYAMA[3], T. KOIKE[2,4], Y. OSHIDA[5], H. AKIMA[4,6]

1. School of International Liberal Studies, Chukyo University, Toyota, Japan; 2. Graduate School of Medicine, Nagoya University, Nagoya, Japan; 3. Kajinoki Medical Clinic, Gifu, Japan; 4. Research Center of Health, Physical Fitness & Sports, Nagoya University, Nagoya, Japan; 5. Minami Seikyo Hospital, Nagoya, Japan; 6. Graduate School of Education and Human Development, Nagoya University, Nagoya, Japan. Corresponding author: Akito Yoshiko, Ph.D. School of International Liberal Studies, Chukyo University, 101 Tokodachi, Kaizu, Toyota, Aichi 470-0393, Japan, Tel: +81 (565) 46-6952, E-mail: yoshiko@lets.chukyo-u.ac.jp

Abstract: *Objectives:* To assess the effects of 24 months training on muscle quality, size, strength, and gait abilities in older adults who need long-term care. *Design:* Non-randomized controlled trial Setting: Kawai Rehabilitation Center and Kajinoki Medical Clinic. *Participants:* Ten older participants who needed long-term care (age, 76.7 ± 5.6 years) were participated as training group (Tr-group) and 10 older men and women who did not require long-term care (age, 72.9 ± 6.6 years) comprised the control group (Cont-group). *Intervention:* Tr-group performed resistive and endurance exercises once or twice a week for 24 months. *Measurements:* Using ultrasound images, echo intensity (EI) and muscle thickness were measured in the rectus femoris and biceps femoris as an index of muscle quality and size. Physical performance was measured before and after the training; performance parameters included knee extension peak torque, 5-m normal and maximal walk test, sit-to-stand and timed up and go test. *Results:* After the training, there was no change in EI, while BF thickness was increased (pre; 1.82 ± 0.29 cm, 24 months; 2.14 ± 0.23 cm, $p < 0.05$) in Tr-group. Walk-related performances were improved after the training in Tr-group (i.e. 5-m walk test and timed up and go test). The percent change of knee extension peak torque explained the percent change of EI in the rectus femoris (regression coefficient = 1.24, R = 0.91, adjusted R2 = 0.82, $p < 0.001$). *Conclusions:* Twenty-four months' training induced muscle hypertrophy and improved physical functions. Increased muscle quality in the rectus femoris could be a key to improved knee extension peak torque, with the potential to eventually reduce the need for long-term care in older individuals.

Key words: Echo intensity, ultrasonography, endurance training, resistance training, twenty-four months, long-term care, older individuals.

Introduction

Sarcopenia is defined as the loss of skeletal muscle with aging, and this condition dramatically decreases the functional abilities of the older (1). As a consequence, it becomes difficult for many older individuals to live independently, necessitating long-term care as progression leads to a bedridden state and/or death. As sarcopenia advances, muscle quality worsens because of the increased fat and connective tissue content within the muscle (2-5). The infiltration of fat into muscle, intramuscular fat (IMF or IntraMAT), is negatively associated with locomotive functions and/or glucose metabolism (6, 7). Thus, prevention of and recovery from physical and metabolic deterioration related to muscle quality are extremely meaningful for the promotion of health in the older individuals.

In earlier studies, physical training is considered an ideal intervention to preserve muscle strength and gait ability that are commonly used to diagnose sarcopenia and frailty. Several studies support the fact that training interventions positively affect physical functional parameters in the older individuals (8, 9). Importantly, Radaelli et al. (10) showed that thigh muscle echo intensity (EI) determined by ultrasonography in the healthy older significantly decreased after 3 months of resistance training. Muscle EI primarily reflects the IMF content and extramyocellular lipid (EMCL) as determined by magnetic resonance techniques (11). Considering this finding, resistance and/or endurance training for the older adults would be recommended to help with independent living by improving muscle metabolism.

Older individuals with sarcopenia and/or frailty requiring long-term care may have difficulty performing high-intensity and incremental training because of their lower functional abilities. Several studies have shown the effects of long-term training (over 8 to 12 months), regardless of whether the intensity was low or moderate (12, 13). Therefore, training continuation may be the key to achieving the effects of training interventions. An interesting observation in these studies was that EI was significantly decreased after 3 to 5 months of training (14, 15). Furthermore, we found that thigh EI decreased after 6 months of training, and it returned to the initial level after 12 months of training (2). It suggested that the physiological significance of this EI fluctuation was because energy resources increased following the increase in muscle metabolism. However, the adaptation of physical training on EI for more than 12 months in this population remains unclear.

The purpose of this study was to assess the effects of long-term (24 months) training continuation on muscle quality, size, strength, and physical functions in older subjects who needed long-term care. We hypothesized that EI continuously increased, along with energy resources of stocked fat in muscle,

Received February 5, 2019
Accepted for publication February 26, 2019

Published online May 23, 2019, http://dx.doi.org/10.1007/s12603-019-1208-8

accompanied by the improvement in muscle size and strength.

Materials and Methods

Study design and recruitment

This study was performed at the Kawai Rehabilitation Center, which was established as part of the Kajinoki Medical Clinic in Gifu, Japan. Importantly, this is a follow-up study to research reported by Yoshiko et al (2). Participants in the training group (Tr-group) had difficulties in performing ADL without long-term care and were certified as requiring long-term health care, which is managed by the Ministry of Health, Labour and Welfare of Japan. As part of their rehabilitation, they visited the rehabilitation center once or twice a week and performed several physical training exercises as described below. Participants who visited the clinic for regular medical checkups comprised the control group (Cont-group). We confirmed that Cont-group did not habitually perform any exercise by screening.

Participant characteristics

Physical characteristics in the Tr- and Cont-groups are shown in Table 1. With respect to physiological parameters, whole muscle mass was measured using the InBody 270 body composition analyzer (InBody Japan Co., Ltd., Tokyo, Japan) through bioelectrical impedance analysis. Skeletal muscle index (SMI) was calculated as follows: SMI (kg/m^2) = muscle mass/height^2.

Table 1
Physical characteristics in the training group (Tr-group) and control group (Cont-group)

	Tr-group (n = 10)	Cont-group (n =10)
Age (years)	76.7 ± 5.6	72.9 ± 6.6
Gender (men : women)	4 : 6	5 : 5
Height (cm)	154.0 ± 7.0	157.0 ± 9.5
Weight (kg)	53.6 ± 8.5	59.8 ± 12.0
BMI (kg/m^2)	22.6 ± 3.4	24.1 ± 3.0
SMI (kg/m^2)	8.3 ± 1.0	9.2 ± 1.5

Values are shown as mean ± SD. BMI, body mass index; SMI, skeletal muscle index.

Ten older men and women requiring long-term care comprised the Tr-group. They had level one to level four requirements for long-term care, which they received at facilities certified by the Ministry of Health, Labour and Welfare Ministry of Japan. The levels of care are based on necessary support time, with level one requiring the least assistance and level seven requiring the most assistance. Support times for housework, medical care, and ADL of > 25 min to < 32 min per day are needed for level one, and support times of > 50 min to < 70 min are needed for level four. Ten older men and women who did not require long-term care comprised the Cont-group.

This study was a nonrandomized-controlled trial. According to the position of the American College of Sports Medicine, physical exercise is effective for promoting health and is recommended for the older (16). We recruited older who did not require long-term care as the control subjects in this study because they had a much lower risk of developing physical and metabolic dysfunction by the lack of exercise intervention during the observation period. All participants were considered free from serious disease by a medical doctor (T.K.). Some participants were taking medication for diabetes, hyperlipidemia, or high blood pressure; however, these medications did not influence hormonal or neuromuscular metabolism. Before the experiment, the purpose, procedures, and risks associated with this study were explained to all participants, all of whom provided written informed consent to participate. All examination protocols were approved by the Institutional Review Board of the Research Center of Health, Physical Fitness and Sports at Nagoya University and conducted in accordance with the ethical principles stated in the Declaration of Helsinki.

Experimental procedure

On the first visit, we explained the purpose and significance of the study, the entire experimental protocol, and the specific training procedures and measurements to all participants. Participants in the Tr-group engaged in the 24 months' training intervention. Before the training and measurement, they underwent a medical assessment. All participants were evaluated by ultrasound examination and functional tests both before and after the training period. During the study period, the participants were requested to avoid changes in their dietary habits and physical activities in their daily life. Participants in the Tr-group completed the appointed 24 months' training intervention and recorded the duration and number of repetitions of the exercises performed on a scoring sheet.

Training program

As part of the rehabilitation program, participants in the Tr-group performed physical training once or twice a week for 24 months. This training program was the same as that previously reported by Yoshiko et al. (2). Before starting the training sessions, the body temperature, resting blood pressure, and overall health condition (sleep duration and levels of fatigue, appetite, and defecation) were checked by care workers. The training program consisted of resistance and endurance training under the supervision of a physical therapist. Resistance and endurance training were randomly performed in each time. The entire session was completed within 2.5 hours. The physical therapist randomly chose three or four out of eight different resistance exercises (hip adduction/abduction, knee extension/flexion, leg press, seated row, back extension/abdominal crunch, back twist, chest press, and shoulder press) to create an individualized exercise program with consideration of the participant's physical condition; for example, if the participant had knee arthralgia, the exercise intensity was reduced or steps were taken to avoid leg exercises. Generally, at least one lower limb exercise and one upper body/abdominal exercise were included to avoid excessive fatigue.

On each training day, the participants performed the resistance exercise programs using a hydraulic-resistance machine (Well-Round; Mizuno Corp., Tokyo, Japan). This device was used because: (1) the participants could not use heavier loads because of their lower physical abilities, (2) the machine was developed for training or rehabilitation in the older individuals with consideration of safety, and (3) scientific evidence of its effectiveness is reported in several studies (17). The participants were instructed to move through the full range of motion for each exercise as quickly as possible. Resistance was controlled by a dial on the resistance machine, which ranged from level one (lowest) to ten (highest), depending on the participant's physical condition. The training intensity was set to approximately 20% to 40% of each participant's maximum effort. Each resistance exercise program continued for 5 min with a 2-min rest between programs; the total resistance exercise time was 15–20 min.

The participants performed endurance training on a NuStep T5 recumbent cross trainer (NuStep LLC, Ann Arbor, MI, USA). The workload was selectable from one (lowest) to ten (highest); it was set as high as possible and continued for 10 min. We checked the rated perceived exertion after the endurance training and confirmed that it had reached 11 to 12 on the Borg scale as well as 40% of maximum effort.

All participants started at the lowest load (dial one) for both resistance and endurance training in the first class to determine the intensity. During the training, we asked the participants whether it was possible to increase the training intensity, and we encouraged increasing the workload if possible.

Physical functional parameters

The participants performed six functional tests: isometric knee extension peak torque (KEPT), 5-m normal-speed walking, 5-m maximal-speed walking, sit-to-stand test, handgrip strength, and timed up and go (TUG) test. These functional tests were chosen because they have been used in many previous studies, and several studies have shown that EI is associated with basic functional capacity and gait ability (5, 18, 19). The isometric KEPT of the right leg was measured using a custom-made dynamometer (Takei Scientific Instruments Co., Ltd., Niigata, Japan) as described in our previous studies (2, 5). The hip was fixed to the dynamometer by a strap, and the knee joint angle was fixed at 90° (180° is fully extended). The maximal KEPT was calculated as the exerted force (N) × the lever arm length of the dynamometer (m). For the 5-m normal- and maximal-speed walking tests, two parallel lines were taped on the floor as the start and finish lines. The participants walked with normal and maximal effort from the start line toward the finish line. The sit-to-stand test was performed to determine the number of times the participant was able to sit on and stand up from a chair as quickly as possible for 30 s with the participant's arms crossed in front of their chest. The height of the seat was 40 cm from the floor. Handgrip strength was assessed in the participants' right hands using a grip dynamometer (Takei Scientific Instruments Co., Ltd.). The participants squeezed the dynamometer as strongly as possible while maintaining an upright posture. For the TUG test, we measured the time it took the participants to rise from a chair, walk 3-m, turn around, walk back to the chair, and sit down. The handgrip strength and TUG tests were conducted twice, and the better result was used for further analysis.

Ultrasound measurements

The subcutaneous fat thickness, muscle thickness (MT), and EI of the mid-thigh were measured using an ultrasound device essentially as described in our previous studies (2, 5, 19). The MT and EI are affected by muscle contraction–induced blood flow and fluid shifts. To avoid these effects, the participants rested on a bed for at least 20 min before the ultrasound measurements. After the rest period, they moved to an examination bed and were placed in the supine position for measurement of anterior regions and the prone position for measurement of posterior regions with their knee joints fully extended. We measured the portion of the right thigh corresponding to the midpoint between the greater trochanter and lateral condyle. The LOGIQ e ultrasound system (GE Healthcare, Duluth, GA, USA) was used to obtain images. This real-time B-mode ultrasonographic device has a 3.8-cm width and 8- to 10-MHz linear array probe for imaging with the following acquisition parameters: frequency, 10 MHz; gain, 70 dB; depth, 4.0 to 6.0 cm; and focus point, 1 (top of the image). The depth was determined depending on the individual participant; it was generally ≤ 6.0 cm, and the same depth was used in each measurement. A water-soluble gel was applied to the scanning head of the probe to achieve acoustic coupling, and extra care was taken to avoid deformation of the muscle morphology when placing the probe on the skin surface. Three frozen images of each section were stored in the digital imaging and communications in medicine (DICOM) format and transferred to a personal computer for later analysis. ImageJ software, version 1.46 (National Institutes of Health, Bethesda, MD, USA) was used for analysis. The thickness of the subcutaneous fat was defined as the distance between the dermis and the upper boundary of the ventral fascia. The MT of the rectus femoris (RF) and biceps femoris (BF) was defined as the distance between the superior border of the subcutaneous fascia and the deep aponeurosis. The subcutaneous fat thickness and MT of the thigh were calculated using the following equations: Thigh subcutaneous fat thickness = (thickness of anterior thigh subcutaneous fat + thickness of posterior thigh subcutaneous fat)/2; thigh MT = (thickness of RF + thickness of BF)/2.

The EI was assessed based on the 256 gray-scale level

Table 2
Subcutaneous fat thickness, muscle thickness, and echo intensity in the training group (Tr-group) and control group (Cont-group)

	Tr-group		**Contr-group**	
	Pre	**24 months**	**Pre**	**24 months**
Subcutaneous fat (cm)				
Anterior	0.86 ± 0.39	0.80 ± 0.36	0.74 ± 0.22	0.68 ± 0.22
Posterior	0.78 ± 0.28	0.78 ± 0.25	0.78 ± 0.32	0.68 ± 0.21
Thigh	0.82 ± 0.31	0.79 ± 0.29	0.76 ± 0.25	0.68 ± 0.19
Muscle thickness (cm)				
RF	1.04 ± 0.24	1.12 ± 0.31	1.29 ± 0.37	1.21 ± 0.38
BF	1.82 ± 0.29	2.14 ± 0.23*	1.71 ± 0.22	1.95 ± 0.31
Thigh	1.43 ± 0.24	1.63 ± 0.18*	1.50 ± 0.23	1.58 ± 0.28
Echo intensity (a.u.)				
RF	77.29 ± 9.98	77.69 ± 11.95	75.76 ± 5.33	78.44 ± 7.10
BF	57.44 ± 8.57	61.43 ± 11.71	66.58 ± 6.78	64.02 ± 5.69
Thigh	67.37 ± 7.60	69.56 ± 8.74	71.17 ± 4.68	71.23 ± 5.12

Values are shown as mean ± SD. a.u., arbitrary units; BF, biceps femoris; RF, rectus femoris; * $p < 0.05$ vs. Pre within group;

using ImageJ software and was expressed in arbitrary units (a.u.). The largest possible rectangular region of interest was established (20), excluding visible fascia and bone, in the RF from the anterior image and in the BF from the lateral image. The mean EI inside the region of interest in the RF and BF was calculated for each image, and the mean value of the EI in three images for each muscle was used for future analyses. The reliability of this methodology was established by Caresio et al. (20). We assessed the intraclass correlation coefficients (ICC, 2.1) from 20 randomly selected participants. ICCs were 0.99 for the RF and 0.91 for the BF ($p < 0.01$). The standard error of the measurement was 0.75 for the RF and 2.73 for the BF. We calculated the EI of the thigh using the following equation: Thigh EI = (RF in EI + BF in EI)/2.

Statistical analysis

All statistical values were reported as mean and standard deviation. Two-way (time × group) analysis of variance with repeated measures over time was used to compare the subcutaneous fat thickness, MT, EI, and physical function parameters. In the case of a two-factor interaction of main effects, the Bonferroni post-hoc test was used to identify significant differences. Stepwise linear regression analysis was performed with KEPT, 5-m normal/maximal walk, or TUG as a dependent variable, and the percent changes of EI in the RF, BF, and thigh, the percent changes of MT in the RF, BF, and thigh, and the percent changes of subcutaneous fat in the anterior, posterior, and thigh as independent variables. The level of significance was set at $p < 0.05$. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0J (IBM Japan, Ltd., Tokyo, Japan).

Results

The results of the subcutaneous fat thickness, MT, and EI determinations are shown in Table 2. MT in the BF and thigh were significantly increased after the training in the Tr-group.

Physical function outcomes are shown in Table 3. The baseline levels of 5-m normal/maximal speed walk time, sit-to-stand test, and TUG test were worse in the Tr-group compared with the Cont-group. The 5-m maximal speed walk time and TUG test were significantly improved after the training in Tr-group.

We further analyzed stepwise multiple regressions for percent change of muscle function and gait abilities (KEPT, 5-m normal/maximal walk and TUG test) as a dependent variable and ultrasound parameters (subcutaneous fat, MT, and EI) as independent variables (Table 4). As a result, only the KEPT could be explained by percent change of EI in RF ($R = 0.91$, $p < 0.001$); there was no dependent variable to explain the 5-m normal/maximal walk and TUG test.

Discussion

Sarcopenia is defined as decreases in muscle mass, strength, and gait ability; it is known as the syndrome of age-related physical alternation. In the process of making the diagnosis of sarcopenia, it is critical whether the muscle mass is over the cut-off value or not. We calculated SMI as an index of muscle mass (Table 1). Considering these values, most of the participants did not fall into the "low muscle mass" category; only one man in the Tr-group had a muscle mass lower than the cut-off value (< 8.87 kg/m^2) presented by Cruz-Jentoft

Table 3
Physical function outcomes in the training group (Tr-group) and control group (Cont-group)

	Tr-group (n = 10)			Cont-group (n = 10)		
	n	Pre	24 months	n	Pre	24 months
5-m normal speed walk (sec)	10	6.47 ±2.65	5.15 ±1.12	10	3.90 ±0.40†	3.89 ±0.60†
5-m maximal speed walk (sec)	10	4.82 ±2.04	3.85 ±1.19*	10	2.96 ±0.31†	2.85 ±0.45†
Sit-to-stand (rep)	10	11.80 ±4.83	14.20 ±3.36	9	21.89 ±6.67†	17.67 ±5.68*
Handgrip strength (kg)	10	24.80 ±8.50	24.93 ±7.66	9	28.64 ±9.76	27.68 ±8.59
TUG (sec)	10	10.22 ±3.30	8.61 ±2.40*	10	7.80 ±1.27†	6.81 ±1.26
Knee extension peak torque (Nm)	10	64.64 ±35.92	65.32 ±28.94	9	70.88 ±26.39	55.23±24.43*

Values are shown as mean ± SD. TUG, timed up and go; * $p < 0.05$ vs. Pre within group; † $p < 0.05$ vs. Tr-group at same timeline

Table 4
Stepwise multiple regression analyses as a dependent variable of percent change of knee extension peak torque

Independent variable	Standardizes regression coefficient	SEE	Constant	Regression coefficient	R	Adjusted R^2	P
Percent change of EI in rectus femoris	0.91	9.25	6.68	1.24	0.91	0.82	< 0.001

Independent variable is percent changes of echo intensity (EI) in rectus femoris, biceps femoris, and thigh, percent changes of muscle thickness in rectus femoris, biceps femoris, and thigh, and percent changes of subcutaneous fat in anterior, posterior and thigh. SEE, standard error of the estimate.

et al. (21). Yamada et al. (22) investigated the prevalence of sarcopenia in community-dwelling Japanese; they focused on age, and found that the risk factor for sarcopenia was increased age ≥ 80 years. The average age of participants was 76.7 ± 5.6 in the Tr-group and 72.9 ± 6.6 in the Cont-group, and it may be suggested that the age was much younger than is typical for the emergence of sarcopenia; however, those in the Tr-group needed long-term care in daily living regardless of whether or not they were not diagnosed with the condition. Legrand et al. (23) found that muscle mass was no different between the older with low physical activity performance and those with normal/high physical activity performance (for both men and women). Furthermore, muscle mass was not selected as the factor to categorize low physical activity performance, implying that there is a possibility that the need for long-term care for assistance with ADL might be less affected by sarcopenia. In our study, we measured MT in two muscles of the thigh as another parameter of muscle size. The thickness of the thigh was significantly increased after 24 months in Tr-group (Table 2). It is possible that our training not only prevented age-related muscle atrophy but also induced muscle hypertrophy, even in older individuals. We previously reported that resistance training using hydraulic resistance machine induced a 15% increase in thigh MT after 12 months, and this rate was similar in our study (approximately 14%), suggesting that the increase in muscle size reached a plateau after 12 months of training (2). On the contrary, McCartney et al. (24) reported that incremental resistance training for 24 months continually increased muscle size through the training period. The participant, circumstance, training regimen, and purpose of the two studies differed; in particular, it was difficult to increase the resistance and frequency for our participants because they needed long-term care and the training was carried out as the part of their rehabilitation program. However, considering a muscle size decrease of 0.6% to 1.2% per year by aging alone (25, 26), our training regimen was effective in preventing the age-related decline in muscle size by preventing the onset of sarcopenia.

We measured EI from the thigh as the parameter of muscle quality, and EI was constant throughout the training intervention (Table 2). The decline in EI by 1.5 to 6.0 months of training has been shown in many previous studies, suggesting a decrease of the fat to muscle ratio (10, 15). In addition, we reported that EI was increased until reaching the baseline level after 12 months training (2). This observation was interpreted as the mechanism of restoring fat in the skeletal muscle as an energy resource [the so-called "athlete paradox" (27)]. Considering this information, we hypothesized that EI increased by continuous training; however, the results did not support this hypothesis. Pruchnic et al. (28) investigated the effect of 3 months' moderate intensity exercise (using walking, running, or stationary cycling) on intramyocellular lipid (IMCL) in older obese subjects. They found that IMCL significantly increased with improvement of insulin sensitivity. Many studies supported this result; however, it is still unclear how the training intensity, duration, type (that is, resistance or endurance), and participants' characteristics affect this result. Our training intensity might be much lower than other reports and thus influence the result. The moderate (50% to 60% maximal oxygen consumption) intensity endurance training induced the increase in IMCL that has been previously reported

(28); however, we determined that the resistance and endurance training intensity reached the "somewhat hard" level based on the Borg scale, suggesting a correspondence to ≤ 40% heart rate maximum. Therefore, it was concluded that the infiltration of fat into skeletal muscle might be determined by training intensity rather than by training duration. Additionally, a previous study showed that the EI primarily reflects the EMCL, not the IMCL, in human thigh muscles (11). Further studies are needed to clarify the relationship between the physiological characteristics of muscle EI and EMCL by considering the parameters of muscle oxidative capacity or mitochondrial function and training response.

Several physical functions improved in the Tr-group after the continuation of training (Table 3). In particular, the gait abilities including walking time, and TUG test improved. Normal walking capacity is one of the factors in the diagnosis of both sarcopenia and frailty (21, 29). Most participants cleared the cut-off values after the training. However, the walking time scores in the Tr-group were statistically slower than those in the Cont-group, even after the training, suggesting that walking capacity remained lower compared with healthy participants. Studenski et al. (30) investigated the relationships between gait speed and survival rate in older men and women. They showed the importance of maintaining gait speed to survive longer. We clearly showed that resistance and endurence training improved 5-m maximal speed walking time (Table 3). Training may contribute greatly to the recovery of gait capacity in the older individuals who need long-term care, eventually making such care unnecessary. The improvement in TUG was also shown in the Tr-group (Table 3). It has been confirmed that the TUG score is related to balance score and ADL capacity (31). Shumway-Cook et al. (32) clarified that the TUG score was significantly slower in older adults with a history of falls compared with those without such a history. They proposed that a TUG score of ≥ 13.5 sec was classified as the "fallers" group. Two participants in the Tr-group had TUG scores more than the cut-off before the training; however, they improved the score to less than the cut-off after the 24 months of training. Furthermore, the difference in TUG scores between the Tr- and Cont-group disappeared after 24 months training. This finding implies that the TUG score in the old needing long-term care reaches the level of the TUG score in subjects not requiring long-term care. Thus it is important to continue the training to prolong the survival rate by preventing falls.

The KEPT did not change in the Tr-group through the 24-month period, although it decreased in the Cont-group (Table 3). Lindle et al. (33) established age- and gender-adjusted regression equations for the isometric KEPT. They showed that isometric KEPT declined 0.7% to 1.2% per year. The rate of KEPT decline in the Cont-group was 22.1%, faster than previously reported. This discrepancy could be explained by the lower number of participants, participants' physical condition, and/or the difference in study design. Actually, KEPT in one participant in the Cont-group could not be measured at 24 months because of physical deconditioning. Nevertheless, our results showed that the training did attenuate the age-related decline in KEPT. Furthermore, as the result of multiple regression analysis, we found that the percent change of KEPT was 82%, explained by that of EI in the RF (Table 4). It has been clearly shown that the KEPT, strength, and power were negatively correlated with quadriceps EI by cross-sectional studies (34, 35). As far as we know, our study provides the first evidence regarding the relationship of muscle quality and KEPT in a longitudinal study. We did not find the change of EI in RF by comparing before- and after-training results; however, there is a possibility that further continuation of concurrent training may increase EI with accompanied enhancement of KEPT. Even more surprisingly, muscle size (that is, MT) was not a factor in explaining the change in KEPT, although MT was strongly associated with muscle function in maximum voluntary contraction (36, 37). From this result, we could conclude whether muscle quality or size is important in maintaining or improving muscle function in older individuals. In further studies, it will be necessary to track the response in EI and KEPT changes over the 24-month training period.

This study had a limitation. The number of participants was relatively small. Twenty six participants in the Tr-group and 21 participants in the Cont-group were initially included in this study, however, half of participants dropped out during the intervention because of difficulty of gaining access to the facility, busy with a job, lower motivation, change of address, injury (fracture or arthralgia) and death, and a few participants could not perform the functional tests because of physical problems on the testing day (pain, communication difficulty, personal relationship problems and so on). Thus, a large-scale study is needed.

In conclusion, resistance and endurance training for 24 months positively affects muscle size and physical functions in older individuals with long-term-care recipients. Fat infiltration within a given muscle as a parameter of muscle quality evaluated by muscle EI did not change through the intervention; however, through training, the enhancement of fat may positively affect the increase in KEPT; in other words, if EI in the RF increases 1.0%, the KEPT also increases 1.2%. These results may suggest that low-intensity concurrent training is effective in improving physical functions with minor changes in muscle morphology in older adults receiving long-term care. This could eventually provide savings in medical care expenditures and care-work operations by helping the individual recover from long-term care.

Acknowledgments: The authors gratefully thank the volunteers for their participation. The authors also thank the training directors (Mr. Takashi Fukatsu, Ms. Naomi Ishimizu, Ms. Noriko Masuda, and Mr. Masanari Kuroki), all of whom are staff members at Kawai Rehabilitation Center, as well as the individuals who measured the physical functional parameters (Drs. Akira Saito, Ryosuke Ando, and Aya Tomita; Ms. Madoka Ogawa, and Mr. Shohei Kondo of Nagoya University).

Ethical Standards and experimental subjects: All examination protocols were approved by the Institutional Review Board of the Research Center of Health, Physical

Fitness, and Sports at Nagoya University, and were conducted in accordance with the guidelines of the Declaration of Helsinki.

Disclosure Statement: The authors declare no conflicts of interest.

Funding Sources: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Evans WJ, Campbell WW. Sarcopenia and age-related changes in body composition and functional capacity. J Nutr. 1993;123(2):465–468.
2. Yoshiko A, Kaji T, Sugiyama H, Koike T, Oshida Y, Akima H. Effect of 12-month resistance and endurance training on quality, quantity, and function of skeletal muscle in older adults requiring long-term care. Exp Gerontol. 2017;98:230–237.
3. Fukumoto Y, Ikezoe T, Yamada Y, et al. Skeletal muscle quality assessed from echo intensity is associated with muscle strength of middle-aged and elderly persons. Eur J Appl Physiol. 2012;112(4):1519–1525.
4. Akima H, Yoshiko A, Hioki M, et al. Skeletal muscle size is a major predictor of intramuscular fat content regardless of age. Eur J Appl Physiol. 2015;115(8):1627–1635.
5. Yoshiko A, Kaji T, Sugiyama H, Koike T, Oshida Y, Akima H. Muscle quality characteristics of muscles in the thigh, upper arm and lower back in elderly men and women. Eur J Appl Physiol. 2018;118(7):1385–1395.
6. Goodpaster BH, Thaete FL, Simoneau JA, Kelley DE. Subcutaneous abdominal fat and thigh muscle composition predict insulin sensitivity independently of visceral fat. Diabetes. 1997;46(10):1579–1585.
7. Boettcher M, Machann J, Stefan N, et al. Intermuscular adipose tissue (IMAT): association with other adipose tissue compartments and insulin sensitivity. J Magn Reson Imaging. 2009;29(6):1340–1345.
8. Binder EF, Yarasheski KE, Steger-May K, et al. Effects of progressive resistance training on body composition in frail older adults: results of a randomized, controlled trial. J Gerontol A Biol Sci Med Sci. 2005;60(11):1425–1431.
9. Gine-Garriga M, Guerra M, Pages E, Manini TM, Jimenez R, Unnithan VB. The effect of functional circuit training on physical frailty in frail older adults: a randomized controlled trial. J Aging Phys Act. 2010;18(4):401–424.
10. Radaelli R, Botton CE, Wilhelm EN, et al. Low- and high-volume strength training induces similar neuromuscular improvements in muscle quality in elderly women. Exp Gerontol. 2013;48(8):710–716.
11. Akima H, Hioki M, Yoshiko A, et al. Intramuscular adipose tissue determined by T1-weighted MRI at 3 T primarily reflects extramyocellular lipids. Magn Reson Imaging. 2016;34(4):397–403.
12. Taaffe DR, Pruitt L, Pyka G, Guido D, Marcus R. Comparative effects of high- and low-intensity resistance training on thigh muscle strength, fiber area, and tissue composition in elderly women. Clin Physiol. 1996;16(4):381–392.
13. Seynnes O, Fiatarone Singh MA, Hue O, Pras P, Legros P, Bernard PL. Physiological and functional responses to low-moderate versus high-intensity progressive resistance training in frail elders. J Gerontol A Biol Sci Med Sci. 2004;59(5):503–509.
14. Scanlon TC, Fragala MS, Stout JR, et al. Muscle architecture and strength: adaptations to short-term resistance training in older adults. Muscle Nerve. 2014;49(4):584–592.
15. Radaelli R, Botton CE, Wilhelm EN, et al. Time course of low- and high-volume strength training on neuromuscular adaptations and muscle quality in older women. Age (Dordr). 2014;36(2):881–892.
16. Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. Med Sci Sports Exerc. 2009;41(7):1510–1530.
17. Takeshima N, Rogers ME, Islam MM, Yamauchi T, Watanabe E, Okada A. Effect of concurrent aerobic and resistance circuit exercise training on fitness in older adults. Eur J Appl Physiol. 2004;93:173–182.
18. Rech A, Radaelli R, Goltz FR, da Rosa LH, Schneider CD, Pinto RS. Echo intensity is negatively associated with functional capacity in older women. Age (Dordr). 2014;36(5):9708.
19. Akima H, Yoshiko A, Tomita A, et al. Relationship between quadriceps echo intensity and functional and morphological characteristics in older men and women. Arch Gerontol Geriatr. 2017;70:105–111.
20. Caresio C, Molinari F, Emanuel G, Minetto MA. Muscle echo intensity: reliability and conditioning factors. Clin Physiol Funct Imaging. 2015;35(5):393–403.
21. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010;39(4):412–423.
22. Yamada M, Nishiguchi S, Fukutani N, et al. Prevalence of sarcopenia in community-dwelling Japanese older adults. J Am Med Dir Assoc. 2013;14(12):911–915.
23. Legrand D, Adriaensen W, Vaes B, Mathei C, Wallemacq P, Degryse J. The relationship between grip strength and muscle mass (MM), inflammatory biomarkers and physical performance in community-dwelling very old persons. Arch Gerontol Geriatr. 2013;57(3):345–351.
24. McCartney N, Hicks AL, Martin J, Webber CE. A longitudinal trial of weight training in the elderly: continued improvements in year 2. J Gerontol A Biol Sci Med Sci. 1996;51(6):B425–B433.
25. Frontera WR, Hughes VA, Fielding RA, Fiatarone MA, Evans WJ, Roubenoff R. Aging of skeletal muscle: a 12-yr longitudinal study. J Appl Physiol. 2000;88(4):1321–1326.
26. Delmonico MJ, Harris TB, Visser M, et al. Longitudinal study of muscle strength, quality, and adipose tissue infiltration. Am J Clin Nutr. 2009;90(6):1579–1585.
27. Goodpaster BH, He J, Watkins S, Kelley DE. Skeletal muscle lipid content and insulin resistance: evidence for a paradox in endurance-trained athletes. J Clin Endocrinol Metab. 2001;86(12):5755–5761.
28. Pruchnic R, Katsiaras A, He J, Kelley DE, Winters C, Goodpaster BH. Exercise training increases intramyocellular lipid and oxidative capacity in older adults. Am J Physiol Endocrinol Metab. 2004;287(5):E857–E862.
29. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146–M156.
30. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. JAMA. 2011;305(1):50–58.
31. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142–148.
32. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. Phys Ther. 2000;80(9):896–903.
33. Lindle RS, Metter EJ, Lynch NA, et al. Age and gender comparisons of muscle strength in 654 women and men aged 20-93 yr. J Appl Physiol. 1997;83(5):1581–1587.
34. Cadore EL, Izquierdo M, Conceição M, et al. Echo intensity is associated with skeletal muscle power and cardiovascular performance in elderly men. Exp Gerontol. 2012;47(6):473–478.
35. Wilhelm EN, Rech A, Minozzo F, Radaelli R, Botton CE, Pinto RS. Relationship between quadriceps femoris echo intensity, muscle power, and functional capacity of older men. Age (Dordr). 2014;36(3):9625.
36. Freilich RJ, Kirsner RL, Byrne E. Isometric strength and thickness relationships in human quadriceps muscle. Neuromuscul Disord. 1995;5(5):415–422.
37. Strasser EM, Draskovits T, Praschak M, Quittan M, Graf A. Association between ultrasound measurements of muscle thickness, pennation angle, echogenicity and skeletal muscle strength in the elderly. Age (Dordr). 2013;35(6):2377–2388.