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Different modalities of exercise to reduce visceral fat mass and cardiovascular risk in metabolic syndrome: the RESOLVE* randomized trial

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A B S T R A C T

Background: Opinions differ over the exercise modalities that best limit cardiovascular risk (CVR) resulting from visceral obesity in individuals with metabolic syndrome (MetS). As little is known about the combined effects of resistance and endurance training at high volumes under sound nutritional conditions, we aimed to analyze the impact of various intensities of physical activity on visceral fat and CVR in individuals with MetS.
Methods: 100 participants, aged 50–70 years, underwent a diet restriction (protein intake 1.2 g/kg/day) with a high exercise volume (15–20 h/week). They were randomized to three training groups: moderate-resistance–moderate-endurance (re), high-resistance–moderate-endurance (Re), or moderate-resistance–high-endurance (rE). A one-year at-home follow-up (M12) commenced with a three-week residential program (Day 0 to Day 21). We measured the change in visceral fat and body composition by DXA, MetS parameters, fitness, the Framingham score and carotid-intima–media-thickness.
Results: 78 participants completed the program. At D21, visceral fat loss was highest in Re (−18%, $p < .0001$) and higher in rE than re (−12% vs. −7%, $p < .0001$). Similarly, from M3, visceral fat decreased more in *high-intensity-groups* to reach a visceral fat loss of −21.5% (Re) and −21.1% (rE) > −13.0% (re) at M12 ($p < .001$). CVR, MetS parameters and fitness improved in all groups. Visceral fat loss correlated with changes in MetS parameters.
Conclusion: Increased intensity in high volume training is efficient in improving visceral fat loss and carotid-intima–media-thickness, and is realistic in community dwelling, moderately obese individuals. High-intensity-resistance training induced a faster visceral fat loss, and thus the potential of resistance training should not be undervalued (ClinicalTrials.gov number: NCT00917917).

1. Introduction

Visceral fat accumulation is a primary cardiovascular risk (CVR) factor, highly related to morbidity and mortality [1]. According to the International Diabetes Federation's (IDF) definition of metabolic syndrome (MetS), abdominal obesity is an essential factor for diagnosis [2]. The significance of visceral obesity appears so clear that some authors have discussed a 'visceral fat syndrome' [3].

In individuals with MetS, lifestyle modification (restrictive diet + physical activity) has priority over pharmaceutical intervention to reduce visceral adiposity [3]. Evidence-based physical activity guidelines for treating MetS remain under debate, especially in long-term interventions. Randomized studies highlight the role of physical activity in reducing metabolic disorders and CVR independent of the modalities (endurance, resistance or both) [4–16]. Comparison of prescribed exercise showed resistance training to be more effective in reducing metabolic risk than endurance training [9,11], and endurance plus resistance yielded better results than endurance alone or

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resistance alone [6,10]. Moreover, the beneficial effects of training on MetS parameters are positively linked to higher training intensities [12,13,16]. However, the current decrease in interest for resistance [17] is probably excessive and that this kind of training could be truly efficient when applied at a sufficient volume [18] and in sound nutritional conditions (sufficient protein intake) [19].

From these observations, we hypothesized that a restrictive diet combined with a high volume (15–20 h/week) mixed training performed at a high intensity would improve visceral fat loss, and that high-intensity-resistance training would result in a greater losses than endurance training.

Hence, the aim was to conduct a one-year follow-up randomized trial to examine the effects of intensive lifestyle intervention on parameters of MetS in obese seniors. The follow-up was initiated by a three-week residential program during which participants progressively learnt the physical exercises and the nutritional information necessary to sustain the program at home. We specifically examined how cardiometabolic risks could be reduced using the Framingham score and the carotid-intima–media-thickness (CIMT) as a measure of atherosclerotic progression. This study is the principal investigation of the RESOLVE trial: REverse metabolic SyndrOme by Lifestyle and Various Exercises.

2. Methods

2.1. Patient recruitment and inclusion criteria

Participants were recruited via advertisements. They provided written informed consent. The study was reviewed and approved by the human ethics committees from St Etienne, France. To be eligible, participants were: aged between 50 and 70 years, symptomatic of MetS [2], with a sedentary lifestyle, stable body weight and stable medical treatment over the previous 6 months, post-menopausal for women, no hepatic, renal, or psychiatric diseases, nor cardiovascular or endocrine diseases except those defining MetS, no HIV infection, no use of medications altering body weight (supplementary file), no restricted diet in the previous year, and with a satisfactory completion of a maximal exercise tolerance test (VO_2 max) (Fig. 1).

For baseline references, data were obtained from an age matched control group of healthy participants without any of the defined criteria of MetS [2] and chronic disease, and no routine medication. They also had to report unchanged lifestyle over the previous 12 months, and less than three hours per week of physical activity (Fig. 1).

2.2. Outcomes

The primary outcome was the change in central fat. Secondary outcomes were the changes in factors defining the MetS, body composition, fitness and CVR.

2.3. Baseline assessments

Central fat, a surrogate of visceral fat, was assessed from dual-energy X-ray absorptiometry (DXA, Hologic QDR 4500 series; Waltham, USA), according to Kamel et al. [20]. Total body mass, fat mass, lean body mass, and bone mineral content of the whole body were measured by DXA. The in vivo coefficients of variation (CV) were 4.2, 0.4 and 0.5% for fat, lean and bone masses, respectively. Our laboratory also reports a CV of 1.6% in central fat measures in 20 participants.

Waist circumference was measured at midpoint between sub-costal and supra-iliac landmarks [21]. Blood pressure and heart rate were measured after 15 min rest, using an automated upper arm sphygmomanometer (SunTech Medical, Model 222).

Strength was evaluated by summing the maximum load of 10 repetitions from three prescribed exercises (bench press, leg extension, biceps curl) [22]. Endurance was assessed by the six-minute walk test (6MWT) [23]. Cardiorespiratory testing on ergocycle was completed initially to determine the specific goals to reach during the exercise training sessions using the linear VO_2-heart rate association [24].

Three-day self-report questionnaires on food intake and physical activity allowed the calculation of daily energy intake and daily energy expenditure. Basal metabolic rate was calculated using the equations of Black [25].

The common carotid artery structure was evaluated using a high-resolution B-mode ultrasound (MyLab30, Esaote SpA, Firenze, Italy) [26]. The CIMT was defined as the distance from the leading edge of the lumen–intima interface to the leading edge of the media–adventitia interface of the far wall. The CIMT of the left CIMTs was measured automatically by dedicated software (MyLab desk 9.0, Esaote, Florence, Italy) according to the Mannheim consensus [27].

Individual risk factor scores were summed to determine the 10-year absolute risk of cardiovascular disease using Framingham score [28].

Routine medications were recorded. All participants were advised to continue their medications.

2.4. Follow-up assessments

All baseline assessments were repeated at 21 days (D21), 3 months (M3), 6 months (M6) and 12 months (M12), with the exception of VO_2-peak measured only at baseline and the CIMT, which was not measured at M12 (Fig. 2). The self-report questionnaires on food intake and physical activity were completed each month.

2.5. Randomization

Participants were randomly assigned, (computer-generated randomization) with stratification according to sex, age and body mass index, to one of the following groups:

- Re—high-*R*esistance–moderate-*e*ndurance—performed 10 repetitions at 70% of one maximal repetition in resistance and 30% of VO_2-peak for endurance training,
- rE—moderate-*r*esistance(30%)–high-*E*ndurance(70%),
- re—moderate-*r*esistance(30%)–moderate-*e*ndurance(30%).

All participants followed the same restrictive diet.

Assessors for all outcomes were blinded to the participants' group assignment. All outcome data remained blinded until the end of the study.

2.6. First stage of intervention: a 3-week residential program

Participants attended lectures and workshops on the MetS taught by dieticians, physicians and coaches dealing with nutrition, cooking and exercise in order to maintain this lifestyle on returning home [18].

Daily throughout the residential program, the patients received both standard and personalized balanced meals prescribed by dieticians. Protein accounted for 15 to 20% of the total energy intake (1.2 g/kg/day to maintain protein homeostasis) [19], lipids 30 to 35%, and carbohydrates the remaining. Their total daily food intake was calculated to enable them to reach a negative energy balance of 500 kcal/day.

The participants were coached daily individually [18], within the context of their assigned group. The same time (15–20 h/week) was spent by all groups in endurance (90 min daily) plus in resistance (90 min four days a week). Exercises differed only in intensity, from 30% to 70%. Participants' heart rate was monitored by Polar™ S810 with instantaneous recording and storage of heart rate values. Endurance training included aquagym, cycling and walking. Resistance training consisted of 8 exercises with free weights and traditional muscle building equipment. Each exercise was performed for three sets of 10 repetitions.

2.7. Second stage of intervention: a 1-year at-home follow-up

From D21 to M12, the participants were required to complete the same training program by themselves. At M3, M6 and M12, the participants were seen by the dietician and physical coach.

A compliance score was determined on the basis of the number of food questionnaires returned (score from 0 to 12 i.e. 12 = 100%) and the number of training sessions undertaken per week (score from 0 to 4, i.e. 4 = 100%). The overall compliance score was the mean of these two scores (nutrition and physical activity).

2.8. Statistical analysis

Data are presented as mean percentage change and standard deviation (SD).

Results of a previous similar intervention [18] showed that a central fat loss of 600 ± 800 g was required to differentiate between physical activity groups. Using this value as the main outcome, we calculated that a sample of 30 participants per group allows a statistical power greater than 80% with an alpha level less than 5%, allowing a dropout rate of 20%.

Statistical analyses were performed with SPSS software, v19. The Gaussian distribution for each parameter was assessed by a Shapiro–Wilk test. In case of non-normal distribution, the data were log-transformed for analysis. A Chi-square test was performed to verify the distribution of gender within each group of participants. Baseline characteristics were compared between groups using an analysis of variance. Longitudinal changes between groups were tested with a one-way ANCOVA with repeated-measures using baseline values as covariates. The primary focus of the analyses was the 12-month change in central fat mass. Matrix of correlation between the main parameters of the MetS was determined using a nonparametric Spearman test. For the repeated measures and in presence of interaction between group and time, the factor time was blocked in order to test the potential differences at each step. We performed a descriptive statistical analysis for participants who dropped out to compare their characteristics with those of participants who completed the program.

2.9. Role of the funding source

The Heart and Diseases Foundation funded this study. The funding source had no role in the design, conduct, or reporting of the study.