



# Responsiveness to muscle mass gain following 12 and 24 weeks of resistance training in older women

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Received: 26 March 2020 / Accepted: 30 April 2020 / Published online: 23 May 2020  
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## Abstract

**Background** Many factors may influence the magnitude of individual responses to resistance training (RT). How the manipulation of training volume and frequency affects responsiveness level for muscle mass gain in older women has not been investigated.

**Aims** This study had the objective of identifying responders (RP) and non-responders (N-RP) older women for skeletal muscle mass (SMM) gain from a 12-week resistance training (RT) program. Additionally, we analyzed whether the N-RP could gain SMM with an increase in weekly training volume over 12 additional weeks of training.

**Methods** Thirty-nine older women (aged  $\geq 60$  years) completed 24 weeks of a whole-body RT intervention (eight exercises, 2–3×/week, 1–2 sets of 10–15 repetitions). SMM was estimated by DXA, and the responsive cut-off value was set at two times the standard error of measurement. Participants were considered as RP if they exceeded the cut-off value after a 12-week RT phase, while the N-RP were those who failed to reach the SMM cut-off.

**Results** Of the 22 participants considered to be N-RP, only 3 accumulated SMM gains ( $P = 0.250$ ) that exceeded the cut-off point for responsiveness following 12 additional weeks of training, while 19 maintained or presented negative SMM changes. Of the 17 participants considered to be RP, all continued to gain SMM after the second 12-week RT phase. No significant correlation was observed between the changes in SMM and any baseline aspect of the participants.

**Conclusions** Our results suggest that some older women are RP, while others are N-RP to SMM gains resulting from RT. Furthermore, the non-responsiveness condition was not altered by an increase of training volume and intervention duration while RP participants continue to increase SMM; it appears that RP continue to be RP, and N-RP continue to be N-RP.

**Keywords** Aging · Strength training · Hypertrophy · Responsivity · Inter-individual variation · Heterogeneity

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## Introduction

Resistance training (RT) has been widely recommended for older adults due to its potential for attenuating and even reversing the aging-induced loss of muscle mass and function, as well as improving other important health-related indicators to augment active-life expectancy [1, 2]. Despite the plethora of data supporting RT for inducing overall positive adaptations in the elderly, previous works have exhibited large inter-individual variations in responses of muscular strength, muscle mass, and functional fitness [3–5]. Following a training period, some individuals demonstrate considerable improvements in a given outcome while others show worsened or no change. These differences lead subjects to be

classified as responders (RP) and others as non-responders (N-RP) [6–8].

Many factors may influence the magnitude of individual responses to RT [9]. With regard to muscle hypertrophy, training variables play a key role in the adaptations, with training volume seeming to have the most impact generally [10, 11]. Moreover, protein intake [12], the inflammatory and anabolic hormonal environment [13, 14], genetic and epigenetic predisposition [6–9] are among various other aspects that can influence RT-induced muscle growth and may explain some of the heterogeneity of the hypertrophic responses within subjects. Several strategies have been proposed to test if N-RP do exist to a specific exercise program. Although subjects considered N-RP to an outcome measure are not always N-RP to other measures [3–5], a larger period of training, preferably with changes in training variables and/or increases in training volume, may be necessary to confirm if these individuals are indeed N-RP [5, 6, 15], especially for gains in muscle mass, which is mostly influenced by these factors [10, 11, 16]. In the elderly, some studies have suggested that protocol duration and multiple assessments might mitigate the presence of N-RP [3–5]. However, how the manipulation of training volume and frequency affects responsiveness level in older women has not been investigated.

Therefore, this investigation is exploratory of a previous experiment [17] and has the purpose of identifying possible RP and N-RP older women for skeletal muscle mass (SMM) gains following a 12-week RT program. After that, it was aimed to verify whether the N-RP could then enhance SMM with an increase in weekly training volume with 12 more weeks of RT. Furthermore, correlations between the changes in SMM with the initial values of SMM, specific blood biomarkers, and dietary intake were explored. It was hypothesized that N-RP would benefit from the increased training volume and duration.

## Methods

### Experimental approach to the problem

The current investigation was exploratory in nature. It is an extension of the data presented previously, which showed similar effects of RT performed two (G2×) versus three (G3×) times per week on muscle mass in older women [17, 18]. The present study was conducted over 30 weeks, with 6 weeks used for data acquisition and 24 weeks directed to the RT program. Weeks 1–2 (pre-training), 15–16 (mid-training), and 29–30 (post-training) were used for assessment of outcome variables. The RT was conducted in two phases of 12 weeks, with weeks 3–14 constituting Phase 1, and weeks 17–28, Phase 2.

## Subjects

The present study is part of a longitudinal research project named ‘Active Aging Longitudinal Study’, which started in September 2012, whose purpose is to analyze the effects of supervised, structured, and progressive RT programs on neuromuscular, morphological, physiological, metabolic, and behavioral outcomes in older women. The recruitment of the sample was carried out through newspaper and radio advertisings. Interested subjects completed detailed health history and physical activity questionnaires and were subsequently admitted to the study if they met specific inclusion criteria: female,  $\geq 60$  years old, physically independent, had no orthopedic conditions that would prevent them from performing the prescribed exercise training or testing associated with the study, and were not receiving hormonal replacement therapy. From 112 older women who applied, 50 met inclusion criteria and were evaluated by a cardiologist (resting 12-lead electrocardiogram test, personal interview, and treadmill stress test when deemed necessary) and released with no exclusions to exercise practice. Eleven women (first 12-week phase: RP = 3, N-RP = 2; second 12-week phase: RP = 3, N-RP = 3) withdrew the study due to personal reasons, traveling, lack of time, health problems or surgeries not related to RT practice. Thirty-nine women ultimately completed the intervention and were included for final analyses (age =  $68 \pm 6$  years; weight =  $65.3 \pm 14.8$  kg; height =  $156.0 \pm 6.4$  cm; body mass index =  $26.7 \pm 5.1$  kg/m<sup>2</sup>). They had not been in any systematized exercise program for six months prior to this study but had a brief 3-month preparatory to RT in the mentioned Project and had not performed RT previously. Written informed consent was obtained from all participants. The procedures were conducted according to the Declaration of Helsinki, and this investigation was approved by the local University Ethics Committee.

### Skeletal muscle mass

Body composition was assessed by dual-energy X-ray absorptiometry (Lunar Prodigy, model NRL 41990, General Electric, Madison, USA). SMM was estimated by a specific equation validated from magnetic resonance imaging which uses values of lower- and upper-limbs lean soft tissue [19]. Both calibration and analysis were carried out by an experienced, skilled laboratory technician, following the manufacturer’s recommendations. The software generated standard lines that set apart the limbs from the trunk and head. The same technician adjusted these lines using specific anatomical points determined by the manufacturer

and performed analyses during the intervention. Previous test–retest scans in 13 participants resulted in an intraclass correlation coefficient of 0.995 and a standard error of measurement (SEM) of 0.290 kg for the SMM. The responsiveness cut-off point for the SMM was set at 0.580 kg, which refers to the value of two times the SEM value [20]. RP participants were considered those who exceeded the responsiveness cut-off value after the first 12-week RT phase, i.e., those who improved SMM in an amount higher than 0.580 kg. On the other hand, N-RP participants were those who presented an absolute change of SMM below the cut-off value of 0.580 kg.

### Blood biomarkers

Venous blood samples were collected into one tube between 7:00 am and 9:00 am after 12 h fasting and after a minimum of 48 h since the last physical exercise session. Five milliliters were withdrawn from a prominent superficial vein in the antecubital space using a clean venous puncture with minimal stasis and placed in a tube containing a dipotassium-methylenediaminetetra-acetic acid as an anticoagulant and preservative. All samples were centrifuged at 3000 rpm for 15 min, and plasma or serum aliquots were stored at  $-80^{\circ}\text{C}$  until assayed. Measurements of serum levels of insulin-like growth factor-1 (IGF-1), testosterone, and C-reactive protein were assessed. The analyses were carried out using a biochemical auto-analyzer system (Dimension RxL Max—Siemens Dade Behring) according to the established literature, consistent with the manufacturer's recommendations.

### Dietary intake

Food intake was assessed by the 24-h dietary recall method applied on three nonconsecutive days (two weeks days and one weekend day) during the first week of the training period (week 3). Participants were given specific instructions regarding how to estimate portion sizes and identify all food and fluid intake from a specialized manual; food models were viewed by participants to enhance precision. Total energy intake, carbohydrate, lipid, and protein content were calculated using nutrition analysis software (Avanutri Processor Nutrition Software, v. 3.1.4; Rio de Janeiro, Brazil). All participants were asked to maintain their routine food and fluid consumption throughout the study.

### RT program

The supervised RT program was performed in the morning hours over the 24 weeks. Physical Education professionals supervised all training period to ensure consistent and safe performance. Participants underwent an RT program composed of eight exercises performed in the following order: chest press,

horizontal leg press, seated row, leg extension, preacher curl, leg curl, triceps pushdown, and seated calf raise. Each exercise was performed in one set of 10–15 repetitions maximum for the first 12 weeks and then increased to two sets of 10–15 repetitions maximum during the last 12 weeks. Participants were given two to three minutes of rest between each exercise. Among the participants, 19 performed RT twice a week (G2 $\times$ ) on Tuesdays and Thursdays, and 20 performed RT three times per week (G3 $\times$ ) on Mondays, Wednesdays, and Fridays [17, 18]. The initial load for all exercises was made based on Physical Education professionals' perception and experience. Progression of training load was individually planned so that when 15 repetitions (in one set at Phase 1, and in two sets at Phase 2) were completed for two consecutive sessions in a specific exercise, weight was increased 2–5% for upper-limb exercises and 5–10% for the lower-limb exercises. During the RT intervention, the volume-load was calculated as load  $\times$  repetitions  $\times$  sets. Participants were asked not to engage in any other type of physical exercise during the intervention period.

### Statistical analyses

The Shapiro–Wilk test verified data distribution. To compare the RT-induced change in SMM between groups, analysis of covariance (ANCOVA) was used to compare the raw differences, with baseline scores as covariates. Non-adjusted values were also presented, although statistical interpretations were made with results from ANCOVA. For the other variables, ANOVAs were used to compare the values of different groups and time-points. The McNemar test was applied to compare whether the proportion of RP and N-RP changed throughout the training phases. Pearson's chi-square test was used to compare the fraction of participants that were from G2 $\times$  or G3 $\times$  groups [17, 18] between the RP and N-RP subgroups. Pearson's correlation test was adopted to test whether there were relationships between SMM and other variables at pre-training, and between the changes in SMM of Phases 1 and 2. Cohen's effect size (ES) was calculated as post-training mean minus pre-training mean divided by the pooled pre-training standard deviation [21]. An ES of 0.00–0.19 was considered as trivial, 0.20–0.49 was considered as small, 0.50–0.79 was considered as moderate, and  $\geq 0.80$  was considered as large [21]. For all analyses, a  $P < 0.05$  was accepted as statistically significant. The data were stored and analyzed using IBM SPSS Statistics, v. 23.0 (IBM Corp., Armonk, NY, USA).

### Results

Training attendance was satisfactory with all participants attaining  $93 \pm 5\%$  of the sessions over the 24 weeks, with no difference between G2 $\times$  ( $93 \pm 5\%$ ) and G3 $\times$  ( $92 \pm 8\%$ )

groups ( $P=0.645$ ), as well as for N-RP ( $92\pm6\%$ ) and RP ( $92\pm6\%$ ) subgroups ( $P=0.830$ ). No adverse event was observed during the intervention. The progression in the training volume-load throughout the 24-week program was also similar between the frequency groups ( $G2\times=199\%$ ,  $G3\times=193\%$ ;  $P=0.245$ ), and between N-RP (200%) and RP (190%) subgroups ( $P=0.519$ ). The number of participants that performed RT two or three times per week was similar between N-RP and RP subgroups ( $P=0.267$ ). In the RP subgroup, 10 subjects were from  $G2\times$ , and 7 were from  $G3\times$ , while in the N-RP, 9 were from  $G2\times$ , and 13 were from  $G3\times$ . No significant difference at pre-training was identified between RP and N-RP for SMM, anthropometry, blood biomarkers, and dietary intake (Table 1).

The N-RP presented no change in upper-limb lean soft tissue (pre-training =  $4.5\pm0.7$  kg; post-training =  $4.5\pm0.7$  kg;  $P=0.379$ ), lower-limb lean soft tissue (pre-training =  $13.8\pm2.1$  kg; post-training =  $13.8\pm2.0$  kg;  $P=0.552$ ), and total body lean soft tissue (pre-training =  $38.1\pm5.1$  kg; post-training =  $38.1\pm4.9$  kg;  $P=0.931$ ). The RP presented significant gains ( $P<0.001$ ) in upper-limb lean soft tissue (pre-training =  $4.1\pm0.9$  kg; post-training =  $4.4\pm0.9$  kg), lower-limb lean soft tissue (pre-training =  $13.0\pm2.5$  kg; post-training =  $13.8\pm2.4$  kg), and total body lean soft tissue ( $36.7\pm6.7$  kg; post-training =  $38.3\pm6.7$  kg). For the changes in estimated SMM, there was observed no significant difference between groups in either time points: pre-training (RP =  $18.65\pm3.9$ ;

N-RP =  $20.27\pm3.2$ ;  $P=0.163$ ), mid-training (RP =  $19.50\pm3.9$ ; N-RP =  $20.29\pm3.1$ ;  $P=0.485$ ), post-training (RP =  $19.92\pm3.8$ ; N-RP =  $20.12\pm3.1$ ;  $P=0.857$ ). All changes in SMM throughout the training periods were significantly greater for the RP group compared to the N-RP group ( $P<0.001$ ), as presented in Table 1. The RP group presented a significant gain (ES = 0.22) from pre-training to mid-training and also from mid-training to post-training (ES = 0.11), although the latter was significantly lower than the former. None of the 22 N-RP participants achieved a gain of SMM above the cut-off point for responsiveness in the second 12-week RT phase. Of the 17 participants who were considered as RP in the first 12 weeks, only 4 gained more than 0.580 kg of SMM in the second training phase, and 13 had an alteration between 0 and 0.580 kg. The N-RP did not present any measurable change following the first 12 weeks of training (ES = 0.01), nor did they make any gain between mid-training and post-training (ES = -0.06). Average percent change from pre-training to mid-training was 4.7% for RP (range 2.9–9.2%), and 0.2% for N-RP (range -3.4 to 2.6%), while from mid-training to post-training change was 2.3% for RP (range 0.2–7.8%) and -0.9% for N-RP (range -5.0 to 2.7%). From pre-training to post-training, the average change was 7.1% for RP (range 4.5–12.6%) and -0.6% for N-RP (range -6.2 to 4.2%). Considering the total sample, a significant ( $F=10.272$ ;  $P=0.002$ ;  $\eta_p^2=0.213$ ; power = 0.903) positive change in SMM was observed from pre-training ( $19.6\pm3.6$ ) to post-training ( $20.1\pm3.4$ ).

**Table 1** Participants' characteristics at pre-training, and changes in SMM after training periods, according to responsiveness subgroups

Variables	RP ( $n=17$ )	N-RP ( $n=22$ )	$P$
Values at pre-training			
Age (years)	$68.7\pm6.3$	$67.8\pm6.1$	0.659
Body mass (kg)	$63.0\pm16.3$	$66.9\pm13.6$	0.416
Height (cm)	$154.2\pm6.7$	$157.5\pm5.9$	0.112
BMI ( $\text{kg}/\text{m}^2$ )	$26.4\pm5.7$	$26.9\pm4.7$	0.723
SMMI ( $\text{kg}/\text{m}^2$ )	$7.8\pm1.4$	$8.2\pm1.0$	0.393
Testosterone (ng/mL)	$0.20\pm0.1$	$0.20\pm0.1$	0.999
IGF-1 ( $\mu\text{U}/\text{mL}$ )	$121.0\pm35.2$	$121.8\pm57.0$	0.960
CRP (pg/mL)	$3.14\pm1.5$	$2.45\pm1.2$	0.116
Energy (kcal/kg/day)	$26.0\pm6.1$	$28.1\pm8.5$	0.380
Carbohydrate (g/kg/day)	$3.9\pm1.1$	$4.3\pm1.4$	0.361
Lipid (g/kg/day)	$0.7\pm0.3$	$0.7\pm0.2$	0.664
Protein (g/kg/day)	$1.1\pm0.3$	$1.0\pm0.4$	0.964
SMM (kg)			
$\Delta\text{Pre to mid}$	$0.83 (0.67, 1.00)^*$	$0.04 (-0.10, 0.18)$	$<0.001$
$\Delta\text{Mid to post}$	$0.40 (0.19, 0.60)^{*}\dagger$	$-0.16 (-0.34, 0.05)$	$<0.001$
$\Delta\text{Pre to post}$	$1.23 (0.92, 1.54)$	$-0.13 (-0.40, 0.14)$	$<0.001$

RP responders, N-RP non-responders, SMM skeletal muscle mass, BMI body mass index, SMMI skeletal muscle mass index, IGF-1 insulin-like growth factor-1, CRP C-reactive protein

\*Significant change ( $P<0.05$ )

$\dagger P<0.05$  vs.  $\Delta\text{Pre to mid}$

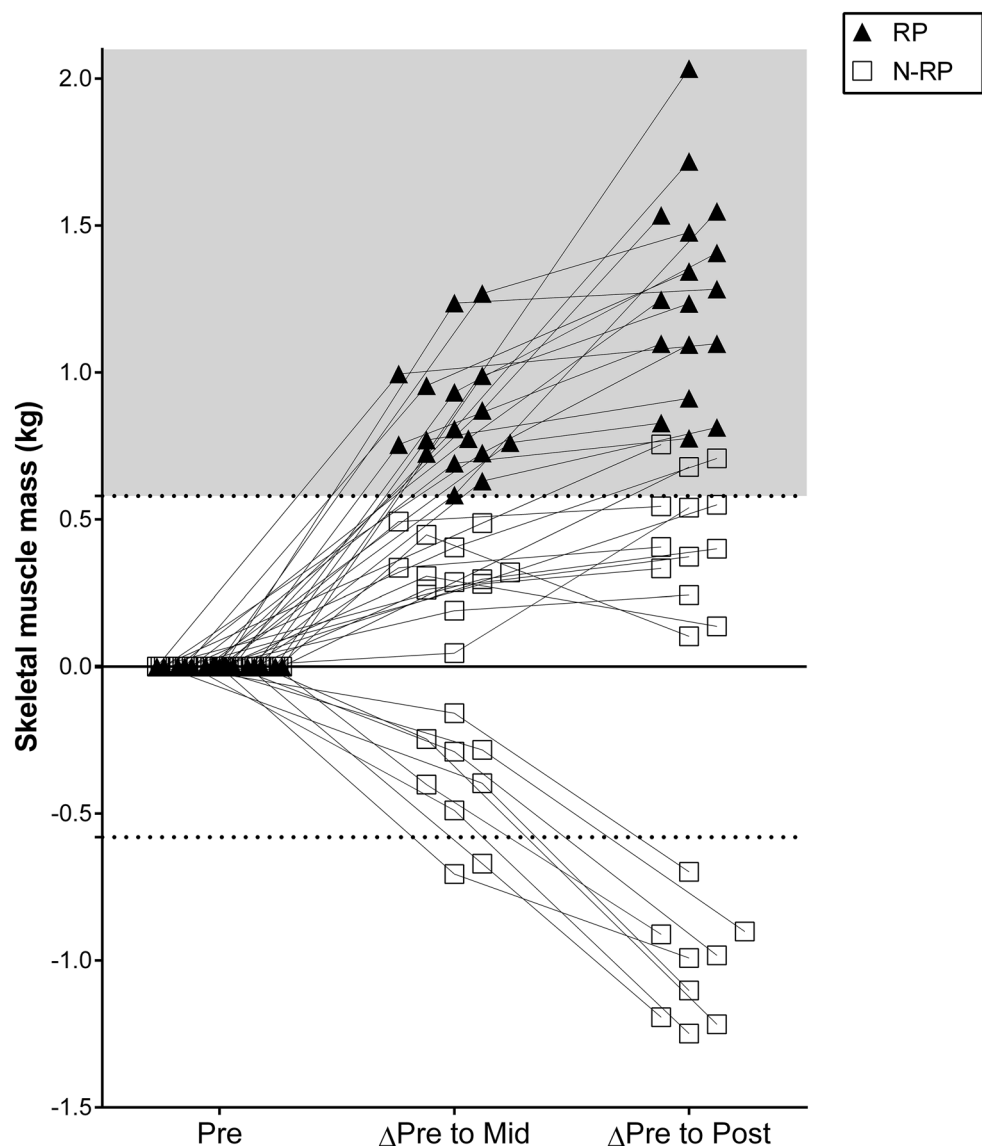
Figure 1 shows the individual values of the changes throughout the program (between pre-training to mid-training, and pre-training to post-training). Across the 24 weeks of RT, of the 22 participants who were considered N-RP, 3 accumulated gains in SMM that surpassed the cut-off point for responsiveness ( $P=0.250$ ), while 19 did not. Within these 19 N-RP, 10 maintained their changes in SMM between 0 and 0.580 kg, and 9 had reductions in SMM. All the RP kept their SMM values above the cut-off line.

No significant correlation was observed between the changes in SMM and the pre-training characteristics of the participants, as presented in Table 2. A positive correlation ( $r=0.697$ ,  $P<0.001$ ) was observed between the changes in SMM after Phase 1 ( $\Delta$ pre-training to mid-training) and the changes in SMM after Phase 2 ( $\Delta$ mid-training to post-training) suggesting that those who had SMM gain initially continued to show increases in the second phase of RT.

## Discussion

The main finding of the current investigation was that the older women who did not show increases in SMM during an initial 12 weeks of RT (i.e., N-RP) also did not obtain gains after an additional 12-week RT period with higher training volume. The proportion of RP and N-RP participants remained similar from the first phase to the end of the RT program, and there were observed significant strong positive correlations between the changes in SMM from pre-training to mid-training with changes from mid-training to post-training. In contrast, refuting our initial hypotheses, no significant association was observed between the changes in SMM and physical characteristics, blood biomarkers, and dietary intake at pre-training.

**Fig. 1** Individual values of the absolute delta of muscle mass between pre-training to mid-training, and pre-training to post-training, according to responders (RP,  $n=17$ ) and non-responders participants (N-RP,  $n=22$ ). The grey area represents where the gains of skeletal muscle mass were above the responsiveness cut-off value (0.580 kg)





**Table 2** Correlations between the changes in SMM and variables related to sample characteristics assessed at pre-training ( $n = 39$ )

Variables (at pre-training)	SMM (kg)			
	$\Delta$ Pre to mid		$\Delta$ Pre to post	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Age (years)	0.119	0.470	0.159	0.332
BMI (kg/m <sup>2</sup> )	−0.266	0.101	−0.268	0.100
SMM (kg)	−0.308	0.085	−0.306	0.098
SMMI (kg/m <sup>2</sup> )	−0.242	0.138	−0.233	0.154
Testosterone (ng/mL)	−0.101	0.539	−0.106	0.521
IGF-1 (μU/mL)	0.096	0.562	0.144	0.381
CRP (pg/mL)	0.108	0.514	0.029	0.860
Energy (kcal/kg/day)	0.046	0.779	−0.092	0.579
Carbohydrate (g/kg/day)	−0.032	0.846	−0.141	0.391
Lipid (g/kg/day)	0.125	0.449	0.017	0.916
Protein (g/kg/day)	0.169	0.303	0.013	0.938

No significant correlation was observed

SMM skeletal muscle mass, BMI body mass index, SMMI SMM index, IGF-1 insulin-like growth factor-1, CRP C-reactive protein

Contrary to previous results for aerobic training [15], training volume in the current study did not eliminate the presence of N-RP. As previously presented, after 12 and 24 weeks of RT, the changes in SMM were similar for those who performed either two or three sessions per week [17]. This is the first indication that training volume does not seem to play a large role in improving SMM in older women. Moreover, the ratio of older women RP to N-RP was not different between the G2× and G3× groups. Also, when the number of sets per exercise was doubled in the second phase of the program, the response pattern did not change. The RP continued to have positive improvements in SMM, while the N-RP continued to show changes below the responsiveness cut-off point. Although participants were only categorically dichotomized above or below the +0.580 kg SMM cut-off, Fig. 1 shows participants with  $\Delta$ pre-training to mid-training SMM greater than 0.580 kg continued to be above that line during the remainder of the training. When individuals with delta values greater than 0 but below the cut-off value, labeled as “false responders” [6], continued to train, they remained within that same range of change throughout. Finally, all subjects who had negatives delta values in the first phase continued to have the same pattern in the second phase, presenting reductions under the two times of the SEM value. A posteriori analyses revealed no significant ( $P > 0.05$ ) difference among these three subgroups for any baseline measure and Phase 1 variables. The positive and significant correlation observed between the  $\Delta$ pre-training to mid-training and  $\Delta$ mid-training to post-training confirmed that changes in SMM are associated throughout the program.

Since there were no differences in the characteristics of the subjects among the subgroups for responsiveness nor any significant correlation of these characteristics with the SMM change, it raises the possibility that a genetic background could explain part of the results observed herein. Although no such analysis was performed, the literature indicates that muscle hypertrophy does have a substantial genetic component [6–9, 22]. Recent findings of Haun et al. [22] revealed that an elevated proportion of type I muscle fiber at the baseline negatively predicts the magnitude of the hypertrophic gain from RT in trained young men. Thus, considering that the percentage of muscle fiber type is highly heritable [9, 23], it can be speculated that individuals who inherited a greater proportion of type I muscle fibers are less likely to gain muscle mass with exercise. In the same way, individuals with more type II fiber percentage tend to have a greater hypertrophic response since this fiber type has a more considerable hypertrophic potential [8]. This seems to be plausible in older women since the aging process leads to a reduction in the innervation of high-threshold fibers and decrease in the proportion of type II fibers [24], which might explain the small improvements or absence of gains in SMM in N-RP individuals. In addition, the reduced hypertrophic response has also been attributed to lower initial values of anabolic hormones and higher values of inflammatory blood markers in older adults, although these results are not universal [13, 14]. Studies with larger and more heterogeneous samples may help to determine whether some blood markers have any influence or association on the gains of muscle mass [14], which was not the case in the present work.

The significant correlation between the responses to the two training phases further highlights the possible genetic dependence of the adaptation in SMM. In older adults, Stec et al. [25] recently observed that ribosome biogenesis was also one determinant factor that may explain RT-induced muscle growth. That is, the ability to gain (or not) muscle mass with the increase of training volume may be dependent on the concomitant rise of ribosomal content to further augment protein synthesis capacity [26, 27], which is an individual-dependent factor [25–27]. Together, these results indicate that if responses to a particular training protocol were strong, responses to another protocol would also be strong [27].

A higher proportion of N-RP participants was revealed in the current study than in previous investigations [4, 5]. However, both Barbalho et al. [4] and Churchward-Venne et al. [5] considered subjects as being RP if they presented a “responsive” adaptation on at least one of their many analyzed outcomes. It is noteworthy that Churchward-Venne et al. [5] found losses in lean body mass (more important than that observed in the present study) after a 24-week RT program with 12 sets/exercise/week in older adults consuming protein supplementation. Additionally, it is important

to emphasize that the aging process typically leads to a decrease in muscle mass, more incisively in women after menopause. The N-RP individuals in the current study did not present a significant mean reduction in SMM after the 24 weeks of training (Table 1), which has important clinical and practical implications for professionals working with this population since the maintenance of SMM plays an essential role in several parameters of good health. A non-exercise control group would be helpful to confirm if the alterations in SMM were lower than those observed for the N-RP subgroup [28].

The current study has some concerns that should be addressed. First, physical activity outside the training environment was not monitored, and dietary intake data were assessed only at baseline. This hinders our ability to determine if there were alterations following the intervention that could influence changes in SMM. With regard to protein intake, although we did not observe a correlation between initial daily protein intake and changes in SMM, it should be noted that the average protein intake was far below (78% of the sample had a protein intake < 1.2 g/kg/day at baseline) what has been recommended [12, 29] and makes it difficult to observe any dose–response relationship. Second, the findings of our study may be particularly related to the prescribed training protocol, whereby not enough volume was present to induce significant changes in SMM in the first 12-week phase when the sample was pooled [17]. In fact, even participants considered RP had gains of SMM of small magnitude. Although we doubled the number of sets per exercise per week from 2 and 4 to 4 and 6, it could still have been considered a small amount. Future studies could investigate whether N-RP can benefit from higher training volumes (e.g.,  $\geq 10$  sets/week) [16]. However, care must be especially taken when dealing with older participants not to cause excessive fatigue or diminish the interest in performing RT. Also, it could be explored if protein intake is a mediator factor on the dose–response between training volume and muscle hypertrophy.

On the other hand, it is essential to highlight the strengths of our study. All training sessions were supervised by professionals with RT experience to ensure participant safety, quality of execution of the movement, and effectiveness. The importance of supervised RT in older adults has been reported in several studies [30]. Moreover, the load adjustments were continuous and based on the participants' individual progress over the course of the RT sessions, which allowed the maintenance of the intensity throughout the intervention. Finally, although a priori calculation of sample size was established for changes in muscular strength [17], the number of subjects here included was ideal for this primary purpose, since there was observed significant gains in muscular strength throughout the study period [17], and for improving SMM as well, since we observed significant

average gains of SMM in both Phase 1 and 2 of the training protocol. Nonetheless, exploring responsiveness to RT still comprises of a long avenue of investigation. More works with larger sample size are needed to verify the magnitude of RP and N-RP for muscle mass gains (for other outcomes, and populations as well) to different training approaches, volume, and variable manipulations.

## Conclusion

Our results suggest that there are older women who are non-responsive to SMM gains from RT programs, and this condition is not altered with the increase of training volume and intervention duration. Thus, it appears that N-RP continue to be N-RP, and RP continue to be RP. Moreover, the changes in SMM seems not to be related to the initial values of specific blood markers (testosterone, IGF-1, and CRP) and the amount of SMM at baseline, but to some as yet undiscovered trigger.

Results of the present study indicate that muscle mass gains could have an important genetic background for the magnitude of the responses in older women, with no meaningful influence of the training volume. In this sense, coaches, clinicians, and strength professionals should perhaps perform the RT prescription for this population with a volume based on the preference of the practitioner focusing on long-term adherence to exercise practice. Thus, other training variables may be taken into consideration to be manipulated for improving muscle mass, as well as other neuromuscular and health-related outcomes, mainly functional fitness and muscular strength, in the elderly.

**Acknowledgements** We would like to express thanks to all the participants for their engagement in this study, the Coordination of Improvement of Higher Education Personnel (CAPES/Brazil) for the scholarship conferred to JPN, WK, GK (master degree), PMC and BDVC (doctoral), and the National Council of Technological and Scientific Development (CNPq/Brazil) for the grants conceded to ASR and ESC. This study was partially supported by the Ministry of Education (MEC/Brazil) and CNPq/Brazil.

**Funding** None.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** Our institutional ethics review board approved the study protocol, and it was in accordance with the Declaration of Helsinki.

**Informed consent** All enrolled patients provided their written, informed consent before participating in the study.

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