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High-volume, heavy-resistance strength training and muscle damage in young and older women

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JEFFREY T. LEMMER,[1] E. JEFFREY METTER,[3] BEN F. HURLEY,[1] AND MARC A. ROGERS[1]
[1]*Department of Kinesiology, College of Health and Human Performance, University of Maryland, College Park 20742;* [2]*Department of Physical Therapy, University of Maryland Eastern Shore, Princess Anne 21853; and* [3]*Gerontology Research Center, National Institute on Aging, Baltimore, Maryland 21224*

Roth, Stephen M., Gregory F. Martel, Frederick M. Ivey, Jeffrey T. Lemmer, E. Jeffrey Metter, Ben F. Hurley, and Marc A. Rogers. High-volume, heavy-resistance strength training and muscle damage in young and older women. *J. Appl. Physiol.* 88: 1112–1118, 2000.—To determine possible age differences in muscle damage response to strength training, ultrastructural muscle damage was assessed in seven 20- to 30-yr-old and six 65- to 75-yr-old previously sedentary women after heavy-resistance strength training (HRST). Subjects performed unilateral knee-extension exercise 3 days/wk for 9 wk. Bilateral muscle biopsies from the vastus lateralis were assessed for muscle damage via electron microscopy. HRST resulted in a 38 and 25% increase in strength in the young and older women, respectively ($P < 0.05$), but there were no between-group differences. In the young women, 2–4% of muscle fibers exhibited damage before and after training in both the trained and untrained legs (P = not significant). In contrast, muscle damage increased significantly after HRST, from 5 to 17% of fibers damaged ($P < 0.01$), in the older women in the trained leg compared with only 2 and 5% of fibers damaged in the untrained leg before and after training, respectively. The present results indicate that older women exhibit higher levels of muscle damage after chronic HRST than do young women.

aging; gender; muscle injury; regeneration; resistance training

AGING IS ASSOCIATED WITH a progressive loss of muscle mass and strength (31), which can result in reduced functional capacity (12). Decreased physical activity is a contributor to sarcopenia (13), and strength training has been shown to significantly increase muscle fiber size and strength in older individuals (22), thus improving functional capacity, even in frail elderly people (9). Both acute and chronic exercise, especially activities involving eccentric muscle actions, are known to elicit ultrastructural muscle damage (10, 19, 25, 27); however, the effects of strength training on muscle ultrastructure have not been clearly defined for skeletal muscle from older individuals.

Several studies have indicated that older animals are more susceptible to acute eccentric exercise-induced muscle damage than are young animals (5, 17). In humans, Fiatarone Singh et al. (8) reported increased muscle damage in both older men and women after 10 wk of strength training, but gender differences were not discussed, and young subjects were not included for comparison. Manfredi et al. (16) found higher levels of muscle damage in older men after acute eccentric exercise compared with young men. We (25) recently reported significant increases in ultrastructural muscle damage in both young and older men after 9 wk of heavy-resistance strength training (HRST), but no differences existed between the groups before or after training. Thus the effects of age on muscle damage response to strength training are unclear.

Two lines of evidence suggest that the response to exercise and aging may differ between men and women. First, Komulainen et al. (14) have reported lower levels of muscle damage in female compared with male rats after "eccentrically biased" downhill running, and lower creatine kinase levels have been reported in women compared with men after strenuous exercise (24). Second, age-associated losses of strength and muscle mass start sooner (15) and are greater in women than men (3, 15, 23), possibly contributing to higher rates of falls (21). Thus whereas HRST programs used in the treatment of sarcopenia appear important for older women, the muscle damage response to HRST is poorly characterized in this population. Therefore, we hypothesized that older women would demonstrate higher levels of muscle damage in response to HRST compared with young women. The present investigation extends our laboratory's previous work in men (25) to examine possible age and gender differences in exercise-induced ultrastructural muscle damage in young and older women before and after 9 wk of unilateral, high-volume HRST.

METHODS

Subject selection. Twenty healthy female subjects volunteered for this study. The subjects consisted of 10 young women between 20–30 yr and 10 older women between 65–75 yr. All subjects were screened by a physician who performed a

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medical history, physical examination, and graded maximal exercise test. All subjects were nonsmokers and free of significant cardiovascular, metabolic, or musculoskeletal disorders. Individuals enrolled in the study had not participated in a regular exercise program for at least 6 mo before their recruitment. After all methods and procedures were explained, the subjects read and signed a written consent form for the project, which had been approved by the Institutional Review Board at the University of Maryland, College Park. All subjects were reminded throughout the study not to alter their regular physical activity levels or dietary habits for the duration of the investigation.

Body composition. Body composition was assessed before and after HRST by using a Lunar DPXL dual-energy X-ray absorptiometer (software version 1.22, Lunar) as previously described (25, 30). Body weight was measured weekly during an exercise session by using a medical beam scale, and subjects were encouraged to maintain their before-training body weight.

Strength testing. Muscle strength was assessed in both quadriceps unilaterally via a one-repetition-maximum (1-RM) test by using the Keiser K-300 pneumatic variable-resistance knee-extension machine, as described previously (25). Briefly, three training sessions were conducted using light resistance before the strength testing to familiarize the subjects with the equipment, training protocol, and proper exercise technique. After the familiarization sessions and before the HRST sessions began, knee-extensor 1-RM strength was assessed. The same investigator administered the 1-RM strength test before and after training, and all testing procedures were standardized based on specific seat and body positions on the Keiser machine. After the 1-RM test, each subject's 5 RM was also determined by using the same procedure to establish the initial resistance for the first regular HRST session.

HRST protocol. Each training session was preceded by a 3-min warm-up on a stationary cycle followed by 5–10 min of static stretching of both quadriceps. The training protocol consisted of 9 wk of unilateral HRST of the knee extensors of the dominant leg with the nondominant leg serving as a control, as described previously (25). The training program consisted of five sets of high-volume (55 total repetitions, including 5 warm-up repetitions during the first set), heavy-resistance knee-extension exercise performed 3 days/wk. The details of the HRST protocol are outlined in detail elsewhere (25). In general, subjects completed a set of five repetitions of knee extension at the 5-RM resistance (after a warm-up set of 5 repetitions). The resistance of subsequent sets was initially set at 5 RM, with the resistance incrementally decreased by the subject to perform a total of 10, 15, and 20 repetitions/set, respectively. Specified rest periods were allowed between sets. An exercise specialist directly supervised the exercise sessions of every subject at every training session to verify compliance with the training protocol. Increases in resistance occurred throughout the 9-wk training program. When a subject completed more than five repetitions at the 5-RM resistance during the third set of 10 repetitions, the 5-RM resistance was increased by a 1- to 2-kg increment during the next training session.

Muscle tissue sampling. Muscle biopsies were taken from each vastus lateralis muscle of a subject before and after the HRST program by using the percutaneous needle-biopsy technique (4). The initial sampling site determined for each subject was 14 cm from the proximal border of the patella at the midline of the quadriceps. The muscle sample was obtained with suction by using a 5-mm Bergstrom biopsy needle, and all biopsies were performed by the same investigator. The biopsy sample taken after training was obtained at a new site 2.5 mm proximal and lateral to the original incision, with the biopsy needle directed into approximately the same muscle position as the first biopsy. The before-training biopsy occurred ~1 wk before the familiarization sessions and 2 wk before the start of the training program. The after-training biopsy occurred 24–48 h after the last training session.

Muscle fixation and analysis. The muscle sample (~50–70 mg) was placed immediately on an ice-chilled watch glass and dissected of all visible blood and adipose and connective tissue. The sample was minced for fixation into eight to ten 0.5- to 1.0-mm cubes. The same investigator dissected and prepared all samples. To control for the possibility of artifacts resulting from the mincing and fixation, biopsy samples were taken from both the trained and untrained (control) leg before and after HRST. The fixation procedure used in the present investigation is well established (8, 10, 16, 19) and has been described in detail previously (25). In general, samples were initially fixed in 2% gluteraldehyde solution before postfixation in 1% osmium tetroxide and staining for positive contrast. Samples were embedded longitudinally in epoxy resin (Spurr's), with five sample blocks obtained from each biopsy. Thick (0.8–1.0 μm) and thin (60–70 nm) sections were obtained, and the thin sections were placed on 75 × 300 copper grids for electron microscopy. The sections on each grid were stained with 2% uranyl acetate and 0.1% lead citrate and were viewed on a Zeiss EM 10 CA electron microscope operated at 80 kV. A representative section on each grid was viewed at ×2,000–12,500 magnification, and micrographs were taken of each fiber. Muscle damage was quantified initially by using images directly from the electron microscope and subsequently confirmed via prepared micrographs. The primary investigator was blind to both the age group and time point during the analysis. A blinded second investigator repeated the analysis separately using the prepared micrographs, and interrater reliability was calculated from the results (Pearson's $r = 0.95$).

Quantification of muscle damage. Each viable muscle fiber was analyzed for ultrastructural muscle damage. Hypercontracted fibers were excluded from the analysis, as the cause of the associated damage was unable to be determined (25). Hypercontracted fibers were defined as exhibiting large areas (a majority of the fiber) of extreme sarcomere shortening, without disruption of Z-band or myofibrillar material, as described previously (25). Previous research suggests that the source of this structural alteration is the biopsy procedure (6, 10). A viable muscle fiber was defined as a transverse or longitudinally oriented fiber with a minimum visible length of 200 μm with minimal muscle hypercontraction. Initially, 40–50 fibers were assessed for each subject, but only 15–40 fibers were analyzed for muscle damage for each subject per time point because of the elimination of hypercontracted fibers. Each fiber was analyzed individually for the extent of damage, and all fibers per subject were assessed for the extent of fiber disruption. The percentage of fibers exhibiting myofibrillar disruption was then calculated for each subject. A disrupted fiber was defined as any fiber containing disruptions in the normal myofibrillar banding pattern. Specifically, fibers exhibiting Z-line streaming or M-band disruption, as well as disruption of the myofilament structure within sarcomeres, were classified as damaged. An area of disruption occupying one to two adjacent myofibrils and/or one to two continuous sarcomeres was classified as a "focal" disruption (19). An area of disruption encompassing 3–10 adjacent myofibrils and/or 3–10 continuous sarcomeres was designated as "moderate" disruption, and an area of disruption

covering >10 adjacent myofibrils and/or continuous sarcomeres was defined as "extreme" (10).

Statistical analysis. The tissue specimens from three young and four older subjects were eliminated from the analysis because of extensive hypercontraction, leaving seven young and six older subjects for statistical analysis. As no significant differences existed in the numbers of fibers within each damage category between groups and the majority of fibers were categorized as "focal" damage, all fibers exhibiting damage were pooled for statistical analysis. Ultrastructural muscle damage and strength test data were analyzed by using a two-factor (2 × 2; time × group) repeated-measures ANOVA. Statistical significance for all ANOVA analyses was accepted at $P < 0.05$. All data are reported as means ± SD.

RESULTS

Physical characteristics and 1-RM strength values. Table 1 outlines the physical characteristics for both groups. Body weight remained stable throughout the training for both groups, and only age and body composition differed significantly between groups ($P < 0.05$). Body composition did not change after HRST in either group. All subjects completed a minimum of 27 supervised exercise sessions over ~9 wk. Strength values were significantly higher for the young women than for the older women before training in both the trained and untrained legs ($P < 0.05$). As shown in Table 1, strength increased significantly in the trained leg of both young and older women, whereas it increased in the untrained leg only in the young women ($P < 0.05$).

Muscle fiber damage. No significant difference in muscle damage existed between groups before training in either the trained or untrained legs (Fig. 1). Muscle damage increased significantly in the trained leg in the older women (5.2 ± 5.8 vs. 16.5 ± 11.3%; $P < 0.01$) but not in the young women (2.0 ± 4.0 vs. 2.9 ± 4.2%; $P =$ not significant) after 9 wk of unilateral HRST. No significant differences in muscle damage were observed in before- and after-training muscle samples obtained from the untrained legs in either group.

Figure 2 is an electron micrograph representation of a normal skeletal muscle fiber not exhibiting myofibrillar disruption or Z-line streaming. In both the young and older women, muscle damage was primarily focal in nature (1–2 damaged sarcomeres) both before and after training in each leg (Fig. 3). Most of the focal damage consisted of "frayed" or smeared sarcomeres with myofibrils showing a disruption from their normal banding pattern, although occasionally only the Z disk of a myofibril would exhibit degeneration. Fibers exhibiting moderate damage were seen in both groups; however, moderately damaged fibers were most often observed in the trained leg of the older women after HRST (Fig. 4). Extreme muscle damage (>10 damaged sarcomeres) was seen only rarely (4 fibers) with no consistent pattern of distribution within or between the groups (Fig. 5). In contrast to our previous findings in young and older men (25), separation of myofibrils, possibly indicating myofibrillar edema, was rarely seen before or after training in either the young or older women. Although not quantified, myofibrillar splitting

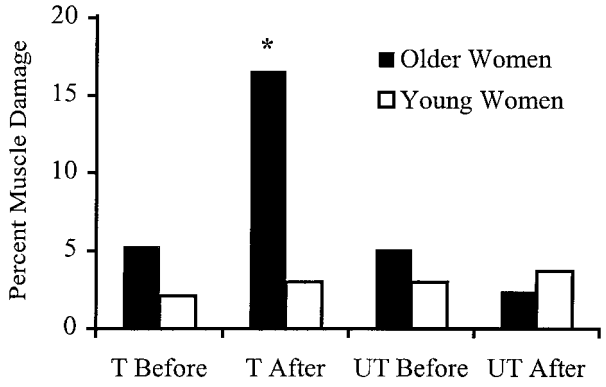

Fig. 1. Percentage of skeletal muscle fibers exhibiting ultrastructural muscle damage for both trained (T) and untrained (UT) legs. Before, before training; After, after training. *$P < 0.05$ vs. T Before.

Table 1. *Subject characteristics and 1-RM strength values for young and older women after 9 wk of unilateral heavy-resistance strength training*

	Young Women		Older Women	
	Before HRST	After HRST	Before HRST	After HRST
Age, yr	26 ± 1*		67 ± 3	
Height, cm	168.5 ± 5.8		157.0 ± 6.1	
Weight, kg	68.1 ± 9.5	69.5 ± 7.1	72.7 ± 7.0	72.9 ± 7.3
Fat, %	30.8 ± 4.7*	31.5 ± 3.4*	40.7 ± 6.4	39.2 ± 6.9
Trained, kg	61.9 ± 17.3*	85.0 ± 18.8*†	42.7 ± 5.4	52.1 ± 8.0†
Untrained, kg	59.7 ± 15.5*	68.6 ± 15.4*†	44.1 ± 5.9	46.9 ± 6.4

Values are means ± SD for $n = 7$ young and 6 older women. 1 RM, 1 repetition maximum; HRST, heavy-resistance strength training. 1-RM strength values are given for the trained and the untrained leg. *Significant difference between groups, $P < 0.05$. †Significantly different from before training, $P < 0.05$.

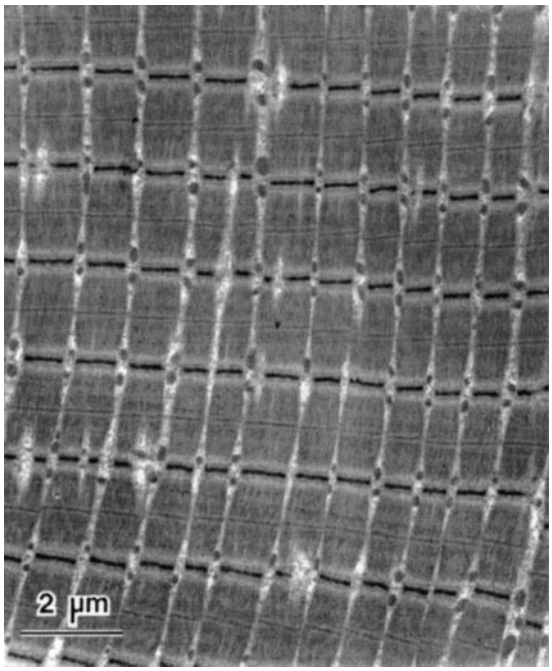

Fig. 2. Electron micrograph representing a normal skeletal muscle fiber free of myofibrillar disruption and Z-line streaming (magnification, ×7,250).

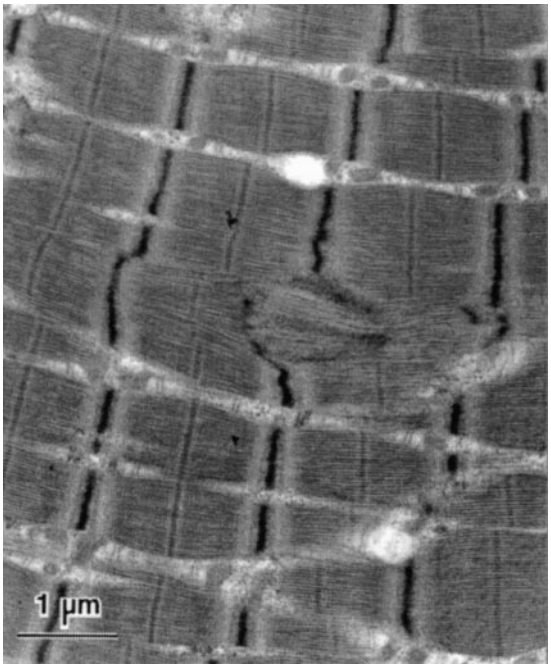

Fig. 3. Micrograph of a longitudinally oriented muscle fiber exhibiting focal muscle damage occupying 2 continuous sarcomeres (magnification, ×14,400).

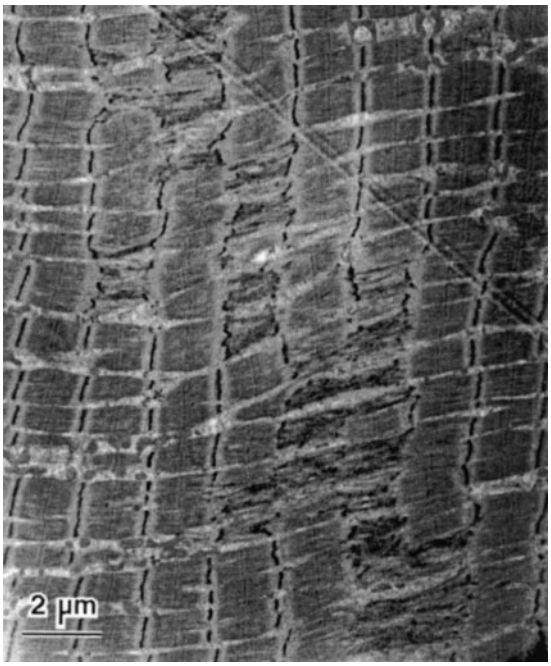

Fig. 5. Micrograph of a muscle fiber exhibiting extreme myofibrillar disruption occupying >10 sarcomeres and associated Z disks (magnification, ×5,750).

was commonly exhibited throughout both trained and untrained biopsies of both groups with no apparent relation to myofibrillar damage, similar to our data in men (25).

Two of the older (postmenopausal) women were taking estrogen replacement medication during the present investigation. Neither subject exhibited baseline muscle damage, and the percentage of fibers exhibiting muscle damage increased to 0 and 17%, respectively, after HRST for these two women. The role of estrogen per se in the muscle damage response to HRST was not a purpose of the present investigation, and estrogen concentrations were not examined.

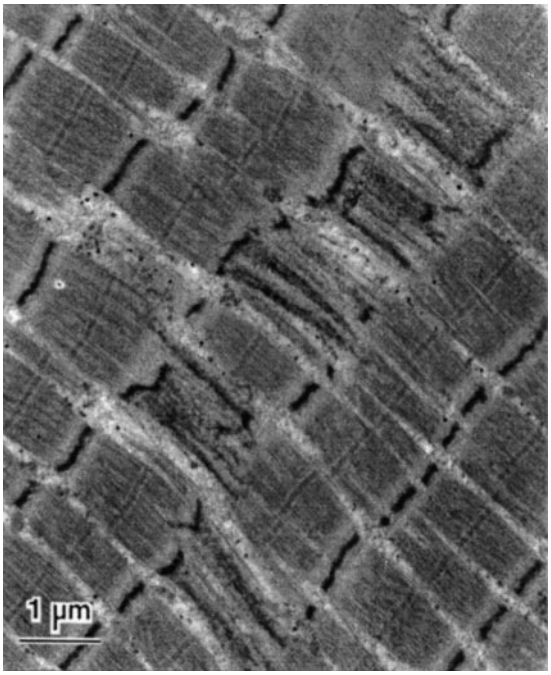

Fig. 4. Micrograph of a muscle fiber exhibiting moderate myofibrillar disruption occupying several adjacent sarcomeres and associated Z disks (magnification, ×11,500).

DISCUSSION

The purpose of the present investigation was to assess ultrastructural muscle damage in previously inactive young and older women before and after 9 wk of HRST. To our knowledge, this is the first investigation to demonstrate an increase in muscle damage after 9 wk of HRST in older compared with young women. In the present study, the extent of muscle damage did not increase in the untrained leg of either group after 9 wk of HRST. Similarly, no increase in damaged fibers was observed in the trained leg of the young women after training. However, the older women exhibited a significant increase in muscle damage, with 17% of muscle fibers exhibiting muscle damage after 9 wk of HRST. Our group has previously reported that both young and older men exhibited increased muscle damage similarly after 9 wk of HRST, with from 0–1 to 6–7% of muscle fibers exhibiting muscle damage before and after training, respectively (Fig. 6) (25). The data from the present investigation indicate a possible age-gender interaction, as the older women exhibited a significant increase in muscle damage to levels twice that of young or older men, whereas young women exhibited no increase in muscle damage from before training.

In the present study, the young women exhibited ~3% of muscle fibers with muscle damage in both the trained and untrained legs before training. In the older

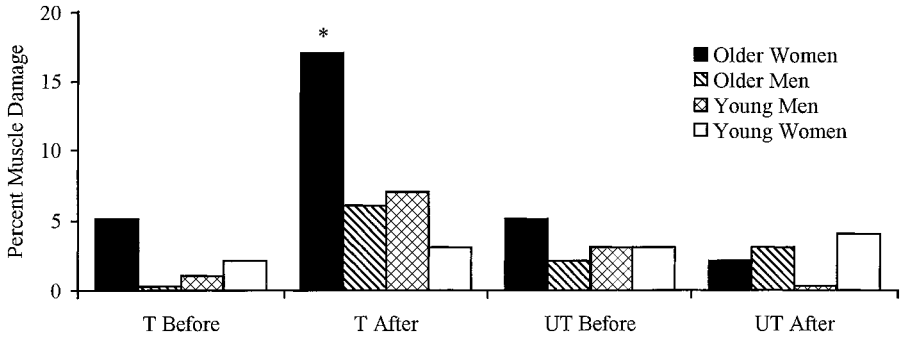

Fig. 6. Percentage of skeletal muscle fibers exhibiting ultrastructural muscle damage for both the T and UT legs in both young and older men (25) and women. Data presented for men are included from our previous report (25). Data were compared by using repeated-measures ANOVA procedures with a Tukey post hoc comparison, which indicated that only the older women demonstrated a significant increase in muscle damage after training. * $P < 0.05$ vs. T Before. No other between- or within-group differences were noted.

women ~5% of fibers displayed damage in both the trained and untrained legs before training, thus indicating no difference in baseline muscle damage between the groups. Whereas previous investigations have suggested that older individuals exhibit higher levels of ultrastructural muscle damage (26, 29), the present results are similar to data reported for young and older men (0–3% of fibers exhibiting damage) (25), as well as for young women (2–4%) (18). Collectively, these data indicate no differences in baseline muscle damage between healthy, physically inactive young and older (65–75 yr) men and women.

Whereas skeletal muscle from older animals appears to be more susceptible to exercise-induced muscle damage (5, 17), the results from studies in humans are less clear. For example, Manfredi et al. (16) reported that older men exhibited higher levels of muscle damage compared with young men after acute eccentric exercise designed to elicit muscle damage. They reported that >90% of muscle fibers exhibited muscle damage in the older men after the exercise compared with values of 5–50% for young men after a similar protocol (16, 20). Fiatarone Singh et al. (8) recently reported significant increases in muscle damage in older subjects (72–98 yr), but young individuals were not included for comparison. Using the same unilateral knee-extension protocol employed in the present study, we recently reported that both young and older men demonstrate similar increases in muscle damage after 9 wk of HRST (25). In that investigation, we reported that only ~7% of muscle fibers exhibited muscle damage in both groups after HRST (25). The present results in women indicate a possible age-related difference in muscle damage response to HRST, with older women demonstrating significantly higher levels of muscle damage after HRST than young women. Furthermore, compared with our previous work, older women exhibited significantly higher levels of muscle damage than young and older men, indicating a possible age-gender interaction.

Gender differences have been noted both in the muscle damage response to strenuous exercise (14) and in the loss of muscle mass and strength with age (3, 23), but gender differences in the muscle damage response to strength training are generally unclear. For example, in college-aged men and women, Staron et al. (27) reported that ~9% of muscle fibers exhibited muscle damage after 8 wk of progressive, lower body strength training, indicating an increase in muscle damage from before training in both groups with no gender differences. Staron et al. (28) had previously reported evidence of muscle damage in strength-trained young women. Fiatarone Singh et al. (8) reported significant increases in muscle damage in older men and women after a 10-wk strength-training program, although gender differences were not indicated. The present results indicate no increase in muscle damage in young women in response to HRST, whereas older women demonstrated a significant increase. Furthermore, compared with our previous work in men (25), the present results indicate that older women appear to demonstrate the greatest increase in muscle damage in response to HRST when young and older men and women are simultaneously compared. The basis for possible gender differences in muscle damage response to strenuous exercise is unknown, but estrogen has been implicated as having a role in muscle damage (1, 2).

Comparison between the present investigation and previous work in our laboratory in men revealed other possible age and gender differences. In both investigations, muscle fibers exhibiting moderate damage were seen predominantly in older men and women after the training protocol and were rarely observed in the young individuals (25). Furthermore, we previously reported that myofibrillar separation or edema was a notable feature in the muscle of both young and older men after 9 wk of HRST (25). Myofibrillar separation was rarely seen in the young or older women after 9 wk of HRST in the present investigation.

The design of the HRST protocol used in the present investigation included several important conditions to assess muscle damage more accurately after strenuous strength training. Muscle samples from the untrained leg allowed the assessment of possible muscle damage due to either the biopsy procedure (6, 27) or the tissue preparation itself. In addition, the unilateral nature of the training provided for consistency across neural input and hormonal signals to the untrained leg. The exercise protocol was designed to overload the muscle to induce both muscle strength and hypertrophy, without subjecting the muscle to high-eccentric forces, which are known to result in muscle damage. Certain limitations should be considered, however, for both the present investigation and other research using the needle biopsy procedure. For example, the invasive

nature of this type of investigation tends to result in lower sample sizes. The tissue samples are small, and the data are assumed to represent structural changes in other areas of the muscle. Furthermore, the data from one particular muscle (e.g., vastus lateralis) may not be representative of the response of other muscles to a similar stimulus.

The levels of muscle damage demonstrated in the present study (~17% of muscle fibers exhibiting damage in the older women after HRST) and our previous report in men (25) indicate that chronic HRST does not elicit a functional deficit in muscle, as both strength and muscle volume (F. M. Ivey, S. M. Roth, R. E. Ferrell, B. L. Tracy, J. T. Lemmer, D. E. Hurlbut, G. F. Martel, E. L. Siegel, J. L. Fozard, E. J. Metter, J. L. Fleg, and B. F. Hurley, unpublished observations) increased significantly in all groups. Furthermore, strength training is considered an important intervention for reversing sarcopenia (11), and the present results provide no basis for suggesting otherwise. The role of muscle damage in muscle adaptation has been discussed previously (7, 8); however, the present investigation was not designed to assess either the mechanism of muscle damage or the role of such damage in muscle adaptation.

In summary, the data presented here indicate that, when combined with our data from men (25), no differences exist in ultrastructural muscle damage before training in young and older physically inactive men and women, contrary to previous reports. Furthermore, older but not young women exhibit a significant increase in ultrastructural muscle damage after 9 wk of high-volume HRST. These results differ from our previous investigation in young and older men (25), indicating a possible age-gender interaction with regard to the muscle damage after HRST.

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