




## Research Article

# Resistance Training Associated with Dietetic Advice Reduces Inflammatory Biomarkers in the Elderly

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Aging is a biological process during which chronic low-grade inflammation is present due to changes in the immune system of the elderly. The main objective of this study is to evaluate the effects of resistance training associated with dietary advice on chronic inflammation in the elderly. We conducted a prospective intervention study in which we evaluated anthropometric parameters and inflammatory biomarkers (CRP, IL-8, CCL-2, and leptin) in 40 elderly people before and after long-term progressive resistance training (19 weeks) associated with dietary advice. The participants trained twice a week on nonconsecutive days, and the training lasted one hour with an intensity of 60-85% of 1-MR. Dietary advice was explained in person and individually focusing on foods rich in compounds with anti-inflammatory and antioxidant properties. Participants were instructed at the beginning of the training program, and dietary advice was reinforced verbally weekly. There was an improvement in body composition evidenced by a reduction in waist circumference and body fat percentage and by the increase in arm circumference, calf circumference, and corrected arm muscle area. In addition, there was a reduction in the inflammatory biomarkers CCL-2 ( $p = 0.01$ ) and leptin ( $p < 0.01$ ). Resistance training associated with dietary guidance can contribute to a healthy aging due to observed improvements in body composition and in the inflammatory profile of the elderly.

## 1. Introduction

The growing number of elderly people in Brazil highlights the peculiarities of this population, which interfere with the social and economic context. Factors such as the presence of mostly chronic diseases and morphological, physiological, and body composition changes tend to affect the nutritional status and the health of the elderly [1–4].

Chronic low-grade inflammation is common in the elderly due to changes in the immune system that lead to dysregulation in cytokine secretion. In addition, as a conse-

quence of changes in body composition, the secretion of proinflammatory cytokines by adipose tissue increases [5–9].

A pertinent issue to be addressed in reducing low-grade chronic inflammation is resistance training. Resistance exercise generates adaptations in the skeletal muscle. It reduces the secretion of proinflammatory cytokines and increases the expression of anti-inflammatory cytokines. In addition, this type of training can decrease adiposity and increase the activity and expression of antioxidant enzymes [10–14].

Still regarding low-grade chronic inflammation, other studies have shown that reductions in the consumption of

saturated fats and simple sugars and increases in the consumption of foods rich in compounds with anti-inflammatory and antioxidant action (such as polyphenols, prebiotics, and omega 3 fatty acids) tend to decrease plasma concentrations of inflammatory biomarkers in the elderly [15–17].

However, the few existing studies on resistance training related to chronic inflammation in the elderly have addressed physical exercise in isolation, without taking into account the possible synergistic effects of dietary advice focusing on foods with anti-inflammatory and antioxidant properties [18–21, 4, 22]. Thus, this study proposes to investigate the effects of resistance training associated with dietary advice focusing on foods rich in compounds with anti-inflammatory and antioxidant actions on low-grade chronic inflammation in the elderly.

## 2. Materials and Methods

**2.1. Ethical Aspects.** This study was conducted according to the guidelines of the Resolution of the National Health Council no. 466/2012. It was approved by the Research Ethics Committee on Humans of the Federal University of Ouro Preto (CAAE: 02761918.0.0000.5150). Participants were duly informed about the risks and benefits and were included in the study after signing an informed consent.

**2.2. Study Design, Selection of Participants, and Eligibility Criteria.** This is a prospective study. We evaluated the following anthropometric parameters: weight, body mass index (BMI), waist circumference (WC), hip circumference (HC), waist-hip ratio (WHR), abdominal circumference (AC), arm circumference (ArmC), calf circumference (CC), and corrected arm muscle area (AMAc). We also evaluated inflammatory biomarkers (CRP, IL-8, CCL-2, and leptin) before and after the long-term progressive resistance training intervention and nutritional advice for 19 weeks.

Participants were recruited through posters posted at the Federal University of Ouro Preto (UFOP) and throughout the community of Ouro Preto. Interested participants performed a face-to-face registration. They were later scheduled for the initial assessment by telephone.

The inclusion criteria were age equal to or above 60 years and absence of problems that prevented physical activity (resistance training). A specialized professional evaluated them. The exclusion criterion was a percentage of attendance in the training program lower than 70%.

The sample calculation was performed using the formula for comparing paired groups with a quantitative variable as proposed by Miot [23], considering a 95% confidence level and 80% power. The sample size was 43 participants.

**2.3. Intervention.** The long-term progressive resistance training happened twice a week on nonconsecutive days and lasted one hour. In the 1<sup>st</sup> and 2<sup>nd</sup> weeks, the participants became familiar with the exercises and equipment and used a minimum load. Later, the 1-MR prediction test was applied. In the 3<sup>rd</sup> and 4<sup>th</sup> weeks, the participants trained with 60% of the 1-MR load; in the 5<sup>th</sup> and 6<sup>th</sup> weeks, they trained with 70% load; and in the 7<sup>th</sup> and 8<sup>th</sup> weeks, they trained with

80% load. From the 9th week, they trained with 85% of the 1-MR load until 19 weeks of training was completed. The number of repetitions suggested was 12-15 repetitions when the percentage of the 1-MR load was 60%, 10-12 repetitions for 70% load, and 6-8 repetitions for 80 and 85% of the 1-MR load [24, 25]. Adherence to resistance training was assessed using the 1-MR test applied before and after training [26].

The dietary advice was based on a list of foods rich in compounds with anti-inflammatory and antioxidant properties [10, 27–31]. The dietary advice was given to study participants by a nutritionist at the beginning of the training program in printed and verbal form. The advice was reinforced verbally every week. Adherence to dietary guidelines was assessed by calculating the total dietary antioxidant capacity (TACd) [32], using R24h [33] applied before and after dietary advice.

Participants were advised to increase the consumption of prebiotic foods (soluble fibers); antioxidants, such as polyphenols; and foods rich in omega 3, as well as to reduce the consumption of saturated fats and simple sugars. Therefore, the recommendation was to eat at least three fruits and two vegetables a day; natural spices (rosemary, turmeric, garlic, and onion), ginger, extra virgin olive oil, and whole grains (oats and flaxseed) once a day; and fish and chestnuts at least three times a week.

**2.4. Anthropometric Measurements.** Weight was measured using a portable Tanita® scale, a capacity of 150 kg, where the participant was weighed barefoot and wearing light clothing. Height was measured using a portable Sanny® anthropometer, spanning 115 to 210 cm [34]. The BMI was calculated using weight and height measurements to classify the nutritional status of the elderly, according to Lipschitz [35].

To measure the circumferences, a flexible and inelastic measuring tape was used. It was divided into centimeters and subdivided into millimeters (with a precision of 1 mm). The measurements followed Lohman et al. [34]. The AMAc was calculated using the equation by Heymsfield et al. [36] and the waist-hip ratio (WHR) was obtained by dividing WC by HC [37]. Skinfolds were measured using a Cescorf® adipometer with a sensitivity of 0.1 mm, reading range of 85 mm, and pressure of 10 g/mm [2, 34]. The BF percentage was estimated by summing four skinfold values, according to the equation of Durnin and Womersley [38].

**2.5. Blood Collection and Analysis of Inflammatory Biomarkers.** The blood collection was performed by a trained professional using intravenous puncture and vacuum system in the anterior area of the arm, in front of and below the elbow, where the medial and cephalic veins are. For the CRP analysis of the serum, a blood tube containing serum separation gel was used. For the analyses of IL-8, CCL-2, and leptin in the plasma, the collection was performed in a blood tube containing EDTA. The tubes remained at rest for 30 minutes. Then, they were centrifuged at 3,000 rpm for ten minutes. After separating the blood components, the aliquots were pipetted and stored.

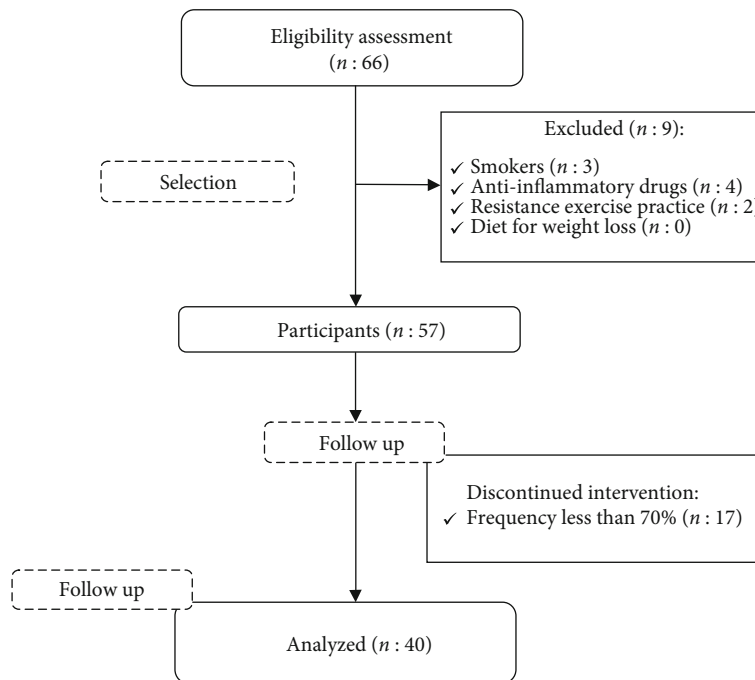


FIGURE 1: Flowchart of the present study.

The CRP dose evaluation was performed using the turbidimetric inhibition immunoassay and a specific kit for the Cobas Integra 400 Plus equipment (Roche®). The analyses of the biomarkers IL-8, CCL-2 (sensitivity from 8 to 1,000 pg/mL), and leptin (sensitivity from 63 to 4,000 pg/mL) were performed using the ELISA method and specific kits from PeproTech® following the manufacturer's protocol.

**2.6. Statistical Analyses.** Data were tabulated and assessed for normality by the Shapiro-Wilk test. The results were expressed as mean and standard deviation in the case of normal data or median (minimum and maximum) if nonparametric. Differences between paired groups were assessed using the paired *t*-test or Wilcoxon test (two groups), depending on data normality. Tests for normality and differences between groups were performed using the GraphPad Prism® software, version 6.0. For all analyses, a level of significance of 5% was adopted.

### 3. Results

The present study had the participation of 40 elderly people (Figure 1), with an average age of  $63.90 \pm 5.80$  years, and among them, 26 (65%) were women.

Regarding adherence to the intervention, there was an increase in performance in the exercises of anterior pull, bench press, and seated row, as assessed by the 1-MR test. There was an increase in TACd calculated by R24h (Figure 2), indicating that the participants adhered to the proposed intervention.

The intervention based on resistance training and dietary advice resulted in a reduction in WC, WHR, and BF percentage and in an increase in ArmC, AMAc, and CC (Table 1).

Regarding inflammatory biomarkers, there was a reduction in plasma CCL-2 concentrations: 299.8 (54.4-950.7) pg/mL (before) and 229.9 (27.9-744.1) pg/mL (after) ( $p = 0.01$ ), and in leptin:  $2,749 \pm 693$  pg/mL (before) and  $2,405 \pm 655$  pg/mL (after) ( $p < 0.01$ ).

However, there were no differences in CRP concentrations: 1.97 (0.27-8.06) mg/L (before) and 1.70 (0.15-7.17) mg/L (after) ( $p = 0.41$ ), and IL-8: 259.6 (198.7-448.7) pg/mL (before) and 258.8 (169.1-491.3) pg/mL (after) ( $p = 0.97$ ), according to Figure 3.

### 4. Discussion

Low-grade chronic inflammation is common with aging and is associated with an increased risk of developing diseases, such as NCDs and sarcopenia. Studies have indicated resistance training to help reduce chronic inflammation in the elderly population. However, the results are still controversial. In addition, existing studies have not addressed dietary advice focusing on foods rich in anti-inflammatory and antioxidant properties in conjunction with training [18–22].

In this scenario, the present study evaluated the effects of resistance training associated with dietary advice on chronic inflammation in elderly people living in the city of Ouro Preto, MG, Brazil. The results show a decrease in plasma concentrations of the inflammatory biomarkers CCL-2 and leptin and an improvement in body composition.

According to Pedersen and Febbraio [39], the muscle is an endocrine organ capable of producing and secreting cytokines, called myokines, in response to muscle contractions. Among myokines, IL-6 stimulates the expression of anti-inflammatory cytokines (IL-1ra and IL-10) and reduces the levels of circulating inflammatory biomarkers, such as

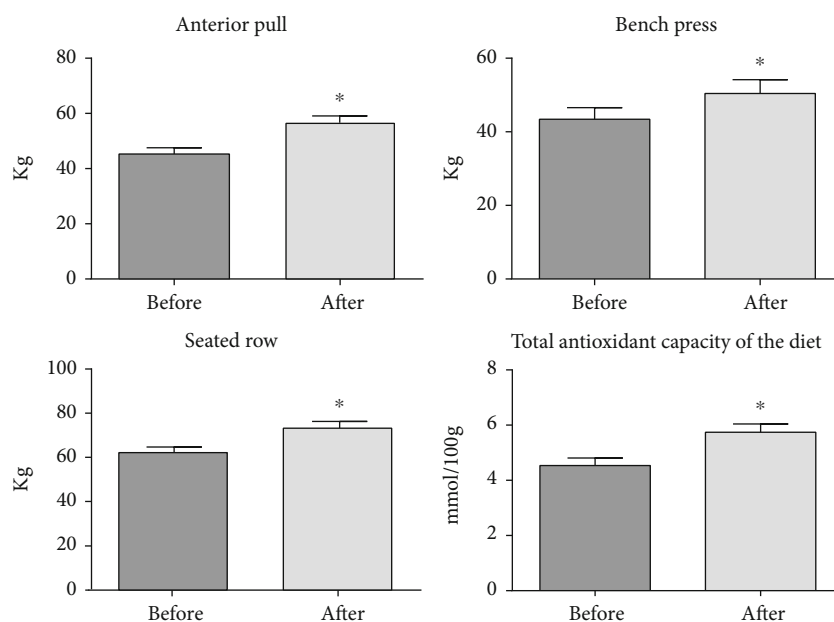


FIGURE 2: Evaluation of adherence to the intervention, performance data obtained by the 1-RM test, and antioxidant capacity of the diet calculated by R24h. \*Difference between paired groups (paired *t*-test or Wilcoxon, *p* value < 0.05).

TABLE 1: Results regarding anthropometric variables before and after the intervention.

Variable	<i>n</i> : 40		<i>p</i> value	$\Delta$
	Before	After		
Weight (kg)	72.08 $\pm$ 13.78	71.95 $\pm$ 13.26	0.82	0.13
BMI (kg/m <sup>2</sup> )	27.68 $\pm$ 4.52	27.62 $\pm$ 4.21	0.78	0.06
WC (cm)	89.43 $\pm$ 10.05	86.53 $\pm$ 10.02	<0.01	2.90
HC (cm)	99.10 (85.40-119.20)	101 (86.80-121)	0.40	-1.90
WHR	0.89 $\pm$ 0.08	0.86 $\pm$ 0.08	<0.01	0.04
AC (cm)	93.80 $\pm$ 12.73	93.22 $\pm$ 12.72	0.55	0.58
ArmC (cm)	30.31 $\pm$ 4.03	31.00 $\pm$ 3.62	0.04	-0.69
AMAc (cm <sup>2</sup> )	37.74 $\pm$ 18.42	44.89 $\pm$ 17.57	<0.01	-7.15
CC (cm)	36 (26.80-42.50)	37.50 (30.30-59.80)	<0.01	-1.50
BF (%)	38.69 $\pm$ 7.00	34.77 $\pm$ 6.13	<0.01	3.75

$\Delta$ : delta (initial-final); BMI: body mass index; WC: waist circumference; HC: hip circumference; WHR: waist-to-hip ratio; AC: abdominal circumference; ArmC: arm circumference; AMAc: corrected arm muscle area; CC: calf circumference; BF (%): percentage of body fat. \*Difference between paired groups (paired *t*-test or Wilcoxon, *p* value < 0.05).

IL-1 $\beta$ , TNF, and chemokines (CCL-2). Thus, skeletal muscle hypertrophy tends to increase the production of IL-6 by the muscle, which could explain the improvement in the inflammatory profile.

Regarding the reduction of plasma CCL-2 concentrations, the finding of this study can also be related to a decrease in visceral and subcutaneous fat since CCL-2 is also produced by the adipose tissue, as well as leptin. Other studies have shown that resistance training is effective in reducing adiposity due to increased metabolic rates at rest, improved insulin sensitivity, and increased sympathetic activity, which reduces visceral fat storage [40, 18, 41–46].

However, there are still few studies evaluating the chronic effects of resistance training on the CCL-2 biomarker in the

elderly. Supposedly, because aerobic exercises have a greater capacity for lipid oxidation due to the increase in the number of mitochondria [40]. In this scenario, Ihalainen et al. [47] corroborate the present study by reporting a decrease in body fat and in the inflammatory biomarkers CCL-2 and leptin after 24 weeks of combined training (resistance and aerobic exercises) in adults. Similarly, Leggate et al. [48] showed a reduction in WC and CCL-2 in obese individuals after high-intensity exercises.

In the elderly, Kelly et al. [49] showed that 12 weeks of aerobic training reduced CCL-2 levels in obese elderly people. On the other hand, Ogawa et al. [50] did not observe changes in the plasma concentrations of CCL-2 in elderly women after 12 weeks of resistance training (once a week).

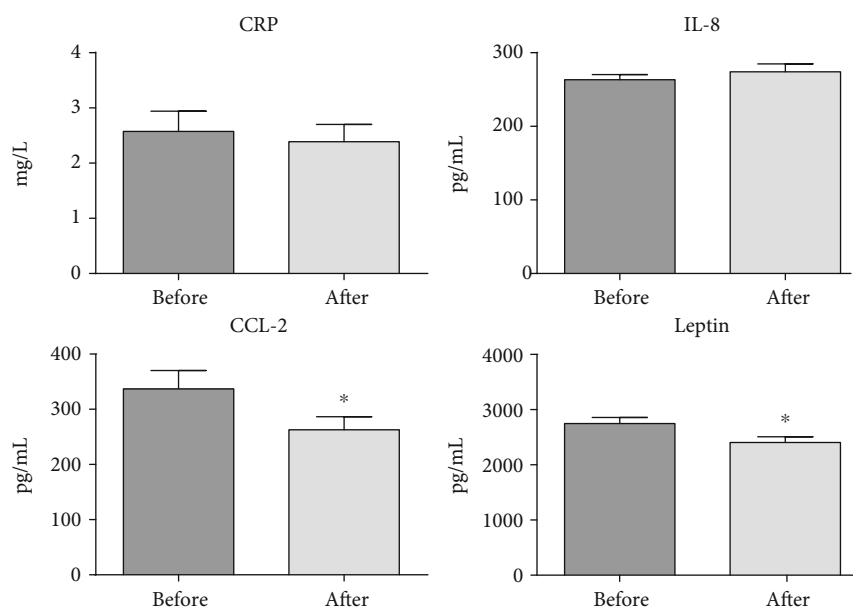


FIGURE 3: Results of inflammatory biomarkers (CRP, IL-8, CCL-2, and leptin) before and after the intervention. \*Difference between paired groups (paired *t*-test or Wilcoxon, *p* value < 0.05).

Considering that the aforementioned studies have emphasized that exercise intensity is relevant to change CCL-2 levels, the progression of intensity (65 to 85% of 1-MR) in the present study may have positively influenced the response of this cytokine.

Another possible mechanism for reducing CCL-2 concentrations involves the production of reactive oxygen species. Resistance training is known to increase glucose uptake in muscles, reducing plasma glucose concentration and consequently the production of reactive oxygen species, which inhibits the NF- $\kappa$ B pathway, responsible for expressing genes that encode proinflammatory cytokines such as CCL-2 [51, 49, 39, 52, 53]. In addition, adaptations resulting from chronic exercise lead to the reduction of reactive oxygen species by increasing the activity of antioxidant enzymes [54, 55, 21, 56].

The reduction in plasma leptin concentrations may also be associated with an improvement in body composition. Pedersen and Febbraio [57] described that myosins produced by the increase in muscle mass neutralize the production of adipokines due to the increase in lipid oxidation in the adipose tissue. Still regarding this scenario, other authors reported that leptin is produced predominantly by white adipose tissue, and its plasma concentration is proportional to the amount of body fat [51, 58, 59]. Thus, the increase in muscle mass and the reduction in body fat, as evidenced in the present study, affected leptin levels in the elderly.

In this scenario, Balducci et al. [60] showed that combined training (resistance and aerobic exercises) for one year, whose intensity of resistance is 80% of 1-MR and the frequency is two times a week, reduces leptin levels in diabetic and obese elderly. Prestes et al. [61] showed a reduction in plasma leptin concentrations in elderly women after 16 weeks of resistance training with a frequency of two times a week.

The changes found can also be justified by better eating habits promoted by dietary advice and evidenced by the increase in TACd. The diet may have foods rich in compounds with anti-inflammatory and antioxidant properties, such as polyphenols, prebiotics, and omega 3 fatty acids [5, 62]. These compounds modulate the Nrf2 signaling pathway, increasing the expression of antioxidant enzymes and reducing the production of reactive oxygen species [5, 63, 51].

Studies have addressed that bioactive compounds present in food can improve leptin resistance by acting in the recovery of signaling between leptin and neurotransmitters and in the transport of this adipokine to the blood-brain barrier [64, 58].

Corroborating the results found in the present study, Shah et al. [65] also observed a reduction in plasma leptin concentrations in obese elderly people after 24 weeks of combined training (resistance and aerobic exercises) associated with a proper diet. In that study, the intensity of resistance exercises was between 65 and 80% of 1-MR, similar as the methodology applied in the present research.

In the present study, the serum levels of CRP did not change, which can be justified by the fact that the elderly had normal values (less than 2 mg/L) before the intervention. According to Gaesser et al. [66], CRP reduction is more common in individuals with high levels of this biomarker before interventions. There were also no differences in plasma IL-8 concentrations. Corroborating this finding, Buford et al. [67] suggested that IL-8 has a local effect on the muscle after resistance training and plasma changes tend not to occur.

The WHO [68] recommends to the elderly population at least 150 minutes of moderate aerobic exercise per week for the control of CNCD, in which chronic low-grade inflammation is directly involved. However, the role of resisted exercise is still little studied [40]. Fragala et al. [24] and Sardeli et al. [69] reported that a resistance exercise program lasting 12



weeks or more, with at least eight exercises and a frequency of three times a week, is effective in reducing proinflammatory cytokines in the elderly.

Thus, this study, using new biomarkers, elucidates the use of relatively simple interventions in the planning of assistance programs for the elderly, including resistance exercises and dietary advice, as a way to reduce health risks.

The absence of a control group to identify the isolated effects of resistance training and dietary advice is a limitation of the study. However, the aim of this study was precisely to demonstrate the synergistic effect of both strategies in reducing low-grade chronic inflammation. The combination of both strategies has been widely reported as more effective than isolated actions regarding physical exercises and changes in eating habits [49, 70–72]. In addition, the study design and adherence to the intervention are strengths of this study.

## 5. Conclusion

The present study shows that long-term progressive resistance training associated with dietary advice for 19 weeks is effective in reducing inflammatory biomarkers (CCL-2 and leptin). In addition, there is a reduction in the anthropometric parameters WC and BF percentage and an increase in ArmC, CC, and AMAc, evidencing a reduction in body fat and an increase in muscle mass. Resistance training associated with dietary advice can contribute to a healthy aging due to observed improvements in body composition and in the inflammatory profile of the elderly.

## Data Availability

This manuscript was prepared based on the Postgraduate in Health and Nutrition that is available at the Institutional Repository of the Federal University of Ouro Preto (<http://www.repositorio.ufop.br/handle/123456789/12340>).

## Conflicts of Interest

Each author of this study declares that there is still no relationship with the companies or manufacturers that will benefit from the results of this study. The authors declare no conflicts of interest.

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