Hypertrophy training improves glycaemic and inflammatory parameters in men with risk factors

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Received: 21.12.2016
Accepted: 29.05.2017

Summary

Background and aims: A close link between metabolic syndrome (MS), insulin resistance, chronic low-grade inflammation and cardiovascular diseases has been highlighted in the literature. However, resistance training (RT) has shown interesting results on inflammatory mediators, adipokines, and insulin-related parameters in this population, although results are still contradictory. This study aimed to investigate the effects of hypertrophy RT on glycaemic, cytokines and adipokines levels in men with MS risk factors.
Methods: Twenty-one untrained men (57.8 ± 7.74 years old) underwent a RT for 15 weeks (3 times per week), comprised of nine exercises performed predominantly in the hypertrophy zone. Blood samples were drawn for analysis of glycaemic, inflammatory and hormonal parameters. Subjects were encouraged to maintain their habitual dietary intake during the intervention and dual-energy X-ray absorptiometry was used to assess body composition.
Results: Levels of interleukin-1 beta (IL-1β), interleukin-6 (IL-6), interleukin-18 (IL-18), tumor necrosis factor alpha (TNF-α), interferon-gamma (IFN-γ), resistin, ghrelin and leptin decreased, while interleukin-10 (IL-10) and adiponectin concentrations increased after RT. Moreover, the intervention improved glycaemic and insulinemic parameters, besides body composition. Body mass, abdominal and waist circumferences, besides total cholesterol and triglycerides levels remained unaltered.
Conclusion: Positive modulation of glycaemic, insulinemic and inflammatory parameters are found in men with MS risk factors after 15 weeks of hypertrophy resistance training, parallel with improvements on body composition and independent of weight loss.

Key words:
Strength training. Inflammation. Health. Diabetes Mellitus. Exercise.

El entrenamiento de hipertrofia mejora los parámetros glucémicos e inflamatorios en hombres con factores de riesgo

Resumen

Antecedentes y objetivos: Se ha destacado en la literatura un estrecho vínculo entre el síndrome metabólico (SM), la resistencia a la insulina, la inflamación crónica de bajo grado y las enfermedades cardiovasculares. Además de varios beneficios, el entrenamiento de resistencia (ER) ha producido resultados contradictorios en citoquinas, citoquinas derivadas de tejido adiposo y niveles de parámetros relacionados con la insulina. Este estudio tuvo como objetivo investigar los efectos del ER de hipertrofia como una sola intervención en los niveles de glucemia, citoquinas y adipoquinas en hombres con factores de riesgo de SM.
Métodos: Veintiún hombres sedentarios (57,8 ± 7,74 años) se sometieron a ER durante 15 semanas (3 veces por semana), compuesto de nueve ejercicios realizados predominantemente en la zona de hipertrofia. Se tomaron muestras de sangre para el análisis de parámetros glucémicos, inflamatorios y hormonales. Los sujetos fueron alentados a mantener su ingesta dietética habitual durante la intervención y se utilizó la absorciometría de rayos X de energía dual para evaluar la composición corporal.
Resultados: Los niveles de interleucina-1 beta (IL-1β), interleucina-6 (IL-6), interleucina-18 (IL-18), necrosis tumoral alfa (TNF-α), interferón gamma (IFN-γ), resistina, grelina y leptina disminuyeron, mientras que las concentraciones de interleucina-10 (IL-10) y adiponectina aumentaron después del ER. También, la intervención mejoró los parámetros glicémico e insulinémico, además de la composición corporal. La masa corporal, la circunferencia abdominal y la cintura, además del colesterol total y los triglicéridos permanecieron inalterados.
Conclusión: La modulación significativa y positiva en los parámetros sistémicos glicémicos, insulinémicos e inflamatorios ha sido encontrada en los hombres con factores de riesgo de SM después de 15 semanas de entrenamiento de resistencia a la hipertrofia, paralelamente con mejoras en la composición corporal e independiente de la pérdida de peso.

Palabras clave:
Entrenamiento de fuerza. Inflamación. Salud. Diabetes Mellitus. Ejercicio.

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Introduction

The metabolic syndrome (MS) comprises insulin resistance, dyslipidemia, hypertension and abdominal obesity, and it is associated with a lifestyle encompassing excessive energetic intake and low physical activity levels[1]. In this regard, it is estimated that 25% of the worldwide' adults have MS[2]. In Brazil, MS prevalence is higher in middle-aged men than aged-matched women, with a prevalence ranging from 34% up to 79%, depending on overweight or obesity status, respectively[3]. Moreover, cardiovascular disorders such as abdominal aortic aneurysm, coronary heart disease, peripheral arterial disease and cerebrovascular diseases are closely related with MS prevalence[4].

One of the main factors related to MS development is abdominal obesity[1]. Adipose tissue is recognized not only as a passive fat storage, but also an active metabolic and endocrine organ that secretes several peptide hormones responsible for energy balance, appetite modulation and inflammation, such as leptin, adiponectin, resistin, interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α)[5]. In this regard, an imbalanced chronic inflammatory status is closely linked to abdominal obesity, atherosclerosis, age-related sarcopenia and type 2 diabetes mellitus (T2DM)[6]. In fact, an infiltration of immune cells in adipose tissue, muscle, liver and pancreas has been associated with a shift from an anti-inflammatory to a pro-inflammatory frame that may disrupt insulin signaling in peripheral tissues and induce β-cell dysfunction[7].

Recent studies have also linked MS and obesity to poorer cancer outcomes including increased risk of recurrence and overall mortality[8]. Considering that higher levels of muscular strength are associated with lower cancer mortality risk in men[9] and in order to avoid the progression of obesity, subclinical inflammation[10] and insulin resistance[11] in middle-aged men, resistance training (RT) has been indicated. However, RT has produced conflicting results on inflammatory cytokines, adipose-derived cytokines (adipokines) and insulin-related parameters levels[12,13]. In fact, most studies concerning RT and high risk populations have utilized training intensities below 80% of one repetition maximum (1RM)[10-12], leaving aside possible benefits of hypertrophy RT programs on inflammatory profile. Therefore, the aim of this study was to investigate the effects of hypertrophy resistance training on glycaemic, cytokines and adipokines levels in men with metabolic syndrome risk factors.

Material and method

Subjects

After advertisements of the study and fully informed about the protocol, twenty-five men were recruited. The following inclusion criteria were considered: untrained[14] men aged between 40 and 65 years, that had at least two MS risk factors, such as triglycerides (TG) levels ≥150 mg/dL or specific drug treatment, high-density cholesterol (HDL) levels ≤40 mg/dL or specific drug treatment, fasting glucose levels ≥100 mg/dL or specific drug treatment, systolic blood pressure ≥130 and/or diastolic ≥85 mmHg or specific drug treatment and waist circumference (WC) ≥90 cm[1]. Moreover, volunteers were instructed to maintain their habitual food intake during the protocol. This study was approved by the Ethics Committee of the Federal University of Santa Maria (UFSM) (permit number: 0032.0.243.000-07), followed the statements of the Declaration of Helsinki and all participants signed a written informed consent.

Anthropometric Measurements

Subjects were weighted in a scale (Plenna, São Paulo, Brazil) and heighted 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) with the software "Body composition with sub regional analysis". Briefly, after 12 h fasting and 24 h without exercises and wearing only a light coat, subjects were laid in the designed corrected position on the DXA table and were instructed to remain still throughout the scanning procedure.

Functional Assessments

All tests described below were performed at same time of day, before and after the RT. A submaximal test was used to estimate 1RM in the bench press, rower machine, leg press and knee flexion machines. This test was utilized to estimate the largest load that an individual can move in a single maximal effort, and thus, to prescribe the training load[15,16]. Resting systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels were measured with a digital sphygmomanometer (Omron, Kyoto, Japan). Furthermore, flexibility of lumbar and hamstring muscles was assessed by the sit-and-reach test[16] and the longest distance reached on the measuring board was registered after three attempts. The cardiorespiratory fitness was assessed by Bruce's modified protocol[17] in a treadmill.

Resistance Training

The supervised RT was performed three days per week during 15 weeks, with 48-72 h of recovery between sessions. The RT protocol was briefly adapted from a previous study[18]. Sessions started with a low-intensity indoor walking for 10 min and was followed by the performance of alternating upper and lower limbs, and trunk exercises. Volunteers performed nine exercises: chest press, leg press, rower machine, leg curl, triceps extension, leg extension, biceps curl, trunk extension and abdominals[19]. The first two weeks of RT consisted of two sets of 15 repetitions at 55% of one repetition maximum (1RM). In weeks 3 and 4, subjects performed three sets of 12 repetitions at 65% 1RM. During weeks 5 to 8, the intensity ranged between 70-75% 1RM, and three sets of 10 repetitions were performed. During the last seven weeks, subjects worked out with three sets of 8 repetitions at 80% 1RM, designed to induce muscle hypertrophy[20]. There were rest periods of 1-2 min between sets and exercises[21]. After training sessions, volunteers performed stretching exercises: upper and lower back, shoulders, arms, chest, abdomen, thighs (back, front, inner and outer) and calves.

Biochemical Assays

Blood samples were drawn in the morning (07:00-08:30 a.m.) from a vein of the antecubital region after 12 h of fasting and 72 h without

exercise. Samples were collected into 4-mL serum separator or EDTA tubes (BD Diagnostics, Plymouth, UK), centrifuged at 1500 g for 15 min and supernatants were frozen at -80 ºC until analysis. Total cholesterol and HDL concentrations were determined using commercially available assay kits (Bioclin, Belo Horizonte, Brazil) on a Cobas MIRA® (Roche Diagnostics, Basel, Switzerland) automated analyzer. Serum TG and glucose levels were determined using commercial kits (Bio Técnica, Varginha, Brazil). The levels of low-density cholesterol (LDL) were estimated[22].

Serum levels of cytokines IL-1β, IL-6, IL-10, IL-18, TNF-α and interferon-gamma (IFN-γ) were determined by enzyme-linked immunosorbent assay (ELISA) using commercial kits (eBIOSCIENCE, San Diego, USA), according to manufacturer's instructions. IL-1β, IL-6 and IL-10 were sensitive to 2 pg/mL. TNF-α and IFN-γ were sensitive to 4 pg/mL and 4 µg/mL, respectively, while IL-18 was sensitive to 37 pg/mL. Plasma adiponectin (R & D Systems, Minneapolis, USA) and resistin (R & D Systems, Minneapolis, USA) were performed by ELISA, which was sensitive to 0.25 ng/mL and 0.023 ng/mL, respectively. Serum leptin and ghrelin (Diagnostic System Laboratories, Leawood, USA) were also analyzed by ELISA, which was sensitive to 0.05 ng/mL and 0.07 ng/mL, respectively. Insulin levels were also measured by ELISA using commercial kits (eBIOSCIENCE, San Diego, USA). Insulin resistance (IR) and beta cell function (BF) indexes were calculated using homeostasis model assessment (HOMA), where HOMA-BF: (fasting insulin [mU/L] x 20) / (fasting glucose [mmol/L] – 3.5) and HOMA-IR: (fasting insulin [mU/L] x fasting glucose [mmol/L]) / 22.5[23].

Nutritional Data

To minimize a possible bias, subjects were encouraged to maintain their habitual dietary intake during intervention and filled in a 3-day diet record before and after the RT. A specific software (Dietwin, São Paulo, Brazil) was used to determine total caloric intake and the amount of macronutrients ingested.

Statistical Analysis

Shapiro-Wilk test was carried out to verify data distribution. Afterwards, Student's t test or Wilcoxon Rank Test were used to determine significant differences between pre and post-training results. 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 ± standard deviation of the mean (SD).

Results

Twenty-one men (57.8 ± 7.74 years old) concluded the RT and were considered in the statistical analysis. Furthermore, the sample comprised three smokers and 18 nonsmokers, 39% of men took antihypertensive agents, 19% took lipid-lowering agents and 4.75% took oral hypoglycemic agents. Table 1 shows the results of submaximal strength test before and after RT. Increases in the load lifted/moved in the bench press ($p < 0.001$), leg press ($p < 0.001$), rower machine ($p < 0.001$) and knee flexion ($p < 0.001$) exercises were registered.

Furthermore, Table 2 demonstrates that RT resulted in significant improvements in hip circumference ($p = 0.028$), body fat ($p = 0.011$), lean mass ($p = 0.018$), and SBP ($p = 0.023$) levels, besides HDL reduction ($p < 0.001$). Moreover, the stretching performed before and after exercise sessions could have improved flexibility ($p = 0.001$). However, body mass, BMI, VO_{2max}, DBP, TG and total cholesterol levels remained unchanged.

Table 1. Load moved in the strength test along intervention (n=21).

Exercises	Before	After
Bench Press (kg)	65.12 ± 16.79	74.11 ± 10.05**
Rower machine (kg)	49.93 ± 6.51	63.38 ± 8.36**
Leg Press (kg)	100.50 ± 14.57	119.03 ± 21.25**
Knee Flexion (kg)	18.46 ± 2.83	22.98 ± 3.42**

Values expressed as mean ± SD. * $p < 0.05$ and ** $p < 0.001$ after *vs.* before the resistance training.

Table 2. Effects of resistance training on anthropometric, functional and biochemical parameters of men with metabolic syndrome (n=21).

Parameters	Before	After
Body Mass (kg)	86.69 ± 13.82	86.32 ± 12.90
BMI (kg/m^2)	28.98 ± 4.43	28.86 ± 4.17
Abdominal Circumference (cm)	105.60 ± 13.60	104.53 ± 13.10
Waist Circumference (cm)	101.30 ± 12.07	100.30 ± 12.18
Hip Circumference (cm)	107.07 ± 10.33	105.31 ± 9.45*
Body Fat Mass (%)	32.51 ± 5.02	31.90 ± 5.15*
Body Lean Mass (%)	64.12 ± 4.73	64.68 ± 4.87*
Systolic Blood Pressure (mmHg)	131.95 ± 16.29	124.23 ± 17.67*
Diastolic Blood Pressure (mmHg)	78.76 ± 9.66	75.52 ± 9.28
Flexibility (cm)	17.73 ± 11.56	21.08 ± 10.97*
VO_{2max} (mL.kg^{-1}•min^{-1})	37.61 ± 7.66	38.41 ± 9.48
Total Cholesterol (mg/dL)	206.61 ± 46.95	208.85 ± 40.96
Triglycerides (mg/dL)	174.87 ± 82.62	176.71 ± 58.62
HDL (mg/dL)	52.04 ± 14.17	43.47 ± 8.78**
LDL (mg/dL)	119.59 ± 43.21	130.03 ± 39.85

Values expressed as mean ± SD. BMI: body mass index. VO_{2max}: maximal oxygen uptake. HDL: high-density cholesterol. LDL: low-density cholesterol. * $p < 0.05$ and ** $p < 0.001$ after vs. before resistance training.

It is observed in Table 3 that RT did not change insulin levels, while it decreased glucose levels ($p < 0.001$), HOMA-IR ($p = 0.003$) and increased HOMA-BF ($p = 0.004$).

No significant differences were found in total ingestion of calories and macronutrients, demonstrating the maintenance of habitual intake during the intervention (Table 4).

Changes in cytokines are given in Figure 1. Serum levels of IL-1β ($p < 0.001$), IL-6 ($p < 0.001$), IL-18 ($p < 0.001$), TNF-α ($p < 0.001$) and IFN-γ ($p < 0.001$) decreased after RT. Moreover, participants showed higher levels of IL-10 ($p < 0.001$) after intervention.

As shown in Figure 2, RT decreased resistin (77.8 ± 5.56 *vs.* 58.57 ± 8.11 ng/mL; $p < 0.001$), ghrelin (49.47 ± 5.7 *vs.* 40.23 ± 7.45 pg/mL; $p < 0.001$) and leptin (140.57 ± 7.76 *vs.* 83.9 ± 10.94 ng/mL; $p < 0.001$)

Table 3. Effects of RT on glycaemic control parameters (n=21).

Exercises	Before	After
Glucose (mg/dL)	121.61 ± 34.28	96.09 ± 29.82**
Insulin (mU/L)	11.47 ± 5.96	10.42 ± 5.62
HOMA-BF (%)	87.25 ± 52.86	188.88 ± 174.7**
HOMA-IR index	3.54 ± 2.65	2.42 ± 1.36*

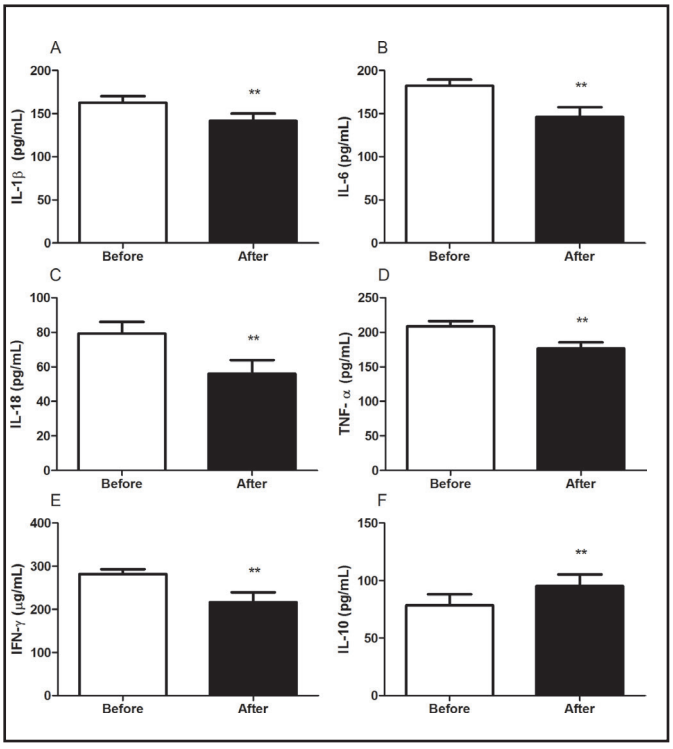
Values expressed as mean ± SD. *p < 0.05 and ** p < 0.001 after ***vs***. before the resistance training. HOMA-BF: homeostasis model assessment insulin resistance β cell function. HOMA-IR: homeostasis model assessment insulin resistance.

Table 4. Total calorie and macronutrients ingested before and after training (n=21).

Variables	Before	After
Total Caloric Intake (kcal)	2,731.19 ± 262.07	2,719.37 ± 220.97
Carbohydrates (g)	317.84 ± 29.57	314.83 ± 26.25
Proteins (g)	109.81 ± 15.22	113.04 ± 12.92
Lipids (g)	113.63 ± 17.85	111.98 ± 14.79

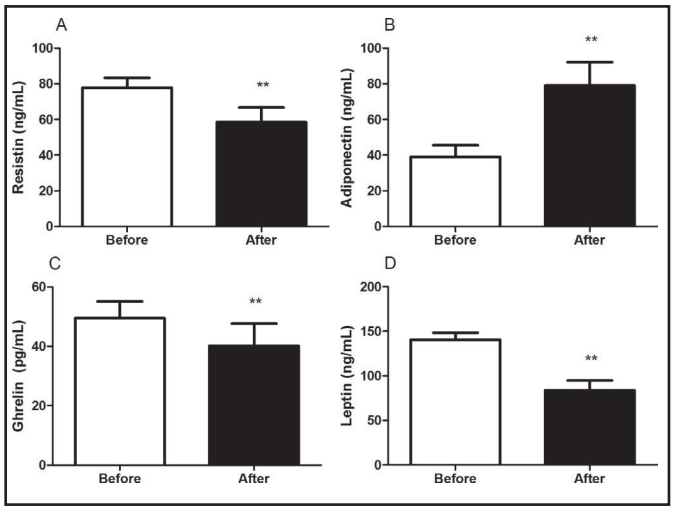
Values expressed as mean ± SD.

Figure 1. Effects of 15 weeks of hypertrophy resistance training on interleukin-1 beta (IL-1β) (A), interleukin-6 (IL-6) (B), interleukin-18 (IL-18) (C), tumor necrosis factor alpha (TNF-α) (D), interferon-gamma (INF- γ) (E) and interleukin-10 (IL-10) (F) levels in 21 men with metabolic syndrome risk factors.



Data are expressed as mean ± SD. * p < 0.05 and ** p < 0.001 after *vs*. before training.

Figure 2. Effects of 15 weeks of hypertrophy resistance training on resistin (A), adiponectin (B), ghrelin (C) and leptin (D) levels in 21 men with metabolic syndrome risk factors.



Data are expressed as mean ± SD. * p < 0.05 and ** p < 0.001 after *vs*. before training.

levels, while it resulted in increased levels of adiponectin (39.09 ± 6.41 *vs*. 79.14 ± 12.98 ng/mL; p < 0.001).

Discussion

This study aimed to investigate the effects of a supervised RT on glycaemic parameters, inflammatory and hormonal profile in men with MS risk factors. The main findings are that 15 weeks of hypertrophy RT reduced several pro-inflammatory cytokines, fasting glucose levels and HOMA-IR, together with improvements in body composition, even in the absence of weight loss. Moreover, RT increased loads moved during 1RM test, indicating a functional efficacy in the stimulus generated from training sessions. RT also resulted in modulation of resistin, ghrelin, leptin and adiponectin concentrations, independently of maintenance of total calorie and macronutrients ingested along the intervention.

Regarding criteria for the MS classification (SBP, DBP, WC, TG, HDL and glucose levels)[1], only fasting glucose concentrations and SBP were positively altered with the RT program. Indeed, a review with meta-analysis concerning the effect of RT on the treatment of MS characteristics and others variables showed no statistically significant effect of RT on HDL, TG and DBP[13]. Nevertheless, in the 13 interventions included in the aforementioned review, RT reduced resting SBP by 6.2 mmHg, similar with our findings. This SBP reduction is more prominent in RT programs with high volume (9 sets weekly per muscle group) than interventions with low volume (4-6 sets weekly per muscle group), and more pronounced in hypertensive patients at baseline[13]. This reduction of SBP induced by RT is independent of weight loss and probably linked with decreased catecholamine levels and systemic vascular resistance, with involvement of sympathetic nervous system and the renin-angiotensin system[13,24].

Changes in fasting glucose levels, HOMA-IR and HOMA-BF were observed after the hypertrophy RT. The improvements of insulin sensitivity and β-cell function in men with MS risk factors are in accordance

with results of another study involving a similar protocol of hypertrophy RT with sedentary, however, young men[18]. Several mechanisms have been proposed to explain reductions in glucose concentrations and insulin resistance after a RT program. Considering that exercise training increases both transporters GLUT-4 messenger RNA (mRNA) and protein expression, it is noteworthy that the expression of GLUT-4 at the plasma membrane of myocytes is associated with increased fiber volume in both slow and fast fibers[25]. Moreover, improvement of insulin-stimulated glucose uptake after exercise training has been attributed to enhanced intracellular postreceptor signaling via phosphatidylinositol 3-kinase (PI3K) activity and/or its phosphorylation[26]. It has also been demonstrated increased protein content of protein kinase B (Akt), *Akt* substrate of 160 kDa (AS160), GLUT4 and hexokinase, besides elevated activities of *Akt* and glycogen synthase in basal and in insulin-stimulated glucose uptake conditions, respectively, both following exercise training in healthy men[27]. Considering that insulin resistance over time leads to T2DM and its secondary complications, an attenuated insulin resistance after RT in men with MS risk factor is of major importance. It may be, therefore, hypothesized that improved β-cell function is due to decreased hepatic gluconeogenesis, attenuated insulin resistance in muscles and slowly wakening of β islets to secrete insulin, together with modulation of cytokines released by myocytes and adipocytes[28].

Furthermore, exercise training may enhance muscular glucose uptake via insulin-independent mechanisms. After six weeks of RT with one leg while the other remained rested, it was reported increased protein content of AMP-activated protein kinase (AMPK) isoforms in trained compared with untrained muscles in healthy and T2DM patients, showing that RT results in an up-regulation of AMPK[29]. In addition, AMPK phosphorylates AS160 in response to muscle contraction, may result in muscle GLUT 4 expression, biogenesis and translocation[30]. Since disturbances in fatty acid metabolism and the consequent accumulation of diacylglycerol and ceramide impair insulin signaling in skeletal muscle, AMPK activation results in the up-regulation of fatty acid oxidation[26].

Following RT, there were reductions in leptin, resistin and ghrelin, as well as elevation in adiponectin levels. Leptin is a hormone released from adipose tissue that affects satiety and energy balance, may trigger the growth of several cancer cells, and when it signals directly to their receptors on the surface of mononuclear white cells (MNC), the syntheses of TNF-α and IL-6 is stimulated[31]. In this regard, IL-10 is an important physiological contributor to the central leptin action mediated by exercise[32]. Adiponectin is another mainly adipose tissue-derived protein inversely correlated with body fat levels and known by improving insulin sensitivity and increasing fat oxidation, presenting anti-atherogenic and anti-inflammatory properties[12,33]. Adiponectin binds to adiponectin receptors AdipoR1 and AdipoR2, producing beneficial on insulin sensitivity, glycaemia and lipid profile via activation of AMPK, peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PPAR-α) and p38 mitogen-activated protein kinase (P38 MAPK) pathways in skeletal muscle, adipose tissue and liver[34,35]. This link between improved glucose metabolism and adiponectin levels, as observed after our RT protocol, highlights a fine crosstalk between the different markers measured.

In an interesting study, the impact of three different intensities of RT on adipokines levels in sedentary elderly subjects was compared. Low (45-50% of 1RM), moderate (60-65% of 1RM) and high (80-85% of 1RM) intensities of training decreased leptin and increased adiponectin levels, however, the greater changes in both adipokines were found in the high-intensity group, showing an intensity-dependent effect[33]. Authors attribute the greater decline in leptin levels induced by the higher intensity due to augmented sympathoadrenal discharge and caloric expenditure, glycogen depletion and acidosis in the repeated sessions, besides long-term decreased body fat stores responsible by leptin secretion[33]. Moreover, only four weeks of intensive aerobic training increased the expression of AdipoR1 and AdipoR2 in skeletal muscle and subcutaneous adipose tissue and circulating adiponectin levels of individuals with normal or impaired glucose tolerance or T2DM[36].

Ghrelin is synthesized and secreted from the stomach and small intestine, being responsible for appetite-stimulating and anti-inflammatory functions[37]. Most investigations have demonstrated no effects of exercise training in the absence of weight loss on ghrelin levels[37]. In this regard, the intensity of our RT protocol may explain this change. A recent study showed that an intervention combining aerobic and resistance exercises produced increased levels of ghrelin and concomitant reductions in CD14+/CD16+ monocytes, possibly via interaction with its receptor, the growth hormone secretagogue receptor[37]. In addition to the discussed above, ghrelin, leptin and adiponectin may lead to the production of several cytokines from MNC[37].

In the present study, hypertrophy RT also positively modulated several cytokines levels, lowering the subclinical low-grade inflammatory status presented in patients with MS. According to the literature, RT has produced discrepant results on cytokines[12], depending on age of subjects, basal levels of cytokines, influence of the last exercise session, biomarkers assessed, differences in subject populations, variation in frequency, duration and intensity of RT, among others. Evidences have shown that TNF-α is the first cytokine produced by the inflammatory cascade, is related to lower muscle mass and it causes insulin resistance by triggering different key steps instead of the normal insulin signaling pathway, while IL-6 is a marker of the MS[38]. Still, IL-18 is closely related to the development of MS[39].

It is important to distinguish the effects of chronic elevated levels of IL-6 (released by adipocytes and/or infiltrated MNC) from the acute and drastic several fold IL-6 augmented levels provoked by muscle contractions (released by myocytes). Contrary to severe infections, exercise-induced IL-6 activation is independent of previous activation of TNF-α[38], since intramuscular IL-6 is regulated by calcium/nuclear factor of activated T cells, AMPK and glycogen/ P38 MAPK[38,40]. Moreover, studies have demonstrated that IL-6 released from myocytes is an essential regulator of skeletal muscle hypertrophy mediated by satellite-cells[41], stimulates glucose uptake, IL-10 production and inhibits TNF-α production[38]. The cumulative effect of transitory increases on IL-6 levels promoted by sessions with resistance exercises is responsible for an important part of the anti-inflammatory effect of RT. Furthermore, taking into account that adipose tissue is an endocrine organ[38], a reduction in the adipose tissue content may influence the production and releasing of pro-inflammatory markers and several adipokines, as confirmed in the present study. Lastly, it has also been shown that RT leads to reduced mRNA expression of toll-like receptor (TLR4) and mRNA TNF-α in monocytes[42].

In conclusion, significant and positive modulation in systemic glycaemic, insulinemic and inflammatory parameters are found in men with MS risk factors after 15 weeks of hypertrophy resistance training.

These findings are parallel with improvements on body composition and independent of weight loss. Thus, the present findings demonstrate that hypertrophy resistance training programs may serve as a strategy for treatment of populations at high cardiovascular risk. Limitations in the current study comprise the absence of a control group.

Acknowledgments

The authors greatly thank the Laboratório de Análises Clínicas (LABIMED) and the Clínica Osteolab (Instituto de Densitometria Óssea) for the technical support and research incentive.

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