Effectiveness of two aerobic exercise programs in the treatment of metabolic syndrome: a preliminary study

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Abstract

The effectiveness of two aerobic exercise programs on the modification of the metabolic syndrome (MS) components and its influence on cardiovascular risk (CVR) was assessed in 16 sedentary women (30-66 years old). The patients were randomized into two groups: continuous exercise (CE), 45 min at 65-70% heart rate reserve (HRR); and interval exercise (IE), five 3-min intervals at 80-85% HRR with 2-min active recovery at 65-70% HRR, after previously obtaining signed informed consent. The MS components were assessed according to the National Cholesterol Education Program/ Adult Treatment Panel III (NCEP/ATP III) criteria, as well as CVR parameters at baseline and after 16 weeks. Data analyses were performed using the Wilcoxon signed test and the Mann-Whitney U-test (Statistical Package for the Social Sciences [SPSS] v.12.0 for Windows; p < 0.05). Both programs were effective in modifying some components (triglycerides [TG], blood pressure); however, IE had a higher percentage of participants without a MS diagnosis by the end of the study (62.5%). CE improved physical fitness by increasing the peak oxygen uptake (VO_{2peak}) and metabolic equivalents (MET) and reducing heart rate recovery, which largely favors the reduction of CVR. (Gac Med Mex. 2014;150:486-93)

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Introduction

The metabolic syndrome (MS) is an entity characterized for clustering a series of cardiovascular risk (CVR) factors, such as abdominal obesity, dyslipidemia, hypertension, glucose intolerance and insulin resistance[1]. Its presence is associated with an increased development of chronic diseases such as cancer and type 2 diabetes mellitus. Additionally, there is a 2-fold increase in the risk for the development of cardiovascular conditions, mortality due to cardiovascular disease and stroke, and a 1.5-fold increase in all-cause mortality[2].

In the past few decades, the prevalence of MS has grown worldwide and has been associated with increased obesity and diabetes[3]. In Mexico, according to the 2006 National Survey on Health and Nutrition (ENSANUT 2006), MS was present in 41.6% of the adult population, and its frequency was higher in women than in men (47.4 *vs.* 34.7%, respectively)[4]. Considering the accelerated increase in overweight and obesity in our country over the past few years (61.8% in the year 2000 and 71.28% in 2012)[5,6], the prevalence of the syndrome is likely to have increased as well.

Most MS-associated risk factors can be modified through lifestyle changes. Increasing physical activity and exercise has been advocated by a number of studies and organizations for the treatment and prevention of metabolic conditions[7,8]; however, "lack of time" remains one of the most quoted barriers to its regular practice[9,10]. Different aerobic exercise models assessing different training intensities, volumes and time have been studied[11-14]. Some authors have established the efficacy of high intensities (90% of maximal heart rate) and low volume; however, its execution may be reduced in this population considering the functional limitations many patients have, including joint pain or deterioration and high CVR, which is why it is essential offering training programs with tolerable intensities and

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efficient volumes that favor the reduction of cardio-metabolic disease risk factors and have an impact on the adoption of lifestyles that decrease sedentarism.

The purpose of this study was to assess the effectiveness of two aerobic exercise programs on the modification of components that define the MS and their influence on CVR.

Material and methods

Sedentary women, aged 30-66 years, diagnosed with MS according to the NCEP/ATP III criteria were included[15]. Patients with a body mass index (BMI) > 40 kg/m^2, uncontrolled or insulin-dependent diabetes, exercise-induced severe arterial hypertension (systolic > 200 mm Hg, diastolic > 110 mm Hg), renal impairment (creatinine > 1.5 mg/dl) or contraindications to the practice of exercise according to the American College of Sports Medicine (ACSM)[16] were excluded from this trial. Pre-participation risk was stratified according to the ACSM.

Patients not complying with 80% attendance to the exercise program were withdrawn from the study. All patients were informed on the objectives and the interventions to be made in the study, and acceptance to participate was established by signing the informed consent form, in compliance with the Declaration of Helsinki for the conduction of research with human beings. The study was approved by the Research Committee of the Instituto Nacional de Rehabilitación (INR).

Study design

Controlled clinical trial carried out at the INR's Centro Nacional de Investigación y Atención en Medicina del Deporte (CENIAMED) of the Ministry of Health. The study was conducted with a convenience sample by making the recruitment of patients over a 12-month time period, which is why the sample size corresponded to the number of patients who agreed to participate and met the inclusion criteria during this period.

Patients meeting the inclusion criteria were randomly assigned in a 1:1 ratio to two parallel groups: continuous exercise (CE) group and intermitent exercise (IE) group. All patients kept a logbook to record the exercise sessions.

Anthropometric measurements were carried out and biochemical parameters were determined to assess the MS components. CVR was evaluated using a maximal stress test, which was established as the patient reaching > 85% of the maximal predicted heart rate on the treadmill, following the modified Bruce protocol[17,18]. All assessments were made at baseline and 16 weeks later for both groups.

During the intervention, the patients continued with their usual diet in order to focus exclusively on the effects of exercise and to avoid interference by other variables, such as dietary habits modification.

Anthropometric assessment

Body weight and height were measured using an electronic scale and stadiometer (Bame brand, model 427, Mexico) with the patients wearing light clothes and, afterwards, the BMI was calculated. Waist circumference was determined at the level of the navel; body density, by means of the Durnin-Womersley equation; fat mass percentage, with Siri's formula, and muscle mass percentage, using Matiegka's four-component method[19-21].

Biochemical assessment

The patients were instructed to avoid alcohol consumption and practicing exercise 24 h before samples were obtained. Blood levels with at least 8-h fasting were determined for glucose (mg/dl), total cholesterol (mg/dl), triglycerides (TG) (mg/dl), high and low-density lipoproteins (HDL and LDL, respectively) (mg/dl) and C-reactive protein (mg/l), all of them in serum. Insulin sensitivity was determined indirectly using the TG/HDL ratio, with resistance established at values > 3.0[22,23], and the cholesterol/HDL ratio to assess the presence of CVR, with low risk being regarded as values < 4.5[24]. The samples were processed at the INR Central Laboratory.

CVR assessment

The patients performed the maximal treadmill stress test following a 12-lead electrocardiogram at rest. The following CVR parameters were measured: heart rate recovery in the 2nd minute after the challenge (Rec Min 2), systolic blood pressure recovery at the 3rd minute post-exercise (PBP3), heart rate at rest (HR_{rest}), indirectly achieved VO_{2peak} and METs.

Exercise program

Both groups were prescribed an individualized and supervised exercise program during 16 weeks (3 days/week). The program was divided in three stages: the first, a 4-week anatomical and physiological adaptation

Table 1. Exercise programs characteristics

Week 0-4: adaptation; equipment: Swiss ball		
Description: proprioception exercises, core strengthening, open and closed kinetic chain exercises		
Frequency: 3 days/week		
Volume: 1 h/day		
Week 5-6: aerobic induction; equipment: treadmill/stationary bike		
Description:		
Frequency: 3 days/week		
Intensity: 65-70% HRR		
Volume: 30 min/day		
Week 7-16: training program; equipment: treadmill/stationary bike		
Description:	CE	IE
Frequency:	3 days/week	3 days/week
Intensity:	65-70% HRR	5 intervals: 3 min (80-85% HRR) with 2-min (65-70% HRR) active recovery
Volume:	45 min/day*	25 min/day*

*Each exercise program considered 5-min warm up and 5-min cool down additional periods.

period in order to achieve adherence to exercise; the second, a 2-week general training period aiming to enhance physical fitness, and the last, which involved the 10-week training program. During the first 4 weeks, proprioception exercises, core strengthening and open and closed kinetic chain exercises were performed in 1-h sessions. Over the next two weeks, aerobic exercise was practiced, 30 min at 60-65% HRR intensity. The training phase for the CE group involved 45 min of exercise at 65-70% HRR, whereas for the IE group it was five 3-min intervals at high intensity (80-85% HRR), with 2-min active recovery (65-70% HRR) between intervals. Both groups had a 5-min warm up with the chosen equipment, at the beginning of the exercise and a 5-min cool down period at the end of it, which added up to 55 min of exercise for the CE group and 35 min for the IE group (Table 1).

Each session was preceded by warm up exercises (joint mobilization and stretching) and stretching exercises were performed at the end. The aerobic exercise sessions were made alternating the treadmill and the stationary bike in order to avoid monotony and to favor adherence to the program. Aerobic work intensity was controlled in all sessions by means of the heart rate using transmitters (Polar Electro, model T31C, Finland), making sure the training load was the assigned one.

Statistical analysis of the results

All analyses were carried out using the SPSS v.12.0 software (Chicago, IL, U.S.A.) for Windows. The results were reported as medians and limits. The Wilcoxon signed-rank test was used for paired data and the Mann-Whitney U-test for independent data, in order to examine the significance of the changes in the study variables within each group and between groups. In all cases, a p-value < 0.05 was considered to be significant.

Results

Initially, the sample was comprised by 36 patients, but during the course of the research, 20 participants were withdrawn from the trial: 16 patients due to lack of adherence, one due to change of residence and the remaining three due to left hand hamate bone fracture, myocardial infarction and left ear surgery; none of these events were related with the exercise program (Fig. 1). At the end of the study, the groups were comprised by eight patients per group. The statistical analysis was conducted with data obtained from these 16 patients. During the exercise programs, the patients reported events such as: dizziness (20.0%), headache (16.6%), hypotension (10.0%) and gonalgia (53.0%), which occurred in isolated sessions, were treated on a timely basis and did not affect the continuity of the program; 80% of the reported events occurred in the CE group, whereas 20% occurred in the IE group. The attendance rate was 94.7% for the CE group and 95.8% for the IE group.

MS components

Both groups were comparable in the MS-defining components baseline values, as well as in the rest of

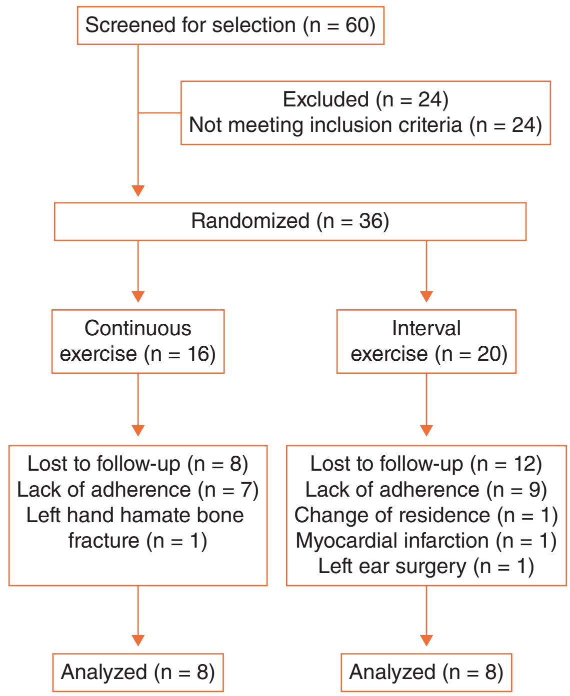

Figure 1. *Patient flow during the study.*

Table 2. MS components according to the ATPIII criteria

	CE		IE	
	Baseline (n = 8)	**Final (n = 8)**	**Baseline (n = 8)**	**Final (n = 8)**
Waist (cm)	93.1 (72.4-127.9)	92.3 (74.2-122.7)	94.8 (83.0-109.0)	94.4 (86.6-106.0)
Glucose (mg/dl)	104.0 (86.8-143.6)	102.8 (83.8-122.7)	100.5 (89.9-120.6)	102.9 (93.6-120.7)
TG (mg/dl)	271.4 (147.8-407.7)	147.2 (85.7-287.3)*	199.7 (156.1-267.2)	136.6 (103.7-309.1)*
HDL (mg/dl)	42.5 (34.0-121.8)	45.2 (12.3-49.9)	43.3 (25.0-115.0)	32.8 (16.2-47.6)*
SBP (mmHg)	115.0 (100.0-160.0)	115.0 (100.0-130.0)	120.0 (100.0-130.0)	110.0 (110.0-120.0)
DBP (mmHg)	80.0 (60.0-90.0)	80.0 (70.0-90.0)	80.0 (60.0-90.0)	80.0 (80.0-80.0)
Number of components	**Number of patients (%)**			
One	–	1 (12.5)	–	2 (25.0)
Two	–	1 (12.5)	–	3 (37.5)
Three	4 (50)	3 (37.5)	5 (62.5)	1 (12.5)
Four	4 (50)	3 (37.5)	3 (37.5)	2 (25.0)

Data presented as medians and limits (minimum-maximum).
*Wilcoxon test ($p < 0.05$).

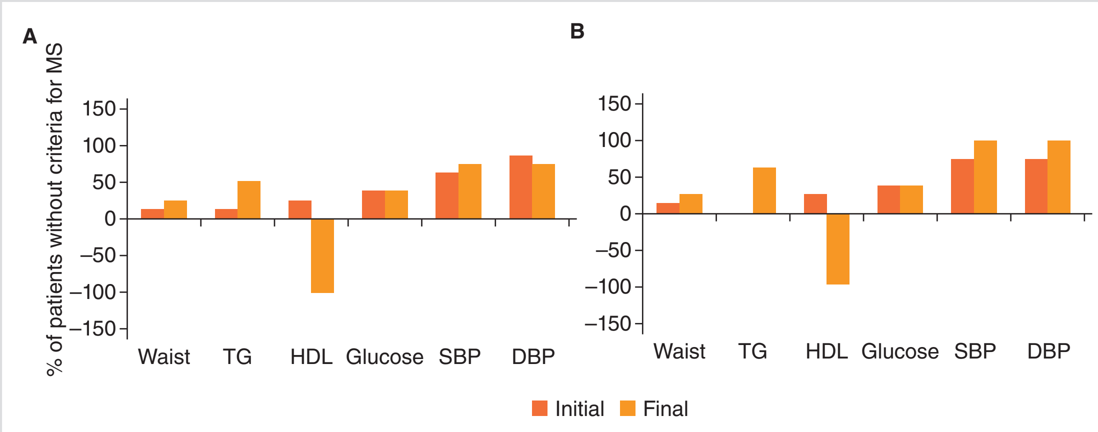

Figure 2. *Modification of ATP III criteria for MS after the exercise programs.* ***A:*** *group with CE.* ***B:*** *group with IE. ATP III criteria: waist > 88 cm, glucose > 100 mg/dl, TG > 150 mg/dl, HDL < 50 mg/dl, SBP ≥ 130 and DBP ≥ 85 mmHg.*

the assessed parameters. After 16 weeks of intervention, there were no important changes between groups (Table 2). TG were decreased significantly in both groups with regard to their baseline values and reached normal values (CE: $Z = -2.521$; $p = 0.012$; IE: $Z = -1.96$; $p = 0.05$), whereas HDL decreased significantly in the IE group ($Z = -1.992$; $p = 0.046$). At the end of the intervention, 25% of CE group participants had no longer MS, as compared with 62.5% in the IE group. The components that reached normality criteria and excluded participants from the diagnosis were, in order of frequency: TG, waist circumference and systolic and diastolic blood pressure (SBP and DBP, respectively) (Fig. 2).

CVR

Resting heart rate decreased in the CE group at 16 weeks ($Z = -2.521$: $p = 0.012$), whereas in the IE group, PBP3 ($Z = -2.380$; $p = 0.017$) and Rec Min 2 ($Z = -2.384$: $p = 0.017$) were improved (Table 3). The CE group improved in VO_{2peak} and MET with regard to baseline values ($Z = -2.333$; $p = 0.020$) (Table 3). The atherogenic index remained at values higher than 4.5 in both groups by the end of the study.

Additional assessments

Both interventions favored weight loss (CE: $Z = -2.524$; $p = 0.012$; IE: $Z = -2.527$; $p = 0.012$) and BMI (CE: $Z = -2.524$; $p = 0.012$; IE: $Z = -2.521$; $p = 0.012$) at the end of the study, whereas CE favored a decrease in fat mass percentage ($Z = -2.240$; $p = 0.025$) and an increase in muscle mass ($Z = -2.173$; $p = 0.030$) (Table 3). The change in TG/HDL ratio was more apparent in the CE group, which reached values suggestive of insulin sensitivity (2.9); however, no significant differences were observed.

Discussion

In this study, the effectiveness of two aerobic exercise programs was assessed in the reduction of components defining the MS, as well as their influence on CVR. The results demonstrated that both proposed programs were effective in modifying some components, which is consistent with those from other studies, where no difference was found between CE and IE[25]; however, IE had a higher percentage of participants no longer meeting the diagnostic criteria for MS at the end of the intervention.

The program for the IE group proposed in this study was effective even with a low training volume (105 min/week) when compared to other programs where volumes of at least 120 min/week and with intensities higher than 90% VO_{2peak} were used[14,26,27], which favored the low rate of adverse events during the study, and thus, it can be proposed as a treatment alternative that implies less time spent and more safety for its execution.

Table 3. MS-related parameters before and after the intervention

	CE		IE	
	Baseline	**Final**	**Baseline**	**Final**
Anthropometric parameters				
Age (years)	48.5 (32.0-66.0)	49.5 (33.0-66.0)	40.0 (31.0-64.0)	40.5 (31.0-64.0)
Height (cm)	1.51 (1.49-1.57)	1.51 (1.49-1.57)	1.58 (1.43-1.71)	1.58 (1.43-1.71)
Weight (kg)	71.3 (48.3-83.7)	66.4 (45.4-79.6)*	73.7 (63.8-101.1)	71.8 (61.6-98.5)*
BMI (kg/m^2)	29.9 (21.2-37.7)	28.3 (20.2-35.8)*	29.5 (27.0-39.0)	28.7 (26.3-37.5)*
Fat mass (%)	37.9 (34.4-43.3)	36.6 (32.6-41.0)*	37.7 (24.9-42.2)	36.6 (21.7-41.8)
Muscle mass (%)	27.4 (22.6-31.5)	29.5 (25.2-31.9)*	27.8 (20.5-37.4)	30.0 (26.6-38.8)
Additional biochemical parameters				
Cholesterol (mg/dl)	235.6 (163.0-279.7)	203.0 (186.2-245.6)	204.2 (149.0-253.6)	198.5 (140.4-235.9)
LDL (mg/dl)	108.0 (87.7-161.5)	144.8 (131.3-186.9)	107.3 (63.3-136.7)	126.8 (92.2-178.1)
TG/HDL	5.1 (2.38-9.5)	2.9 (1.9-17.2)	4.4 (1.3-10.6)	3.7 (3.3-19.0)
TC/HDL	5.08 (2.30-6.96)	6.86 (3.92-15.09)	4.91 (2.03-6.32)	7.04 (5.35-11.73)
CVR				
VO_{2peak} ($ml*kg^{-1}*min^{-1}$)	35.1 (16.5-35.1)	45.4 (24.5-45.4)*	35.1 (24.0-45.4)	35.1 (24.0-45.4)
MET	10.05 (4.7-10.0)	12.9 (7.0-12.9)*	10.0 (6.8-12.9)	10.0 (6.8-12.9)
HR_{rest} (bpm)	90.0 (76.0-96.0)	72.0 (55.0-86.0)*	74.5 (53.0-100.0)	73.5 (54.0-87.0)
PBP3	0.8 (0.73-1.4)	0.63 (0.59-1.6)	0.78 (0.46-0.93)	0.63 (0.37-0.71)*
Rec Min 2 (bpm)	38.5 (22.0-52.0)	42.5 (27.0-65.0)	38.5 (31.0-60.0)	40.5 (33.0-62.0)*

Data presented as medians and limits (minimum-maximum).
*Wilcoxon test ($p < 0.05$).

With regard to the influence of the programs on the metabolic components of the syndrome, it has been established that aerobic exercise increases sensitivity to peripheral insulin through an enhanced coordination between the release of glucose (higher capillary perfusion), membrane surface transport (glucose transporter type 4 [GLUT-4] receptors activity) and intracellular flow of the substrate due to glycolysis[28]. Although insulin sensitivity is not a component for the diagnosis of the syndrome, it plays an important role in the prediction of the development of type 2 diabetes mellitus and in the risk for cardiovascular diseases. In this study, neither of both programs produced a significant decrease in fasting glucose levels; however, a decrease was observed in the TG/HDL ratio, suggesting there was an improvement in peripheral response.

The TG/HDL ratio has been used as a marker to determine insulin resistance because it is easy to be measured at low cost; however, its usefulness in different populations has been questioned due to ethnical factors[29]. Although the cut-off point of 3 in the Mexican-American population shows high sensitivity and especificity values (64.1 and 71.1%, respectively)[30], its application should be considered cautiously in the Mexican population due to the high prevalence of hypertriglyceridemia and hypoalphalipoproteinemia in the country[31], which suggests that the cut-off point could be different.

Both programs influenced on the lipid metabolism and are effective in the reduction of TG levels; total cholesterol levels did not show relevant changes, and an increase in LDL levels was observed, which was non-significant. Conversely to that what was expected, there was no increase in HDL concentrations, which even decreased significantly in the IE group.

The increase in HDL levels has been associated with a rise in VO_{2peak}, higher caloric uptake and a decrease in body fat mass[32-34]. In this study, the CE group improved significantly the VO_{2peak} and reduced the fat mass percentage; however, these changes did not favor the increase in HDL. The decrease in the levels of these proteins following the interventions can be explained as a modification in their structure and their inflammatory/anti-inflammatory properties. Kraus et al. observed that aerobic exercise at different volumes and intensities modifies HDL concentration and favors its conversion into longer particles with cardioprotective function (HDL_2 subspecies), even in the absence of significant weight loss; and Roberts et al. demonstrated that, after an intervention with diet and exercise in subjects with CVR factors, the protective capability of HDL to prevent LDL oxidation increases even when its concentration decreases, suggesting that the lifestyle modification-associated anti-inflammatory function should be more important than HDL levels when the atherogenic risk is assessed[35,36].

In this study, the TC/HDL ratio remained without significant changes in both groups, indicating the presence of risk for cardiovascular conditions. Importantly, only HDL total concentration was measured, without the HDL_2 and HDL_3 subspecies being determined. A 12-week aerobic exercise program with a caloric uptake of at least 1,500 kcal/week has been shown to be enough to generate a change among HDL subspecies, which results in a healthier cholesterol distribution without an apparent change in its concentration[37]. The exercise programs designed for this study promoted a caloric uptake of 1,639 and 2,603 kcal/week for the IE and CE groups, respectively, which was sufficient stimulus to achieve a better cholesterol distribution.

The exercise programs proposed in the present study did not show significant differences in terms of CVR reduction; however, the CE group improved the VO_{2peak} and MET values with regard to their baseline values. It has been established that for each MET of increase in functional capability, mortality is reduced by 15-19%[38,39], whereas for each ml*kg^{-1}*min increase in aerobic capacity, there is a 9-10% cardiovascular mortality reduction[40]. On the other hand, the IE group reduced the PBP3 and improved the Rec Min 2, which may indicate a decrease in the risk for coronary heart disease[41,42].

This study included a 6-week exercise-induction program prior to the specific aerobic programs, which allowed for patients to better adhere to the training program and to prevent lesions, since exercises proposed for this program favor proprioception, neuromotor coordination and improve core stability[43,44].

This study has several limitations: the number of participants that completed the intervention was small considering the initial number of patients who agreed to participate and the prevalence of MS in our country; lack of adherence to the program was significant, which is why it is important to conduct studies assessing the reasons for this behavior; the diet was not controlled, which could have influenced on the absence of changes in some variables, although the aim of the study was to evaluate the effect of exercise *per se*; and it was not possible to assess the HDL subspecies in order to confirm that the changes observed with both programs promoted the anti-inflammatory status. On the other hand, the main strengths were: supervision of the patients during the execution of the exercise programs in order to ensure that the work-up done was at the established intensities and volumes, and the follow-up of adverse events during the execution of the programs in order to establish the difficulties of patients to perform the exercise, which contributed to promote the safety of the study.

An aerobic exercise program requiring less time spent and with intensities that allow for the patient to practice it regularly may influence on the prevention of MS components progressing to specific disorders, such as cardiovascular conditions and type 2 diabetes[45]. The IE program proposed in this study might be an effective treatment alternative with regard to the time required for its execution, with similar effects to CE programs that involve large volumes; however, further studies are required including larger numbers of patients, which will allow for the conclusion to be strengthened.

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