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Muscle mass and strength gains following 6 months of resistance type exercise training are only partly preserved within one year with autonomous exercise continuation in older adults

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ABSTRACT

Introduction: Although resistance type exercise training (RT) effectively increases muscle mass and strength in older individuals, it remains unclear whether gains in muscle mass and strength are maintained without continued supervised training. We assessed the capacity of older individuals to maintain muscle mass and strength gains one year after partaking in a successful RT program.

Methods: Fifty-three healthy older adults performed a 24-wk supervised RT program. Upon the cessation of the training program, participants were not provided with any advice or incentives to continue exercise training. One year after completion of the training program, all participants were contacted and invited back to the laboratory to assess anthropometrics, body composition (DXA), quadriceps muscle cross-sectional area (CSA) (CT-scan), muscle strength (1RM knee extension/leg press), and muscle fiber characteristics (muscle biopsy). Following primary analyses on all participants that responded to the invitation ($n = 35$), participants were divided into two groups: individuals who had continued to perform exercise training on an individual basis (EXER group; $n = 16$) and individuals who had not continued to perform any regular exercise (STOP group; $n = 19$) after completing the RT program.

Results: The initial increases in quadriceps CSA (+506 ± 209 and +584 ± 287 mm^2) and knee extension strength (+32 ± 12 vs +34 ± 10 kg) after the 24-wk RT program did not differ between the STOP and EXER group (all $P > 0.05$). One year after discontinuation of the RT program, participants had lost muscle mass ($P < 0.01$), with a greater decline in *quadriceps* CSA in the STOP vs EXER group (−579 ± 268 vs −309 ± 253 mm^2, respectively; $P < 0.05$). Muscle strength had decreased significantly compared to values after completing the RT program ($P < 0.01$), with no differences observed between the STOP vs EXER group (knee extension: −21 ± 8 vs −18 ± 8 kg, respectively; $P > 0.05$), yet remained higher compared with values before the RT program ($P < 0.05$).

Conclusion: Though prolonged RT can effectively increase muscle mass and strength in the older population, muscle mass gains are lost and muscle strength gains are only partly preserved within one year if the supervised exercise program is not continued.

1. Introduction

The progressive loss of skeletal muscle mass and strength with age, also known as sarcopenia, is associated with the development of frailty, functional impairments, and increased risk of morbidity and mortality (Evans, 1997; Fielding et al., 2011). Resistance type exercise training (RT) is an effective intervention strategy to counteract the loss of muscle mass and strength in both older men and women (Churchward-Venne et al., 2015; Dirks et al., 2017; Leenders et al., 2013a, 2013b; Tieland et al., 2012). Even in the very old population, substantial improvements in skeletal muscle mass, strength, and functional capacity have been demonstrated following RT (Fiatarone et al., 1994; Tieland et al., 2012). In addition, on a muscle fiber level, it has been observed that both older men and women maintain their capacity to increase muscle fiber size (Leenders et al., 2013a).

Although RT represents an effective interventional strategy to combat sarcopenia, gains in skeletal muscle mass and strength generally dissipate when regular exercise training is interrupted (Bickel et al.,

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2011; Correa et al., 2013; Correa et al., 2016; Fatouros et al., 2005; Ivey et al., 2000; Kalapotharakos et al., 2007; Kalapotharakos et al., 2010; Lemmer et al., 2000; Sherk et al., 2012; Staron et al., 1991; Trappe et al., 2002; Yasuda et al., 2015; Yasuda et al., 2014). Only limited data is available on the impact of exercise maintenance on skeletal muscle mass and strength preservation following prolonged RT in older adults. Trappe et al. (2002) demonstrated that prescribing a maintenance dose of exercise, equivalent to one-third of the weekly volume of the initial RT program, is sufficient to maintain muscle mass and strength gains for up to 6 months in older adults ($n = 5$) when compared with subjects undergoing strict detraining ($n = 5$). Furthermore, Bickel et al. (2011) reported that older adults require a higher exercise maintenance dose to maintain skeletal muscle mass and strength following a supervised exercise training program when compared with young adults. These studies indicate that older adults may need to be prescribed with a certain exercise dose to prevent or attenuate the loss of skeletal muscle mass and strength that were previously gained in a RT program. Clearly, research is warranted to establish whether older adults are able to preserve gains in skeletal muscle mass and strength after discontinuing their participation to a prolonged RT program. The first aim of the present study was therefore to assess the capacity of older individuals to maintain their gains in muscle mass, strength, and functional performance during one year after discontinuing an effective 24-week supervised RT program.

In addition to the RT induced gains in skeletal muscle mass, strength, and function, an indirect benefit of a supervised RT program could be that older adults adopt a more healthy, active lifestyle (King, 2001). Besides the behavioral aspects associated with the participation in an exercise training program, the concomitant gains in muscle strength may increase the capacity to perform activities of daily living that were previously considered unrealistic. However, it remains unknown whether older adults autonomously incorporate exercise in their daily routine and/or adopt a more active life style after an exercise training program, and whether those who do will be more likely to maintain the exercise induced benefits. Therefore, the second aim of the current study was to compare individuals who continued to perform (unprescribed) RT on an individual basis, and individuals who did not continue to partake in any resistance type exercise activities on their ability to preserve muscle mass, strength and function at 1 year follow-up after completing the initial exercise training program. We hypothesized that individuals who continued to perform some form of RT on an individual basis would be more likely to retain their previous gains in muscle mass, strength, and function when compared with individuals who no longer participated in any regular exercise activities.

2. Methods

2.1. Subjects

Fifty-three healthy older adults were included to participate in a 24-weeks supervised RT program. Medical history of all participants was evaluated and an oral glucose tolerance test and resting and exercise 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, type 2 diabetes patients were excluded from participation. All participants were living independently and had no history of participating in any structured exercise training program over the past 5 y. All participants were informed on the nature and possible risks of the experimental procedures, before their written informed consent was obtained. The supervised RT study was approved by the Medical Ethics Committee of the Maastricht University Medical Centre+. This study was part of a greater project investigating the impact of nutrition and exercise interventions to increase muscle mass and strength in older adults, for which the main study outcomes have been previously published (Churchward-Venne et al., 2015; Leenders et al., 2013a, 2013b; Snijders et al., 2017).

Upon the cessation of exercise training program, participants were not provided with any advice or incentives to continue exercise training. At that stage no plans were made for a follow-up assessment. One year after completion of the RT program, all participants were contacted and invited back to the laboratory to repeat all measurements performed before and after the supervised RT program. All returning participants were again informed on the nature and possible risks of the experimental procedures, before their written informed consent was obtained. The 1 y follow-up measurements were approved as an amendment to the original medical ethical application by the Medical Ethics Committee of the Maastricht University Medical Centre+. A total of 35 of the 53 subjects who had participated in the supervised training program agreed to partake in the 1 y follow-up measurements. Subjects were subdivided (based on self-report) into two groups: individuals who had continued to perform RT on an individual basis (defined as exercise performed at least biweekly, with lifting weights during lower-body exercise being a main component of the exercise performed; $n = 16$, EXER group) and individuals who had not continued to perform any regular weight-lifting exercise ($n = 19$, STOP group) after completing the 24 weeks supervised RT program. See Supplemental Table 1 for group allocation based upon self-reported sport activities. As we did not initially plan to include these subjects in a follow up study, we were unable to collect further details with regard to the exercises performed during the 1 y follow up period (e.g., exact intensity and dose/volume of exercise).

2.2. Supervised resistance type exercise training program

The initial RT program was performed three times per week for 24 weeks, as described previously (Leenders et al., 2013a). In short, following a 5 min warm-up on a cycle ergometer, four sets (8 repetitions at 80% of 1RM) of leg press and knee extension machines (Technogym, Rotterdam, the Netherlands) and three sets on the chest press and horizontal row were performed every training session. The vertical lateral pull-down and abdominal crunches were alternated with biceps curls and triceps extensions between subsequent exercise sessions (2–3 sets). Resting periods of 1.5 and 3 min were allowed between sets and exercises, respectively. Participants were personally supervised throughout the exercise training program. Each exercise session ended with a 5 min cool-down on a cycle ergometer.

2.3. Body composition

Body composition was assessed by Dual-Energy X-ray Absorptiometry (DXA; Discovery A, QDR Series; Hologic, Bradford, MA). Whole-body and regional fat and fat free mass were determined by using the system's software package Apex version 2.3 (Wind River, Alameda, CA). Anthropometrics data were assessed using standardized procedures; bodyweight by digital weighing scale to within 100 g; height by stadiometer to within 0.5 cm; and circumferences to within 1 mm using a measuring tape, with waist measured midway between the lowest rib and the iliac crest with the subject standing at the end of a gentle expiration, and hips measured at the greater trochanters.

Anatomical cross-sectional area (CSA) of the *quadriceps* muscle was assessed by CT scanning (Philips Brilliance 64, Philips Medical Systems, Best, the Netherlands) as described previously (Leenders et al., 2013a). In short, the scanning characteristics were as follows: 120 kV, 300 mA, rotation time of 0.75 s, and a field of view of 500 mm. With the subjects 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. Muscle area of the right leg was selected between 0 and 100 Hounsfield units (Goodpaster et al., 2000), after which the quadriceps muscle was selected by manual tracing using ImageJ software (version 1.45d; National Institutes of Health, Bethesda, MD) (Strandberg et al., 2010).

2.4. Muscle strength assessment

Maximum strength was assessed by 1-RM strength tests on leg press and knee extension machines (Technogym). During a familiarization trial, proper lifting technique was demonstrated and practiced and maximum strength was estimated using the multiple repetitions testing procedure (Verdijk et al., 2009). In an additional session, at least 1 week before muscle biopsy collection, each subject's 1 RM strength was determined as described previously (Leenders et al., 2013a).

2.5. Physical performance measures

To assess lower and upper extremity physical performance, a sit-to-stand test and a handgrip test were performed. 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 attempts was used for analysis (Guralnik et al., 1994). Data on maximal grip 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 for left and right were added and are reported.

2.6. Muscle biopsy sampling

Muscle biopsies were taken from the right leg of each subject in the morning after an overnight fast. After local anesthesia was induced, percutaneous needle biopsy samples (50–80 mg) were collected from the *vastus lateralis* muscle, approximately 15 cm above the patella (Bergstrom, 1975). Any visible non-muscle 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 analyses.

2.7. Immunohistochemistry

From all biopsies, 5-μm-thick cryosections were cut at −20 °C. Care was taken to properly align the samples for the cross-sectional muscle fiber analyses. Muscle biopsies were stained to determine type I and type II muscle fiber distribution, fiber size, myonuclear and satellite cell content, as described in detail previously (Leenders et al., 2013b). In short, the slides were incubated with primary antibodies against laminin (polyclonal rabbit anti-laminin; 1:50 dilution; Sigma), MHC-I (myosin heavy chain) (A4.840, 1:25 dilution; Developmental Studies Hybridoma Bank, Iowa City, IA, U.S.A.) and CD56 (1:40 dilution; BD Biosciences). Appropriate secondary antibodies were applied: Alexa Fluor® 647-conjugated goat anti-(rabbit IgG), Alexa Fluor® 555-conjugated goat anti-(mouse IgM) and Alexa Fluor® 488-conjugated streptavidin (1:400, 1:500 and 1:200 dilution respectively; Life Technologies). Nuclei were stained with DAPI (0.238 μM; Life Technologies). 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).

2.8. Statistics

Data are expressed as mean ± SD. First, baseline characteristics between groups (follow-up vs lost to follow-up) were compared by means of an independent samples *t*-test. Likewise, RT induced changes were analyzed using a repeated measures ANOVA with time (pre vs 24 wks) as within subject factor and group (follow-up vs lost to follow-up) as between subject factor.

Secondly, the impact of RT and 1 year follow-up in all the participants included in the 1 year follow up ($n = 35$), was assessed by one-way ANOVA with time (pre vs 24 wks vs 1 year follow-up) as within subject factor, and Bonferroni corrected pairwise comparisons in case a significant effect of time was observed. To assess the impact of unsupervised resistance exercise continuation after the supervised RT program, a two-way repeated measures ANOVA with time (pre vs 24 wks vs 1 year follow up) as within subject factor and group (EXER vs STOP) as between subject factor was used. For the muscle biopsy parameters, repeated measures ANOVA with fiber type (Type I vs Type II) and time (pre vs 24 wks vs 1 year follow up) as within subject factors and, where appropriate, group (EXER vs STOP) as between subject factor was used. In case of a significant *time* × *group* interaction, Bonferroni corrected pairwise comparisons were used within each group separately for each time (i.e., to determine the effect of time within the EXER and STOP group separately), as well as within each time point to assess potential group differences. In case of a significant main effect of time, pairwise comparison with Bonferroni correction was performed to locate differences. Significance was set at $P < 0.05$. All calculations were performed using SPSS version 22.0 (SPSS version 22.0, IBM Corp., USA).

3. Results

Note that for all the data included here, the baseline (pre-RT) and the 24 week (post-RT) data were previously reported in the original study (Leenders et al., 2013a, 2013b), and have now been combined with the newly generated 1 y follow up data.

3.1. Follow-up versus lost to follow-up

Fifty-three healthy older adults participated in the initial RT program. In 35 participants a 1 y follow-up measurement was performed. With the exception of the sit-to-stand test, no differences in baseline characteristics and/or response to the initial RT program were observed between individuals who were included in the present study (1 y follow-up; $n = 35$) and those who were lost to follow-up ($n = 18$) (*time* × *group* interaction effect: $P > 0.05$ on all parameters; see Supplemental Tables 2 and 3).

3.2. Body composition

3.2.1. All follow-up participants

No significant changes in bodyweight and waist-to-hip ratio were observed in response to the 24-week RT program, nor in the 1 y follow-up period (Table 1). A significant main effect of time was found for BMI ($P < 0.05$), however, no significant differences between time points could be located using pairwise comparisons. Whole body and leg lean mass increased significantly in response to the initial 24 weeks of RT

Table 1

Body composition before (pre), after 24 weeks of resistance type exercise training (post), and 1 y follow-up in healthy older adults.

	Pre ($n = 35$)	Post (24 wks) ($n = 35$)	1 y follow-up ($n = 35$)
Weight (kg)	75.6 ± 13.0	75.9 ± 12.6	76.0 ± 12.8
BMI (kg/m^2)[1]	25.7 ± 2.7	25.8 ± 2.6	26.0 ± 2.7
Leg volume (L)	7.8 ± 1.1	7.9 ± 1.2*	8.0 ± 1.1*
Waist-to-hip ratio	0.93 ± 0.07	0.94 ± 0.08	0.94 ± 0.07
Whole body lean mass (kg)	53.6 ± 11.3	55.0 ± 11.2*	53.9 ± 11.4**
Whole body fat mass (kg)	19.9 ± 5.0	18.9 ± 4.7*	19.9 ± 5.1**
Leg lean mass (kg)	17.1 ± 3.7	17.8 ± 3.8*	17.1 ± 3.9**
Leg fat mass (kg)	6.3 ± 1.9	6.0 ± 1.8*	6.3 ± 2.0**

Data are presented as Mean ± SD.

* Significantly different compared with pre ($P < 0.05$).

** Significantly different compared with post ($P < 0.05$).

[1] Significant main effect of time ($P < 0.05$), but pairwise comparison showed no significant differences between time points.

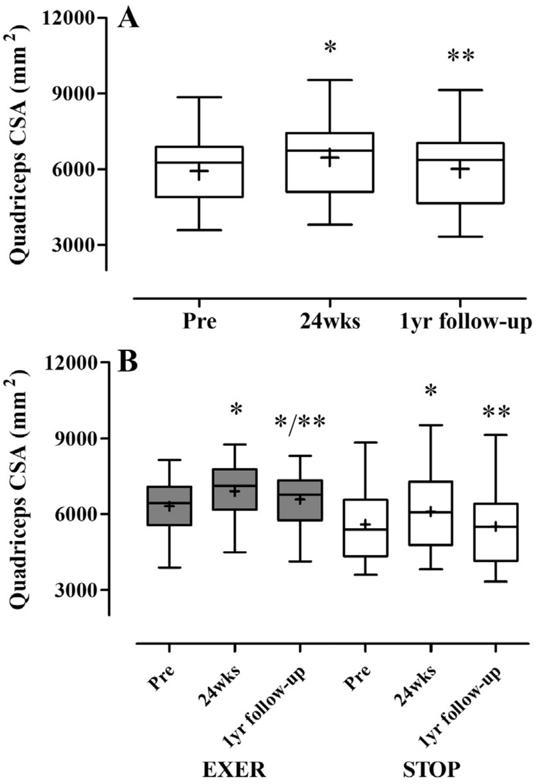

Fig. 1. Quadriceps muscle cross-sectional area (CSA) before (pre) and after 24 wks of the initial resistance type exercise training (RT) program and 1 y follow-up in all participants (n = 35; A) and quadriceps muscle CSA (B) divided in participants who continued to perform RT (EXER, n = 16) or individuals who had stopped to perform any resistance type exercise (STOP, n = 19). Boxes represent interquartile (25th to 75th percentile) ranges, whiskers represent the maximal and minimal values, and the horizontal line and cross indicate the median and mean, respectively. *Significantly different compared with pre, $P < 0.05$. **Significantly different compared with 24 wks, $P < 0.05$. ***Significantly different compared with EXER group, $P < 0.05$.

and had returned to baseline at the 1 y follow-up measurement (Table 1; $P < 0.05$). *Quadriceps* muscle CSA increased significantly following the RT program and returned to baseline at the 1 y follow-up measurement (from 5927 ± 1337 to 6468 ± 1428 and 6012 ± 1434 mm^2, respectively; $P < 0.05$: Fig. 1A).

3.2.2. STOP versus EXER

Bodyweight, BMI and leg volume were at all time points significantly greater in the EXER compared with the STOP group (main effect of group, $P < 0.05$). No significant changes over time were observed for bodyweight in both groups. A significant main effect of time ($P < 0.05$) was found for BMI (Table 2). However, no significant differences between time points were observed using pairwise comparisons. Leg volume increased significantly in response to 24 weeks of RT in both groups (Table 2; $P < 0.05$) and did not differ at the 1 y follow-up assessment. No significant changes over time were observed for waist-to-hip ratio in both groups (Table 2).

Whole body lean mass was significantly greater in EXER compared with the STOP group (main effect of group, $P < 0.05$; Table 2). A significant *time* × *group* interaction ($P < 0.05$) was observed for whole body lean mass. In response to the initial 24 weeks of RT, whole body lean mass increased significantly in both the STOP and EXER group ($P < 0.05$). Subsequently, whole body lean mass had returned to baseline levels in the STOP group, and whole body lean mass remained unchanged in the EXER group at the 1 y follow-up assessment compared with the post exercise training time point (Table 2). Whole body fat mass decreased significantly in response to the RT program ($P < 0.05$) and returned to baseline levels at the 1 y follow-up assessment ($P < 0.05$) with no differences between groups (Table 2). A significant main effect of group was observed for leg lean mass ($P < 0.05$; Table 2), indicating that leg lean mass was significantly greater in the EXER compared with the STOP group. For leg lean mass, a tendency for a *time* × *group* interaction was observed ($P = 0.058$). Leg lean mass increased significantly in response to the RT program ($P < 0.05$) and returned to baseline levels at the 1 y follow-up assessment ($P < 0.05$) for both groups. In response to the RT program leg fat mass decreased significantly ($P < 0.05$), and returned to baseline levels at the 1 y follow-up assessment ($P < 0.05$), with no differences between groups.

Overall, *quadriceps* muscle CSA tended to be greater in the EXER compared with the STOP group (main effect of group, $P = 0.068$). A significant *time* × *group* interaction ($P < 0.05$) for *quadriceps* muscle CSA was observed. In response to the RT program, *quadriceps* muscle CSA increased significantly in both the STOP and EXER group (from 5599 ± 308 to 6105 ± 349 mm^2 and from 6316 ± 315 to 6900 ± 304 mm^2, respectively; $P < 0.05$: Fig. 1B). *Quadriceps* muscle CSA had returned to baseline in the STOP group, whereas it remained slightly elevated in the EXER group at the 1 y follow-up measurement (Fig. 1B).

3.3. Muscle strength and physical function

3.3.1. All follow-up participants

In response to the RT program 1RM strength on leg press (from 175 ± 45 to 222 ± 53 kg; $P < 0.05$) and knee extension (from 79 ± 19 to 112 ± 25 kg; $P < 0.05$) increased significantly. Although 1RM leg press and knee extension strength had decreased at the 1 y follow-up assessment, they remained significantly higher when compared with baseline values ($P < 0.05$). Handgrip strength (left + right) increased significantly with RT (from 71 ± 22 kg to 74 ± 25 kg; $P < 0.05$) and had returned to baseline at the 1 y follow-up measurement (72 ± 24 kg). In response to the RT program the time to complete the sit-to-stand test improved significantly (from 8.1 ± 1.6 to 6.5 ± 1.4 s; $P < 0.05$), which was maintained at the 1 y follow-up assessment (6.2 ± 1.1 s).

3.3.2. STOP versus EXER

Knee extension muscle strength was significantly greater in the EXER compared with the STOP group (main effect of group, $P < 0.05$). The changes in knee extension and leg press muscle strength did not differ between the EXER and STOP group (Fig. 2B–D). Handgrip strength increased significantly with RT ($P < 0.05$) and had returned to baseline values at the 1 y follow-up measurement, with no differences between groups ($P < 0.05$). The time to complete the sit-to-stand test had improved significantly following the training program ($P < 0.05$), which was maintained at the 1 y follow-up assessment, with no differences between groups.

3.4. Muscle fiber cross-sectional area and composition

3.4.1. All follow-up participants

A significant main effect of fiber type ($P < 0.05$) was observed, indicating that type II muscle fiber CSA was significantly smaller compared with type I muscle fiber CSA. A significant *fiber type* × *time* interaction ($P < 0.05$) was observed for muscle fiber CSA. Whereas type I muscle fiber CSA remained unchanged, type II muscle fiber CSA increased significantly in response to 24 wks of RT ($P < 0.05$), but was not different compared to either pre- or post-training values at the 1 y follow-up time point (Table 3). Muscle fiber type distribution (expressed as % of total fiber as well as expressed as % area occupied) remained unchanged over time (Table 3).

3.4.2. STOP versus EXER

No significant differences were observed in both type I and type II

Table 2

Body composition before (pre), after 24 weeks (post) of resistance type exercise training, and 1 y follow-up assessment in healthy older adults who stopped (STOP) or continued to perform strength training (EXER) during the 1 y follow-up period.

	Pre		Post (24 wks)		1 y follow-up	
	STOP ($n = 19$)	EXER ($n = 16$)	STOP ($n = 19$)	EXER ($n = 16$)	STOP ($n = 19$)	EXER ($n = 16$)
Weight (kg)[1]	69 ± 11	83 ± 12‡	70 ± 11	83 ± 11‡	69 ± 10	84 ± 11‡
BMI (kg/m^2)[2]	24.7 ± 2.2	26.8 ± 2.9‡	24.9 ± 2.3	26.8 ± 2.7‡	24.9 ± 2.1	27.3 ± 2.7‡
Leg volume (l)[1]	7.3 ± 1.2	8.3 ± 0.8‡	7.5 ± 1.2*	8.4 ± 0.9‡*	7.7 ± 1.1*	8.5 ± 0.8*‡
Waist-to-hip ratio	0.91 ± 0.07	0.96 ± 0.06	0.92 ± 0.08	0.95 ± 0.07	0.93 ± 0.07	0.95 ± 0.07
Whole body lean mass (kg)[1,3]	48.9 ± 10.3	59.3 ± 10.0‡	50.6 ± 1.7*	60.2 ± 9.7*‡	48.8 ± 10.2**	60.0 ± 9.9‡
Whole body fat mass (kg)[2]	18.6 ± 4.8	21.4 ± 5.0	17.9 ± 4.9*	20.2 ± 4.4*	18.6 ± 4.9**	21.5 ± 4.9**
Leg lean mass (kg)[1]	15.4 ± 3.3	19.0 ± 3.2‡	16.0 ± 3.6*	19.6 ± 3.2‡*	15.3 ± 3.5*	19.3 ± 3.2‡*
Leg fat mass (kg)[2]	6.2 ± 2.0	6.4 ± 1.7	5.9 ± 2.0*	6.1 ± 1.6*	6.2 ± 2.2**	6.4 ± 1.9**

Data are Mean ± SD. EXER: individuals who continued to perform any resistance type exercise after the exercise training program. STOP: individuals who did not continue to perform any resistance type exercise after the exercise training program.

* Significantly different compared with pre ($P < 0.05$).

** Significantly different compared with post ($P < 0.05$).

‡ Significantly different compared with STOP ($P < 0.05$).

[1] Significant main effect of group ($P < 0.05$).

[2] Significant main effect of time ($P < 0.05$), with no significant differences in post-hoc pairwise comparison (Bonferroni correction).

[3] Significant *time* × *group* interaction ($P < 0.05$).

muscle fiber CSA between the EXER and STOP at baseline. For both type I and type II muscle fiber CSA and fiber type distribution, the changes over time (described above) were not different between the EXER and STOP group (Table 4).

3.5. Myonuclear and satellite cell content

3.5.1. All follow-up participants

For myonuclear content a significant main effect of fiber type was observed, indicating that type II muscle fiber myonuclear content was significantly lower compared with type I muscle fibers (Table 3, $P < 0.05$). A significant *fiber type* × *time* interaction (Table 3, $P < 0.05$) was observed for muscle fiber myonuclear content. In

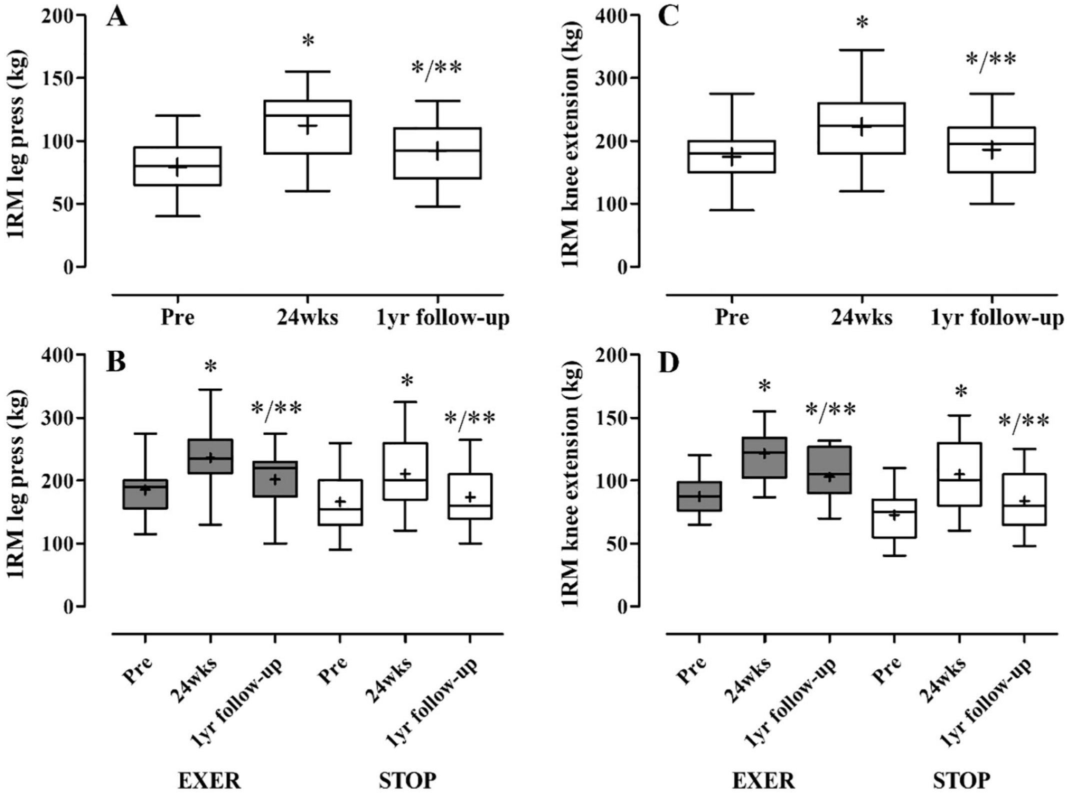

Fig. 2. One repetition maximum (1RM) leg press (A and B) and knee extension (C and D) before (pre) and after 24 wks of the initial resistance type exercise training (RT) program and 1 y follow-up in all participants ($n = 35$; A and C) and divided in participants who continued to perform RT (EXER, $n = 16$) or individuals who had stopped to perform any resistance type exercise (STOP, $n = 19$) (B and D). Boxes represent interquartile (25th to 75th percentile) ranges, whiskers represent the maximal and minimal values, and the horizontal line and cross indicate the median and mean, respectively. *Significantly different compared with pre, $P < 0.05$. **Significantly different compared with 24 wks, $P < 0.05$.

Table 3

Muscle fiber characteristics before (pre), after 24 weeks (post) of resistance type exercise training, and 1 y follow-up in healthy older adults.

		Pre (n = 26)	Post (24 wks) (n = 26)	1 y follow-up (n = 26)
Fiber type distribution (%)	I	55 ± 15	55 ± 14	55 ± 14
	II	45 ± 15	45 ± 14	45 ± 14
Fiber type distribution (CSA%)	I	61 ± 17	58 ± 15	59 ± 15
	II	39 ± 17	42 ± 15	41 ± 15
Muscle fiber CSA (μm^2)[1,2]	I	5663 ± 1115	6011 ± 1367	5835 ± 1768
	II	4384 ± 1108	5422 ± 1763*	5000 ± 1731
Nuclei (per fiber)[1,2]	I	3.7 ± 0.8	3.8 ± 0.8	3.4 ± 0.9
	II	2.9 ± 0.7	3.4 ± 0.9*	2.9 ± 0.9**
Myonuclear domain (μm^2)	I	1562 ± 295	1611 ± 312	1713 ± 291
	II	1533 ± 340	1622 ± 325	1746 ± 293
SC per fiber[2]	I	0.076 ± 0.029	0.087 ± 0.038*	0.062 ± 0.041$^{*/**}$
	II	0.048 ± 0.023	0.078 ± 0.046*	0.040 ± 0.021$^{*/**}$

Data are presented as Mean ± SD. CSA: cross-sectional area.

* Significantly different compared with pre ($P < 0.05$).

** Significantly different compared with post ($P < 0.05$).

[1] Significant *fiber type* × *time* interaction ($P < 0.05$).

[2] Significant main effect of fiber type ($P < 0.05$).

contrast to type I muscle fibers, a main effect of time ($P < 0.05$) was observed for type II muscle fiber myonuclear content. In response to the RT program, type II muscle fiber myonuclear content increased significantly ($P < 0.05$) and returned to baseline at the 1 y follow-up assessment (Table 3). No difference in myonuclear domain size was observed between type I and type II muscle fibers. Myonuclear domain size tended to increase over time (Table 3, main effect of time $P = 0.054$).

A significant main effect of fiber type ($P < 0.05$) was observed for muscle fiber satellite cell content, indicating that type I muscle fiber satellite cell content was significantly higher compared with type II muscle fibers. A tendency was observed for *fiber type* × *time* interaction ($P = 0.074$) for satellite cell content. Type I and type II muscle fiber satellite cell content increased significantly in response to 24 wks of RT (Table 3, $P < 0.05$). At the 1 y follow-up assessment type I and type II muscle fiber satellite cell content had decreased again and were significantly lower compared with baseline values ($P < 0.05$).

3.5.2. *STOP versus EXER*

A significant *fiber type* × *time* interaction ($P < 0.05$) was observed for muscle fiber myonuclear content. For both type I and II muscle fiber myonuclear content, the changes over time did not differ between the STOP and EXER groups (Table 4). For type I and type II myonuclear domain size a significant main effect of time ($P < 0.05$) was observed in both groups, however, no significant difference could be located using pairwise comparisons.

A significant *fiber type* × *time* × *group* interaction ($P < 0.05$) was observed for muscle fiber satellite cell content. Whereas type I muscle fiber satellite cell content remained unchanged over time, type II muscle fiber satellite cell content increased significantly in response to RT, and returned to baseline values at the 1 y follow-up assessment in the STOP group. In the EXER group, a main effect of time was observed with a tendency ($P = 0.076$) for type I and type II muscle fiber satellite cell content to increase in response to RT. Subsequently, type I and type II muscle fiber satellite cell content decreased at the 1 y follow up time point ($P < 0.05$) and was lower compared with baseline values ($P < 0.05$) in the EXER group.

4. Discussion

The present study shows that exercise training induced gains in skeletal muscle mass are lost after 1 year following the initial 24 weeks of supervised RT in older adults. Although muscle strength and physical function also declined during the 1 y follow up, they remained significantly higher compared with baseline levels. Interestingly, the loss of muscle mass was attenuated when some level of (unsupervised) resistance type exercise was maintained in the older participants, whereas changes in muscle strength and muscle fiber characteristics did not differ from those participants who had not performed any resistance type exercise during the 1 year follow up.

RT is known to be an effective intervention strategy to combat age-related sarcopenia in older adults. Likewise, the present study shows a substantial increase in skeletal muscle mass, strength and physical function in response to 24 wks of RT in older adults, which is in line with previous publications (Bickel et al., 2011; Correa et al., 2013; Correa et al., 2016; Fatouros et al., 2005; Fiatarone et al., 1994; Ivey et al., 2000; Kalapotharakos et al., 2007; Kalapotharakos et al., 2010; Lemmer et al., 2000). However, muscle mass and strength gains have been reported to dissipate when regular resistance exercise training is

Table 4

Muscle fiber characteristics before (pre), after 24 weeks (post) of resistance type exercise training, and 1 y follow-up assessment in healthy older adults who stopped (STOP) or continued to perform strength training (EXER) during the 1 y follow-up period.

		Pre		Post (24 wks)		1 y follow-up	
		STOP (n = 12)	EXER (n = 14)	STOP (n = 12)	EXER (n = 14)	STOP (n = 12)	EXER (n = 14)
Fiber type distribution (%)	I	53 ± 12	57 ± 18	54 ± 11	55 ± 18	53 ± 15	58 ± 14
	II	47 ± 12	43 ± 18	46 ± 11	45 ± 18	47 ± 15	42 ± 14
Fiber type distribution (CSA%)	I	61 ± 14	60 ± 21	58 ± 13	57 ± 18	58 ± 16	60 ± 14
	II	39 ± 14	40 ± 21	42 ± 13	43 ± 18	42 ± 16	40 ± 14
Muscle fiber CSA (μm^2)[1]	I	5915 ± 1042	5368 ± 1042	5752 ± 1574	6312 ± 1065	5948 ± 2015	5704 ± 1506
	II	4234 ± 1130	4559 ± 1105	4982 ± 1616*	5938 ± 1854*	4884 ± 1841	5135 ± 1664
Nuclei (per fiber)[1]	I	3.7 ± 0.9	3.7 ± 0.7	3.7 ± 1.0	3.8 ± 0.4	3.5 ± 0.9	3.4 ± 1.0
	II	2.8 ± 0.9	3.0 ± 0.6	3.2 ± 1.0*	3.6 ± 0.6**	2.9 ± 1.0**	2.9 ± 0.9**
Myonuclear domain (μm^2)	I	1631 ± 324	1481 ± 246	1570 ± 365	1659 ± 243	1703 ± 305	1724 ± 287
	II	1553 ± 410	1509 ± 252	1584 ± 341	1665 ± 314	1677 ± 250	1827 ± 329
SC per fiber[2]	I	0.087 ± 0.030	0.063 ± 0.024	0.086 ± 0.038	0.087 ± 0.033	0.082 ± 0.040	0.038 ± 0.028$^{*/**}$
	II	0.044 ± 0.022	0.053 ± 0.024	0.086 ± 0.057*	0.067 ± 0.025	0.048 ± 0.024**	0.032 ± 0.024$^{*/**}$

Data are Mean ± SD. CSA: cross-sectional area. EXER: individuals who continued to perform any resistance type exercise after the exercise training program. STOP: individuals who did not continue to perform any resistance type exercise after the exercise training program.

* Significantly different compared with pre ($P < 0.05$).

** Significantly different compared with post ($P < 0.05$).

[1] Significant *fiber type* × *time* interaction ($P < 0.05$).

[2] Significant *fiber type* × *time* × *group* interaction ($P < 0.05$).

interrupted (Bickel et al., 2011; Correa et al., 2013; Correa et al., 2016; Fatouros et al., 2005; Ivey et al., 2000; Kalapotharakos et al., 2007; Kalapotharakos et al., 2010; Lemmer et al., 2000; Sherk et al., 2012; Staron et al., 1991; Trappe et al., 2002; Yasuda et al., 2015; Yasuda et al., 2014). In accordance, the present study shows that muscle mass (DXA-scans) and *quadriceps* muscle CSA (CT-scans) had returned to baseline levels 1 year after discontinuation of the initial RT program. Though we also observed a decline in muscle strength during the 1 y follow-up period, 1RM strength remained significantly higher compared with baseline values. Furthermore, the positive impact of RT on physical function (i.e. sit-to-stand test) had remained intact at the 1 y follow-up assessment. These results seem to agree with other work in the area demonstrating a greater and/or faster loss of skeletal muscle mass when compared with strength or function loss after discontinuing exercise (Bickel et al., 2011; Correa et al., 2013; Correa et al., 2016; Ivey et al., 2000; Yasuda et al., 2014). It has been hypothesized that neuromuscular adaptations (e.g. improved motor unit activation, improved coordination of agonists, and/or inhibition of antagonists (Hakkinen et al., 1998)) that affect muscle strength and performance, may persist longer than what appears to be more temporary exercise induced muscle growth. Likewise, recent meta-analysis studies (Peterson et al., 2010; Peterson et al., 2011) reported an overall greater increase in muscle strength in response to exercise training (25 to 29%) when compared to the gain in muscle mass (5–7%) in older adults. This clear mismatch between muscle growth and strength gains during resistance exercise training may make it less surprising that the loss of muscle mass is also different from the loss of muscle strength during detraining. From a clinical perspective, the ability to maintain muscle strength and function, independently of muscle mass, is of major importance in ambulatory function as well as fall risk in the older population. However, this does not exclude the probability that preserving exercise induced gains in muscle mass likely yield even greater (metabolic) health and functional benefits in older adults.

Beside the RT induced gains in skeletal muscle mass, strength, and function, an indirect beneficial effect of any exercise training program would be to change behavior and support older adults to adopt a more active life style, including the implementation of RT in their weekly routine. Only limited data is available on the impact of maintaining some level of exercise on preservation of skeletal muscle mass and strength gains obtained in a prolonged resistance exercise training program in older adults (Bickel et al., 2011; Trappe et al., 2002). Though these studies indicate that exercise prescription can be used to maintain the beneficial effects of an initial exercise training program, it remains unknown whether this can also be achieved by older adults autonomously. Therefore, after the initial analysis of all 'follow up' participants in the present study ($n = 35$), we assessed whether individuals who continued to perform some form of (unprescribed) RT on an individual basis would preserve more of their muscle mass, strength, and function when compared with individuals who had not continued regular weight-lifting exercise. It is important to note that the 1 y follow-up assessment was not part of the original study design but was initiated and submitted to the local ethics committee > 6 months after subjects had completed the original 24-week exercise training study. Consequently, participants were not provided with any advice or incentives to continue exercise training after finishing the initial RT program and were previously not informed about any follow-up assessment. Of all participants included at the 1 y follow up assessment (i.e., $n = 35$ out of a potential total of $n = 53$), 45% ($n = 16$) reported to have continued with some sort of strength training, including lower-body exercises, after the initial 6 month resistance exercise training program and were subsequently allocated in the EXER group. Almost all subjects (15 out of 16 subjects) in the EXER group had continued to perform resistance exercise training at a local gym, one subject performed the strength training at home. Interestingly, only 2 subjects indicated to perform resistance exercise training up to 3 times per week as was performed during the initial 6 month resistance exercise training program, whereas all others subjects within the EXER group indicated to visit the gym not > 2 times per week to perform their strength training exercises. Unfortunately, we were not able to further specify the exact exercises performed as well as exercise intensity/volume used by the participants during the 1 year follow-up, which clearly is a limitation of the present study. Nevertheless, this is the first study to provide a unique insight in the question whether older adults would be able to *autonomously* maintain the initial beneficial health outcomes of a supervised RT program. In accordance to our hypothesis, we report a greater loss (*time* × *group* interaction, $P < 0.05$) in *quadriceps* muscle CSA in the STOP (−9.5%) compared with the EXER (−4.5%) group during the 1 y follow-up. Furthermore, whole-body lean mass was better preserved in the EXER vs STOP group (time × group interaction, $P < 0.05$), and leg lean mass tended (*time* × *group* interaction, $P = 0.058$) to decline more in the STOP (−4.4%) compared with the EXER group (−2.6%) during the 1 y follow-up period. Interestingly, skeletal muscle mass appeared to be better maintained in the EXER group, yet no differences were observed in the preservation of muscle strength and/or physical function during the 1 y follow-up between groups. In other words, continuing to perform (unsupervised) strength training autonomously resulted in attenuated loss of muscle mass, but did not result in a reduction in the loss of muscle strength and function after the initial RT program. This, again, highlights the mismatch between the loss of muscle mass and strength/function after exercise training cessation. Altogether the present study confirms previous findings that supervised RT programs augment skeletal muscle mass, strength, function and overall health in older adults, however, many of these health benefits dissipate after cessation of the supervised exercise program. Whereas the initial strength gains were partially preserved, gains in muscle mass had completely disappeared 1 y after RT cessation. While (self-reported) continuation of some form of resistance exercise appears to be beneficial with regards to maintaining some of the muscle mass gains, it is evident that older adults may require a more supervised approach and/or a better education (i.e., on the required characteristics of an exercise program such as intensity/ volume) for them to continue profiting from all the benefits of RT. These results are a clear call for action to not simply set up lifestyle/exercise training programs for a set amount of time, but emphasis should be directed to the sustainability of an intervention strategy (King, 2001), e.g. exercise education and implementing guided exercise training in the weekly routine of older adults.

In the present study, we also evaluated the impact of exercise training and detraining in older adults on the muscle fiber level. We assessed whether the increase in myonuclear and satellite cell content typically observed with RT in older adults is maintained when the exercise program is discontinued. Muscle satellite cells are the only source to provide additional nuclei in skeletal muscle and, as such, they are found to be critical in muscle fiber regeneration, repair and/or more long-term fiber adaptation in vivo in humans (Snijders et al., 2015). However, we (Snijders et al., 2014; Verdijk et al., 2014) and others (McKay et al., 2013; McKay et al., 2012; Nederveen et al., 2015) have shown that type II muscle fiber satellite cell content and function declines with aging. Accordingly, it has been hypothesized that satellite cells may have an important role in the development of sarcopenia and/or mal-adaptive response to exercise training in older adults (Snijders et al., 2015). We are the first to show that the exercise training induced increase in type II muscle fiber satellite cell content is not maintained 1 y after the initial exercise training program had finished. Furthermore, the return of satellite cell content was observed in both the STOP as well as the EXER group. This suggests that a more sustained exercise stimulus is required to maintain the exercise training induced increase in satellite cell content in muscle tissue of older adults. In rodents it has been reported that exercise (Bruusgaard et al., 2010) or pharmacological (Egner et al., 2013) induced increases in myonuclear content are not lost during subsequent periods of detraining. It has been postulated that this retention of myonuclei might be responsible for the accelerated return of muscle mass and strength after a period of inactivity in previously trained individuals, a phenomenon which has been termed 'muscle memory' (Gundersen, 2016). However, no studies have yet assessed whether exercise induced myonuclear accretion is maintained after exercise cessation in humans. In the present study we show that the RT induced increases in myonuclear content are not retained in older adults. Hence, these results do not support the hypothesis that myonuclei are retained infinitively following an exercise training program. Whether these results are specific to older adults, remains to be established.

We conclude that older adults participating in a 6 month supervised RT program will largely lose their muscle mass gains within one year after exercise discontinuation. Although muscle strength and physical function also decline after exercise discontinuation, part of the functional benefits were still maintained after 1y follow up. Maintenance of some level of unsupervised RT attenuated the decline in muscle mass, but does not appear to suffice to preserve all prior gains in muscle mass and strength in older adults. We propose that older adults will likely require a more supervised approach and/or a better education on the required exercise characteristics to continue profiting from all the benefits of RT.

Conflict of interest and funding disclosure

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.exger.2019.04.002.

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