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Effect of cardiac rehabilitation program on the Framingham risk score and C-reactive protein after CABG

Efeito de um programa de reabilitação cardíaca sobre o escore de Framingham e proteína C-reativa pós-revascularização do miocárdio

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Abstract

Introduction: Coronary artery bypass grafting (CABG) does not have an effect on the etiopathogenic factors of atherosclerosis, thus, it is crucial to control risk factors. **Objective:** To analyze the effect of a cardiac rehabilitation (CR) program on cardiovascular risk factors, the Framingham risk score (FRS) and levels of C-reactive protein (CRP) of patients undergoing CABG. **Methods:** A descriptive, cross-sectional and retrospective study was conducted with a sample of 49 patients, who were participating in a program (24 weeks). Body mass index (BMI), waist circumference (WC), FRS, risk (%) of developing coronary artery disease in 10 years (CAD risk), serum levels of LDL-c, triglycerides (TG) and CRP were assessed. **Results:** The variables BMI, WC, LDL-c, TG, CRP levels, FRS and CAD risk showed significant reductions (p<0,001). **Conclusion:** The program was effective in reducing cardiovascular risk factors, FRS, as well as the decrease in CRP levels.

Keywords: Myocardial Revascularization; Risk Factors; Rehabilitation Centers; Secondary Prevention.

Resumo

Introdução: A cirurgia de revascularização do miocárdio (CRM) não atua nos fatores etiopatogênicos da aterosclerose, dessa forma o controle destes fatores torna-se crucial. **Objetivo:** Analisar o efeito de um programa de reabilitação cardíaca (RC) sobre fatores de risco cardiovasculares, Escore de Framingham (EF) e níveis de proteína C reativa (PCR) de pacientes submetidos à CRM. **Métodos:** Trata-se de um estudo transversal e retrospectivo com uma amostra 49 pacientes participantes de um programa de RC (24 semanas). Índice de massa corporal (IMC), circunferência da cintura (CC), EF, risco de desenvolvimento de doença arterial coronariana em 10 anos (risco DAC), níveis séricos de LDL-c, triglicerídeos (TG) e PCR foram avaliados. **Resultados:** As variáveis IMC, CC, LDL-c, TG, PCR, Pontuação no EF e o risco DAC apresentaram reduções significativas (p<0,001). **Conclusão:** O programa foi eficaz na redução de fatores de risco cardiovascular, no EF, bem como na diminuição dos níveis de PCR.

Descritores: Revascularização Miocárdica; Fatores de Risco; Centros de Reabilitação; Prevenção Secundária.

Introduction

Cardiovascular diseases are the leading cause of death and disability in Brazil and worldwide. According to data from the World Health Organization, 7.4 million deaths occurred worldwide in 2012 due to coronary artery disease (CAD)[1]. In Brazil, data from the Informatics Department of the Unified Health System (DATASUS) show that cardiovascular disease represents approximately 30% of the overall causes of death. More than 80,000 hospital admissions occurred in Brazil in February 2014 because of circulatory system diseases[2]. Despite advances in clinical therapeutics and percutaneous coronary intervention, coronary artery bypass grafting (CABG) is a safe procedure that is performed worldwide, presenting low mortality and morbidity rates in the overall population. This procedure may control persistent ischemia and its progression to acute myocardial infarction and provide symptomatic relief [3]. However, vascular graft failure is a common finding in patients following CABG surgery and most commonly associated with atherosclerosis[4]. Atheroma formation is associated with the same factors as in the native arteries and occurs by a similar process.

Lifestyle changes with a focus on regularly scheduled physical activity, adoption of healthy eating habits, smoking cessation and the use of drugs in general, besides strategies to moderate the impact of stress, are considered essential components of cardiovascular rehabilitation and secondary prevention for patients with CAD [5,6].

Based on the best available scientific evidence, in the context of secondary prevention, specifically in CABG patients, the focus of cardiac rehabilitation (CR) programs is interventions based on physical activity[7]. In this sense, there is significant evidence confirming that the Framingham risk score can be used to evaluate the effects of different types of preventive strategies, including physical training[8]. This score is based on clinical and laboratory variables, and it is widely accepted and recommended by the National Cholesterol Education Program's Adult Treatment Panel III to estimate 10-year cardiovascular disease events risk[9].

C-reactive protein (CRP) is the most extensively studied inflammatory biomarker in atherogenic process, which has become the standard for the prediction of cardiovascular risks, due to the discovery of high-sensitivity techniques for its determination, its stable plasmatic concentrations, and its relatively low costs. Although CRP is a nonspecific inflammatory marker, it is a strong independent predictor for coronary heart disease risk and events[10]. It may be of great use in the identification of patients at high risk, as a therapeutic target in large populations, besides adding a prognostic indicator to the Framingham risk score[11].

Previously published studies showing that CR participation is associated with improvements in coronary heart disease risk factor control, as well as long-term follow-up and adherence to secondary prevention medications[12,13]. In addition, given that patients undergoing CABG typically have more severe CAD and risk factors, they likely derive a greater benefit from CR than patients with more limited coronary artery disease[14]. However, the effects of cardiac rehabilitation program on cardiovascular risk using the Framingham risk score, specifically in CABG patients, have been largely unexplored in the literature and require further elucidation. Therefore, the purpose of this study was to analyze the effects of a phase II CR program on cardiovascular risk factors, the Framingham risk score and CRP levels of patients undergoing CABG.

Material and Methods

A retrospective, cross-sectional study guided was conducted by review of medical records of patients undergoing CABG who were participants in a phase II CR program of the Outpatient Cardiology Clinic of Hospital Universitário de Santa Maria (HUSM), Santa

Maria, RS, Brazil, from November 2013 to December 2014.

The eligibility criteria included patients undergoing CABG, 50 to 65 years of age, a clinical course without complications during hospitalization and agreement to participate. Patients with chronic obstructive pulmonary disease, unstable angina, acute decompensated heart failure, acute pericarditis or myocarditis, complex arrhythmias, uncontrolled hypertension, severe orthopedic or neurological disorders, uncontrolled diabetes, labyrinthitis were excluded.

Data collection occurred between April and June 2015; the variables were collected from the patient's medical record, from the time of admission until discharge from the program. The independent variables analyzed were medical history, physical examination, and data from the intraoperative, and postoperative periods.

The outcome measures include body mass index (BMI), which was calculated as the ratio between total body weight (kg) and height (m^2), and waist circumference (WC) which was measured at lowest circumference between the superior border of the iliac crest and below the lowest rib with an inelastic tape [precision 0.1 cm (Sanny®, São Paulo, Brazil)], the cut-off point adopted for males was WC > 102 cm and for females WC > 88 cm[9]. Serum CRP concentrations were measured using turbidimetric immunoassay and cardiovascular risk was calculated by the Framingham risk score[15], which presents the following components: (a) age; (b) total cholesterol (TC) (enzymatic colorimetric method); (c) high-density lipoprotein cholesterol (HDL-C) (selective inhibitor); (d) systolic and diastolic blood pressure (SBP and DBP); (e) current cigarette smoking (smoking at least 100 cigarettes during their lifetime and current smoking every day or some days)[16]; (f) diagnosis of diabetes (fasting blood glucose greater than or equal to 126 mg/dl)[17]. In this study, participants were classified according to their 10-year cardiovascular disease (CVD) risk as low (<10% 10-year CVD risk), medium (10–20% CVD risk), or high >20% CVD risk[15]. The outcome measures were collected pre and post CR program.

Cardiac Rehabilitation Program

All patients participated in the CR program for a period of 24 weeks, with two sessions per week. Each session lasted 60 minutes, and all sessions were under the direct supervision of a physical therapist. The training program consisted of a combination of aerobic and resistance exercises, 30 minutes of aerobic exercise on a treadmill and exercise bike, 20 minutes of resistance exercises for the arms (latissimus dorsal m.,biceps brachii m., triceps brachii m., deltoid m., trapezius m., pectoralis major m., pectoralis major m., and rhomboid m) and legs (femoral quadriceps m., hip adductors m. and hip abductors m.) with dumbbells, ankle weights, or elastic bands (3 sets of exercises for each muscle group performed with 10 repetitions with the intensity adjusted to 50% of the load of one maximum repetition - 1MR), and 10 minutes of stretching and relaxation[18]. Heart rate, blood pressure, and peripheral oxygen saturation were measured at the beginning, during, immediately after, and five minutes after each session.

The study was approved by the Research Ethics Committee of Universidade Federal de Santa Maria (UFSM) under protocol no. 16149813.3.0000.5346, and was conducted in accordance with the Brazilian Regulatory Guidelines and Standards on Research Involving Human Subjects, according to National Health Council Resolution no 466/2012.

Sample size calculation

Estimated to obtain a significance level of 5% ($p<0.05$) and a power of 80% (WinPepi version 10.5), considering standard deviation of the low-density lipoprotein cholesterol (LDL-c) variable of 1.23 mg/dl according to Cooper et al.[19], a sample of 43 patients was calculated.

Statistical analysis

Data were analyzed using SPSS s software, version 20.0. The Shapiro-Wilk test was used to assess the normality of the variables, and were log-transformed to normalize the distribution. Categorical data are presented as absolute frequencies and percentages. Continuous data with normal distributions are expressed as mean and standard deviation. Student's t-test for paired samples was used to compare the data before and after the intervention, except for the categorical variables, which were compared by the Chi-square test. A value of $p<0.05$ was considered statistically significant.

Results

The medical records of 49 patients were examined. All patients were submitted to chest physiotherapy during the immediate postoperative period (Phase 1). The sociodemographic, anthropometric and clinical characteristics are presented in Table 1. No adverse events were observed during the CR, and adherence to the program was considered excellent.

Significant reductions in BMI ($p<0.001$), WC ($p<0.001$), TC ($p<0.001$), LDL-C ($p<0.001$), triglycerides (TG) ($p<0.001$), SBP ($p<0.001$), DBP ($p=0.016$), and CRP levels ($p<0.001$), and increases in HDL-C levels ($p<0.001$), were observed between before and after the intervention (Table 1).

It is worth noting that in the pre-intervention period, 75.5% (n=37) of the patients were smokers, and after the training, all reported that they had stopped smoking. Reduction in glucose levels was also observed, since 26 patients (60.5%) showed values higher than 126 mg/dl in the first assessment; in the second assessment, these values were observed in only 17 patients (39.5%).

The Framingham risk score before and after the intervention was significantly lower ($p<0.001$) (Fig. 1A). The mean 10-year CVD risk also showed a significant decrease after the intervention ($p<0.001$) (Fig. 1B).

Table 1: Demographic and clinical characteristics of patients

Variables	Pre CR (n=49)	Post CR (n =49)	P-value
Age (years)	58.3 ± 10.8	-	-
Male gender, n (%)	32 (65.3)	-	-
Duration of hospitalization after surgery (days)	6.9 ± 1.6	-	-
Ejection fraction (%)	61.0 ± 10.7	63.7 ± 10.9	0.004
NYHA			
I, n (%)	31 (63.3)	37 (75.5)	N.S
II, n (%)	12 (24.5)	9 (18.4)	N.S
III, n (%)	6 (12.2)	3 (6.1)	N.S
Anthropometric measurements			
BMI (Kg/m^2)	27.6 ± 3.5	23.9 ± 2.7	<0.001
WC (cm)	102.6 ± 9.8	90.9 ± 8.6	<0.001
Lipid profile			
TC (mg/dL)	209.5 ± 42.7	151.3 ± 28.7	<0.001
HDL-c (mg/dL)	37.5 ± 6.2	48.9 ± 8.0	<0.001
LDL-c (mg/dL)	126.8 ± 27.3	80.9 ± 15.1	<0.001
TG (mg/dL)	196.0 ± 41.0	128.0 ± 50.8	<0.001
Inflammatory biomarker			
CRP (mg/dL)	1.4 ± 0.4	0.2 ± 0.1	<0.001
Blood pressure			
SBP (mmHg)	129.3 ± 15.0	118.2 ± 12.7	<0.001
DBP (mmHg)	78.5 ± 11.6	74.1 ± 8.3	0.016
Medication, n (%)			
Acetylsalicylic acid	40 (81.63)	38 (77.55)	N.S
Clopidogrel	3 (6.1)	2 (4.0)	N.S
Statin	32 (65.30)	30 (61.22)	N.S
Diuretics	7 (14.2)	6 (12.2)	N.S
ACEI or ARB	9 (18.36)	7 (14.2)	N.S
Beta-blockers	20 (40.81)	18 (36.73)	N.S

Data are expressed as mean ± standard deviation or absolute values and percentage. ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; BMI: body mass index; CR: cardiac rehabilitation; CRP: C-reactive protein; DBP: diastolic blood pressure; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; NYHA: New York Heart Association; SBP: systolic blood pressure; TC: total cholesterol; TG: triglycerides; WC: waist circumference.

Regarding 10-year CVD risk scores, before the exercise program, the individuals were classified in the following risk categories: 16.3% were classified as low risk, 46.9% as medium

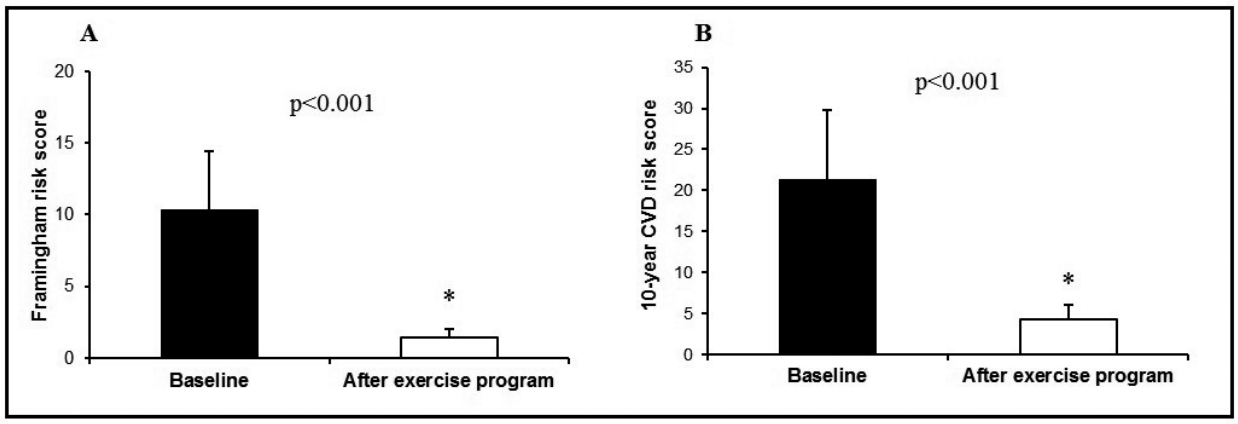

Figure 1: The Framingham risk and 10-year CVD risk scores before and after exercise program
(A) Framingham risk score before and after exercise program. (B) 10-year CVD risk score before and after exercise program. *Chi Square test p < 0.05.

risk, and 38.8% as high risk. After the program, 87.7% were classified as low risk, 12.2% as medium risk (only 6 patients), and 0 patients as high risk (p<0.001).

Discussion

The present study found that a phase II CR program reduced the Framingham risk score, CRP levels, 10-year CVD risk score, and variables associated with cardiovascular risk in patients undergoing CABG. To the best of our knowledge, this is the first study to address the effects of a 24-week training program in reduced the Framingham risk score and CRP levels exclusively in CABG patients.

In Brazil, the use of Framingham risk score is recommended by the Ministry of Health as a strategy to identify individuals at risk of cardiovascular disease[20]. CR programs are accepted and established as a nonpharmacological therapeutic intervention of patients undergoing CABG[21]. In this study, the decrease in the cardiovascular risk score reinforced the importance of physical exercise in this population of patients, and suggests the potential role of the Framingham risk score in secondary prevention.

The present study applied a combined aerobic and resistance training program for a 6-month period. Other studies have shown a significant reduction in Framingham risk score after implementation of exercise training program[22,23]; those studies, however, differ from the current study for several reasons: study population, longer duration and higher weekly frequency.

Studies have demonstrated that measurement of CRP may be used for the follow-up of patients with cardiovascular diseases[24], which is a potential strategy for the secondary prevention. A recent systematic review and meta-analysis of 43 studies involving 3575 participants divided into healthy patients and patients with heart disease, revealed that exercise interventions reduced CRP levels in adults irrespective of the presence of heart disease, which reinforces the anti-inflammatory effects of physical exercise[25]. In a non-randomized study, Moghadam and Azizinejad[26] observed a significant reduction in CRP levels in CABG patients after of aerobic training for eight months. Regarding body composition, the results of the present study showed a significant decrease in BMI and WC after the training program. In the pre-training, most of the sample was classified as pre-obese and obese. After the CR program, patients were classified as eutrophic and pre-obese. In a recent study conducted by Gomadam et al.[27], 40% of patients were obese, and an additional 40% were overweight; the authors showed that a 12-week CR program did not effects on weight loss.

Xu et al.[28], using a similar protocol to that used in our study, recently showed that physical training in 61 patients submitted to percutaneous transluminal coronary angioplasty promoted a decrease in WC values, according to the results of the present study.

With regard to lipid profile, in the present study a decrease in TC, LDL-C and TG levels and an increase in HDL-C levels were observed, after intervention, there was an improvement in lipid profile. Aikawa et al.[29], using a similar protocol to that used in our study, did not observe improvements of lipid profile in patients undergoing CABG after 12 weeks of combined training; however, the authors emphasize that the sample size (n=11) was insufficient.

In the present study, it was observed that combined aerobic and resistance training reduced resting levels SBP and DBP and this result was similar to those reported by Hussein et al.[30], which showed that combined resistive and aerobic exercise three times per week for 36 sessions produces a significantly reduced in the SBP levels of obese coronary patients.

Strengths and Limitations

We consider that our results are relevant because even a training program just performed 2 times per week improved the variables analyzed. Furthermore, these findings are consistent with results from previous studies performed at higher weekly frequency and longer duration.

The decrease in the cardiovascular risk score, and the CRP levels of patients undergoing CABG demonstrated in this study reinforced the importance of physical exercise in this population of patients, and suggests the potential role of the Framingham risk score in secondary prevention. This could be expected to lead to better clinical and therapeutic management, follow-up and prognosis of patients.

The present study has limitations. First, our study had a non-randomized design. Second, the study was conducted in a single center, which limits the generalization of the findings, and patient data were collected retrospectively. Retrospective studies may be subject to selection and measurement biases (data obtained from medical records). However, these limitations do not invalidate the study results.

Conclusion

The present study found that a phase II CR program, based on combined aerobic and resistance training over a period of 24 weeks, reduced the Framingham risk score, CRP levels, 10-year CVD risk score, and variables associated with cardiovascular risk in patients undergoing CABG. Future research is needed based on multicenter studies, with a prospective design, to provide definitive proof of these benefits.

References

1. World Health Organization. Cardiovascular diseases (CVDs). Geneva: WHO; 2016.
2. Cesar LA, Ferreira JF, Armaganijan D, Gowdak LH, Mansur AP, Bodanese LC, et al. Guideline for Stable Coronary Artery Disease. Arq Bras Cardiol 2014; 103(2 Suppl.2): 1-59.
3. Santos CA, Oliveira MAB, Brandi AC, Botelho PHH, Brandi JCM, Santos MA, et al. Risk factors for mortality of patients undergoing coronary artery bypass graft surgery. Rev Bras Cir Cardiovasc. 2014;29(4):513-20.
4. Pashneh-Tala S, MacNeil S, Claeyssens. The tissue-engineered vascular graft—past, present, and future. Tissue Eng Part B Rev. 2016;22(1): 68-100.
5. Herdy AH, López-Jiménez F, Terzic CP, Milani M, Stein R, Carvalho T, et al. South American guidelines for cardiovascular disease prevention and rehabilitation. Arq Bras Cardiol. 2014;103(2 Suppl 1):1-31.
6. Conraads VM, Van Craenenbroeck EM, Pattyn N, Cornelissen VA, Beckers PJ, Coeckelberghs E, et al. Rationale and design of a randomized trial on the effectiveness of aerobic interval training in patients with coronary artery disease: the SAINTEX-CAD study. Int J Cardiol. 2013;168(4):3532-6.

7. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren WM, et al. European guidelines on cardiovascular disease prevention in clinical practice (version 2012): the fifth joint task force of the European society of cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts). Int J Behav Med. 2012;19(4):403-88.

8. Lazzarotto AR, Pereira FB, Harthmann AA, Bazzo KO, Vicenzi FL, Sprinz E. Treinamento físico no risco de doença isquêmica cardíaca em sujeitos HIV/AIDS em uso de TARV. Rev Bras Med Esporte. 2014;20(3):233-36.

9. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002;106:3143-21.

10. Shrivastava AK, Singh HV, Raizada A, Singh SK. C-reactive protein, inflammation and coronary heart disease. The Egyptian Heart Journal. 2015;67(2): 89-97.

11. Ridker PM. Inflammation, C-reactive protein, and cardiovascular disease: moving past the marker versus mediator debate. Circ Res. 2014;114(4):594-5.

12. Armstrong MJ, Sigal RJ, Arena R, Hauer TL, Austford LD, Aggarwal S, et al. Cardiac rehabilitation completion is associated with reduced mortality in patients with diabetes and coronary artery disease. Diabetologia. 2015;58(4):691-8.

13. Shah ND, Dunlay SM, Ting HH, Montori VM, Thomas RJ, Wagie AE, et al. Long-term medication adherence after myocardial infarction: experience of a community. Am J Med. 2009;122(10):961.e7-13.

14. Pack QR, Goel K, Lahr BD, Greason KL, Squires RW, Lopez-Jimenez F, et al. Participation in cardiac rehabilitation and survival after coronary artery bypass graft surgery: a community-based study. Circulation. 2013;128(6):590-7.

15. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use primary care: The Framingham Heart Study. Circulation. 2008;117(6):743-53.

16. Jamal A, King BA, Neff LJ, Whitmill J, Babb SD, Graffunder CM. Current cigarette smoking among adults—United States, 2005–2015. MMWR Morb Mortal Wkly Rep 2016;65:1205-11.

17. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2006;29 Suppl 1:S43–S48.

18. Hermes BM, Cardoso DM, Gomes TJ, Santos TD, Vicente MS, Pereira SN, et al. Short-term inspiratory muscle training potentiates the benefits of aerobic and resistance training in patients undergoing CABG in phase II cardiac rehabilitation program. Braz J Cardiovasc Surg. 2015;30(4):474-81.

19. Cooper LL, Rong J, Benjamin EJ, Larson MG, Levy D, Vita JA, et al. Components of hemodynamic load and cardiovascular events: the Framingham Heart Study. Circulation. 2015;131(4):354-61.

20. Soares TS, Piovesan CH, Gustavo AS, Macagnan FE, Bodanese LC, Feoli AM. Hábitos alimentares, atividade física e escore de risco global de Framingham na síndrome metabólica. Arq Bras Cardiol. 2014;102(4):374-82.

21. Anderson L, Oldridge N, Thompson DR, Zwisler AD, Rees K, Martin N, et al. Exercise-based cardiac rehabilitation for coronary heart disease: cochrane systematic review and meta-analysis. J Am Coll Cardiol. 2016;67(1):1-12.

22. Gidlow CJ, Cochrane T, Davey R, Beloe M, Chambers R, Kumar J, et al. One-year cardiovascular risk and quality life changes in participants of a health trainer service. Perspect Public Health. 2014;134(3):135-44.

23. Rautio N, Jokelainen J, Pölönen A, Oksa H, Peltonen M, Vanhala M, et al. Changes in lifestyle modestly reduce the estimated cardiovascular disease risk in one-year follow-up of the Finnish diabetes prevention program (FIN-D2D). Eur J Cardiovasc Nurs. 2015;14(2):145-52.

24. Viana PADC, Petto J, Santos ACN, Barojas MM, Oliveira FTO, Correia LCL. Effect of a regular aerobic exercise program on c-reactive protein among people at risk for cardiovascular disease. Rev Bras Cardiol. 2014;27(3):172-9.

25. Hammonds TL, Gathright EC, Goldstein CM, Penn MS, Hughes JW. Effects of exercise on c-reactive protein in healthy patients and in patients with heart disease: A meta-analysis. Heart Lung. 2016;45(3):273-82.

26. Moghadam AJ, Azizinejad S. Study of high sensitive c-reactive protein (HS-CRP) after cardiac rehabilitation program in patients undergoing isolated CABG. Int J Biomed Sci. 2016;12(4):143-8.

27. Gomadam PS, Douglas CJ, Sacrinty MT, Brady MM, Paladenech CC, Robinson KC. Degree and direction of change of body weight in cardiac rehabilitation and impact on exercise capacity and cardiac risk factors. Am J Cardiol. 2016; 15;117(4):580-4.

28. Xu L, Zhao H, Qiu J, Zhu W, Lei H, Cai Z, et al. The different effects of BMI and WC on organ damage in patients from a cardiac rehabilitation program after acute coronary syndrome. Biomed Res Int. 2015;2015:942695.

29. Aikawa P, Cintra ARS, Oliveira Júnior AS, Silva CTM, Pierucci JD, Afonso MS, et al. Reabilitação cardíaca em pacientes submetidos à cirurgia de revascularização do miocárdio. Rev Bras Med Esporte. 2014; 20(1):55-8.

30. Hussein N, Thomas M, Prince D, Zohman L, Czojowski P. Effect of combined resistive and aerobic exercise versus aerobic exercise alone on coronary risk factors in obese coronary patients. J Clin Exp Cardiolog. 2015;6:361.