Effects of Resistance Training on Muscle Size and Strength in Very Elderly Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Resistance training increases muscle size and strength in very elderly adults: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Background: Effects of resistance training on muscle strength and hypertrophy are well-established in adults and younger elderly. However, less is currently known about these effects in the very elderly (i.e., 75 years of age and older).

Objective: To examine the effects of resistance training on muscle size and strength in very elderly individuals.

Methods: Randomized controlled studies that explored the effects of resistance training in very elderly on muscle strength, handgrip strength, whole-muscle hypertrophy, and/or muscle fiber hypertrophy were included in the review. Meta-analyses of effect sizes (ESs) were used to analyze the data.

Results: Twenty-two studies were included in the review. The meta-analysis found a significant effect of resistance training on muscle strength in the very elderly (difference in ES = 0.97; 95% confidence interval [CI]: 0.50, 1.44; $p = 0.001$). In a subgroup analysis that included only the oldest-old participants (80+ years of age), there was a significant effect of resistance training on muscle strength (difference in ES = 1.28; 95% CI: 0.28, 2.29; $p = 0.020$). For handgrip strength, we found no significant difference between resistance training and control groups (difference in ES = 0.26; 95% CI: –0.02, 0.54; $p = 0.064$). For whole-muscle hypertrophy, there was a significant effect of resistance training in the very elderly (difference in ES = 0 30; 95% CI: 0.10, 0.50; $p = 0.013$). We found no significant difference in muscle fiber hypertrophy between resistance training and control groups (difference in ES = 0.33; 95% CI: –0.67, 1.33; $p = 0.266$). There were minimal reports of adverse events associated with the training programs in the included studies.

Conclusions: We found that very elderly can increase muscle strength and muscle size by participating in resistance training programs. Resistance training was found to be an effective way to improve muscle strength even among the oldest-old.

Key points:

►We found that very elderly adults can increase their muscle strength and size by participating in resistance training programs.

►These effects were observed with resistance training interventions that generally included low weekly training volumes and frequencies.

►There were minimal reports of adverse events associated with the training programs.

1 Introduction

Dynapenia is the age-associated loss of muscle strength [1]. Low muscle strength increases the risk of mobility limitations and mortality in older adults [1-4]. Sarcopenia is a progressive skeletal muscle characterized by a degenerative loss of muscle mass and function [5]. It is associated with an increased likelihood of physical disability, falls, fractures, and mortality [5]. Resistance training is the most widely recognized mode of exercise for increasing muscle strength and muscle size. The effectiveness of resistance training in achieving these outcomes among youth, adults, and older adults is well established [6-8]. The effects of resistance training on older adults have been recently reviewed by Fragala et al. [9]. However, this review considered studies conducted among adults aged 50 years and older, with less focus placed on the effects of resistance training on muscle strength and hypertrophy in the very elderly (i.e., 75 years of age and older) [10, 11].

Muscle hypertrophy occurs when muscle protein synthesis exceeds muscle protein degradation over time [12]. Research has established that, compared to their younger counterparts, older adults experience a reduced muscle protein synthetic response to protein intake, a physiological adaptation termed "anabolic resistance" [13]. Muscle hypertrophy in response to resistance training is associated with myonuclear addition via satellite cell recruitment [14]. In this context, data suggest that resistance training induces significant addition of myonuclei per muscle fiber in young adults [15]. However, no significant satellite cell or myonuclear addition was found in older adults that performed 12-16 weeks of resistance training [15, 16]. Therefore, some researchers speculate that there might be an age-related ceiling above which an individual cannot further increase muscle size with resistance training [17]. Additionally, there are estimates that older individuals have up to a 47%

reduction in the number of motor units, and this reduction might be associated with compromised gains in muscle strength with resistance training in this population [18, 19].

The seminal work by Fiatarone et al. [20] suggested that participation in resistance training increases muscle strength and muscle size, even at the advanced stages of aging. In this single-arm study, ten participants with an average age of 90 years (range: 86 to 96 years) performed eight weeks of resistance training. After the intervention, knee extension one-repetition maximum (1RM) strength improved by 15 kg, accompanied by an increase in quadriceps muscle size of 9%. However, in a more recent randomized controlled study [16], 12-weeks of resistance training in a group of participants aged 83 to 94 years did not significantly increase their muscle size.

In 2013, a systematic review by Stewart et al. [11] provided a summary of studies that explored the effects of different modes of physical training (including resistance training) on muscle size and strength in adults aged 75 years or older. Even though this review concluded that resistance training is an effective exercise intervention for increasing muscle size and strength in this age group, the conclusions were based only on two included studies. It is important to note that several studies that satisfied the inclusion criteria of Stewart et al. [10] were not identified and included in the review [21-29]. Furthermore, since 2013, new original studies have been published on this topic, adding new relevant data to further our understanding of muscular adaptations to resistance training in very elderly adults [16, 30-34].

The aim of this systematic review and meta-analysis was, therefore, to examine the effects of resistance training on strength and muscle size in very elderly individuals. A systematic review on this topic is needed, given that: (a) the evidence presented in studies examining the effects of resistance training in this age group is conflicting; and (b) there are no recent systematic reviews on this topic. Findings on this topic could have a substantial public health impact because the very elderly represent one of the fastest-growing age groups in the population, and it is estimated that only 8.7% of adults aged 75 years or older participate in muscle-strengthening activities [35, 36].

2 Methods

2.1 Search strategy

For this systematic review, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [37]. In total, we searched through nine databases: Academic Search Elite, CINAHL, ERIC, Open Access Theses and Dissertations, Open Dissertations, PsycINFO, PubMed/MEDLINE, Scopus, and SPORTDiscus. In all of these databases, we used the following search syntax (or equivalent) to search through titles, abstracts, and keywords of indexed documents: ("very elderly" OR "oldest old" OR "oldest-old" OR "very old" OR "advancing age" OR "advancing years" OR "old-old" OR "old old" OR septuagenarian* OR nonagenarian* OR octogenarian* OR centenarian* OR "75 and older" OR "80 and older" OR "85 and older" OR "90 and older" OR "95 and older" OR "75 years" OR "80 years" OR "85 years" OR "90 years" OR "95 years") AND ("resistance training" OR "resistance exercise" OR "weight lifting" OR "weightlifting" OR "strength exercise" OR "strength training" OR "strengthening" OR "resistive exercise" OR "resistive training") AND ("muscle hypertrophy" OR "muscular hypertrophy" OR "muscle mass" OR "lean body mass" OR "fat-free mass" OR "fat free mass" OR "muscle fiber" OR "muscle size" OR "muscle fibre" OR "muscle thickness" OR "cross-sectional area" OR "cross sectional area" OR "computed tomography" OR "magnetic resonance imaging" OR "muscle power" OR "strength" OR "1RM" OR "isokinetic" OR "isometric"). We also performed secondary searches that consisted of: (a) screening the reference lists of studies that were included in the review; and (b) examining the reference lists of previous related reviews [7, 11, 38-43]. To reduce the probability of study selection bias, two authors of the review (JG and AG) conducted the study selection independently. After both authors completed their searches, the lists of included and excluded studies were compared between them. Any discrepancies between the two authors in the included and excluded studies were resolved through discussion and agreement. The databases were searched on January 20th, 2020.

2.2 Inclusion criteria

Studies that satisfied the following criteria were included in the review: (a) the participants were aged 75 years or older; (b) the participants were randomized into the intervention and control group(s); (c) the exercise intervention was comprised of resistance training while the control group did not exercise; (d) the study assessed muscle strength and/or muscle size pre- and post-intervention; and (e) the training protocol lasted for a minimum of six weeks. All forms of strength tests, including isotonic, isometric, isokinetic, and handgrip tests were deemed relevant. For muscle hypertrophy, we considered studies that assessed changes at the whole-muscle (macroscopic methods) and/or muscle fiber level (microscopic methods).

2.3 Data extraction

In each of the included studies, we extracted the following data: (a) author names and year of publication; (b) characteristics of the sample size, including their age and sex; (c) specifics of the resistance training intervention (e.g., the number of performed sets, exercise selection); (d) adverse events reported during the intervention (if any); (e) exercise used for the muscle strength test and/or body site and tool used for the muscle hypertrophy assessment; and (f) pre and post-intervention mean ± standard deviation (SD) of the strength and/or hypertrophy outcomes. For the studies that reported standard errors, we converted them to SDs. Two authors of the review (JG and FS) performed the data extraction independently. After both authors completed the data extraction from all studies, the coding sheets were compared between the authors. In case of any discrepancies in the data extraction files, the data was re-checked from the studies.

2.4 Methodological quality

The methodological quality of the included studies was assessed using the 27-item Downs and Black checklist [44]. This checklist evaluates different aspects of the study design, with items 1–10 referring to reporting, items 11–13 referring to external validity, items 14–26 referring to internal validity, and item 27 referring to statistical power. Given that the included studies explored the effects of a resistance training intervention, the standard 27-item checklist was modified by adding two items, item 28 and item 29. Item 28 was on the reporting of adherence to the training program, while item 29 was related to training supervision. For each item—including items 28 and 29—one point was allocated to the study if the criterion was satisfied; no points were allocated if the criterion was not satisfied. The maximum possible score on the modified version of the Downs and Black checklist was, therefore, 29 points. Based on the summary score, studies that had 21–29 points were classified as being of 'good quality', studies with 11–20 points were classified as being of 'moderate quality', while studies that scored less than 11 points were considered to be of 'poor quality' [45, 46] The methodological quality assessment was performed independently by two authors (JG and AG), with discussions and agreement for any observed differences in the initial scoring.

2.5 Statistical analysis

The meta-analyses for strength and hypertrophy outcomes were performed on the training intervention minus control difference in relative effect sizes (ESs). The data for strength and hypertrophy were converted to relative ES, calculated as the posttest-pretest mean change in each group, divided by the pooled pretest SD, with an adjustment for small sample bias [47]. The variance of the ESs depends on the within-subject posttest-pretest correlation. Given that this correlation was not reported in any of the included studies, when possible it was estimated by back-solving from paired t-test *p*-values or SDs of posttest-pretest change scores. Among studies for which the correlation could be derived from the available data, the median value was 0.85. A more conservative value of 0.75 was used for all studies. Sensitivity analyses (not presented) were performed using correlations ranging from 0.25 to 0.85, and their results were consistent with those using 0.75. In order to account for correlated ESs within studies, we used a robust variance meta-analysis model, with an adjustment for small samples [48]. In the main meta-analysis for muscle strength, we included all available studies. A sensitivity analysis was performed by excluding the two studies [26, 29] that used upper-body exercises for the strength test. In a subgroup analysis, we explored the effects of resistance training on muscle strength only among the “oldest-old” (i.e., 80+ years). Handgrip strength was analyzed separately from other strength tests as this test is commonly used alone in predicting mortality and functional declines in the very elderly [49]. For hypertrophy, the following meta-analyses were performed: (a) for whole-muscle hypertrophy outcomes; and (b) for muscle fiber cross-sectional area (CSA). All differences in ESs were presented with their 95% confidence intervals (95% CIs). These differences were interpreted as: “trivial” (≤0.20); “small” (0.21–0.50); “medium” (0.51–0.80); and “large” (>0.80). The potential presence publication bias was checked by examining funnel plot asymmetry and calculating trim-and-fill estimates. The trim-and-fill estimates (not presented) were similar to the main results. Heterogeneity was explored using the I^2 statistic, with values of ≤50%, 50–75%, and >75% indicating low, moderate, and high levels of heterogeneity, respectively. All meta-analyses were performed using the robumeta package within R version 3.6.1 and the trim-and-fill analyses were calculated using the metafor package [50, 51]. Group differences were considered statistically significant at $p < 0.05$.

3 Results

3.1 Study selection

The total number of search results in the nine databases was 2076. After excluding 2016 search results based on title or abstract, 60 full-text papers were read. Of the 60 full-text papers, 17 studies were included. Secondary searches resulted in another 1559 search results and with the inclusion of five additional papers (Figure 1). Therefore, the final number of included studies was 22 [16, 21-34, 52-58]. Of note, in two cases, the strength and whole-muscle hypertrophy data were published separately from muscle fiber CSA data, even though the data collection was carried out in the same cohort [16, 30, 52, 53]. Additionally, one group of authors published the data on strength, whole-muscle CSA, and muscle fiber CSA in three separate papers, even though the data was collected in a single study [54-56].

3.2 Study characteristics

3.2.1 Muscle strength outcomes

In the seventeen studies that explored muscle strength outcomes and met the inclusion criteria, the pooled number of participants was 880 (84% females; Table 1). The median sample size per study was 38 (range: 14 to 144 participants). The interventions lasted from 8 to 18 weeks. Training frequency was from 1 to 3 days per week. Eleven studies used isometric strength tests, four used isotonic strength tests, and three used isokinetic tests (one used both isometric and isokinetic tests). Two studies employed tests on upper-body exercises, while the remaining studies used lower body exercises (Table 2). Eight studies assessed handgrip strength (Table 2).

3.2.2 Hypertrophy outcomes

In the nine studies that explored hypertrophy outcomes and met the inclusion criteria, the total sample size was 204 participants (67% females; Table 1). The median sample size per study was 26 participants (range: 23 to 49 participants). The interventions lasted from 10 to 18 weeks, with a training frequency of 2 to 3 days per week. Six studies reported data on whole-muscle hypertrophy. For this outcome, studies used computed tomography (three studies), B-mode ultrasound (two studies), and magnetic resonance imaging (one study). Three studies explored changes at the muscle fiber level. All studies assessed lower-body hypertrophy. The training programs used in the studies are summarized in Table 2.

3.3 Methodological quality

The average score on the modified 29-item Downs and Black checklist was 25 (range: 21 to 28 points). All studies were classified as being of good methodological quality. Scores on all items of the checklist are reported in Table 3.

3.4 Meta-analysis results for muscle and handgrip strength

The meta-analysis found a significant effect of resistance training on muscle strength in the very elderly (difference in ES = 0.97; 95% CI: 0.50, 1.44; p = 0.001; I^2 = 87%; Figure 2). In the sensitivity analysis, there was a significant effect of resistance training on lower-body muscle strength in the very elderly (difference in ES = 0.96; 95% CI: 0.48, 1.45; I^2 = 87%; p = 0.001). In a subgroup analysis that included only the oldest-old participants (80+ years of age), there was a significant effect of resistance training on muscle strength (difference in ES = 1.28; 95% CI: 0.28, 2.29; p = 0.020; I^2 = 86%; Figure 3). For handgrip strength, we found no significant difference between resistance training and control groups (difference in ES = 0.26; 95% CI: –0.02, 0.54; p = 0.064; I^2 = 51%; Figure 4).

3.5 Meta-analysis results for whole-muscle and muscle fiber hypertrophy

For whole-muscle hypertrophy, there was a significant effect of resistance training in the very elderly (difference in ES = 0.30; 95% CI: 0.10, 0.50; p = 0.013; I^2 = 0%; Figure 5). We found no significant difference in muscle fiber hypertrophy between resistance training and control groups (difference in ES = 0.33; 95% CI: –0.67, 1.33; p = 0.266; I^2 = 7%; Figure 6).

4 Discussion

The main finding of this systematic review and meta-analysis is that resistance training increases muscle strength in very elderly people, even among the oldest-old. We also found that resistance training results in muscle hypertrophy at the whole-muscle level in very elderly. The ES for strength and whole-muscle hypertrophy was large and small, respectively. Even though the pooled ES favored resistance training for muscle fiber hypertrophy and handgrip strength, these effects were not statistically significant.

4.1 Muscle strength

We found that resistance training produced substantial increases in muscle strength in the very elderly. Increases in muscle strength were also observed in a subgroup analysis of studies that included the oldest-old suggesting that resistance training enhances muscle strength even at an advanced stage of aging. Xue et al. [59] reported that dynapenia is associated with increased mortality risk. Findings from the "Health, Aging and Body Composition Study" further indicated that knee extension strength—as measured by isokinetic dynamometry—is associated with a reduced risk of mortality [3]. Dynapenia also increases the risk of physical disability and reduces physical performance [1]. Therefore, muscle strength is identified as one of the key muscle qualities for physical independence in the very elderly [1, 4]. After the age of 75 years, muscle strength annually declines by about 2% to 4% (ES: 0.17 to 0.24) for those who do not perform regular resistance exercise [60-62]. Our findings suggest that participation in resistance training over 8 to 18 weeks, with a frequency of 1 to 3 days per week, can restore strength that has been potentially lost over several years of inactivity. Research has also established that lower limb muscle weakness is an important risk factor for falls in the older population [63]. When considering only the studies that used lower-body exercise for the strength test, an ES of 0.96 (95% CI: 0.48, 1.45) was found. These data highlight that increasing muscle strength through resistance training participation could be of great health benefit for the very elderly. Our findings are, therefore, highly relevant from a public health perspective. Moreover, data suggests that only 8.7% of adults aged 75 years and older participate in muscle-strengthening activities [36]. Thus, it is clear that finding ways to further promote participation and adherence to muscle-strengthening activities in this age group is of considerable public health interest.

4.2 Handgrip strength

The handgrip strength test is widely used to evaluate muscle strength as it is noninvasive and inexpensive [64]. Given its simplicity, this test is often utilized in epidemiological studies [49]. In the sample of included studies, the pooled ES favored resistance training condition, but the effect was not statistically significant ($p = 0.064$). In one of the included studies, resistance training focused exclusively on the lower body, but strength was evaluated using the handgrip test [31]. This might not be entirely appropriate, given that the largest increases in strength are expected for the muscle groups that were covered in the training program [65, 66]. Indeed, one study reported that 24 weeks of whole-body resistance training produced a substantial increase in 1RM knee extension and leg press strength (on average by 21 and 45 kg, respectively), that were not accompanied by any significant changes in handgrip strength [67]. In line with this finding, some authors have speculated that there is only a limited ability to increase handgrip strength in adulthood [68]. While handgrip strength testing can certainly provide valuable information about physical functioning, the use of this test may, in some cases, provide limited insights into the efficacy of a given resistance training program.

4.3 Whole-muscle hypertrophy

We found that very elderly individuals can increase muscle size despite their advancing age, although the expected improvements may be small to modest (ES = 0.30; 95% CI: 0.10, 0.50). Nonetheless, the finding that the very elderly can increase their muscle size is highly relevant, given that sarcopenia may increase the risk of falls and fractures, increase frailty, decrease functional independence and quality of life as well as increase the risk of chronic disease and all-cause mortality [4]. There are estimates that in the very elderly muscle size is reduced at a rate of 0.64% to 0.98% per year (ES: 0.14 to 0.23) [60, 62]. Our results suggest that resistance training interventions lasting from 10 to 18 weeks with a training frequency of 2 to 3 days per week can increase muscle size that was potentially lost over multiple years of aging. This finding is of public great health importance, if we consider estimates that the prevalence of sarcopenia in adults older than 75 years ranges from 27% to 60% [69].

4.4 Muscle fiber hypertrophy

Despite the findings observed for whole-muscle hypertrophy, we did not find significant increases in muscle fiber CSA, even though in the sample of included studies the pooled ES of 0.33 favored resistance training. The lack of a significant finding in this analysis could be attributed to the small pooled sample size. Specifically, only three studies with a combined sample of 53 participants were included in this analysis. The small sample sizes in individual studies for this outcome were probably due to the difficulties in collecting muscle biopsy samples in this age group. In a group of 87 older adults that were considered for a Bergstrom needle muscle biopsy, only 19% to 59% of participants had adequate levels of muscle mass needed for biopsy sampling (depending on factors such as sex, age, and frailty) [70]. Furthermore, some participants had suboptimal muscle thickness, suggesting that multiple samples might be required to obtain an adequate amount of muscle for the analysis. While future studies are needed to elucidate possible effects of resistance training on muscle fiber hypertrophy in the very elderly, there may be challenges in collecting the necessary data.

4.5 Adverse events

A recent systematic review reported that fear of a heart attack, stroke, or even death, is one of the most common barriers to participation in resistance exercise for older adults [71]. Therefore, when conducting exercise intervention studies among older adults, the reporting of adverse events associated with the training intervention is essential. The included studies reported minimal adverse events (Table 2). Specifically, in some studies, there were reports of muscle soreness following the exercise sessions, and in one study there was an exacerbation of preexisting osteoarthritis in one participant (Table 2). There were no reported serious events directly related to exercise interventions. These results suggest that resistance training can be safe, even for the very elderly.

4.6 Methodological quality

All included studies were of good methodological quality. Therefore, the results presented herein were not confounded by studies with poor methodological quality. Nonetheless, it is worth noting that four included studies did not report participants' adherence to the training program [22, 33, 34, 58]. Adherence to a given training program is one of the key variables that influence its overall efficacy [72]. Therefore, future studies should ensure that adherence data are reported.

4.7 Strengths and limitations of the review

The strengths of this review are that: (a) the search for studies was conducted through nine databases using a search syntax with a broad range of relevant search terms; and (b) 17 studies with over 800 participants were included in the analysis for muscle strength, which allowed for an additional subgroup analysis including only the oldest-old. This review's main limitation is that the meta-analysis on muscle fiber hypertrophy included only three studies with a combined sample of 53 participants. Besides, there was high heterogeneity in the analysis for muscle strength. However, it should be considered here that the effects from all studies in this analysis were in the same direction (i.e., favoring of resistance training), but their overall effectiveness varied. The variation in ESs could be associated with the differences between studies in duration, training programs, and strength tests.

4.8 Suggestions for future research

The included studies generally utilized only one type of strength test. Given that the studies used isotonic training programs, it might be expected that resistance training would have the greatest effect on isotonic strength [73, 74]. However, the majority of studies used isometric tests to evaluate changes in muscle strength. Ultimately, the small number of studies employing isotonic and isokinetic strength assessments limits the ability to further subanalyze the effects of resistance training on strength in different tests. Isotonic and isokinetic strength tests were used only in four and three studies, respectively (Table 2). Therefore, future studies on the topic may consider utilizing isotonic, isometric, and isokinetic strength measures in the same group of participants to directly explore if the effects of resistance training in the very elderly vary between different strength tests.

5 Conclusion

This systematic review and meta-analysis found that the very elderly can increase their muscle strength and size by participating in resistance training programs. Moreover, resistance training was found to be an effective way to improve muscle strength even among the oldest-old. Importantly, the resistance training interventions generally included low weekly training volumes and frequencies, suggesting that a relatively low time commitment is needed to reap these benefits. There were minimal reports of adverse events associated with the training programs in the included studies, thus suggesting that resistance training can be a safe mode of exercise for the very elderly. More research is needed on the effects of resistance training on handgrip strength and muscle fiber hypertrophy.

Data Availability Statement

The datasets generated and analyzed during the current systematic review and meta-analysis are available from the corresponding author on reasonable request.

Contributors

JG conceived the idea for the review. JG and AG conducted the study selection quality assessment. JG and FS conducted the data extraction. JO performed the statistical analysis. JG drafted the initial manuscript. All authors contributed to data interpretation, writing of the manuscript, and its revisions.

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Conflict of Interest

Jozo Grgic, Alessandro Garofolini, John Orazem, Filip Sabol, Brad J. Schoenfeld and Zeljko Pedisic have no conflicts of interest that are directly relevant to the content of this article.

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