



Original/Deporte y ejercicio

Positive effects of resistance training on inflammatory parameters in men with metabolic syndrome risk factors

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Summary

Background: evidences have shown a strongly association between metabolic syndrome (MS), cardiovascular diseases and chronic low-grade inflammation, being this last, related with the occurrence of sarcopenia and atherosclerosis. Despite several benefits, the effects of resistance training (RT) on inflammatory profile are controversial. Thereby, this study aims to investigate the effects of a RT on the inflammatory profile of men with MS risk factors.

Methods: fifteen sedentary men (57.53 ± 7.07 years old) with 2 or more MS components underwent a RT for 14 weeks (3 times per week), with intensity ranging between 40 and 70% of one repetition maximum. The dual-energy X-ray absorptiometry was used to body composition assessment and serum was collected to evaluate biochemical and inflammatory parameters before and after the RT.

Results: despite the absence of changes in body weight, total muscular content and biochemical parameters, the individuals demonstrated a reduction on body fat content ($p < 0.05$). Furthermore, the RT resulted in lower circulating levels of tumor necrosis factor alpha and interleukin-6 ($p < 0.05$), in higher levels of interleukin-10 ($p < 0.05$) and in the stabilization of interleukin-1 beta and interferon-gamma concentrations. It was concluded that a moderate RT benefits inflammatory profile, contributing to a lower risk of cardiovascular diseases.

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Key words: Health. Cardiovascular diseases. Exercise. Cytokines. Adiposity.

EFFECTOS POSITIVOS DEL ENTRENAMIENTO DE RESISTENCIA EN LOS PARÁMETROS INFLAMATORIOS DE HOMBRES CON FACTORES DE RIESGO DE SÍNDROME METABÓLICO

Resumen

Introducción: la evidencia muestra la relación entre síndrome metabólico (SM), enfermedades cardiovasculares e inflamación crónica de bajo grado, que está relacionada con la aparición de sarcopenia y aterosclerosis. A pesar de muchos beneficios, los efectos del entrenamiento de resistencia (ER) sobre la inflamación son controvertidos. Este estudio tiene como objetivo investigar los efectos de 14 semanas de ER en el perfil inflamatorio de hombres con factores de riesgo para SM.

Métodos: quince varones sedentarios ($57,53 \pm 7,07$ años) con 2 o más componentes del SM fueron sometidos a un ER moderado durante 14 semanas (tres veces a la semana), con una intensidad que oscila entre 40 y 70% de una repetición máxima. La absorciometría dual de rayos X se utilizó para la evaluación de la composición corporal y el suero se recogió para evaluar los parámetros bioquímicos e inflamatorios antes y después de la ER.

Resultados: a pesar del mantenimiento de la masa corporal, la masa muscular total y los parámetros bioquímicos, hubo una reducción en la grasa corporal ($p < 0,05$). Además, el ER disminuyó los niveles de factor de necrosis tumoral alfa e interleucina-6 circulante ($p < 0,05$), aumentó la concentración de interleucina-10 ($p < 0,05$) y mantuvo la interleucina-1 y el interferón-gamma. Se concluyó que 14 semanas de ER moderado provocan beneficios sobre el perfil inflamatorio, contribuyendo a la reducción del riesgo cardiovascular.

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Palabras clave: Síndrome metabólico. Ejercicio. Citocinas. Adiposidad.

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Abbreviations

1RM: one repetition maximum.
CRP: C reactive protein.
CVD: cardiovascular diseases.
DBP: diastolic blood pressure.
DXA: dual-energy X-ray absorptiometry.
ELISA: enzyme-linked immunosorbent assay.
HDL: high-density cholesterol.
IFN- γ : interferon-gamma.
IL-1 β : interleukin-1 beta.
IL-6: interleukin-6.
IL-10: interleukin-10.
LDL: low-density cholesterol.
MS: metabolic syndrome.
NF κ B: nuclear factor kappa B.
RT: resistance training.
SBP: systolic blood pressure.
SPSS: Statistical Package for Social Sciences.
T2DM: type 2 diabetes mellitus.
TNF- α : tumor necrosis factor alpha.

Background

The metabolic syndrome (MS) is defined as the clustering of risk factors, including central obesity, dyslipidemia, hypertension, insulin resistance and type 2 diabetes mellitus (T2DM)¹, being related to the high occurrence of several cardiovascular diseases (CVD)¹. In this sense, it is known that a sedentary lifestyle and an incorrect diet result in the increased prevalence of MS and the regular practice of physical exercises have been recommended for the prevention and treatment of this syndrome².

Several evidences have shown a close relationship between MS, visceral obesity and chronic low-grade inflammation³. The chronic low-grade inflammation is characterized by an increase of circulating proinflammatory cytokines levels, being related to disorders such sarcopenia, osteoporosis, atherosclerosis and T2DM³⁻⁵. In obese individuals, leucocytes infiltrate in the abdominal adipose tissue and produce several proinflammatory cytokines³. Among the proinflammatory predictors of CVD and stimulators of higher rates of skeletal muscle catabolism are interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF- α)⁶. In contrast, interleukin-10 (IL-10) acts inhibiting the production of interleukin-1 beta (IL-1 β) and TNF- α ⁴.

The physical exercise has been strongly recommended for the prevention and treatment of MS, obesity and low-grade inflammation. Specifically, the regular practice of resistance training (RT) has been efficient in slowing down the progress of several age-related chronic diseases⁷, in the prevention of various causes of mortality⁸, in the increase of caloric expenditure, muscle mass and resting metabolic rate⁹ and in the decreasing hepatic lipogenesis¹⁰. However, the effects of RT as a single intervention

on inflammatory profile have produced controversial results¹¹⁻¹⁶.

Considering that the chronic low-grade inflammation is associated with sarcopenia, strength losses and cardiovascular diseases^{3,5}, this study aims to investigate the effects of a resistance training program on inflammatory parameters of men with metabolic syndrome risk factors.

Methods

Subjects

As the study was advertised on website and local institutional newspapers, eighteen men were recruited to participate after being informed about the protocol. The inclusion criteria applied were: sedentary (without participating in structured exercises for at least 6 consecutive months prior to starting the intervention) men, age between 45 and 75 years and the presence of at least two factors of MS classification: triglycerides levels \geq 150 mg/dL or specific drug treatment, high-density cholesterol (HDL) levels \leq 40 mg/dL or specific drug treatment, fasting glucose levels \geq 100 mg/dL or specific drug treatment, systolic blood pressure \geq 130 and/or diastolic \geq 85 mmHg or specific drug treatment and waist circumference \geq 90 cm¹⁷. Besides, the subjects were asked to maintain their habitual food intake during the intervention. This study was approved by the institutional Ethics Committee (number 0032.0.243.000-07) and followed the statements of the Declaration of Helsinki. All the participants signed a written informed consent.

Resistance Training

The supervised RT was performed three days per week during 14 weeks, with a minimal of 48-72 h of recovery between sessions. The first two weeks of the RT consisted of one set of 15 repetitions and two sets of 17 repetitions in five exercises for whole muscles, respectively, at 40% of one repetition maximum (1RM). From weeks 3 to 10, subjects performed three sets of 15 repetitions at 60% 1RM, with the number of exercises increasing until 12. During the last four weeks, the subjects performed three sets of 12 repetitions at 70% 1RM¹² in the following exercises: lat pull down, bench press, rower machine, triceps pulley extension, biceps curl, trunk extension, abdominal curl, leg-press, knee flexion, ankle plantar flexion, hip abduction and adduction¹, during 1 h in average. In the beginning of sessions, warm-up was performed through a low intensity walking indoor for 10 min. In the end, stretching was performed individually. The stretching exercises varied with the sessions and were directed to stretch upper and low back, shoulders, arms, chest, abdomen, thighs (back, front, inner and outer) and calves.

Functional Assessments

All the tests described below were performed by the same researcher and at same time of day, before and after the 14th week of RT. To estimate the largest load that an individual can move in a single maximal effort and thus prescribe the training load, a submaximal test was used to estimate the 1RM in the bench press, rowing machine, leg press and knee flexion exercises¹⁸. Cardiorespiratory fitness was assessed by Bruce's modified protocol in a treadmill¹⁹. The levels of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured after the subjects sat quietly for 5 min with a digital sphygmomanometer (Omron, Kyoto, Japan). Furthermore, the flexibility of lumbar and hamstring muscles were assessed by the sit-and-reach test²⁰ and the longest distance reached on the measuring board was registered after three attempts.

Anthropometric Measurements

The subjects were weighted in a scale (Plenna, São Paulo, Brazil) and height was evaluated with a stadiometer (Cardiomed, Curitiba, Brazil). The abdominal circumference was measured with a spring-loaded metal tape (Cardiomed, Curitiba, Brazil). Body composition was determined using dual-energy X-ray absorptiometry (DXA) with a densitometer machine (Hologic QDR Discovery, Waltham, USA). Briefly, after 12 h fasting and 24 h without exercises and wearing only a light coat, subjects lay supine on the DXA table with their arms adequately separated from their trunk and were instructed to remain still throughout the scanning procedure.

Biochemical Assays

Blood samples were collected from a vein of the antecubital region after 12 h of fasting and 72 h without physical exercise practice. Samples were collected into serum separator tubes (BD Diagnostics, Plymouth, United Kingdom) and centrifuged at 1500 g for 15 min. Then, serum was frozen at -80°C until analysis. The triglycerides, total cholesterol, HDL and glucose levels were determined spectrophotometrically with commercially available assay kits (Labtest, Lagoa Santa, Brazil). The concentration of low-density lipoprotein cholesterol (LDL) was estimated²¹. The serum levels of cytokines IL-1 β , IL-6, IL-10, TNF- α and interferon-gamma (IFN- γ) were determined by enzyme-linked immunosorbent assay (ELISA) using commercial kits for human (eBIOSCIENCE, San Diego, USA), according to manufacturer's instructions. Lipid and glucose parameters were analyzed with samples in duplicate, while inflammatory parameters were performed with samples in triplicate.

Nutritional Data

To minimize a possible bias, subjects were encouraged to not alter their habitual dietary intake during the intervention and completed a 3-day diet record in the beginning and in the end of the RT. The 3-day diet record included Sunday, Monday and Tuesday analysis. To determine total caloric intake and the amount of macronutrients ingested, it was utilized a specific software (Dietwin, São Paulo, Brazil).

Statistical Analysis

The Shapiro-Wilk test was carried out to verify data normality. Afterwards, Student's *t* test or Wilcoxon Rank Test were used to determine significant differences between the pre and post-training means. Statistical Package for Social Sciences (SPSS 14.0, Chicago, USA) was used and statistical significance was set at $p < 0.05$. Data were expressed as mean \pm standard deviation of the mean (SD).

Results

Of the 18 volunteers who started participating in the study, 15 individuals (57.53 ± 7.07 years old) concluded the RT and were considered in the statistical analysis (three individuals were excluded due the absence in more than 25% of RT sessions). Besides, the sample comprised two smokers, six former smokers and seven nonsmokers. Furthermore, 40% of men took antihypertensive agents, 33.3% took lipid-lowering agents and 20% took oral hypoglycemic agents. Among the fifteen subjects, the adherence to RT was of 82.34%. In table I, it is demonstrated that TR did not result in significant changes in most anthropometric, functional and biochemical characteristics. However, total body fat content decreased with the RT ($p = 0.041$).

Table II exhibits the results of the submaximal strength test before and after the RT. Increases in the load lifted/moved in the bench press ($p < 0.001$), leg press ($p < 0.001$), rowing machine ($p < 0.001$) and knee flexion ($p = 0.003$) exercises were observed.

No significant differences were reported in the total caloric intake and the amount of macronutrients ingested of carbohydrates, proteins and lipids, demonstrating the maintenance of habitual intake during the intervention (Table III).

Figure 1 shows the impact of RT on serum levels of cytokines. It was observed that RT decreased TNF- α (174.2 ± 56.59 vs. 140 ± 23.25 pg/mL; $p = 0.011$) (B), IL-6 (155 ± 50.18 vs. 124 ± 26.73 pg/mL; $p = 0.019$) (D), and IL-10 levels (86.53 ± 34.93 vs. 108.53 ± 24.76 pg/mL; $p = 0.037$) (E). However, the IL-1 β ($p = 0.074$) (A) and INF- γ levels ($p = 0.084$) (C) did not change significantly after the intervention.

Table I
Anthropometric, functional and biochemical characteristics of men with metabolic syndrome risk factors before and after the resistance training

Parameters	Before	After
Body Mass (kg)	89.24 ± 15.5	88.82 ± 14.77
BMI (kg/m ²)	29.82 ± 5	29.68 ± 4.81
Abdominal Circumference (cm)	106.47 ± 11.34	105.28 ± 10.66
Total Body Fat Content (kg)	29.78 ± 9.19	28.57 ± 8.71*
Total Muscle Mass (kg)	54.91 ± 5.56	55.29 ± 5.99
Systolic Blood Pressure (mmHg)	122.2 ± 20.26	118.33 ± 16.86
Diastolic Blood Pressure (mmHg)	73.66 ± 9.65	69.80 ± 9.83
VO ₂ max (mL/kg ⁻¹ ·min ⁻¹)	32.29 ± 10.32	33.47 ± 11.34
Glucose (mg/dL)	96.03 ± 11.85	105.87 ± 23.36
Total Cholesterol (mg/dL)	156.38 ± 41.09	166.37 ± 45.68
Triglycerides (mg/dL)	162.46 ± 71.23	159.46 ± 90.37
HDL (mg/dL)	42.9 ± 14.91	46.78 ± 17.98
LDL (mg/ dL)	80.99 ± 31.52	80.19 ± 49.09

Values expressed as mean ± SD. BMI: body mass index. VO₂max: maximal oxygen uptake. HDL: high-density cholesterol. LDL: low-density cholesterol. * p < 0.05 after vs. before resistance training.

Table II
Load lifted/moved in the strength test pre and post-training

Exercises	Before	After
Bench Press (kg)	43.98 ± 11.40	61.36 ± 15.90**
Leg Press (kg)	98.28 ± 22.67	122.20 ± 20.09**
Rower machine (kg)	44.76 ± 13.80	57.18 ± 9.80**
Knee Flexion (kg)	27.22 ± 7.16	41.6 ± 13.65*

**p < 0.01 and *p < 0.01 after vs. before the resistance training.

Table III
Caloric intake and amount of macronutrients ingested along the resistance training

Variables	Before	After
Total Caloric Intake (kcal)	2171.14 ± 461.17	2137.93 ± 494.78
Carbohydrates (g)	242.97 ± 51.54	233.89 ± 65.19
Proteins (g)	97.31 ± 20.86	106.16 ± 22.05
Lipids (g)	94.42 ± 25.50	88.50 ± 24.85

Values expressed as mean ± SD.

Discussion

This study aimed to investigate the effects of a supervised RT on inflammatory profile in men with metabolic syndrome risk factors. The main findings are that RT provoked improvements in inflammatory

and anthropometric (body fat content) parameters, independently of significant changes in body mass and in the factors of MS classification. Furthermore, RT promoted increases in exercise load during 1RM test, indicating a functional adaptation to the stimulus generated from RT sessions.

Evidences have demonstrated that the age-related skeletal muscle catabolism and sedentary lifestyle contribute to the high prevalence of metabolic disorders^{5,22}. In this sense, a recent review and meta-analysis demonstrated that RT, as a single intervention, is not able to change total cholesterol, triglycerides, HDL, LDL and diastolic blood pressure²², as the results obtained in this study. Furthermore, beneficial alterations in inflammatory biomarkers associated with the physical training are not dependent of weight loss, conflicting with some previous studies^{23,24}.

Although the regular practice of resistance exercise provides several health benefits^{7,9,10}, the effects of RT on cytokines parameters are inaccurate. In the present study, 14 weeks of moderate RT resulted in lower levels of serum TNF-α and IL-6 and higher levels of IL-10 in men with MS, while IL-1β and IFN-γ levels was not altered. However, other investigations with RT protocols in individuals with considerable cardiovascular risk did not find changes in circulating inflammatory markers after intervention^{11-13,25-28}. Possible reasons for conflicting results may include age of the participants, basal levels of cytokines, influence of the last exercise session, besides frequency, duration and intensity of training.

Studies demonstrate that positive effects of RT on inflammatory profile vary according to the biomar-

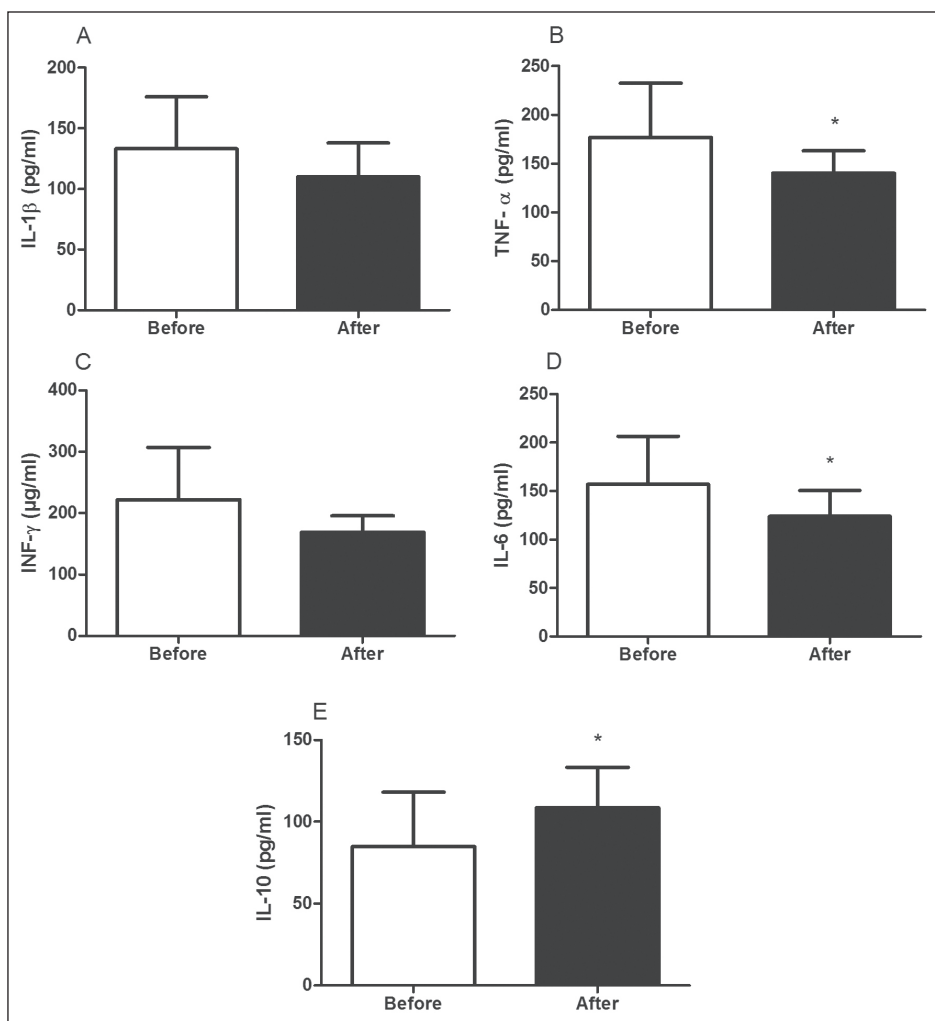


Fig. 1.—Effects of resistance training on circulating levels of interleukin-1 beta (IL-1 β) (A), tumor necrosis factor alpha (TNF- α) (B), interferon-gamma (INF- γ) (C), interleukin-6 (IL-6) (D), interleukin-10 (IL-10). * $p < 0.05$ after vs. before the resistance training.

kers. For instance, four months of RT with post-menopausal women decreased IL-6 levels, despite the maintenance of TNF- α and interleukin-15 concentrations¹⁵. Similarly, 12 weeks of RT lowered TNF- α , leptin and C reactive protein (CRP) levels, although the maintenance of other plasma and subcutaneous adipose tissue inflammatory markers levels in postmenopausal women¹⁴. However, 32 weeks of resistance exercise decreased IL-6 levels in elderly men, without modifying IFN- γ , TNF- α and CRP concentrations²⁹. In this regard, protocols of RT with lower week frequency and amount of exercises induced decreasing of CRP, IFN- γ , serum amyloid A and heat shock protein 70, respectively, despite the unchanged levels of TNF- α and IL-6^{16,30}.

Considering that adipose tissue is an endocrine organ⁴, a reduction in the adipose tissue content may influence the production and releasing of proinflammatory markers, as confirmed in the present study. It is highlighted that the found body fat content reduction derives from the RT, since caloric intake and amount of macronutrients did not change along the intervention. The IL-6 releasing from adipose tissue and im-

mune cells is linked with several disorders, characterizing the chronic low-grade inflammation status. In contrast, investigations have demonstrated that IL-6 released by skeletal muscle during the physical exercise stimulates the lipolysis, the IL-10 production and inhibits the TNF- α production⁴. In this sense, *in vivo* and *in vitro* studies have demonstrated that IL-6 release from myocytes is an essential regulator of skeletal muscle hypertrophy mediated by satellite-cells³¹. The physical training also reduces skeletal muscle mRNA toll-like receptor 4 (TLR4) and TNF- α ⁶, possibly influencing circulating cytokines levels.

Other several mechanisms have been proposed to explain the positive effects of RT on inflammatory parameters in previously sedentary individuals. It has been suggested that anti-inflammatory effects of RT are mediated by the modulation of cytokines production not only in the adipose tissue, but also in the skeletal muscle and peripheral blood mononuclear cells³². Another hypothesis is that RT results in reduced expression of TLR4 in monocytes, as previously demonstrated³³. Indeed, TLR4 is known to activate the nuclear factor kappa B (NF κ B), inducing the expres-

sion of proinflammatory cytokines such TNF- α and IL-6³⁴. Furthermore, investigations have demonstrated that physiological adjustments to muscle contraction involves functional changes in macrophages, reducing the production of TNF- α and IL-1 β due anti-inflammatory cytokines, such as IL-10^{34,35}. In this regard, it is known that higher levels of proinflammatory cytokines stimulate the migration of monocytes to the arterial layer and its conversion in macrophages, originating atherosclerosis lesions⁴.

In conclusion, these results suggest that 14 weeks of moderate resistance training induces positive and favorable effects on inflammatory profile in men with metabolic syndrome risk factors, contributing to the decrease of cardiovascular risk. The lack of control group may be considered a limitation of this study.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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