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Original article

Is it possible that a cardiac rehabilitation program can reduce the cardiovascular risk in individuals with metabolic syndrome?

É possível que um programa de reabilitação cardíaca reduza o risco cardiovascular em indivíduos com síndrome metabólica?

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ABSTRACT

Background: Metabolic syndrome is a complex disorder represented by a set of cardiovascular risk factors usually related to central fat deposition, insulin resistance, hypertension, and dyslipidemia. It is associated with accelerated atherosclerosis in response to chronic inflammation and vascular endothelial dysfunction, increasing overall mortality. **Objective:** We aimed to evaluate the effect of a cardiac rehabilitation program on cardiovascular risk factors in patients with metabolic syndrome. **Methods:** This is prospective interventional study. All patients underwent a 20-session cardiac rehabilitation program with aerobic and resisted exercises as well as an educational program for lifestyle changes. **Results:** Forty-seven patients participated in the present study. After the cardiac rehabilitation program (CRP), a significant reduction ($p = 0,0092$) for cardiovascular risk and fatigue ($p > 0.001$) was observed; 78% of the patients had positive effects on physical capacity, 72% of the patients presented HbA1c reduction, 51% increased HDL-cholesterol, 70% reduced total cholesterol, 63% reduced triglycerides, 61% reduced systolic blood pressure and 53% reduced diastolic blood pressure. **Conclusion:** Cardiac rehabilitation program with aerobic and resisted exercises associated with educational program for lifestyle changes is an effective approach in the treatment of patients with metabolic syndrome mainly seen by a reduced cardiovascular risk factors and reducing fatigue, improved physical capacity and reduced components of metabolic syndrome.

Keywords: metabolic syndrome; diabetes; cardiac rehabilitation; lifestyle.

RESUMO

Introdução: A síndrome metabólica é uma desordem complexa representada por um conjunto de fatores de risco cardiovascular geralmente relacionados à deposição central de gordura, resistência à insulina, hipertensão e dislipidemia. Está associada à aterosclerose acelerada em resposta à inflamação crônica e disfunção endotelial vascular, aumentando a mortalidade geral. **Objetivo:** O objetivo foi avaliar o efeito de um programa de reabilitação cardíaca sobre os fatores de risco cardiovascular em pacientes com síndrome metabólica. **Métodos:** Este é um estudo prospectivo de intervenção. Todos os pacientes foram submetidos a um programa de reabilitação cardíaca de 20 sessões com exercícios aeróbicos e resistidos, além de um programa educacional para mudanças no estilo de vida. **Resultados:** Quarenta e sete pacientes participaram do presente estudo. Após o programa de reabilitação cardíaca, observou-se redução significativa ($p = 0,0092$) para risco cardiovascular e fadiga ($p > 0,001$); 78% dos pacientes tiveram efeitos positivos na capacidade física, 72% dos pacientes apresentaram redução do HbA1c, 51% aumentaram o colesterol HDL, 70% reduziram o colesterol total, 63% reduziram os triglicerídeos, 61% reduziram a pressão arterial sistólica e 53% reduziram a pressão arterial diastólica. **Conclusão:** Programa de reabilitação cardíaca com exercícios aeróbicos e resistidos associado a um programa educacional para mudanças no estilo de vida é uma abordagem eficaz no tratamento de pacientes com síndrome metabólica por redução dos fatores de risco cardiovascular e redução da fadiga, melhora da capacidade física e redução dos componentes da síndrome metabólica.

Palavras-chave: síndrome metabólica; diabetes; reabilitação cardíaca; estilo de vida.

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Introduction

Metabolic Syndrome (MS) is a complex disorder represented by a set of cardiovascular risk factors usually related to central fat deposition, insulin resistance, hypertension, and dyslipidemia. It is associated with cardiovascular disease increasing overall and cardiovascular mortality up to two and threefold, respectively. Studies have shown that the prevalence of MS is high and varies with age [1]. Its prevalence accounts for up to 21.8% and 23.7% of subjects with unadjusted and adjusted age matched peers, respectively [2]. Prevalence increases from 6.7% among subjects aged 20-29 years to 43.5% and 42.0% for subjects aged 60-69 and at over 70 years, respectively [3].

Health-related lifestyle can be a very effective strategy that is being used mainly in the prevention of chronic degenerative diseases [4]. Some studies have already shown positive associations between health-related lifestyle and components of MS improvement: systemic arterial blood, hypertriglyceridemia, high blood glucose and HDL-c reductions. In addition, cardiac rehabilitation programs are considered adequate strategies for overall survival; it includes physical training, eating habits reeducation, smoke cessation and stress management [5].

Adopting a healthy lifestyle associated to a cardiopulmonary rehabilitation program may be an effective low-cost alternative treatment to reduce cardiovascular diseases risks, fatigue and loss of functional capacity associated to MS [6-10]. The aim of this study was to evaluate the effectiveness of a cardiac rehabilitation program and a therapeutic healthy lifestyle approach on the cardiovascular risk factors, fatigue and functional capacity of MS in adult volunteers.

Methods

This is a prospective study. The Research Ethics Committee of UNASP approved this research under the number 2.170.175, in agreement with Resolution No. 466/2012 of the National Health Council and Declaration of Helsinki (WMA, 2013) [11].

The sample of this study consisted of 47 patients with MS invited to participate in our facility Cardiac Rehabilitation Program (CRP). Both genders participated in the study who presented minimally 3 of the 5 criteria for MS; also subject aged between 40 and 60 years old. Patients with MS receiving chemotherapy, with hemodynamic instability and uncontrolled arrhythmias were excluded.

To evaluate cardiovascular risk, the Framingham Questionnaire was used; to assess individual's lifestyle we used the Individual Lifestyle Profile (PEVI) [12] questionnaire, and to evaluate global fatigue, the Chalder's Fatigue Scale [13]. Every questionnaire was performed pre and post rehabilitation.

For cardiovascular risk assessment, all patients underwent measurements of total and fractioned cholesterol, triglycerides, fasting blood glucose, blood pressure, weight, body mass index (BMI) and abdominal circumference. Also, patients performed an incremental lower limb test (BRUCE treadmill protocol) [14] and a six-minute walk test. All patients accomplished a comprehensive cardiac rehabilitation program.

Framingham cardiovascular risk has a score of 0 to 25 points, and the higher the score, the higher the cardiovascular risk.

The global fatigue was assessed using the Chalder scale, which has six questions. All individuals should have answered the first two questions, and only individuals who responded positively to the first two questions should have answered the last four questions. The last four questions were ought to quantify the individual's overall fatigue, and the higher the score, the greater the fatigue.

To assess total, fractionated cholesterol (HDL-C, LDL-C) triglycerides, fasting glucose and Hb1Ac all participants underwent venous blood collection. Total cholesterol below 200 mg/dl was considered normal. Reference values for LDL cholesterol were < 130 mg/dl, for HDL in men was > 40 mg/dl and in women was > 50 mg/dl. Triglycerides were normal when the value found was below 150 mg / dl on an empty stomach. For glycosylated hemoglobin (Hb1Ac) a normal value was considered between 4.0 and 5.6%

Body composition

BMI was classified according to criteria proposed by the World Health Organization (BMI < 18.5 kg/m² was considered as low weight, BMI between 18.5 and 24.9 kg/m² as eutrophic; BMI betwwen 25 and 29.9kg/m² as overweight; BMI between 30 and 34.9 kg/m² as grade I obesity; BMI between 35 and 39.9kg/m² as grade II obesity and BMI > 40 kg/m² as grade III obesity. For the elderly population aged 60 or over in this study, the classification recommended by the WHO was adopted in which BMI up to 18.49 kg/m2 is classified as low weight, between 18.5 to 24.99 k /m² as eutrophic, between 25 and 29.9 kg/m² as overweight and > 30kg/m² as obesity.

MS was defined using the International Diabetes Federation (IDF) diagnosis criteria. It include five components: waist circumference, blood pressure, high-density lipoprotein (HDL) cholesterol, triglycerides and fasting glucose. 3 abnormal results assume the MS diagnosis.

Cardiac rehabilitation program

Patients with metabolic syndrome performed a comprehensive rehabilitation program with 20 sessions, each lasting 60 minutes, 4 times per week. All patients were assessed by our team doctors and then referred to rehabilitation. Each session had 30 minutes of aerobic training for lower limbs on a treadmill. This training started with 3 minutes of warm-up, with 2.6 km/h of speed, twenty-two minutes at a fixed speed and treadmill inclination ranging from 60 to 80% intensity of the maximum value reached during the Bruce protocol; finally, the last five minutes had 2.7km/h speed decreased for cool down purposes.

Upper limbs and lower limbs strengthening exercises comprised of 15 minutes each; 2 sets of 10 reps for each exercise (with dumbbells and ankle weights ranging from 1 to 3 kg, theraband and Swiss ball). Specific loads were given for each individual and an interval of 60 seconds between each exercise was provided.

The participants were encouraged to practice health-promoting practices, through classes three times per week by our physiotherapists, athletic trainers, and nutritionists. Adoption of a diet rich in fruits and vegetables was oriented to meet metabolic targets [15] (mostly 3 to 5 times a day of fruit intake - the diet provided was comprehensive and, generally, oriented to all). No individual diet consult was provided; we oriented physical activity practice for at least 30 minutes three times a week, breathing fresh air and frequent water intake, smoking cessation and avoidance of alcoholic beverages and soft drinks, 7-8 h/day of sleeping period, adequate exposure to sunlight [16].

Statistical analysis

The Shapiro-Wilk normality test was used to evaluate the distribution of data in relation to normality. The data are presented in mean and standard deviation, the paired test was used to compare the differences between the anthropometric variables and the functional capacity before and after intervention within groups. Proportions were analyzed using the chi square test. Univariate logistic regression analysis was used to identify which baseline variables were significantly associated with being a non-responder treatment patient. Due to the small number of non-responder patients, a multivariate logistic regression model was performed including the four baseline variables that showed the strongest association for being a non-responder in the univariate analyses. $p < 0.05$ was considered as statistically significant.

Study Design

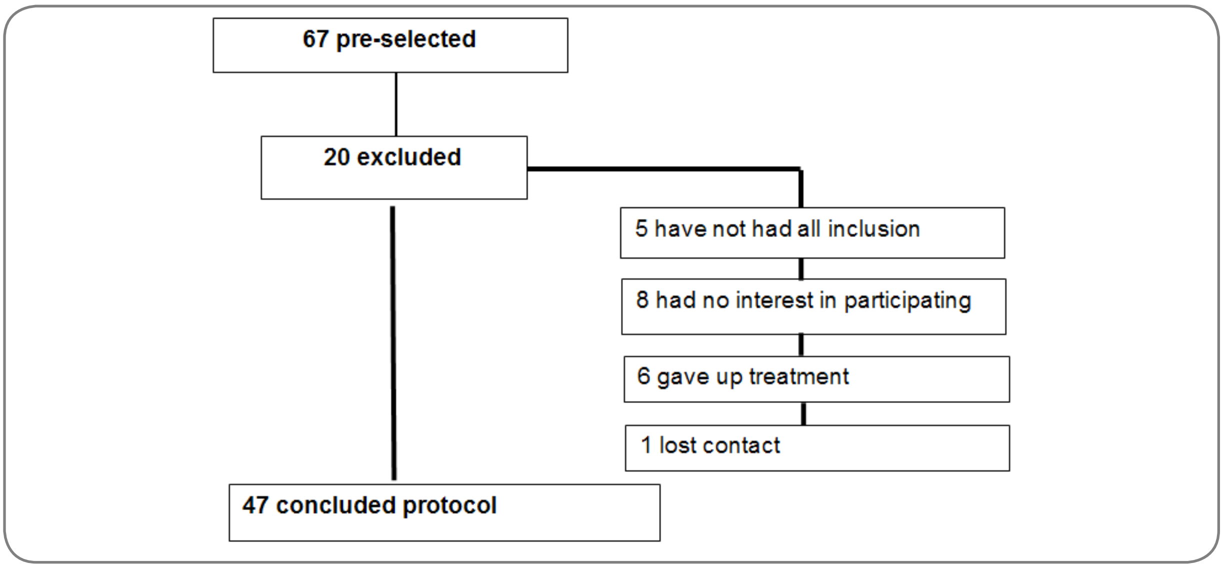

Figure 1 – Selection of the participants

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Results

The sample consisted of 47 patients with metabolic syndrome; out of these, 70.2% were female (n = 33). Sample's age ranged from 53 to 69 years. BMI was classified according to criteria proposed by the World Health Organization [17].

29.5% patients with grade I obesity, 27.7% with grade II obesity and 23.4% with grade III obesity. Initially, only 8% of patients had their blood arterial hypertension controlled, 55% of patients had total cholesterol over 200 mg/dl, 64.2% had low HDL, 31.9% had high LDL and 76.5% had high triglycerides.

None of the women presented belly obesity; on the other hand, 28% of men presented abdominal circumference < 102 cm. After the cardiac rehabilitation program there was an increase in patients' proportion who had controlled blood pressure and total cholesterol lower than 200 mg/dl (table I).

Table I - Demographic characteristics at baseline and after cardiac rehabilitation

Variables	Pre-rehabilitation (%)	Post-rehabilitation (%)	p
Man (%)	14(29.8)	14 (29.8)	0.98
Woman (%)	33(70.2)	33 (70.2)	0.98
Age (years)	59.5 ± 8.1	59.5 ± 8.1	0.98
Overweight	14 (29.5)	15 (31)	0.87
Obesity, degree I	13 (27.7)	13 (27.7)	0.95
Obesity degree II	11 (23.4)	11 (23.4)	0.94
Obesity degree III	8 (17)	6 (12)	0.92
Glycosylated hemoglobin < 7	17 (36.1)	18 (38.2)	0.89
SBH Controlled	8 (17)	20 (42)	0.001
Total cholesterol > 200 mg/dl	26 (55)	31 (65)	0.03
HDL cholesterol			
Man < 40mg/dl (%)	9 (64.2)	8 (57.1)	0.87
Woman < 50mg/dl (%)	19 (57.5)	21 (63.6)	0.84
LDL > 135 mg dl	15 (31.9)	10 (21.2)	0.21
Triglycerides > 150 mg/dl	36 (76.5)	36 (76.5)	0.98
Waist circumference			
Woman < 88cm (%)	0 (0)	0 (0)	
Man <102 cm (%)	4 (28)	4 (28)	0.99

IMC = Índice de Massa Corporal; TC6'= teste de caminhada de seis minutos; HbA1c = hemoglobina glicosilada; DP = desvio padrão

Após o programa de reabilitação cardíaca, foi possível observar que 55,3% dos pacientes reduziram o IMC e 59,6% reduziram a obesidade da barriga. A fadiga geral reduziu significativamente (p > 0,001). Observou-se também aumento da distância percorrida em seis minutos no SMWT (p > 0,001) e teste de duração do protocolo de Bruce (p = 0,0008) (Tabela II).

Table II - Comparison of anthropometric results and physical capacity before and after intervention

Variables	Pre-rehabilitation Mean ± SD	Post- rehabilitation Mean ± SD	p
BMI (kg/m²)	34.1 ± 5.5	33.8 ± 5.4	0.377
Waist circumference (cm)	111.0 ± 11.2	109.5 ± 11.5	0.268
Global fatigue (score)	2.0 ± 1.6	0.6 ± 1.2	0.001
SMWT (meters)	509.2 ± 78.1	565 ± 93.7	0.001
Bruce Protocol (minutes)	10.0 ± 3.5	12.2 ± 3.2	0.0008
Dyspnea SMWT (score)	3.5 ± 3.0	3.4 ± 3.0	0.497
Dyspnea Bruce (score)	3.1 ± 2.7	2.7 ± 2.5	0.177
Festins glucose (mg/dl)	129.9 ± 53	117.7 ± 31.3	0.017
HBA1C (mg/dl)	7.1±1.9	6.8 ± 1.6	0.13

BMI = Body Mass Index; SMWT = six minutes walking test; HBbA1c = glycosylated hemoglobin; SD = standard deviation

Figure 1 compares the Framingham scores before and after the cardiac rehabilitation program. At the end of the program, the cardiovascular risk reduction was statistically significant in our patients with metabolic syndrome (p = 0.0092, Figure 1).

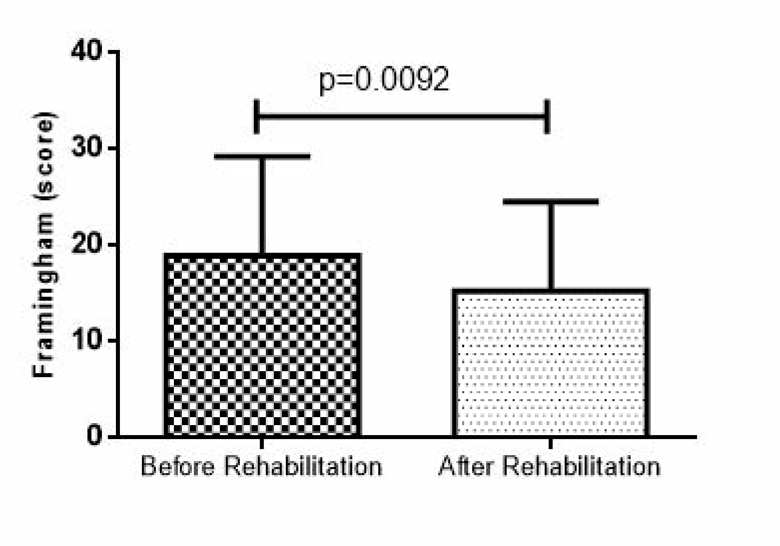

Figure 2 - Comparison of the Framinghan score for cardiovascular risk before and after rehabilitation

Among the entire cohort of 47 subjects, we identified 29 individuals considered as "non-responders" (Non-responders were defined as subjects that continued to have diagnostic criteria for metabolic syndrome after cardiac rehabilitation). Table III describes the baseline univariate predictors for being a non-responder. BMI, waist circumference, fasting glucose, total cholesterol, hypertriglyceridemia, were all significant predictors of being a non-responder to treatment; also lower HDL-cholesterol levels and exercise tolerance (Bruce protocol and six-minute walking distance) were significant variables either (table III).

Table III - Univariate baseline predictors of being a non-responder to cardiac rehabilitation and lifestyle programs in patients with metabolic syndrome

Variables	Odds ratio	95% CI	p
Waist circumference > 113 cm (median)	2.88	1.98 to 3.6	0.001
BMI > 31 kg/m² (median)	2.01	1.74 to 3.6	0.004
Fasting glucose > 131 mg/dl (median)	1.78	1.25 to 2.5	0.021
SMWT < 491 meters (median)	1.63	1.15 to 2.3	0.034

BMI = Body Mass Index; SMWT = six minutes walking test.

We created a multivariate logistic regression model containing the four baseline variables most closely associated with being a non-responder patient considering the univariate analyses (Table IV). High waist circumference, BMI and fasting glucose, low physical capacity in the six-minute walk test were variables that remained significant predictors of maintaining the diagnosis of MS (table IV).

Table IV - Multivariate predictors of being a non-responder to cardiac rehabilitation and exercise training programs in the entire metabolic syndrome cohort

Variables	Odds ratio	95% CI	p
BMI > 31 kg/m² (median)	1.4	1.03 a 3.21	0.0005
Waist circumference > 113 cm (median)	3.4	2.31 a 6.32	0.0001
Fasting glucose > 131 mg/dl (median)	1.34	1.54 a 4.3	0.001
Systolic arterial blood rest > 140 mmHg (median)	1.12	0.87 a 1.92	0.45
Diastolic arterial blood > 85 mmHg (median)	1.05	0.78 a 2.4	0.54
Total cholesterol	1.2	1.0 a 2.3	0.049
LDL cholesterol > 170 mg/dl (median)	1.7	1.08 a 4.6	0.015
HDL cholesterol < 40mg/dl (median)	0.52	-2.1 a -1.0	0.021
Hypertriglyceridemia > 234 mg/dl (median)	1.42	1.24 a 4.35	0.032
Bruce protocol > 9,5 minutes (median)	0.24	-2.5 a -4.9	0.002
SMWT < 491 meters (median)	2.85	1.80 a 4.95	0.005

BMI = Body Mass Index; SMWT = six minutes walking test

Discussion

The objective of this study was to evaluate the effect of a cardiac rehabilitation program on cardiovascular risk factors of patients with metabolic syndrome. Among the main results of this study, we can highlight that, after the cardiac rehabilitation program, there was reduction for cardiovascular risk (Framingham score). 78% of our patients had a positive effect on physical ability, 72% had hemoglobin glycosylated reduction, 51% increased HDL cholesterol, 70% reduced total cholesterol, 63% reduced triglycerides, 61% reduced SBP, 53% reduced DBP and 5% reduced overall fatigue.

Pontes et al. [18], while evaluating the effects of physical exercises in metabolic syndrome patients, also noticed significant reductions in cardiovascular risk assessed by the Framingham Score. Other authors showed that physical inactivity is one of the leading modifiable risk factors for global mortality in these patients - an estimated 20% to 30% increased risk of death compared with those who are physically active [19]. Physically active people of all age groups have higher levels of cardio-respiratory fitness, health, wellness and a lower risk for developing several chronic medical illnesses, including cardiovascular disease - compared with those who are physically inactive [20,21]. Another study [22], also obtained significant values for reduction of cardiovascular risk with exercise and life style changes in a sample of obese, hypertensive and dyslipidemic women.

The positive effects to reduced cardiovascular risk caused by the aerobic training are associated with the speed and load imposed on the treadmill. Pontes et al. [18] confirm that disease burden imposes a positive impact on the cardiorespiratory performance. In this study, training speed was based on maximal heart rate and a load of 60 to 80% of maximum HR was applied. When performing exercise in this modality, some effects are known such as the increase of the shear stress mediated by the flow in the arteries walls that improves endothelial function. This mechanism increases the synthesis and release of nitric oxide that leads to endothelium vasodilation and inhibits multiple processes involving atherogenesis and thrombosis [23].

One of the ways to reduce cardiovascular risk is to reduce blood pressure. The mechanism for blood pressure reduction is already well described both at short and long term; the short term it is due to the release of pro-vasodilation factors by the vascular endothelium after moderate to high intensity load exercise. In the long term, it occurs by vascular neo-formation in the muscles during anaerobiosis [24]. Reductions of only 2 mmHg in diastolic blood pressure can substantially reduce the risk of diseases and deaths associated with hypertension [25].

Aerobic training may reduce the risk of death from cardiac events due to reduced ventricular tachyarrhythmias by reducing sympathetic activity and increasing parasympathetic (vagal) activity, as evidenced by increased heart rate variability and increased baroreceptor sensitivity [23].

When assessing fatigue by Chalder's scale, patients in our study reported a significant decrease in fatigue after CRP. Fatigue symptoms may be due in part to the inability of the muscle to use oxygen reducing heart overload [26-28]. Physical exercise is able to reverse this situation through adaptations of skeletal muscle, such as improvement of mitochondrial capacity, decrease of insulin resistance [3] and reduction of systemic oxidative stress and improvement in well-being [29].

A systematic review with a meta-analysis [30] that evaluated cardiovascular risk factors during exercise testing in metabolic syndrome patients observed significant mean reductions in waist circumference, blood pressure, HDL cholesterol, glucose and triglycerides.

Aerobic and resistive physical exercises have positive effects on insulin sensitivity [27]. One study showed that exercises have effects on insulin sensitivity between 12 and 48 hours after exercise, but these changes returned to pre-activity levels 3 to 5 days after the last exercise session. Exercise improves the dyslipidemic profile by increasing the ability of muscle tissue to consume fatty acids and increases the activity of the lipoprotein lipase enzyme in the muscle, causing an improvement in dyslipidemia in individuals with MS [31].

As previously shown [32,33], therapeutic lifestyle changes and cardiac rehabilitation programs can be extremely beneficial for MS patients. Other studies have seen clinical improvement in MS patients such as ours [34,35]. For instance, Met Fit program showed significant reductions in waist circumference, body fat, systolic and diastolic blood pressures in those patients accomplishing a comprehensive 12 week sessions of 45 minutes of exercise and 45 minutes of education. The target 150 to 200 minutes weekly exercise and 5% loss in body weight were achieved by all patients [34]. Another study showed a significant improvement at 6 weeks and at 6 months period in waist circumference, body weight, diastolic blood pressure, and total cholesterol occurred in 240 patients with MS after a cardiometabolic program [35].

This study brings important clinical applications mainly related to the fact that cardiac rehabilitation program and small lifestyle changes may improve cardiovascular risk in patients with MS. The limitations of this study are related to the fact that we only measured the behavior of these variables after the cardiac rehabilitation program, not being able to measure the effects over a long period, as well as to follow other end points such as hospitalization and mortality. However, this cannot invalidate our results.

Conclusion

After evaluating the effect of the cardiac rehabilitation program on the cardiovascular risk factors, physical capacity, and metabolic changes in patients with metabolic syndrome, our study can conclude that this is an effective result in the treatment of these patients by reducing cardiovascular risk factors, fatigue, blood pressure, triglycerides, total cholesterol and LDL cholesterol and fasting glucose and improving physical ability and HDL cholesterol.

Conflict of interest
No conflict of interest with relevant potential.

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Own financing.

Authors' contributions
conception and design of the study: Porto EF; **Data collection and analysis:** Brandão AD, Reis KLP, Ribeiro NM, Figueiredo P; **Data interpretation:** Figueiredo P, Castro AAM; **Writing and substantial revision of the work:** Castro AAM, Fausto DM, Porto EF.

References

1. Kuschnir MCC, Bloch KV, Szklo M, Klein CH, Barufaldi LA, Abreu GDA, Moraes AJ PD. ERICA: prevalence of metabolic syndrome in Brazilian adolescents. Rev Saúde Pública 2016;50(11):256-68. doi:

10.1590/S01518-8787.2016050006701

2. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287(3):356-9. doi: 10.1001/jama.287.3.356

3. Tjønna AE, Lee SJ, Rognmo Ø, Stølen TO, Bye A, Haram PM, *et al.* Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome. Circulation 2008;118(4):346-54. doi: 10.1161/CIRCULATIONAHA.108.772822

4. Porto EF, Souza AC. Health promotion and lifestyle: limitations and perspectives. Lifesytle Journal 2016;4(2):7-9. doi: 10.19141/2237-3756.lifestyle.v3.n2.p7-10

5. Takahara M, Shimomura I. Metabolic syndrome and lifestyle modification. Rev Endocr Metab Dis 2014;15(4):317-27. doi: 10.1007/s11154-014-9294-8

6. Lavie CJ, Milani RV. Cardiac rehabilitation and exercise training programs in metabolic syndrome and diabetes. J Cardiopulm Rehabil 2005;25(2):59-66. doi: 10.1097/00008483-200503000-00001.

7. Savage PD, Banzer JA, Balady GJ, Ades PA. Prevalence of metabolic syndrome in cardiac rehabilitation/secondary prevention programs. American Heart Journal 2005;149(4):627-31. doi: 10.1016/j.ahj.2004.07.037

8. Lavie CJ, Morshedi?Meibodi A, Milani RV. Impact of cardiac rehabilitation on coronary risk factors, inflammation, and the metabolic syndrome in obese coronary patients. J Cardiometab Syndr 2008;3(3):136-40. doi: 10.1111/j.1559-4572.2008.00002.x

9. Galvão TF, Pereira MG. Systematic reviews of the literature: steps for preparation. Epidemiol Serv Saúde 2014;23(1):183-4. doi: 10.5123/S1679-49742014000100018

10. Santos CMDC, Pimenta, CADM, Nobre MRC. The PICO strategy for the research question construction and evidence search. Rev Latinoam Enferm 2007;15(3):508-511. doi: 10.1590/s0104-11692007000300023

11. World Medical Association (WMA). Declaration of Helsinki. [Internet]. 2013 [cited 2021 Jun 12]. Available from: http://www.wma.net/en/ 30publications/10policies/b3/

12. Castro JBP, Souza Vale RG, Aguiar RS, Silva Mattos R. Perfil do estilo de vida de universitários de Educação Física da cidade do Rio de Janeiro. Revista Brasileira de Ciência e Movimento 2017;25(2):73-83. doi: 10.18511/rbcm.v25i2.6234

13. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright S, Wallace EP. Development of a fatigue scale. Journal of Psychosomatic Research 1993;37(2):147-53. doi: 10.1016/0022-3999(93)90081-P

14. Karvonen JJ, Kentala E, Mustalam O. The effects of training on heart rate: a "longitudinal" study. Ann Med Exp Biol Fenn 1957;35:307-15. doi: 10.1038/sj.jhh.1002173

15. Fung TT, Hu FB, Wu K, Chiuve SE, Fuchs CS, Giovannucci E. The Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets and colorectal cancer. Am J Clin Nutr 2010;92(6):1429-35. doi: 10.3945/ajcn.2010.29242

16. Meira MDD, Abdala GA, Teixeira CA, Ninahuaman MFM, Moraes MCL. Profile of adult lifestyle of São Paulo south zone. Life Style Journal [Internet]. 2015 [cited 2021 Jun 12];2(2):29-45. https://revistas.unasp.edu.br/LifestyleJournal/article/view/607

17. World Health Organization (WHO). The top 10 causes of death. 2016 [cited 2018 April 15]. Available from: http://www.who.int/mediacentre/factsheets/fs310/en/index3.html

18. Pontes HT, Araujo SP, CorrêA CD, Cerqueira PA, Oliveira NC, Portes LA. Supervised physical activity and metabolic syndrome components of women assisted in primary health care. J Metabolic Synd 2012;1(111):2167-0943. doi: 10.4172/2167-0943.1000111

19. Fletcher GF, Landolfo C, Niebauer J, Ozemek C, Arena R, Lavie CJ. Promoting physical activity and exercise: JACC health promotion series. J Am Coll Cardiol 2018;72(14):1622-39. doi: 10.1016/j.jacc.2018.08.2141

20. Ozemek C, Lavie CJ, & Rognmo Ø. Global physical activity levels-Need for intervention. Prog Cardiovasc Dis 2019;62(2):102-7. doi: 10.1016/j.pcad.2019.02.004

21. Lavie CJ, Ozemek C, Carbone S, Katzmarzyk PT, Blair SN. Sedentary behavior, exercise, and cardiovascular health. Circ Res 2019;124(5):799-815. doi: 10.1161/CIRCRESAHA.118.312669

22. Chagas EFB, Bonfim MR, Brondino NCM, Monteiro HL. Physical exercise and cardiovascular risk factors in obese women in the postmenopausal period. Rev Bras Med Esporte 2015;21(1):65-9. doi: 10.1590/1517-86922015210101834

23. Leon AS, Franklin BA, Costa F, Balady GJ, Berra KA, Stewart KJ, Lauer MS. Cardiac rehabilitation

and secondary prevention of coronary heart disease. Circulation 2005;111:369-76. doi: 10.1161/01.CIR.0000151788.08740.5C

24. Porto EF, Kumpel C, Portes LA, Leite JRO. Comparative study between two methods of supervised and semi-supervised cardiac rehabilitation on maximal oxygen consumption and functional capacity. Rev Soc Cardiol Estado de São Paulo [Internet]. 2007 [cited 2021 Jun 12];17(2):18-24. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/lil-461835

25. Ciolac EG, Guimarães GV. Ejercicio físico y síndrome metabólico. Rev Bras Med Esporte 2004;10(4)319-24. doi: 10.1590/S1517-86922004000400009

26. Pozehl B, Ducan K, Hertzog M. The effects of exercise training on fatigue and dyspnea in heart failure. Eur J Cardiovasc Nurs 2008;7(2):127-132. doi: 10.1016/j.ejcnurse.2007.08.002

27. Jackson L, Leclerc J, Erskine Y, Linden W. Getting the most out of cardiac rehabilitation: a review of referral and adherence predictors. Heart 2005;91(1):10-14. doi: 10.1136/hrt.2004.045559

28. Mann DL, Reid MB. Exercise training and skeletal muscle inflammation in chronic heart failure: feeling better about fatigue. J Am Coll Cardiol 2003;42(5):869-72. doi: 10.1016/S0735-1097(03)00847-7

29. Windthorst P, Mazurak N, Kuske M, Hipp A, Giel KE, Enck P, Nieb A, Zipfel S, Teufel M. Heart rate variability biofeedback therapy and graded exercise training in management of chronic fatigue syndrome: An exploratory pilot study. J Psychosom Res 2017;93:6-13. doi: 10.1016/j.jpsychores.2016.11.014

30. Pattyn N, Cornelissen VA, Eshghi SRT, Vanhees L. The effect of exercise on the cardiovascular risk factors constituting the metabolic syndrome. Sports Med 2013;43(2):121-33. doi: 10.1007/s40279-012-0003-z

31. Chagas EFB, Bonfim MR, Brondino NCM, Monteiro HL. Physical exercise and cardiovascular risk factors in obese women in the postmenopausal period. Rev Bras Med Esporte 2015;21(1):65-9. doi: 10.1590/1517-86922015210101834

32. Milani RV, Lavie CJ. Prevalence and profile of metabolic syndrome in patients following acute coronary events and effects of therapeutic lifestyle change with cardiac rehabilitation. Am J Cardiol 2003;92(1):50-4. doi: 10.1016/s0002-9149(03)00464-8.

33. Lavie CJ, Milani RV, O'Keefe JH. Dyslipidemia intervention in metabolic syndrome: emphasis on improving lipids and clinical event reduction. Am J Med Sci 2011;341(5):388-93. doi: 10.1097/MAJ.0b013e31821483fa

34. Rubenfire M, Mollo L, Krishnan S, Finkel S, Weintraub M, Gracik T, Kohn D, Oral EA. The metabolic fitness program lifestyle modification for the metabolic syndrome using the resources of cardiac rehabilitation. J Cardiopulm Rehabil Prev 2011;31:282-9. doi: 10.1097/HCR.0b013e318220a7eb

35. Rodriguez-Escudero JP, Somers VK, Heath AL, Thomas RJ, Squires RW, Sochor O, Lopez-Jimenez F. Effect of a lifestyle therapy program using cardiac rehabilitation resources on metabolic syndrome components. J Cardiopulm Rehabil Prev 2013;33(6):360-70. doi: 10.1097/HCR.0b013e3182a52762