

Muscle hypertrophy response to resistance training in older women

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CHARETTE, SUSAN L., LAWRENCE McEVOY, GISELA PYKA, CHRISTINE SNOW-HARTER, DAVID GUIDO, ROBERT A. WISWELL, AND ROBERT MARCUS. *Muscle hypertrophy response to resistance training in older women*. *J. Appl. Physiol.* 70(5): 1912–1916, 1991.—We conducted a 12-wk resistance training program in elderly women [mean age 69 ± 1.0 (SE) yr] to determine whether increases in muscle strength are associated with changes in cross-sectional fiber area of the vastus lateralis muscle. Twenty-seven healthy women were randomly assigned to either a control or exercise group. The program was satisfactorily completed and adequate biopsy material obtained from 6 controls and 13 exercisers. After initial testing of baseline maximal strength, exercisers began a training regimen consisting of seven exercises that stressed primary muscle groups of the lower extremities. No active intervention was prescribed for the controls. Increases in muscle strength of the exercising subjects were significant compared with baseline values (28–115%) in all muscle groups. No significant strength changes were observed in the controls. Cross-sectional area of type II muscle fibers significantly increased in the exercisers ($20.1 \pm 6.8\%$, $P = 0.02$) compared with baseline. In contrast, no significant change in type II fiber area was observed in the controls. No significant changes in type I fiber area were found in either group. We conclude that a program of resistance exercise can be safely carried out by elderly women, such a program significantly increases muscle strength, and such gains are due, at least in part, to muscle hypertrophy.

postmenopausal women; muscle strength; exercise; muscle biopsy; type I and type II muscle fibers; cross-sectional fiber area

AGE-RELATED DECREASES in muscle strength and mass have frequently been observed in humans (8, 13, 17, 18). Increasing predominance of type I muscle fibers, atrophy of type II fibers, and degenerative changes in peripheral nerve and neuromuscular junctions have been demonstrated with consistency in older subjects (13, 16–18, 24–26). It is not well understood to what extent these changes reflect fundamental age-dependent alterations in muscle as opposed to environmental influences, such as diminished activity or altered hormonal milieu.

The decreased muscle strength of older individuals is at least partly reversible by resistance exercise (11, 12, 23). Resistance training clearly promotes muscle fiber hypertrophy in young men (20, 29, 30), and recent evidence (11, 12) suggests that increased strength in elderly

men reflects muscle hypertrophy. Most studies in this area have been carried out in men, and very little work has addressed the physiological response of women to strength training. Earlier studies of exercise in women used inappropriate methods, such as indirect anthropometry, to estimate muscle hypertrophy, and strong evidence for hypertrophy in women was not forthcoming (22, 33). However, Staron et al. (28) have recently published the results of a 20-wk weight training program in college women in whom substantial improvements in strength were accompanied by significant hypertrophy of all muscle fiber types, as determined from biopsies of the vastus lateralis muscle.

Particularly lacking has been any systematic inquiry into the training responses of elderly women. Agre et al. (1) reported strength gains in older women after a program of aerobic and light-resistance exercise. Recently, Fiatarone et al. (11) demonstrated that high-resistance training leads to significant gains in muscle strength, midthigh muscle area, and functional mobility in frail elderly adults. However, we are not aware of any studies that have directly examined by muscle biopsy the capacity of older women to achieve muscle hypertrophy with resistance exercise of moderate to high intensity. The scarcity of research in this particular area is unfortunate in view of the increased fracture risk in older women (9) and in view of the fact that muscle strength is related to both bone mass (5) and the risk of falls in frail elders (32). If resistance exercise were shown to increase muscle strength in older women, such a program might provide an effective strategy to improve bone strength and decrease the risk of falls, thereby decreasing the risk of fracture. We report here the results of such an experiment.

METHODS

Subjects. Twenty-seven healthy women aged 64–86 yr [mean 69.9 ± 1.0 (SE)] were recruited from the Palo Alto community. Volunteers were randomly assigned to control or exercise groups and were admitted to the Aging Study Unit, a clinical investigation ward, for a comprehensive screening procedure including a health history questionnaire, physical examination, standard electrolyte panel, and resting electrocardiogram (ECG) to verify that there were no preexisting disabilities or illnesses

TABLE 1. Primary muscle(s) involved in resistance exercises

Exercises	Muscle Group
Leg press	Quadriceps group
Leg flexion	Hamstrings group
Leg extension	Quadriceps group
Hip abduction	Gluteus medius
Hip adduction	Adductor magnus
Hip flexion	Iliopsoas
Hip extension	Gluteus maximus

that would preclude participation in a weight training program of moderate intensity. Subjects in the study were either sedentary or mildly to moderately active women, but none was currently involved in any type of resistance exercise program. The protocol was approved by the Human Subjects Committee of Stanford University, and subjects provided written consent before enrollment.

Submaximal exercise evaluation. As a screening procedure, all subjects assigned to the exercise group completed a submaximal graded exercise test on a bicycle ergometer. Blood pressure and ECG were monitored during the test as were the perceived rate of exertion and subjective experience of pain. The test was conducted by an exercise test technologist certified by the American College of Sports Medicine.

Strength testing. After formal instruction in the use of the weight-training equipment, all subjects underwent an initial assessment of muscle strength at the Musculoskeletal Research Laboratory, Veterans Administration Medical Center, Palo Alto, CA (MSRL). Seven exercises were selected to assess the strength of the hips and legs (Table 1). Leg presses were performed on a Universal Spartacus (Universal Gym Equipment, Cedar Rapids, IA); leg flexion and extension were performed on a Marcy Leg Trainer (Marcy Physical Fitness Products, Alhambra, CA). Hip adduction, abduction, extension, and flexion were executed on a Universal Total Hip Trainer (model 993494, Universal Gym Equipment).

Muscle strength was measured by the one repetition maximum (1-RM) method for each exercise. 1-RM is defined as the weight that can be lifted no more than one time with acceptable form. "Acceptable form" means that the exercise is performed primarily by the specified muscle groups without the use of momentum or any changes in body position, other than those directly resulting from the movement of the weight, during the exercise motion. When this criterion for acceptable form was not satisfied, the last successfully performed weight was noted as the 1-RM.

Before the start of the strength testing session, each subject walked for 5–10 min and then, under the guidance of the study coordinators, stretched the major muscle groups to be tested. After this initial warm-up period, subjects received detailed instructions and performed each exercise several times at very low resistance to enhance familiarization and warm-up. Each 1-RM test began at a weight near the suspected maximum to minimize fatigue resulting from repetition. Most subjects required no more than five repetitions to determine maximum

strength. All exercises were repeated with weight increments of 2.5–10 lb, depending on the exercise, until the subject could not lift additional weight with acceptable form. A 30-s rest period separated repetitions of the same exercise, with a 2-min rest between exercises. In our laboratory, the coefficient of variation for repeated measures is 2–5% for all strength tests in older women.

These strength measurements served as baseline values for both controls and exercisers. In addition, the preliminary 1-RM values were used to calculate the initial training load of 65% of 1-RM for the exercise group. Strength testing was repeated at the end of the 2nd wk to monitor increases in strength measurements resulting from familiarization with the equipment as well as the training program. Strength testing was conducted again after the 7th and 12th wk of training, thus dividing the final 10 wk of training into two 5-wk training blocks. Final strength values were determined for both the exercisers and controls at the end of the training period.

Training. Subjects in the exercise group engaged in a 12-wk weight training program consisting of the seven resistance exercises for the leg and hip listed in Table 1. Training sessions were conducted 3 days/wk at the MSRL and were carried out in groups under direct supervision by the study personnel. Each session began with a 10-min walk followed by a period of stretching. Three sets of six repetitions of each exercise were performed during each training session. After 2 wk of training, the number of sets of leg extension and leg press was increased from three to six to increase the total work performed by the quadriceps group. Adequate rest was permitted between sets to minimize the effect of muscular endurance in performing the increased exercise. Subjects carried out each repetition at a specified tempo. The concentric phase of the repetition was performed over 2 s, and the eccentric phase was executed over 3 s.

The initial level of exercise was set at 65% of 1-RM for the first 5 wk, 70% for the next 4 wk, and 75% for the last 3 wk. In addition to these increases in intensity, the 1-RM values were adjusted immediately before weeks 3 and 8 of training to accommodate increases in maximal strength. Accordingly, most exercisers experienced load increases at the end of 2, 5, 7, and 9 wk and finished the training period with 3 wk of training at 75% of the 7-wk 1-RM.

Subjects in the control group did not participate in the training program. They were instructed to maintain their normal level of activity and were specifically asked not to start a new exercise regimen during this 12-wk period. The controls were informed that they could participate in a similar training program after completion of the study. In addition, frequent contact was maintained with the controls to sustain their level of interest and to confirm follow-up appointments.

Muscle biopsies. Needle biopsies were taken from the vastus lateralis muscle of the nondominant thigh under local anesthesia (Xylocaine, 1%) from all subjects at the beginning and on completion of the study. The Bergström biopsy trephines had a 5-mm internal bore, and samples were taken under light suction (4). Initial biopsies were obtained before the initiation of exercise, and

follow-up specimens were completed within 1 wk of the final exercise session.

The biopsy site on each occasion was at the midlateral thigh at a point 6 in. proximal to the lateral femoral condyle, and the second biopsy was taken from the incision site of the first biopsy. Each sample was oriented under a stereoscope, placed in mounting medium (Tissue-Tek II OCT compound), and frozen in isopentane cooled to its freezing point in liquid nitrogen (10). The specimens were stored at -80°C until histochemical analysis could be performed.

Muscle histology. Muscle samples were cut into cross-sections, 8- μm thick, in a cryostat (Histostat, model 975C, Cambridge Instruments, Buffalo, NY) at -20°C . The cross sections were stained for myofibrillar ATPase at pH 9.4 after preincubation at pH 9.7 to differentiate type I and type II fibers (10). No attempt was made in this study to analyze fiber subtypes.

Manual planimetry was performed on each muscle cross-section to determine fiber area, using the Bioquant Digitizing Morphometry program on a personal computer at a magnification of $\times 660$ (R and M Biometrics, Nashville, TN). Slides were analyzed in random sequence, and subject identity was not disclosed until consensus values for all specimens had been obtained. Two operators independently measured the area of 20 randomly selected type I and type II muscle fibers from each sample; both operators made two area measurements for each fiber (6). Only those fibers without artifact, with distinct cell borders, and with no tendency toward longitudinal cuts were included in the analysis (6). The mean cross-sectional area for each fiber type was determined from these 20 fibers (6, 14). The interobserver coefficient of variation for fiber area measurements was 3.7%.

The prevalence of type I and type II fibers was calculated for all specimens; 200 fibers, or all countable fibers if there were fewer than 200 fibers in the sample, were counted by one operator to determine these ratios (7, 14).

Data analysis. Data were maintained on a personal computer, and analysis was accomplished with the Statview II statistical package (Abacus Concepts, Berkeley, CA). Analysis included descriptive measures for all variables, paired *t* tests to compare initial and final values, factorial analysis to assess differences between controls and exercisers both before and after the training, and the coefficient of variation to determine the intra- and inter-operator error for fiber area measurements. All statistical analyses were two tailed. Results are given as means \pm SE.

RESULTS

General. Of the original population of 27 women, 5 (4 exercisers and 1 control) did not complete the study. One volunteer showed cardiac ischemic changes during submaximal stress testing and was excluded. Another subject experienced sufficient discomfort after initial strength testing that she declined further participation. Three volunteers left the study because of intercurrent illness unrelated to the training protocol. For the remaining 22 women (14 exercisers and 8 controls) protocol compliance was excellent. Ninety percent of exer-

TABLE 2. *Physical characteristics of exercise and control groups*

Group	n	Age, yr	Body Weight, kg	Height, m
Exercise	13	69.8 \pm 1.2	59.2 \pm 1.9	1.62 \pm 0.02
Control	6	67.7 \pm 1.7	58.8 \pm 1.7	1.63 \pm 0.04

Values are means \pm SE; n, no. of subjects.

cisers completed all training and testing sessions, and no training-related injuries were sustained. However, one or more biopsy specimens was inadequate for analysis in one exerciser and two controls. Thus the data reported below represent the 13 exercisers and 6 controls who satisfactorily completed the protocol and provided technically adequate biopsy material. Characteristics of these 19 subjects are summarized in Table 2. No significant baseline differences in age, weight, or height were found between the control and exercise groups at either the beginning or the end of the study.

Muscle strength. All initial strength values were similar for controls and exercisers (Table 3). After training, the exercise group demonstrated significant increases in strength for each exercise (Table 3), with the largest percent change on the leg curl (115 \pm 27%) and the smallest percent changes on the leg press (28.3 \pm 6%) and hip extension (28.3 \pm 4%).

The control group showed no significant pre-post differences for any of the seven exercises. The final 1-RM values were significantly different between the controls and exercisers for all exercises ($P < 0.001$ to $P < 0.05$) except the leg press ($P = 0.19$).

Muscle histology. The distribution of fiber types (means \pm SE) was 35.8 \pm 0.06% type I and 64.2 \pm 0.06% type II for the control group and 47.5 \pm 0.04% type I and 52.5 \pm 0.04% type II for the exercise group at baseline. The fiber type distributions determined from the second biopsies were not significantly different from the baseline values for both groups. In addition, differences in fiber distribution between control and exercise groups did not achieve statistical significance ($P > 0.10$).

Type I and type II mean fiber areas did not differ significantly between the two groups at the beginning of the study (Table 4). Neither controls nor exercisers experienced a significant change in type I fiber area over the course of the study. In the exercise group, a significant increase in mean type II fiber area of 20.1 \pm 6.8% ($P = 0.02$) was observed, with a mean increase of 456 \pm 169 μm^2 (Table 4). Type II fiber area in the control group did not change significantly.

A correlation matrix was run to compare changes in areas of both type I and type II fibers with baseline and final strength variables and with changes in strength. No significant associations emerged.

DISCUSSION

The results of this study confirm that a progressive weight-training program can produce significant strength gains in elderly women. Such gains are associated with increases in type II muscle fiber area and support the conclusion that skeletal muscle of elderly women retains the capacity to undergo hypertrophy.

TABLE 3. Initial and final strength values for exercisers and controls

Exercises	Exercisers 1-RM, kg		Controls 1-RM, kg		Difference, kg		%Change	
	Pre	Post	Pre	Post	Exercisers	Controls	Exercisers	Controls
Leg extension	18.4±1.6	33.9±2.1*	23.1±1.1	23.5±1.4	15.5	0.4	92.6±12.6	1.5±3.2
Curl	7.3±1.3	15.0±0.9*	10.8±1.7	10.6±1.6	7.7	-0.2	115.3±27.4	-1.1±2.9
Press	62.7±2.8	79.5±3.5*	66.3±4.2	71.2±4.8	16.8	4.9	28.3±5.7	7.5±3.6
Hip abduction	13.4±1.0	24.4±1.4*	15.3±1.9	15.3±1.9	11.0	0.0	90.6±13.2	2.6±9.3
Adduction	25.6±1.4	33.7±1.4*	25.9±4.0	25.6±2.9	8.1	-0.3	33.9±6.2	5.3±10.2
Extension	38.1±1.7	48.4±1.6*	35.5±4.6	39.5±2.9	10.3	4.0	28.3±3.7	15.2±6.7
Flexion	12.8±1.0	23.8±0.9*	13.1±2.7	13.0±2.1	11.0	-0.1	95.8±13.2	5.1±10.2

Values are means ± SE for 13 exercisers and 6 controls. 1-RM, 1 repetition maximum. * Different from Pre, $P < 0.001$.

Our subjects showed a marked increase in strength for each of seven exercises. The magnitude of these increases ranged from 28 to 115% of baseline values. These increases showed much more consistency from one site to the next when expressed as absolute increments and ranged from 7.7 to 16.8 kg, with the greatest increase occurring in the leg press. Although the percent increase was greatest in the leg curl, the absolute gain in strength was only 7.7 kg. Although Fiatarone et al. (11) and Frontera et al. (12) have previously shown that older people gain strength after dynamic high-resistance training, our study is the first to demonstrate that elderly women can safely engage in a high-resistance training program consisting of more than two exercises and involving muscle groups beyond the leg extensors and flexors.

The mechanisms responsible for these improvements in strength remain unclear (12, 16, 23). Two suggested mechanisms that may underlie training-induced increases in muscle strength include 1) an improvement in neuromuscular recruitment and 2) muscle hypertrophy, or an increase in muscle size due to an increase in the size of individual myocytes (19). Moritani and de Vries (22, 23) proposed that the primary basis for the strength gain in older men is enhanced neuromuscular recruitment rather than muscle hypertrophy. Their conclusion is problematic, because they used anthropometric methods to estimate muscle mass, and this technique does not provide an accurate assessment of hypertrophy. In contrast, Frontera et al. (12) provided radiological and morphological evidence of muscle hypertrophy in older men after a 12-wk program of resistance training.

In confirmation and extension of the report of Fiatarone et al. (11), our study demonstrates that older women who participate in a resistance training program similar to that of Frontera et al. (12) experience muscle hypertrophy as evidenced by increased muscle fiber area. The 20% increase in the cross-sectional area of type II muscle fibers that we observed is similar to the 27.6% increase reported by Frontera et al. for older men but remains

considerably less than the 45% increase found in young women by Staron et al. (28). At present, it is not possible to conclude whether this lower response reflects differences in training regimen or an age-related constraint on hypertrophy.

Although we found a significant increase in the area of type II fibers, no significant change in type I fibers was observed. It is possible that this type of resistance exercise is relatively selective for type II fibers (15, 29–31). However, Frontera et al. (12) and Staron et al. (28) reported significant increases in type I fiber area in their subjects. The reason for this discrepancy is not immediately clear but could be related to differences in training regimen. For example, our subjects did not receive the endurance stress that was imposed by these regimens, both of which involved demanding warm-up periods of aerobic activity. In addition, the protocol of Staron et al. involved exercise to exhaustion over a 20-wk period.

We note that our mean values for type I fiber area approximate those reported for a large population of younger women (27) and a smaller number of older women (3). However, we found that our mean value for type II fiber area was smaller than those previously noted for young women (27, 28). Decreased type II fiber area in older women could reflect an age-related alteration in physical activity or, alternatively, an inherent response of muscle to age. Because our subjects showed type II fiber hypertrophy after high-intensity resistance training, our results appear to favor the first hypothesis.

Although one might predict that changes in fiber area would correlate with changes in strength, we were unable to document any such relationship. This experience is not unique. Frontera et al. (12) found no correlation between changes in strength and muscle hypertrophy on biopsy. Similarly, no correlation has been observed between changes in muscle strength and changes in muscle cross-sectional area as measured by anthropometry (23, 34) or computed tomography (2, 11, 12). The increase in fiber area that we observed does not preclude a simulta-

TABLE 4. Initial and final muscle fiber areas

Group	n	Type I Fiber Area, μm^2		Type II Fiber Area, μm^2		Pre-Post Fiber Area Difference, μm^2		%Change in Fiber Area	
		Pre	Post	Pre	Post	Type I	Type II	Type I	Type II
Exercise	13	3,967±200	4,205±212	2,532±101	2,988±144*	238	456	7.3±5.3	20.1±6.8
Control	6	4,631±378	4,427±296	2,941±287	2,273±133	-204	-668	-6.1±8.1	-18.3±10.9

Values are means ± SE; n, no. of subjects. * Different from Pre, $P < 0.02$.

fiber area that we observed does not preclude a simultaneous improvement in neuromuscular recruitment, as proposed by Moritani and de Vries (23). In fact, Milner-Brown et al. (21) demonstrated improved synchronization of motor units after resistance training. Such an improvement could contribute to the observed lack of correlation between strength gain and hypertrophy response.

Our results leave unresolved a number of issues concerning the response to training of elderly women. These include the biochemical correlates of muscle hypertrophy, the effects of training on various fiber subtypes, and possible constraints on strength gains with longer or more intense training. Nonetheless, the results suggest that resistance training of high intensity can be safely carried out by elderly women, such a program significantly increases strength, and these gains are due, at least in part, to type II fiber hypertrophy. Such results support the idea that resistance training may be a useful model to examine the effects of exercise on posture, gait, and bone mass in older women.

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