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Elderly Men and Women Benefit Equally From Prolonged Resistance-Type Exercise Training

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This study compares the effects of 6 months resistance-type exercise training (three times per week) between healthy elderly women (n = 24; 71 ± 1 years) and men (n = 29; 70 ± 1 years). Muscle mass (dual-energy x-ray absorptiometry–computed tomography), strength (one-repetition maximum), functional capacity (sit-to-stand time), muscle fiber characteristics (muscle biopsies), and metabolic profile (blood samples) were assessed. Leg lean mass (3% ± 1%) and quadriceps cross-sectional area (9% ± 1%) increased similarly in both groups. One-repetition maximum leg extension strength increased by 42% ± 3% (women) and 43% ± 3% (men). Following training, type II muscle fiber size had increased, and a type II muscle fiber specific increase in myonuclear and satellite cell content was observed with no differences between genders. Sit-to-stand time decreased similarly in both groups. Glycemic control and blood lipid profiles improved to a similar extent in both women and men. A generic resistance-type exercise training program can be applied for both women and men to effectively counteract the loss of muscle mass and strength with aging.

Key Words: Sarcopenia—Muscle mass—Strength—Function—Men—Women.

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AGING is accompanied by the progressive loss of muscle mass and muscle strength, referred to as sarcopenia (1). The loss of muscle mass and strength leads to a substantial decline in functional capacity, an increased risk of falls and fractures, and an increased risk of developing chronic metabolic diseases (2,3). The relative loss of muscle mass and strength with age has been reported to be similar for men and women (4). However, the loss of muscle mass and strength may represent a greater health concern in women, as older women tend to suffer more from physical disabilities than older men (5). Effective interventions are required to prevent or treat the detrimental consequences of muscle mass and strength loss in both elderly women and men.

Resistance-type exercise training has been well established as an effective treatment strategy to counteract the loss of muscle mass and strength in the elderly population (6–9). Even in the very old population, substantial improvements in muscle mass, strength, and functional capacity have been observed following prolonged resistance-type exercise training (10). Also, at the muscle fiber level, it has been shown that both elderly men (11) and women (12) maintain the capacity to augment muscle fiber size and function. Despite the overwhelming evidence showing the efficacy of resistance-type exercise training to increase muscle mass and strength in the elderly population, there is much discrepancy on the proposed benefits of resistance-type exercise training in elderly women versus men. Previous work has suggested that muscle mass and strength gains following prolonged resistance-type exercise training are either similar (13,14), smaller (15–17), or even greater (18) in older women compared with older men. As it remains unclear whether women benefit to the same extent from prolonged resistance-type exercise training as men, there is still no consensus on whether resistance-type exercise training programs should be specifically tailored for gender.

Given the conflicting data on gender-based differences in the skeletal muscle adaptive response to prolonged resistance-type exercise training, the purpose of this study was to assess whether elderly men and women adapt differently to a generic prolonged resistance-type exercise training program. In this study, we compare structural, functional, and metabolic adaptations to prolonged resistance-type exercise training on a whole body, muscle, and muscle fiber level. We hypothesized that elderly men experience greater absolute but not relative gains in skeletal muscle mass and strength compared with women following 3 and 6 months of generic resistance-type exercise training.

As such, we speculate that a single generic resistance-type exercise training program can be applied successfully in both elderly men and women. The latter would greatly facilitate the implementation of exercise training programs in the older population.

In this study, we selected 60 healthy elderly men ($n = 31$) and women ($n = 29$) to participate in a generic 24-week resistance-type exercise training program (three sessions per week). Prior to and after 12 and 24 weeks of exercise training, we assessed skeletal muscle mass, muscle strength, functional capacity, muscle fiber characteristics, and metabolic profile. This study compares the clinical benefits of resistance-type exercise training between older women and men and addresses the question whether the same generic exercise program can be used for both genders.

Methods

Participants

A total of 29 healthy, elderly women (70 ± 1 years) and 31 healthy, elderly men (71 ± 1 years) volunteered to participate in a 24-week resistance-type exercise training program. Seven participants dropped out (two men and five women) during the study, one because of a heart attack that occurred at home, one because of a transient ischemic attack that occurred at home, and the other five participants dropped out because of time constraints. Medical history of all participants was evaluated and an oral glucose tolerance test and resting electrocardiogram and submaximal electrocardiogram were performed prior to selection. Exclusion criteria were defined that would preclude successful participation in the exercise program, and included (silent) cardiac or peripheral vascular disease and orthopedic limitations. Furthermore, as insulin resistance and/or type 2 diabetes have been associated with a more progressive loss of muscle mass and strength with aging (19), type 2 diabetes patients were excluded from participation (20). All participants were living independently and had no history of participating in any structured exercise training program over the past 5 years. All participants were informed on the nature and possible risks of the experimental procedures, before their written informed consent was obtained. This study was approved by the Medical Ethics Committee of the Maastricht University Medical Centre+ and is part of a greater project investigating the impact of combined dietary and exercise interventions to increase muscle mass and strength in different elderly populations (21–23).

Study Design

Before, during, and after exercise intervention, anthropometric measurements (height, body mass, waist–hip ratio, and leg volume [24]), strength assessment (one-repetition maximum [1RM]), computed tomography, and dual-energy x-ray absorptiometry scans were performed, and muscle biopsies, blood samples, 24-hour urine, and dietary intake and physical activity records were collected.

Exercise Intervention Program

Supervised resistance-type exercise training was performed three times a week for a 24-week period. Training consisted of a 5-minute warm-up on a cycle ergometer, followed by four sets on both the leg-press and leg-extension machines (Technogym, Rotterdam, The Netherlands). In addition, three sets were performed on the chest press and horizontal row, and (alternating) vertical lat pull and abdominal crunches, or biceps curl and triceps extension, followed by a 5-minute cooling-down period on a cycle ergometer. During the first 4 weeks of training, the workload was increased from 60% of 1RM (10–15 repetitions in each set) to 75% of 1RM (8–10 repetitions). Starting at week 5, four sets of eight repetitions were performed at 75%–80% of 1RM on leg press and leg extension. For the upper body exercises, two sets were increased to three sets starting in week 5. Resting periods of ~90 seconds between sets and ~3 minutes between exercises were allowed. Workload intensity was adjusted based on the 1RM tests (performed at week 4, 8, 12, 16, and 20). In addition, workload was increased when more than eight repetitions could be performed in three out of four sets. On average, participants attended 90% ± 1% of the scheduled exercise sessions in both groups.

Dietary Intake and Physical Activity Standardization

Standardized meals were provided to all participants the evening prior to each test day. The participants were instructed to refrain from strenuous physical activity for at least 3 days prior to testing. On all test days, participants arrived at the laboratory by car or public transportation following an overnight fast. To assess potential changes in habitual daily food intake and physical activity during the 6-month intervention period, the participants recorded 4 days weighted dietary intake records and 2 days physical activity records. Dietary intake was recorded before, after 4, 8, 12, 16, 20, and 24 weeks of intervention. Dietary records were analyzed with Komeet (Komeet, 4.059 BaS Nutrition Software, Arnhem, The Netherlands). Habitual physical activity was recorded before, after 12 and 24 weeks of intervention. For every type of activity, a mean equivalent task (MET) score was assigned to express the intensity of a specific activity as previously defined (25). One MET unit equals resting energy expenditure (ie, ~1 kcal per kg body weight per hour [25]). Energy expenditure was calculated as mean MET-hour/day (26).

Body Composition

Body composition and bone mineral content were measured with dual-energy x-ray absorptiometry (Hologic, Discovery A, QDR Series, Bradford, MA). Whole-body

and regional lean mass, fat mass, and bone mineral content were determined using the system's software package Apex version 2.3. Anthropometrics were measured by trained observers with standard technique; weight by digital scale to within 100 g; height by stadiometer to within 0.5 cm; circumferences to within 1 mm using a measuring tape, with waist midway between the lowest rib and the iliac crest with the participant standing at the end of gentle expiration, and hips at the greater trochanters (27). All body composition measurements were assessed before, after 12 and 24 weeks of the exercise program.

Anatomical cross-sectional area (CSA) of the *quadriceps* muscle was assessed by computed tomography scanning (Philips Brilliance 64, Philips Medical Systems, Best, The Netherlands) before, after 12 and 24 weeks of the exercise intervention program (3 days after strength assessment and prior to muscle biopsy collection). The scanning characteristics were as follows: 120 kV, 300 mA, rotation time of 0.75 second, and a field of view of 500 mm. While the participants were lying supine, legs extended and their feet secured, a 3-mm thick axial image was taken 15 cm proximal to the base of the patella. The exact scanning position was measured and marked for replication at subsequent visits. Muscle area of the right leg was selected between 0 and 100 Hounsfield units (28), after which the quadriceps muscle was selected by manual tracing using ImageJ software (version 1.45d, National Institute of Health, MD [29]). Using the described approach, we determined the CV for repeated scans (1 week apart) to be 0.8%. All analyses were performed by two investigators blinded to participant coding; intraclass correlation coefficients for inter- and intrainvestigator reliability were 1.0 and 1.0, respectively.

Muscle Biopsy Sampling

Three days prior to the onset of the intervention, after 12 weeks of intervention, and immediately after cessation of the intervention (4 days after final strength testing), skeletal muscle biopsies were taken from the right leg of each participant, in the morning following an overnight fast. After local anesthesia was induced, percutaneous needle biopsy samples (50–80 mg) were collected from the *vastus lateralis* muscle, ~15 cm above the patella (30). Any visible nonmuscle tissue was removed immediately, and biopsy samples were embedded in Tissue-Tek (Sakura Finetek, Zoeterwoude, The Netherlands), frozen in liquid nitrogen-cooled isopentane, and stored at −80°C until further histological analyses.

Immunohistochemistry

From all biopsies, 5-µm thick cryosections were cut at −20°C. Pre, 12 week, and 24 week samples from each participant were mounted together on uncoated glass slides. Care was taken to properly align the samples for cross-sectional fiber analyses. Muscle biopsies were stained for muscle fiber typing and myocellular satellite cell content as described previously (31), with slight modifications. In short, the slides were incubated with primary antibodies against major histocompatibility complex-I (A4.840, Developmental Studies Hybridoma Bank, Iowa City, IA), CD56 (BD Biosciences, San Jose, CA), and laminin (polyclonal laminin, Sigma, Zwijndrecht, The Netherlands). After washing (phosphate-buffered saline), slides were incubated with biotinylated goat anti-mouse IgG (Vector Laboratories, Burlingame, CA) to optimize staining results for CD56. After another wash, appropriate secondary antibodies were applied: goat anti-mouse IgM AlexaFluor555 and goat anti-rabbit IgG AlexaFluor647 (Molecular Probes, Invitrogen, Breda, The Netherlands), for major histocompatibility complex-I and laminin, respectively, and Streptavidin AlexaFluor488 (Vector Laboratories) for CD56. Nuclei were stained with 4,6-diamidino-2-phenylindole (0.238 µM; Molecular Probes). After a final washing step, all slides were mounted with cover glasses using Mowiol (Calbiochem, Amsterdam, The Netherlands).

Images were visualized and automatically captured at ×10 magnification with a fluorescent microscope equipped with an automatic stage (IX81 motorized inverted microscope, Olympus, Hamburg, Germany). The image was centered and focused on each section, after which the microscope was programmed to automatically capture a series of images to record the entire section. All images were then pasted together to reproduce a single image file of the entire biopsy section, including all four fluorescent channels (ie, a 4,6-diamidino-2-phenylindole UV excitation filter [360–370 nm] for the nuclei, a fluorescein isothiocyanate excitation filter [470–495] for CD56, a tetramethyl rhodamine isothiocyanate excitation filter [540–570 nm] for major histocompatibility complex-I, and a Cy5 excitation filter [590–650 nm] for laminin). Using ImageJ software, individual fibers were localized using the laminin outline, and a Region of Interest list was created listing all individual fibers. Muscle fiber type (fiber%) and fiber CSA were measured for each separate muscle fiber. As such, mean muscle fiber size was calculated for the type I and type II muscle fibers separately. Subsequently, the number of myonuclei and the number of satellite cells were measured for each separate muscle fiber. Satellite cells were identified at the periphery of muscle fibers and stained positive for both CD56 and 4,6-diamidino-2-phenylindole (31). For each biopsy, myonuclear and satellite cell content was calculated for the type I and type II muscle fibers separately. As a measure of fiber circularity, form factors were calculated using the following formula: $(4\pi \cdot CSA)/(perimeter)^2$. All image recordings and analyses were performed by an investigator blinded to subject coding. No differences in fiber circularity were observed over time or between groups. Mean numbers of 442 ± 24, 403 ± 21, and 425 ± 20 muscle fibers were analyzed in the biopsy samples collected at baseline and after 12 and 24 weeks of intervention, respectively.

Strength Assessment

Maximum strength was assessed by 1RM strength tests on leg-press and leg-extension machines and for the upper body exercises (Technogym). During a familiarization trial, proper lifting technique was demonstrated and practiced, and maximum strength was estimated using the multiple repetitions testing procedure (32). In an additional session, at least 1 week prior to muscle biopsy collection, each participant's 1RM was determined as described previously (33). 1RM testing is preferred to evaluate changes in muscle strength during resistance-type exercise training (34). Therefore, 1RM tests were repeated for upper body and leg exercises after 4, 8, 12, 16, and 20 weeks of intervention and 2 days after the last training session of the intervention program.

Physical Performance Measures

To assess lower and upper extremity physical performance, a sit-to-stand test and a hand grip test were performed prior to the onset of the intervention, after 12 weeks of intervention, and immediately after cessation of the intervention. For the sit-to-stand test, the participants were instructed to fold their arms across their chest and to stand up/sit down five times, as fast as possible, from a seat at 0.42 m from the floor. Time was recorded from the initial sitting to the final standing position. The fastest out of two rises was used for analysis (35). Data on maximal handgrip strength were obtained using a JAMAR handheld dynamometer (model BK-7498, Fred Sammons, Inc., Burr Ridge, IL). Grip strength was measured three times with each hand. The highest value using the stronger hand is reported (36).

Blood Samples

Before and after 24 weeks of intervention, fasting blood samples were collected to determine basal plasma glucose and insulin concentrations, plasma amino acid and lipid profiles, serum creatinine, and blood-glycated hemoglobin (HbA1c) content. Blood (10 mL) was collected into ethylenediaminetetraacetic acid-containing tubes and serum tubes. Ethylenediaminetetraacetic acid tubes were immediately centrifuged at 1,000*g* for 10 minutes at 4°C and the serum tubes were centrifuged at 1,000*g* for 15 minutes at 21°C after allowing the blood to clot for 90 minutes at 21°C. Aliquots of plasma and serum were immediately frozen in liquid nitrogen and stored at −80°C until further analysis. Plasma insulin concentrations were determined using an Insulin RIA Kit (LINCO Research Inc., St Charles, MO). Reagents to determine plasma glucose, triglycerides, total cholesterol, and high-density lipoprotein (HDL) cholesterol were from ABX Diagnostics (Montpellier, France). Plasma-free fatty acid concentrations were analyzed with the NEFA C test kit from Wako Chemicals (Neuss, Germany). As plasma triacylglycerol concentrations were less than 4.5 mmol/L, plasma low-density lipoprotein (LDL) cholesterol could be calculated by LDL cholesterol = total cholesterol − HDL cholesterol − triacylglycerol/2.2 (in mmol/L). Serum creatinine concentrations were determined using the Jaffe rate method on a Synchron LX Systems analyzer (Beckmann Coulter Inc., Fullerton, CA). To determine blood HbA1c content, 3 mL blood was collected in ethylenediaminetetraacetic acid containing tubes and analyzed by high-performance liquid chromatography (Bio-Rad Variant II 4, Munich, Germany). Total serum testosterone and sex hormone–binding globulin (SHBG) concentrations were measured using reagents from Roche Diagnostics (Mannheim, Germany), and assays were run on a Modular Analytics E170 analyzer (Hitachi Data Systems, Santa Clara, CA). The intra-assay CVs are 2.7%–1.8% and 1.1%–1.7% for low to high concentrations of testosterone and SHBG, respectively. Bioavailable testosterone was calculated as non-SHBG-bound testosterone using a formula described and validated previously (37).

Statistics

Data are expressed as means ± *SEM*. Baseline characteristics between groups were compared by means of an independent samples *t* test. Training-induced changes were analyzed using repeated measures ANOVA with time (pre, 12 weeks, 24 weeks) as within-participants factor and gender as between-participants factor. In case of significant main effects or interactions, *post hoc* testing with Bonferroni correction and/or separate analyses within groups was performed where appropriate. In addition to the repeated measures analysis, relative changes over time were calculated and analyzed by independent *t* test to detect potential differences between groups. Because the results for both analyses were identical, we report both absolute and relative changes but only present *p* values for the repeated measures analyses, unless otherwise stated. Significance was set at $p < .05$. All calculations were performed using SPSS version 17.0 (Chicago, IL).

Results

Participants

Participants' characteristics are provided in Table 1. In total, 53 participants completed the resistance-type exercise training program, 24 women (71 ± 1 years) and 29 men (70 ± 1 years). Men were taller and heavier with a lower body fat percentage (fat%) and a lower HbA1c level compared with the women. No significant changes in bodyweight, height, and body mass index were observed over time. Systolic blood pressure significantly decreased between 12 and 24 weeks of intervention in both the women (from 138 ± 3 to 133 ± 4 mmHg) and the men (140 ± 2 to 134 ± 2 mmHg), with no differences between genders ($P < .0001$). Diastolic blood pressure decreased significantly between 12 and 24 weeks of intervention, with no differences between genders (from 74 ± 2 to 69 ± 2 mmHg in women and from 76 ± 2 to 70 ± 2 mmHg in men; $p < .0001$).

Table 1. Subjects' Characteristics

	Women (n = 24)	Men (n = 29)
Age (yr)	71 ± 1	70 ± 1
Body weight (kg)	65.6 ± 1.6	84.3 ± 1.7*
Height (m)	1.63 ± 0.01	1.77 ± 0.01*
Body mass index (kg/m^2)	24.6 ± 0.4	27.0 ± 0.5*
Fat (%)	32 ± 1	23 ± 1*
Basal plasma glucose (mmol/L)	5.4 ± 0.1	5.6 ± 0.1
HbA1c (%)	5.8 ± 0.1	5.5 ± 0.1*

Notes: All values represent means ± *SEM*. HbA1c = blood glycosylated hemoglobin. Data were analyzed using independent samples t test.
*Significantly different from women ($p < .05$).

Body Composition

Prior to the exercise intervention, women and men differed in whole-body lean mass, leg lean mass, and bone mineral content (Table 2). The resistance training program resulted in an absolute increase in whole-body lean mass of 1.2 ± 0.2 and 1.2 ± 0.3 kg in the women and men, respectively ($p < .001$), with no differences between groups ($p = .94$). Leg lean mass increased by 3% ± 1% (0.5 ± 0.1 kg) and 3% ± 1% (0.6 ± 0.1 kg) in the women and men, respectively ($p < .001$), with no differences between groups ($p = .69$). The increase in lean mass was accompanied by a 5% ± 2% and 6% ± 1% decrease in fat mass, respectively ($p < .001$). No significant differences were observed for the intervention effects between women and men for any of the dual-energy x-ray absorptiometry variables (Table 2). At baseline, bone mineral content was significantly lower in the women compared with the men (1.9 ± 0.1 kg vs 2.8 ± 0.1 kg). No changes were observed in bone mineral content during the 6-month intervention (data not shown).

Skeletal Muscle Hypertrophy

At baseline, quadriceps CSA was significantly smaller in women compared with the men (46.6 cm^2 vs 68.8 cm^2, respectively). Following the first 12 weeks of intervention, quadriceps CSA had increased by 8% ± 1% (3.5 ± 0.5 cm^2) and 7% ± 1% (4.6 ± 0.5 cm^2) in the women and men, respectively ($p < .001$), with no differences between genders (Figure 1). During the subsequent period from week 12 to week 24, we observed a significant gender × training interaction ($p < .05$). Whereas no significant increase

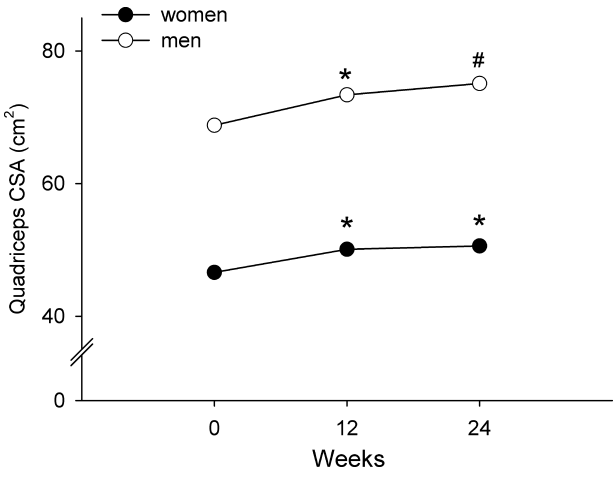

Figure 1. Mean (±*SEM*) quadriceps CSA before and after 12 and 24 wk of resistance-type exercise training in elderly women and men. Data were analyzed using repeated measures ANOVA with time as a within-participants factor and gender as a between-participants factor. A significant time × gender interaction was observed between 12 and 24 wk of intervention ($p < .05$). *Significantly different from before the intervention, $p < .001$. #Significantly different from wk 0 and 12, $p < .001$.

in quadriceps CSA was observed in the women, CSA further increased by 1.7 ± 0.4 cm^2 in the men during the last 12 weeks of exercise training. Nonetheless, the percentage change in quadriceps CSA between 12 and 24 weeks of intervention did not differ significantly between the women (1% ± 1%) and men (2% ± 1%).

At baseline, muscle fiber CSA was significantly smaller in the type II versus the type I muscle fibers in both the women (3167 ± 216 μm^2 vs 5103 ± 271 μm^2) and the men (5126 ± 193 μm^2 vs 5802 ± 209 μm^2), respectively. In addition, prior to intervention type II muscle fiber CSA was significantly smaller in the women compared with the men (Figure 3A). In contrast to the type I muscle fibers, type II muscle fiber CSA significantly increased in both the women (from 3167 ± 216 μm^2 to 3891 ± 269 μm^2) and the men (from 5126 ± 193 μm^2 to 6120 ± 325 μm^2), with no differences between groups (Figure 3). Likewise, the relative increase in type II muscle fiber CSA was comparable between the women and the men (29% ± 7% vs 24% ± 7%, respectively; $p = .68$). Type I and type II muscle fiber percentage did not

Table 2. Body Composition

	Women (n = 24)			Men (n = 29)		
Week	0	12	24	0	12	24
Total mass (kg)	65.6 ± 1.6	66.2 ± 1.6	65.9 ± 1.6	84.3 ± 1.7	84.7 ± 1.6	84.3 ± 1.7
Lean mass (kg)	42.5 ± 0.9	43.5 ± 0.9*	43.7 ± 1.0*	62.2 ± 1.0	63.3 ± 1.1*	63.4 ± 1.0*
Leg lean mass (kg)	13.6 ± 0.4	13.9 ± 0.4*	14.0 ± 0.4*,#	19.8 ± 0.3	20.2 ± 0.4*	20.4 ± 0.4*,#
Fat mass (kg)	21.2 ± 0.9	20.7 ± 0.9*	20.3 ± 0.9*,#	19.3 ± 1.0	18.6 ± 0.9*	18.1 ± 0.9*,#
Fat (%)	32.1 ± 0.8	31.0 ± 0.8*	30.5 ± 0.8*,#	22.6 ± 0.8	21.8 ± 0.8*	21.2 ± 0.8*,#

Notes: All values represent means ± *SEM*. Data were analyzed using repeated measures ANOVA with time as within-subjects factor and gender as between-subjects factor. No time × gender interaction was observed.
*Significantly different from wk 0.
#Significantly different from wk 12.

change over the 6 months of exercise intervention. However, the specific type II muscle fiber hypertrophy resulted in an increase in type II muscle fiber area percentage in the women and the men (from 38% ± 2% to 43% ± 2%; $p < .05$). No gender differences were observed.

Myonuclear and Satellite Cell Content

In line with the smaller type II versus type I muscle fiber size, myonuclear content was lower in the type II versus type I muscle fibers at baseline in both the women (2.5 ± 0.2 vs 3.4 ± 0.2 nuclei per fiber) and men (3.4 ± 0.2 vs 4.0 ± 0.2 nuclei per fiber) ($p < .001$). In addition, type II muscle fiber myonuclear content was significantly lower in the women compared with the men ($p < .01$). In contrast to the type I muscle fibers, the number of myonuclei per type II muscle fiber significantly increased in both the women (from 2.5 ± 0.2 to 2.7 ± 0.2) and men (from 3.4 ± 0.2 to 3.8 ± 0.2) ($p < .05$), with no differences between groups. At baseline, satellite cell content was significantly lower in the type II versus type I muscle fibers in both the women (0.039 ± 0.005 vs 0.075 ± 0.005 satellite cells per muscle fiber) and men (0.047 ± 0.004 vs 0.067 ± 0.005 satellite cells per muscle fiber) ($p < .001$), with no differences between genders. Whereas there was only a tendency for satellite cell content to increase in the type I muscle fibers ($p = .065$), the number of satellite cells per type II muscle fiber significantly increased following 24 weeks of resistance-type exercise training (Figure 3B; $p < .01$). The increase in satellite cell content was apparent for both the women (from 0.039 ± 0.005 to 0.064 ± 0.014) and the men (from 0.047 ± 0.004 to 0.070 ± 0.005), with no differences between groups.

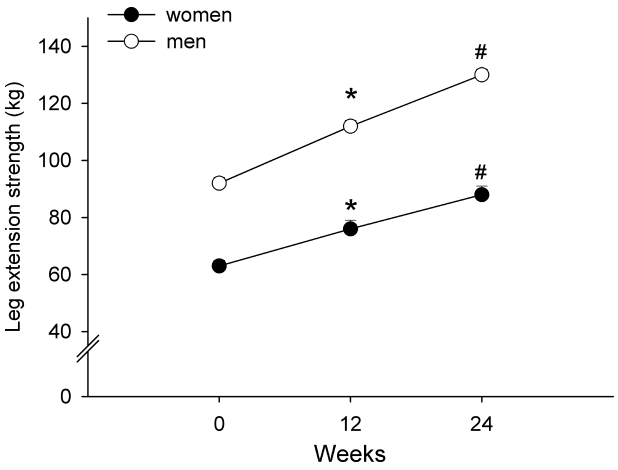

Figure 2. Mean (±*SEM*) leg extension 1RM before and after 12 and 24 wk of resistance-type exercise training in elderly women and men. Data were analyzed using repeated measures ANOVA with time as a within-participants factor and gender as a between-participants factor. A significant time × gender interaction was observed ($p < .001$). *Significantly different from baseline, $p < .001$. #Significantly different from wk 0 and 12, $p < .001$.

Muscle Strength

Prior to intervention, muscle strength was lower in the women compared with the men (Figure 2). In response to training, leg-press 1RM increased by 31% ± 3% in the women (from 138 ± 5 to 179 ± 5 kg; $p < .001$) and by 26% ± 2% in the men (from 207 ± 4 to 260 ± 2 kg; $p < .001$). No significant gender × training interaction was observed for leg-press 1RM. In contrast, for leg-extension 1RM, a significant gender × training interaction was observed, indicating that strength gains were larger in the men compared with the women ($p < .002$). However, relative strength gains for both the leg extension and leg press did not differ between the women and men (42% ± 3% vs 43% ± 3% and 31% ± 3% vs 26% ± 2%, respectively). For all upper body exercises, both absolute and relative strength gains were similar for men and women (on average 42% ± 3% and 47% ± 3%, respectively).

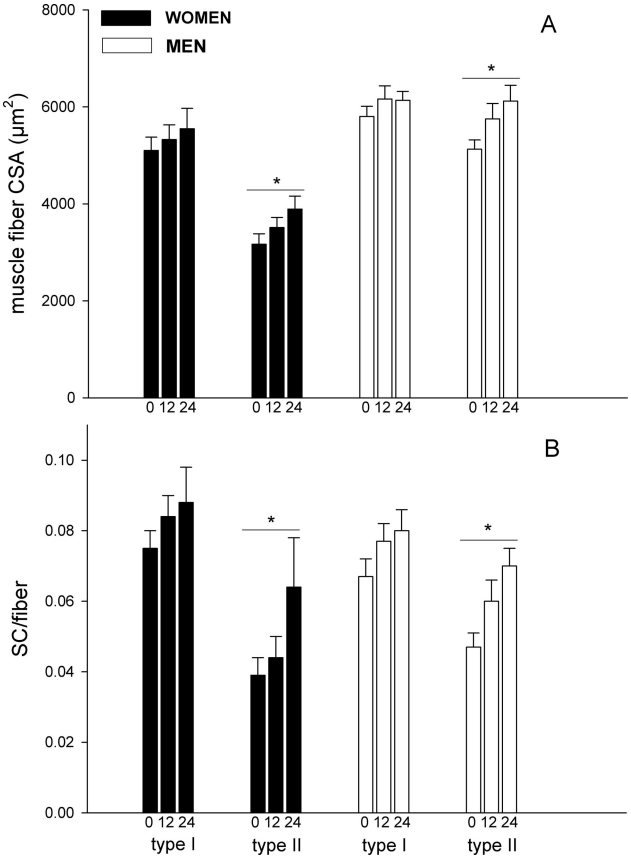

Figure 3. (**A**) Mean (±*SEM*) muscle fiber cross-sectional area (CSA) for type I and type II muscle fibers before and after 12 and 24 wk of resistance-type exercise training in elderly women and men. Data were analyzed using repeated measures ANOVA with time as within-participants factor and gender as between-participants factor. No time × gender interactions were observed. *Significant increase over time $p < .01$. (**B**) Mean (±*SEM*) number of satellite cells (SC) per type I and type II muscle fiber before and after 12 and 24 wk of resistance-type exercise training in elderly women and men. Data were analyzed using repeated measures ANOVA with time as within-participants factor and gender as between-participants factor. No time × gender interactions were observed. *Significant increase over time $p < .01$.

Physical Performance

Prior to the exercise intervention, no significant differences were observed in sit-to-stand time between women and men (7.7 ± 0.3 second vs 7.8 ± 0.3 second, respectively). After 24 weeks of intervention, sit-to-stand time had decreased significantly by 18% ± 2% and 19% ± 2%, respectively ($p < .001$). No significant differences were observed between women and men. At baseline, handgrip strength was significantly lower in the women compared with the men (26 ± 1 kg vs 43 ± 2 kg, respectively). No changes in handgrip strength were observed over time.

Glycemia and Lipidemia

Prior to intervention blood HbA1c contents (5.8% ± 0.1% vs 5.5% ± 0.1%) and whole-body insulin sensitivity indices (oral glucose insulin sensitivity: 454 ± 8 vs 427 ± 9) differed significantly between the women and men, respectively ($p < .05$; Table 3). All other baseline measures of glycemic control did not differ between women and men. Over time, a significant decline in blood HbA1c content was observed in both the women and men (from 5.8% ± 0.1% and 5.5% ± 0.1% to 5.7% ± 0.1% and 5.4% ± 0.1%, respectively; $p < .02$). Accordingly, we also observed an increase in insulin sensitivity index and oral glucose insulin sensitivity over time. For all measures, no interaction was observed with gender. At baseline, plasma LDL, HDL, and total cholesterol concentrations were higher in the women compared with the men (Table 3). Over time significant improvements in total cholesterol and LDL were observed in both groups with no difference between genders.

Hormonal Profiles

At baseline, average serum concentrations of total testosterone, bioavailable testosterone, and SHBG concentrations averaged 0.79 ± 0.13 nmol/L, 0.18 ± 0.02 nmol/L, and 89.52 ± 8.32 nmol/L in the women and 17.08 ± 1.15 nmol/L, 6.14 ± 0.32 nmol/L, and 56.00 ± 3.99 nmol/L in the men. Whereas obvious gender differences were observed for all hormones, no significant changes over time and no time × gender interactions were observed.

Creatinine and Urinary Nitrogen

Serum creatinine concentrations were within the normal range (>60 μmol/L) prior to the intervention. At baseline, women differed significantly from men (77.0 ± 2.6 μmol/L vs 91.5 ± 2.9 μmol/L, respectively). No changes were observed over time in either group. Creatinine clearance was within the normal range (>60 mL/min per 1.73 m^2) prior to the intervention. At baseline, no significant differences were observed between the women and men (82.2 ± 3.1 vs 87.5 ± 4.7 mL/min per 1.73 m^2, respectively). No changes were observed over time in either group. Prior to the intervention, 24-h nitrogen balance was 1.3 ± 0.4 g/day in the women and −0.1 ± 0.5 g/day in the men. Nitrogen balance did not change over time in either group.

Discussion

In this study, we show that traditional, prolonged resistance-type exercise training effectively increases muscle mass, strength, and functional performance and improves metabolic profile in both elderly men and women. No gender differences were observed in the adaptive response to prolonged resistance-type exercise training. Elderly men and women benefited equally from the same generic resistance-type exercise training regimen.

Resistance-type exercise training has been well established as an effective treatment strategy to counteract the loss of muscle mass and strength in the elderly population (6–10,31,38–43). Yet, whether there are gender specific differences in the adaptive response to prolonged resistance-type exercise training in the elderly population remains equivocal. Whereas some report gender-specific

Table 3. Glycemic Control and Plasma Lipid Concentrations

	Women (n = 24)		Men (n = 29)	
Week	0	24	0	24
Glycemic control				
Plasma glucose (mmol/L)	5.4 ± 0.1	5.2 ± 0.1	5.6 ± 0.1	5.7 ± 0.1
Plasma insulin (mU/L)	13.7 ± 1.2	13.2 ± 1.3	14.5 ± 0.9	14.5 ± 0.9
HbA1c (%)	5.8 ± 0.1	5.7 ± 0.1*	5.5 ± 0.1	5.4 ± 0.1*
Insulin sensitivity index	3.8 ± 0.4	4.2 ± 0.3*	3.1 ± 0.3	3.4 ± 0.4*
Oral glucose insulin sensitivity	454 ± 8	475 ± 10*	427 ± 9	440 ± 8*
Plasma lipid concentrations				
Free fatty acids (μmol/L)	456 ± 34	430 ± 41	450 ± 30	424 ± 34
Triglycerides (mmol/L)	1.11 ± 0.11	1.14 ± 0.10	1.25 ± 0.07	1.20 ± 0.09
Total cholesterol (mmol/L)	6.84 ± 0.19	6.43 ± 0.18*	5.83 ± 0.21	5.62 ± 0.21*
High-density lipoprotein (mmol/L)	1.92 ± 0.08	1.97 ± 0.08	1.55 ± 0.08	1.59 ± 0.09
Low-density lipoprotein (mmol/L)	4.46 ± 0.18	3.98 ± 0.18*	3.76 ± 0.18	3.53 ± 0.17*

Notes: All values represent means ± *SEM*. HbA1c = blood glycosylated hemoglobin. Data were analyzed using repeated measures ANOVA with time as within-subjects factor and gender as between-subjects factor. No time × gender interaction was observed.

*Significantly different from wk 0.

differences in the adaptation to prolonged resistance-type exercise training (15,16,18), others fail to detect differences in the impact of prolonged exercise training on structural, functional, and/or metabolic adaptations between men and women (14,17). This study is the first to assess differences in gains in muscle mass and strength, increases in functional capacity, as well as metabolic adaptation following prolonged, resistance-type exercise training in a large cohort elderly men and women. On the whole-body level, we show that increases in lean mass are similar between the elderly women and men (Table 2). The increase in whole-body lean mass was mainly attributed to the increase in leg lean mass which was ~3% in both women and men. These data are in line with Bamman et al. (15), who reported similar absolute gains in whole-body lean mass in women and men in response to 26 weeks of knee extensor training. Several studies also reported a significant increase in thigh muscle CSA ranging from 2% to 9% following resistance-type exercise training in men (7,8,44) and women (45,46). However, these studies did not make a comparison between genders to assess whether men and women respond to the same extent. By actually comparing the response to 9 weeks of (unilateral) resistance-type exercise training between genders, Tracy et al. (17) reported a greater absolute increase in quadriceps muscle volume in elderly men compared with women. However, percent increases in muscle volume were similar between the women and men (17). Our study confirms these latter findings, indicating that whereas absolute increases in quadriceps CSA are greater in men compared with women ($6.2 \pm 0.6\,cm^2$ vs $4.0 \pm 0.4\,cm^2$, respectively), the relative increase in muscle mass remains similar between men and women (~9%).

The loss of skeletal muscle mass with aging is associated with specific type II muscle fiber atrophy (33,47,48). In agreement, we observed that type II muscle fiber CSA was significantly smaller than type I fiber CSA in both the women and men (Figure 3). Comparisons with type I and II muscle fiber size of muscle tissue collected in young adults from our laboratory (33) as well as others (47,48), clearly show that specific type II muscle fiber atrophy is a hallmark of senescent muscle. Furthermore, we confirm and extend on our previous findings in men (31) by showing that type II muscle fiber atrophy with aging is associated with a specific decline in type II muscle fiber satellite cell content in both elderly men and women. In line with previous observations (9,49,50), type II muscle fiber CSA increased following resistance-type exercise training, with no significant changes in type I muscle fiber CSA. This study extends on these data by the comparison of changes in type I and II muscle fiber size between the men and women (Figure 3A). Type II muscle fiber CSA increased by 29% ± 7% and 24% ± 7% in the women and men, respectively, after training. We detected no gender differences in muscle fiber hypertrophy following 3 and 6 months of resistance-type exercise training. In accordance, we observed a type II muscle fiber specific increase in myonuclear and satellite cell content, with no differences between groups (Figure 3B). This is the first study to show that the lower type II muscle fiber size and satellite cell content with aging can be enhanced to the same extent in both elderly men and women by prolonged resistance-type exercise training. This seems to be at odds with previous data by Bamman et al. (15) who reported that muscle fiber hypertrophy was greater in men compared with women. However, the latter findings were observed in a relative small group ($n = 14$, with only 5 women included) compared with the present findings ($n = 53$, with 24 women included). Therefore, we conclude that type II muscle fiber hypertrophy is achieved in both men and women, with no apparent differences between genders. As a consequence of the training-induced gain in type II muscle fiber CSA, the relative type II muscle fiber atrophy observed prior to intervention was no longer apparent after 24 weeks of intervention in the men. In contrast, despite the substantial 29% ± 7% type II muscle fiber hypertrophy, muscle fiber size was still significantly smaller in the type II versus type I muscle fibers after 24 weeks of intervention in the women. The latter clearly shows the relevance of effective interventions to maintain or even increase type II muscle fiber size in women, as baseline type II muscle fiber size is even more compromised in the women compared with the men. Importantly though, muscle tissue in both older women and men is still capable of inducing satellite cell proliferation, differentiation, and fusion of new myonuclei into existing muscle fibers, resulting in type II muscle fiber hypertrophy.

The loss of strength with aging is generally greater than that can be predicted based on the loss of muscle mass (51). This is likely attributed to changes in muscle quality (ie, the maximal strength per unit of muscle mass) as well as impairments in neuromuscular function (52). Goodpaster et al. (28) showed that fat infiltration of the muscle is associated with lower muscle strength per CSA. As such, intermuscular adipose tissue infiltration likely represents an important contributor to the loss of muscle quality and, therefore, the loss of muscle strength and function with aging.

In line with the more pronounced decline in muscle strength versus muscle mass with aging, we observed a massive increase in muscle strength following the onset of exercise training in our volunteers. Various resistance-type exercise training studies in elderly population, using different training and testing methods, have observed increases in 1RM leg-extension muscle strength ranging from 27% to 113% (7,9,10,15,17,45,53). In this study, absolute strength increases appeared to be lower in the women compared with the men. The latter was apparent for both the leg-press (41 ± 3 kg vs 53 ± 3 kg) and leg-extension (26 ± 2 kg vs 38 ± 2 kg) exercises. The larger absolute increase in leg press compared with the leg extension can be explained by the different nature of the exercises, that is, multijoint versus isolating the quadriceps muscle (34). However, when expressed relative to preintervention

values increases in strength were similar between women and men for the leg-press (31% ± 3% vs 26% ± 2%) and leg-extension (42% ± 3% vs 43% ± 3%) exercise. These findings confirmed the observations by Tracy et al. (17) who studied whether gender affects the increase in muscle strength due to resistance-type exercise training in the elderly population over a period of 9 weeks. Although they showed a greater absolute increase in muscle strength for the men compared with the women, the relative changes were comparable between genders (27% vs 29%, respectively). Bamman et al. (15) also observed substantial increases in muscle strength over 26 weeks of training. They confirmed that men gained more absolute strength than women. We speculate that baseline differences in muscle strength may at least partly explain previously reported differences in the increase in muscle strength between genders. This is confirmed by the positive correlation between baseline leg-extension strength and the absolute increase in leg extension ($r = .31$, $p < .05$) and the positive correlation between baseline leg-press strength and the absolute increase in leg press ($r = .33$, $p < .05$) observed in this study. Furthermore, when correcting for baseline strength values by calculating percentage changes, the gender differences in strength gains had completely disappeared.

It is clear that several daily tasks, such as rising from chair, climbing stairs, and walking are influenced by muscle strength, especially in older people (54). The clinical relevance of increasing muscle strength in the elderly population was shown by Capodaglio et al. (55) and Fiatarone et al. (10), who observed improvements in functional capacity following resistance-type exercise training. Nevertheless, gender comparisons of the increase in functional capacity following resistance-type exercise training are lacking. In this study, we also assessed functional parameters; sit-to-stand time and handgrip strength. Sit-to-stand time improved significantly in both the women and the men. Although there is a large difference in muscle strength between genders, the increase in strength due to resistance-type exercise training improves sit-to-stand time to the same extent in both women and men. Notably, whereas there were large gender differences in muscle mass and strength already at baseline (even when corrected for body mass), functional capacity measured as sit-to-stand time was similar for the men and women. This supports the idea that functional capacity is not merely explained by muscle strength, but other factors such as neurological function should also be taken into account. No changes were observed over time in handgrip strength in either women or men. Though a potentially relevant marker in large cross-sectional studies (56), this study clearly shows that handgrip strength does not represent a clinically relevant and/or valid measure to assess individual changes in muscle function in response to prolonged resistance-type exercise training programs.

Together with the increases in muscle mass, strength, and function, we also observed significant improvements in several risk factors for metabolic disease. These improvements are normally attributed to the impact of prolonged endurance-type exercise training. Glycemic control improved similarly in both the women and the men as evidenced by a 0.1% decrease in HbA1c as well as a significant increase in insulin sensitivity index and oral glucose insulin sensitivity. Our findings confirm previous studies in middle-aged participants and elderly women (57–59) and extend on those findings by showing that resistance-type exercise training improves whole body insulin sensitivity and glycemic control to the same extent in elderly women and men. The improvement in glycemic control was accompanied by an improvement in the lipid profile. In addition, we observed significant improvements in both total cholesterol and LDL in the women as well as in the men, with no differences between genders. These findings confirmed the observations of Martins et al. (60), supporting a role for resistance-type exercise also in the prevention and/or treatment of chronic metabolic disease in the elderly population. It should be noted that elderly women are at a greater risk of developing insulin resistance due to a further decline in muscle mass which will affect the fat mass/muscle mass ratio. This will make women even more susceptible for ectopic lipid deposition and insulin resistance.

It has been suggested that gender-related differences in the hypertrophic response to resistance-type exercise training may be attributed to differences in anabolic hormones, especially gender-related hormones such as testosterone. Among the hormones measured in serum, we observed obvious gender differences for testosterone concentrations. However, serum concentrations did not change over time for any of the hormones, and no relations were found between serum hormone concentrations and the response to resistance-type exercise training. These findings lend support to the assumption that hormonal profile may not be as important in the general response to resistance-type exercise training as was previously assumed (61,62).

Although previous studies have shown the efficacy of resistance-type exercise training in both elderly men and women, this is the first study to compare the impact of prolonged resistance-type exercise training on such an extensive range of measurements between elderly men and women. We show that despite differences in the absolute increase in muscle mass and strength, there are no differences in the relative training response between women and men. This study clearly shows that the same generic resistance-type exercise training program is applicable in both elderly women and men to counteract the loss of muscle mass and function with aging. The latter greatly facilitates the implementation of training in a practical setting, enabling generic group sessions (for both men and women) on traditional training equipment. The increase in muscle mass and strength will attenuate the risk for functional impairments, thereby improving quality of life at an advanced age. Combined with an improvement

in metabolic risk profile, these findings indicate that resistance-type exercise training is the best approach to counteract the negative consequences related to the loss of muscle mass and function with aging in both elderly women and men.

We conclude that gender does not affect skeletal muscle mass and strength gains or improvements in functional capacity and metabolic profile in response to prolonged resistance-type exercise training in the elderly population. As such, elderly women and men benefit equally from a resistance-type exercise training program allowing them to prevent and treat the loss of muscle mass and function and reduce the risk of developing chronic metabolic disease.

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