Archives of Gerontology and Geriatrics 81 (2019) 171–175

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

Resistance training performed with single-set is sufficient to reduce cardiovascular risk factors in untrained older women: The randomized clinical trial. Active Aging Longitudinal Study

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ARTICLE INFO

Keywords:
Aging
Strength training
Chronic diseases
Blood biomarkers

ABSTRACT

The purpose of this study was to analyze the effect of a single-set RT program on CVD-risk parameters in untrained older women. Forty-eight older women (> 60 years) were randomly assigned to two groups. The training group (SS) performed a 12-week RT program comprised of single sets (10–15 repetitions) in 8 exercises performed 3 times per week. The control group remained pursued normal daily activities with no exercise intervention. Each participant was evaluated for total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), very low-density lipoprotein (VLDL), triglycerides (TG), glucose (GLU) and, C-reactive protein (CRP). TC, LDL, GLU and CRP were reduced significantly ($p < 0.05$) after exercise intervention in the exercise group. The composite Z-score of the cardiovascular risk was also significantly reduce compared to control group ($P < 0.05$). We conclude that a 12-week RT program performed with a single-set per exercise is sufficient to reduce cardiovascular diseases risk components.

1. Introduction

Cardiovascular diseases (CVD) are the leading cause of mortality worldwide, affecting a large part of the older population, especially women. Cardiovascular disease risk factors appear to be exacerbated by the effect of menopause (Kengne, Batty, Hamer, Stamatakis, & Czernichow, 2012; Maltais, Desroches, & Dionne, 2009; Pearson, 2003). Several strategies for health improvement have been studied in older adults, including exercise. Among the wide array of exercises, resistance training (RT) has been suggested as an excellent intervention to attenuate age-related dysfunctions and promote health and wellness for older populations (ACSM, 2009a, 2011; Fisher, Steele, Gentil, Giessing, & Westcott, 2017; Westcott, 2012).

A growing body of evidence supports the benefits of RT for improving health-related parameters, such as reducing body fat (Cunha et al., 2018), ameliorating bone mineral density (Huovinen et al., 2016), enhancing blood biomarkers (Padilha et al., 2015; Ribeiro, Deminice, et al., 2017; Tomeleri et al., 2016), and increasing muscle mass and strength (Ribeiro, Schoenfeld, et al., 2015). The muscular adaptations from RT follow a dose-response relationship (ACSM, 2009b, 2011; Borde, Hortobágyi, & Granacher, 2015; Csapo & Alegre, 2016; Krieger, 2009, 2010) whereby greater improvements appear to accompany more frequency exposures and greater volumes of training. The American College of Sports Medicine guidelines indicate that older adults should perform RT at least twice a week with one set per exercise for major muscle groups (ACSM, 2011). In a recent review, Fisher et al. (2017) provided information regarding the possible health benefits when practicing RT in a low dosage format (i.e., one set per exercise of 3–10 weight-stack machine exercises performed 2 times a week). However, none of the above-mentioned studies reported the benefits of RT on inflammatory and CVD-risk markers. Thus, there is no evidence to confirm whether a minimal dose of RT is sufficient to promote significant changes in these variables in elderly individuals.

There are many metabolic variables that are related to the risk of CVD, such as blood glucose, C-reactive protein (CRP), total cholesterol, triglycerides, and lipoproteins (i.e., low-density lipoprotein, high-

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https://doi.org/10.1016/j.archger.2018.12.012
Received 13 November 2018; Received in revised form 21 December 2018; Accepted 21 December 2018
Available online 24 December 2018
0167-4943/

density lipoprotein and very low-density lipoprotein). While previous studies have indicated that the RT affects those variables (Cunha et al., 2018; Padilha et al., 2015; Ribeiro, Deminice, et al., 2017; Tomeleri et al., 2016), none have determined if the previously recommended low-dose / single-set RT (ACSM, 2011; Fisher et al., 2017) is sufficient to alter any of these risk factors.

Therefore, the purpose of this study was to assess the effect RT performed with single-set RT on CVD-risk parameters in untrained older women. We hypothesized that RT performed in this dose would be sufficient to reduce CVD-risk factors compared to a non-exercising control group.

2. Methods

2.1. Subjects

This study is part of a longitudinal research project named "Active Aging Longitudinal Study", begun in September 2012, with the purpose of analyzing the behavior of neuromuscular, morphological, physiological, metabolic and behavioral indicators in older women submitted to resistance training.

For this phase of the project, 56 physically independent and untrained older women (≥ 60 years old) volunteered to participate in this study. The sample was preliminarily selected through interview or clinical referrals. The initial inclusion criteria required participants to be: 60 years of age or older, female, physically independent, without cardiopathologies or musculoskeletal disorders that could impede physical exercise. In addition, they must not have been involved in the systematic practice of regular physical activity more than once a week over the preceding six months prior to the start of the study. Furthermore, participants could not be diabetic, have uncontrolled hypertensive or be undergoing hormone therapy. Finally, only those participants who were evaluated by a cardiologist and released for the practice of the RT without any restrictions were included in the study. Following these restrictions, 48 older women qualified to participate and were randomly assigned to one of the two groups: a training group that performed a single-set RT program (SS, n = 25), or a non-exercise control group (CG, n = 23). Adherence to training sessions was satisfactory with all participants reaching a minimum of 85% of the total sessions.

Written informed consent was obtained from all participants after being provided with a detailed description of investigation procedures. This investigation was conducted according to the Declaration of Helsinki and approved by the local University Ethics Committee.

A blinded researcher was responsible for generating random numbers (computer-generated random numbers) for participant allocation. Participants were randomly assigned to one of two groups: control croup (CG) and Single-set (SS). Sample size was estimated using G*Power (version 3.0.10, Universitat Kiel, Germany). Data from previous studies from our laboratory in which RT was the exercise intervention model were used for sample size estimation (Ribeiro, Tomeleri, et al., 2015; Tomeleri et al., 2016, 2017). We based the calculation on an effect size of 0.70, an α level of 0.05, and a power $(1 - \beta)$ of 0.80. The sample size estimation indicated that it would be necessary to include at least 42 participants (21 per group). Considering a drop-out rate, we recruited 50 older women who were randomly assigned into one of two groups of the study.

2.2. Experimental design

The total duration of the study was 16 weeks, of which the first two weeks (1–2 weeks) were used for familiarization with the RT program exercises and pre-training measurements, while the last two weeks (weeks 15–16) were intended for post-training measurements. The intervention period lasted 12 weeks (weeks 3–14). Anthropometric dimensions, body fat, lipid profile, CRP, and glucose were measured pre- and post-training.

2.3. Anthropometry

Body mass was measured to the nearest 0.1 kg using a calibrated electronic scale (Balmak, Laboratory Equipment Labstore, Curitiba, PR, Brazil), and height was measured to the nearest 0.1 cm with a stadiometer attached on the scale. Participants wore light clothes and no shoes. Body mass index was calculated as body mass in kilograms divided by the square of height in meters.

2.4. Biochemical analysis

Upon arrival at the laboratory, participants rested in a seated position for at least 5 min. Venous blood samples were collected into one tube between 7:00 am and 9:00 am after a 12 h fast and a minimum of 72 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 dipotassiumethylenediaminetetra-acetic acid (EDTA) as an anticoagulant and preservative. All samples were centrifuged at 3000 rpm for 15 min, and plasma or serum aliquots were stored at −80 °C until assayed. Inter- and intra-assay coefficients of variation were < 10% as determined in human plasma. Measurements of serum levels of high-sensitivity C-reactive protein (CRP), glucose (GLU), total cholesterol (TC), high-density lipoprotein (HDL-c), and triglycerides (TG) were determined by standard methods in a specialized hospital laboratory. The LDL-c was calculated using the Friedewald, Levy, and Fredrickson (Friedewald, Levy, & Fredrickson, 1972) equation: LDL-c = TC − (HDL-c + TGL / 5). The analyses were carried out using a biochemical auto-analyzer system (Dimension RxL Max - Siemens Dade Behring) according to established methods in the literature consistent with the manufacturer's protocol.

2.5. Composite Z-score

The Z-score of the percentage changes (from pre- to post-training) of the raw data for each parameter was calculated. Moreover, a composite Z-score derived from the average of the components was calculated as following formula: (-1 x HDL-c Z-score) + (LDL-c Z-score) + (VLDL-c Z-score) + (TC Z-score) + (TG Z-score) + (GLU Z-score) + (C-reactive protein Z-score)/ 7.

2.6. Resistance training program

The RT training program was based on recommendations for an older population (ACSM, 2009a, 2011; Fisher et al., 2017). All participants were personally supervised by physical education professionals. The sessions were performed 3 times per week on Mondays, Wednesdays, and Fridays. The exercises were performed in the following order: chest press, horizontal leg press, seated row, knee extension, preacher curl (free weights), leg curl, triceps pushdown, and seated calf raise. Participants completed 1 set of 10–15 repetitions for each exercise, while the control group was instructed to maintain their daily activities and not to perform RT. The sets were performed until repetition failure, defined as the inability to perform the exercise with proper form or volitional fatigue. Participants were instructed to inhale during the eccentric phase and exhale during the concentric phase while maintaining a constant velocity of movement at a ratio of approximately 1:2 s (concentric and eccentric phases, respectively). The rest interval between each exercise was ~ 2 min. The training load was consistent with the prescribed number of repetitions for each exercise. The duration of each RT session was approximately 20 min. Progression in each exercise was planned when the upper limits of the repetitions-zone were completed for two consecutive training sessions, and resulted in weight increase of 2–5% for upper limb exercises and 5–10% for lower limb exercises to the next session (ACSM, 2009a).

2.7. Statistical analyses

Student's *t*-test for independent samples was used for comparison between groups for general characteristics at baseline, percentage changes, and the composite Z-score. To examine differences among groups for changes in TC, TG, LDL, HDL, VLDL, GLU and CRP, a two-way analysis of covariance (ANCOVA) for repeated measures was performed with the baseline scores used as a covariate to eliminate possible influence of initial score variance on training outcomes (Senn, 2013; Van-Breukelen, 2006; Vickers & Altman, 2001). When the F-ratio was significant, the Bonferroni *post hoc* test was employed to identify mean differences between pre- and post-training raw data. Significance was accepted at $P < 0.05$. Effect size (ES) was calculated as post-training minus pre-training mean divided by the pre-training standard deviation (Cohen 1992), where an ES of 0.00 – 0.19 was considered trivial, 0.20 – 0.49 was considered as small, 0.50 – 0.79 as moderate, and ≥ 0.80 as large (Cohen 1992). The data were analyzed using STATISTICA software version 10.0 (STATSOFT INC., TULSA).

3. Results

The anthropometric characteristics of the participants at baseline and after intervention are presented in Table 1. There was no statistically significant difference between groups.

Table 2 presents the values at pre- and post-intervention period according to groups for the cardiovascular risk diseases parameters. Significant interaction (group x time) was observed for TC, LDL-c, GLU, and CRP, where only the SS group presented significant changes after the intervention period ($P < 0.05$). No significant effect was observed for TG, HDL-c, and VLDL-c ($P > 0.05$). The covariate means as well as the adjusted post-training scores are presented in Table 4.

Table 3 presents the ES values according to groups as well as the differences between them. Differences of large magnitude were observed for GLU and LDL-c. A moderate magnitude difference was observed for TC while the difference for CRPwas of small magnitude. Training differences for TG, HDL-c, and VLDL-c differences were of trivial magnitude. All differences were favoring the SS group.

The composite Z-scores of the percentage changes from pre- to post-training for cardiovascular diseases risk of both groups are presented in Fig. 1. A significant difference between them was observed ($P = 0.001$), whereby the SS group presented higher negative values in comparison to control group, showing an increased protective effect to cardiovascular diseases risk (mean and standard deviation of composite Z-score: single-set RT: −0.31 ± 0.47 [CI 95% −0.51 to −0.11]; control group: 0.34 ± 0.34 [CI 95% 0.19 to 0.49]).

4. Discussion

The main and novel finding observed in our study was that RT performed in single-set per exercise is sufficient to improve some blood biomarkers related to cardiovascular disease risk. Our previous hypothesis that single-set RT would be sufficient to induce reduced CVD-risk was confirmed. To our knowledge, this is the first study to observe the adaptive responses in blood biomarkers of older women from RT performed in a single-set configuration.

Previous studies have found reductions in CRP, TC, TG, LDL-c, and GLU after RT program (Calle & Fernandez, 2010; Lera-Orsatti et al., 2014; Mavros et al., 2014; Ribeiro, Tomeleri, et al., 2015; Ribeiro, Schoenfeld, et al., 2016; Tomeleri et al., 2016). Studies from our laboratory have observed reduced CRP, TC, TG, LDL-c, GLU and increased HDL-c values following RT performed three times a week with three sets per exercise (Ribeiro, Schoenfeld, et al., 2016; Tomeleri et al., 2016). The unique approach in the current investigation using a lower training volume compared to previous studies limits comparisons that can be made between them. Nevertheless, other investigators have not found a significant effect of RT on selected blood biomarkers following 12-to-24 month interventions (Nikseresht, Sadeghifard, Agha-Alinejad, & Ebrahim, 2014; Simonavice et al., 2014). These divergent results can be at least partly due to different experimental designs between studies, such as differences in volume and/or intensities of training, study duration, characteristics of participants (i.e., middle-age obese men (Nikseresht et al., 2014), and breast cancer survivors (Simonavice et al., 2014), and baseline levels of blood biomarkers (Calle & Fernandez, 2010; Lera-Orsatti et al., 2014).

In the current study, overall changes induced by RT in blood biomarkers were expressed by a composite Z-score. This approach may be an important tool to estimate the effect of training on CVD-risk because it considers the overall response on biomarkers of a RT program, allowing the ability to draw inferences of the intervention as whole as opposed to isolated outcomes. This approach showed that single-set RT performed three times per week (as recommended for general benefits (2011, ACSM, 2009b) was sufficient to change the CVD risk factors in older women.

Although our study was not able to identify the mechanisms responsible for these alterations, we can speculate on some possibilities. TC and LDL-c were significantly reduced after intervention period, showing that RT may play an important role in making improvements in these markers during the early stages of training in untrained older women (Mann, Beedie, & Jimenez, 2014). Furthermore, HDL-c levels remained stable after 12-week of RT while it decreased in CG. Previous studies have also observed beneficial effects of RT on lipid profile (Conceição et al., 2013; Ribeiro, Tomeleri, et al., 2015; Tomeleri et al., 2016), and suggested mechanisms were related to an increased ability of skeletal muscle to use fat for energy source (Mann et al., 2014; Wolfe, 2006).

Elevated blood glucose is another blood biomarker related to cardiovascular disease risk. GLU showed a significant reduction after 12-week of one-set RT which was expected since the glycolytic pathway is essential for generating energy when performing RT (Lambert & Flynn, 2002). Another possible mechanism for GLU reduction might be the improvement in insulin sensitivity induced by RT (Phillips & Winett, 2010).

The CRP is an important risk factor for cardiovascular diseases (Kengne et al., 2012; Pearson, 2003), and in the current study there was a significant reduction in the RT group versus CG. A possible mechanism for this could be related to the product of myokines produced by muscle contraction which yields an anti-inflammatory characteristic that antagonizes the effects of pro-inflammatory cytokines, favoring a reduction in inflammation and CRP (Pedersen & Febbraio, 2008).

The results observed in our study can help the formulation of RT

Table 1
General characteristics of the participants at baseline and after intervention. Data are presented as mean and standard deviation.

	Control (n = 23) Pre-training	Post-training	Single-set (n = 25) Pre-training	Post-training	Interaction P-value
Age (years)	69.04 ± 4.45	–	71.40 ± 5.71	–	0.12
Body mass (kg)	64.13 ± 12.09	64.50 ± 12.41	70.50 ± 14.65	70.62 ± 14.78	0.53
Height (cm)	155.67 ± 5.60	155.02 ± 5.70	157.73 ± 7.52	157.58 ± 7.49	0.35
Body mass index (kg/m^2)	26.39 ± 4.55	26.78 ± 4.80	28.26 ± 5.01	28.37 ± 5.14	0.13

Table 2
Participants' scores at pre-and post- intervention. Data are presented as mean and standard deviation.

	CG (n = 23)		Single-set (n = 25)		Interaction
	Pre	Post	Pre	Post	P-value
TC (mg/d/L)	204.47 ± 26.18	215.04 ± 26.33	208.04 ± 45.82	196.08 ± 38.60*	0.003
TG (mg/d/L)	109.78 ± 42.13	111.82 ± 39.07	132.44 ± 54.12	125.16 ± 55.76	0.31
LDL-c (mg/dL)	122.73 ± 24.45	133.81 ± 23.72	120.68 ± 40.37	102.81 ± 30.69*	0.001
HDL-c (mg/dL)	59.78 ± 17.94	58.34 ± 16.80	61.92 ± 19.08	60.12 ± 17.04	0.90
VLDL-c (mg/dL)	21.96 ± 8.35	21.93 ± 8.07	22.47 ± 9.50	21.41 ± 9.42	0.49
GLU (mg/dL)	88.82 ± 10.69	99.47 ± 10.43	105.16 ± 18.07	96.16 ± 12.38*	0.001
CRP (mg/L)	2.73 ± 1.92	2.83 ± 1.41	2.71 ± 1.17	2.34 ± 1.02*	0.01

Note: * $P < 0.05$ vs pre. TC = total cholesterol; TG = triglycerides; LDL-c = low density lipoprotein cholesterol; HDL-c = high density lipoprotein cholesterol; VLDL-c = very low-density lipoprotein cholesterol; GLU = glucose; CRP = C- reactive protein.

Table 3
Effects sizes values of the training groups.

	Control (n = 23)	Single-set (n = 25)	Relative effect size
TC	0.33	−0.37	0.70 (moderate)
TG	0.04	−0.15	0.19 (trivial)
LDL-c	0.34	−0.55	0.89 (large)
HDL-c	−0.08	−0.10	0.02 (trivial)
VLDL-c	0.0	−0.12	0.12 (trivial)
GLU	0.74	−0.63	1.37 (large)
CRP	0.06	−0.24	0.30 (small)

Note: Relative effect size = control minus single-set. Effect size interpretation: 0.00 - 0.19 = trivial, 0.20-0.49 = small, 0.50-0.79 = moderate, and ≥ 0.80 = large. TC = total cholesterol; TG = triglycerides; LDL-c = low density lipoprotein cholesterol; HDL-c = high density lipoprotein cholesterol; VLDL-c = very low-density lipoprotein cholesterol; GLU = glucose; CRP = C- reactive protein.

prescriptions in older women who wish to accede to an exercise routine in order to promote improvement in their health status. Furthermore, our investigation corroborated and is in complement with the recent review that showed that a minimal dose of RT (20 and 60 min per week) is sufficient to improve health in aging populations (Fisher et al., 2017). Since time constraints are often a barrier to RT practice, it is important to note that the type of training offered in this study (i.e., short time sessions) can be an important tool in adherence to RT practice (Fisher et al., 2017).

This study has some limitations. It is important to note that the results reported here are specific to untrained older women and cannot necessarily be extrapolated to other populations. We were not able to monitor physical activity levels outside of the study environment, which may have confounded results by increasing caloric expenditure and facilitation to changes observed; however, all participants were instructed to maintain their normal level of physical activity. Furthermore, other biomarkers such as IL-6, TNF-α, IL-1β could exalt the findings found here; however, the variables analyzed are also

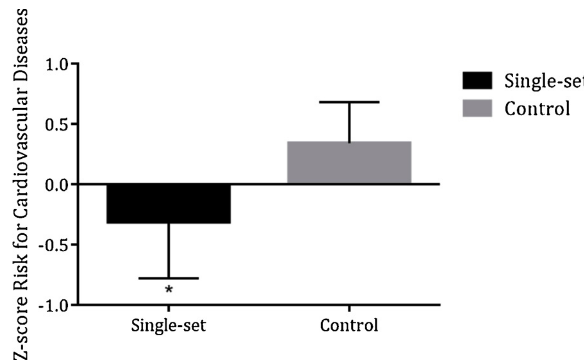

Fig. 1. Composite Z-score of the percentage changes from pre- to post-training of the cardiovascular risk according to groups in older women. * = $P < 0.05$ vs. Control.

important biomarkers related to health and cardiovascular diseases.

5. Conclusion

We conclude that a 12-week RT program performed with single-set per exercise is sufficient to reduce some cardiovascular diseases risk components. This investigation suggest that a minimal dose of RT is able to initiate improvements in the health of older women.

Conflict of interests

The authors declare that they have no conflict of interests regarding the publication of this paper.

Acknowledgments

We would like to express thanks to all the participants for their engagement in this study, the Coordination of Improvement of Higher

Table 4
Adjusted mean by ANCOVA to post-test.

		Control Group (n = 23)		Single-set (n = 25)	
	Covariate Mean	Mean	95%CI	Mean	95%CI
TC (mg/d/L)	206.33	216.21	206.28 – 226.13	195.00	185.49 – 204.52
TG (mg/d/L)	121.58	122.17	112.29 – 132.04	115.64	106.18 – 125.10
LDL-c (mg/dL)	121.66	133.30	123.81 – 142.80	103.28	94.17 – 112.39
HDL-c (mg/dL)	60.89	59.28	56.42 – 62.13	59.26	56.52 – 62.00
VLDL-c (mg/dL)	22.22	22.15	20.14 – 24.16	21.21	19.28 – 23.13
GLU (mg/dL)	97.7	103.84	99.94 – 107.74	92.13	88.41 – 95.85
CRP (mg/L)	2.72	2.82	2.55 – 3.09	2.35	2.09 – 2.51

Note: TC = total cholesterol; TG = triglycerides; LDL-c = low density lipoprotein cholesterol; HDL-c = high density lipoprotein cholesterol; VLDL-c = very low-density lipoprotein cholesterol; GLU = glucose; CRP = C- reactive protein.

Education Personnel (CAPES/Brazil) and the National Council of Technological and Scientific Development (CNPq/Brazil) This study was partially supported by Ministry of Education (MEC/Brazil) and CNPq/Brazil.

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