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Physical Training Programs After Coronary Artery Bypass Grafting

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Abstract

Exercise-based rehabilitation is considered an important adjunct therapy for secondary prevention in patients with coronary artery disease, mainly in populations with coronary artery bypass graft (CABG) and percutaneous coronary intervention. Thus, the increasing number of cardiac surgeries along the years is enlarging the participation of patients in cardiac rehabilitation programs. Encouraging exercise-based cardiac rehabilitation might decrease in-hospital stay, speed returns to work and reduce costs in public health. Recently, two training modalities of exercise gained much attention in cardiac rehabilitation programs: continuous exercise and high-intensity interval aerobic training (HIIAT). The aim of this chapter is to review the effects of HIIAT in patients that undergone to CABG or other cardiac surgeries regarding clinical and physiological parameters such as death, cardiovascular outcomes, aerobic capacity, anaerobic capacity, quality of life and other parameters, beyond to evaluate the feasibility and safety of HIIAT in this patient's group.

Keywords: coronary artery bypass grafting, high-intensity interval training, exercise intensity, cardiac rehabilitation, physical activity

1. Introduction

At the beginning of the twentieth century, the treatment of heart disease was based on few medicines and unconditional rest over weeks or months. The idea that exercise could overload cardiac pump and increase mortality changed facing the evidence that maintaining physical training and activity under supervision quickly reinsert patients to social-economic life.

This concept could be used for patients in a stable status with acute coronary syndromes, heart failure, post-coronary artery bypass graft (CABG), post-percutaneous coronary intervention (PCI), and most of cardiovascular disease.

Currently, exercise-based rehabilitation is considered an important adjunct therapy for secondary prevention in patients with coronary artery disease mainly in populations undergone CABG and PCI. Thus, physical training was included as Class I recommendation for both healthy subjects and those with coronary artery disease as a central point in cardiac rehabilitation (CR) programs [1–4].

In this chapter, we will discuss exercise physiology, clinical assessments, CR programs and the effects of exercise on cardiac outcomes in patients with coronary artery disease and more specifically patients that undergone CABG.

2. Exercise physiology

Exercise physiology uses some basic principles, and the terms that we will use in the present chapter are described as follows: physical activity as any bodily movement, exercise as physical activity to stress and train, aerobic exercise as exercise that stresses the oxygen transport system, resistance exercise as exercise that stresses musculoskeletal system, and exercise training as exercise performed in a repetitive way to improve cardiovascular (aerobic) or musculoskeletal (resistance) systems. Two main types of exercise have been proposed with beneficial health effects on subjects with CHD: interval aerobic training (IAT) and continuous aerobic training (CAT). IAT uses a balanced or equal time-periods between work and rest. CAT uses a steady-state exercise.

Three variables are important to understand the physiology of exercise: maximal oxygen uptake (VO_2), myocardial oxygen uptake (MO_2), and ventilatory threshold (VT).

VO_2 is the amount of oxygen consumed during exercise, and this variable maintains a closed correlation with the amount of energy used.

Fick describes an equation where cardiac output (Q) = VO_2 /difference between arterial and venous oxygen content ($\Delta A-V \text{O}_2$). So, $\text{VO}_2 = \Delta A-V \text{O}_2$ multiplied by Q . Q might be calculated by the product of heart rate (HR) and cardiac stroke volume. Q and $\Delta A-V \text{O}_2$ increases during exercise training.

Maximum exercise capacity is measured as maximum VO_2 ($\text{VO}_{2\text{max}}$), and it reflects the maximal oxygen transported during exercise before being limited by fatigue or dyspnea. This variable evaluates all together: cardiac, respiratory, muscle-skeletal and vascular systems.

Often diseased patients do not achieve their $\text{VO}_{2\text{max}}$ and the term peak VO_2 ($\text{VO}_{2\text{peak}}$) should be preferred. $\text{VO}_{2\text{peak}}$ is the highest level attained by a patient in the absence of fulfilling the criteria for $\text{VO}_{2\text{max}}$ [5]. The metabolic equivalent (MET) is defined as the oxygen requirement in the resting awake individual, and it is equal to 3.5 ml/Kg/min.

The MO_2 can be estimated multiplying HR by systolic blood pressure, also named double product. MO_2 is not determined by the external work-rate exercise, but rather by the exercise work-rate relative to maximal exercise capacity.

The VT is the divergence of VO_2 and carbon dioxide production (VCO_2) curves, and it is due to production of lactic acid. In the beginning of exercise both VO_2 and VCO_2 curves increases in same magnitude. Throughout exercise, the lactic acid is buffered by bicarbonate and it increases exhalation of additional CO_2 , achieving VT. VT denotes exercise tolerance and represent the maximal constant workrate that can be sustained during submaximal exercise.

3. Cardiac rehabilitation program

World Health Organization defines cardiovascular, pulmonary and metabolic rehabilitation as the integration of interventions called “non-pharmacological actions,” to ensure the best physical, psychological and social conditions for the patient with cardiovascular, pulmonary and metabolic diseases.

Based on scientific evidence and proven economic advantages, the ethical medical practice guidelines recommends cardiovascular, pulmonary and metabolic rehabilitation for patients with atherosclerotic coronary disease, heart failure, arterial hypertension, peripheral arterial disease, metabolic diseases (obesity, metabolic syndrome and diabetes mellitus), chronic lung disease, and for subjects with risk factors for cardiovascular diseases such as smoking, dyslipidemia, glucose intolerance, excessive stress, long-term sedentary, and patients with chronic nephropathy. In this context, prescription of training programs is highlighted for the therapeutic benefit of physical exercise which in certain situations should occur under specialized supervision [6].

In the immediate post-operative period, rehabilitation is based on standard protocols that take more regard the current clinical status and the cardiac pump like left ventricular ejection fraction. Cycle ergometer or treadmill tests are not performed routinely during hospitalization, and the decision to use maximum HR to stop exercise is not suitable. Additionally, most of patients are under beta-blockers and their HR response to exercise will be reduced.

The coordinator of the CR team should focus on several clinical parameters during exercise such as important blood pressure changes—high blood pressure or blood pressure fall during exercise—arrhythmia, syncope or pre-syncope, rales, moderate to severe dyspnea (Borg scale > 14), the onset of angina or claudication. Additionally, upper body motion must be hold by 4 weeks until surgical wound knitting, and 3 or 4 months for pushups and other strenuous exercises.

After the hospital discharge, patients with coronary artery diseases or those that undergone CABG need the referral and the assistant physician consent to perform CR. Before, patients get analysis of their clinical condition and feasibility for performing physical training [6]. Some physicians requiring imaging functional tests like cardiac scintigraphy to assess the baseline perfusion after CABG. The scintigraphy may be performed with a treadmill test or

pharmacological stress, like dipyridamole. If the assessment were performed associate to a treadmill test this data can be used as additional information about physiological cardiovascular status, like VO_2 , MET, maximal heart rate achieved, chronotropic reserve.

3.1. Phases of CR program

Beyond pharmacological treatment, it is fundamental that patients with heart failure, coronary artery disease or after CABG should be included in an CR program. For the patient's optimal development with improvement in quality of life, it is necessary the participation of a team with different specialties. The CR program aims to improve physiological, clinical and psychological state of the cardiac patient, based on a multidisciplinary intervention of physician, surgeons, physiotherapists, nutritionists, nurses, physiologists, and psychologists.

Secondary prevention and CR are an integral part of the management strategy after revascularization, and it is associated with reductions in morbidity and mortality in a cost-effective way and can further ameliorate symptoms [7, 8].

Traditionally, the CR program can be divided in phases, as follows:

Phase 1: Performed in hospitalized patients. It will introduce the patient to an active and productive life and aims to ensure that the patient will have discharge with the best physical and psychological conditions. Initially, CR was applied for recovery following myocardial infarction or CABG. Currently, it should include patients submitted to PCI by balloon or by stent implantation, heart valve surgeries, congenital heart surgeries, cardiac transplantation, patients with stable angina pectoris and subjects with risk factors for CAD such as subjects with diabetes, hypertension, metabolic syndrome, chronic nephropathy and chronic lung disease. Phase 1 begins after the patient has been considered clinically compensated due to the optimization of the clinical treatment and/or the use of an interventional procedure. In this phase, a combination of low-intensity physical exercise is indicated as well as stress management techniques, and education in relation to risk factors. The duration of this phase has decreased in recent years, due to shorter hospitalizations [6].

Phase 2: This is the first extra-hospital step. It begins immediately after discharge and / or a few days after a cardiovascular event or cardiovascular, pulmonary and metabolic decompensation. Estimated duration: 3–6 months, and in some cases may be more extensive. It can work in a structure that is part of the hospital complex or another environment suitable for physical exercise (sports club, sports gym, gym, etc.). The ideal team should include doctor, physiotherapist, physical education teacher, nurse, nutritionist and psychologist. It must have the basic resources to handle emergencies. It works with sessions supervised by the physiotherapist and/or physical education teacher. The exercise program should be individualized, in terms of intensity, duration, frequency, training modality and progression. There must always be resources for the accurate measurement of heart rate and blood pressure checking, besides the possibility of eventual verification of oxygen saturation, blood glucose determination and electrocardiographic monitoring. Part of this phase is an educational program aimed at lifestyle modification, with emphasis on dietary reeducation and strategies for smoking cessation. The rehabilitation in this phase has as main objective to contribute to the

early return of the patient to his social and work activities, in the best possible physical and emotional conditions [6].

Phase 3: Estimated duration of 6–24 months. This is the immediate treatment for the patients discharged from phase 2, but can be started at any stage of the disease evolution. It is not necessary to follow previous phases. Therefore, low-risk patients who did not participate in phase 2 are good candidates. The supervision of exercises should be done by a professional with specialization in physical exercise (physical education teacher and/or physiotherapist), and must have the coordination of a physician and have the conditions for possible cardiac monitoring and determination of oxygen saturation. It is recommended that other important professionals also integrate the team: nurse, nutritionist and psychologist. The main objective is the improvement of the physical condition and quality of life and other procedures that contribute to the reduction of the risk of clinical complications, such as the strategies for smoking cessation and food reeducation [6].

Phase 4: It is a long-term program, of indefinite duration. Activities are not necessarily supervised and should be appropriate to the availability of time for the maintenance of the physical exercise program and the preferences of patients in relation to recreational sports activities. The material and human resources available should also be considered. At this stage, patients after each medical evaluation, especially when undergoing ergometric tests, should be evaluated and oriented in practice by some supervised exercise sessions. The periodicity to realize the ergometric tests should not exceed 1 year. The main objectives of this phase are to increase and to maintain physical fitness. It is not mandatory that this phase be preceded by phase 3. The rehabilitation team should propose activities that are more appropriate for each one. Patients should be periodically and systematically contacted by the CR team, even by telephone, at least once every 6 months [6].

Within the CR session, each professional can choose to carry out different activities, among which are: aerobic training proper, which can be performed with cycle ergometer, sliding bands, climber or simply with walks guided by trained personnel; resistance exercises, strength exercises, coordination exercises, flexibility exercises and, in phases 3 and 4, specific exercises that have similarity to the work performed by the patient or to the activities performed.

The aerobic training can be performed using two types of exercises:

- A. a continuous method (CAT), which is characterized by the application of an uninterrupted load, that means, without pause or periods of rest during the work. This method can be extensive or intensive, finding the difference between both in the intensity of the exercise.
- B. an interval aerobic training—IAT method, that contains intervals of rest. When the work is high or moderate intensity, active intervals are used, whereas if the functional capacity of the patient is low, passive recovery intervals are used.

The intensity and duration of aerobic exercises are used to obtain greater benefits for the cardiovascular system and metabolism and have been explored in recent research.

At the beginning of the twenty-first century, research using high-intensity interval aerobic training (HIIAT) was carried out to improve the performance of athletes in competitions.

Examples of protocols of high-intensity interval training (HIIT) applied in studies in trained health volunteers are described as follow:

1. In moderately-trained healthy males. The HIIT interventions consisted of the following parts: (1) 8 min of a warm-up at a speed of 50% $\text{VO}_{2\text{max}}$; (2) interval exercise: total duration of 12 min, work/rest ratio = 1, work intensity 100% $\text{VO}_{2\text{max}}$, rest intensity 60% $\text{VO}_{2\text{max}}$, work and rest duration of 15 s, 30 s, or 60 s (three different groups); (3) a cool-down: 3 min at 5 $\text{km}\cdot\text{h}^{-1}$. All HIIT interventions were identical over the total duration, work/rest ratio, relative work and rest intensity [9].
2. In healthy adults enrolled in non-randomized study. The protocol was low-volume, HIIT consisting of 60 s work and 60 s recovery (60 s/60 s) repeated for 10 repetitions has previously been found to produce beneficial cardiopulmonary, cellular, and metabolic adaptations in healthy and at-risk populations, however using several combinations of work and recovery intensities based in varying percentages of peak power output (PPO) that consisted of the following work/recovery intensities (80% PPO/0% PPO; 80% PPO/50% PPO; 100% PPO/0% PPO and; 100% PPO/50% PPO). In a 100/50 group showed an increasing of PPO and $\text{VO}_{2\text{max}}$ compared to other groups and, the researchers concluded that use of the 80/0, 80/50, and 100/0 protocols would be appropriate for individuals who are at the low to moderate end of the cardiopulmonary fitness spectrum [10].
3. In healthy young men that performed eight 20 s bouts at 130% of the velocity associated with the $\text{VO}_{2\text{max}}$ on a treadmill with 10 s of passive rest in HIIT protocol. In this study, the researchers compared to moderate continuous training (MCT), which performed 30 min running on a treadmill at a submaximal velocity equivalent to 90–95% of the heart rate associated with the anaerobic threshold for data related to oxygen consumption and energy expenditure (EE) were measured during the protocols and the excess post-exercise oxygen consumption (EPOC) was calculated for both sessions. The results showed that post-exercise EE and EPOC values were higher after HIIT, suggesting that supramaximal HIIT has a higher impact on EE and EPOC in the early phase of recovery when compared to MCT [11].

The good response to exercise in health volunteers excited researchers that have been start investigating the benefits of IAT in patients with heart failure during rehabilitation or in patients after CABG. One protocol that showed be effective after CABG consisted of 8 min warm-up, 4 times of 4-min intervals at 90% of maximum heart rate, pauses of 3-min walking at 70% maximum heart rate, and 5 min cool-down after session [12]. This protocol enrolled patients referred to a residential rehabilitation center 4–16 weeks postoperatively, and they excluded heart failure, inability to exercise, or drug abuse. All patients performed a treadmill ergospirometry test before rehabilitation program to evaluation and prescription of exercise intensity and to determine the peak $\text{VO}_{2\text{peak}}$ pre- and post-training. Ergospirometry is a functional capacity test that noninvasively studies the pathophysiology of the respiratory and cardiovascular systems under conditions of physical stress, objectively evaluating the degree of functional limitation and its mechanism [13]. The ergospirometry have the advantage over conventional treadmill test because it calculates the VT.

Some studies performed the cardiopulmonary test on a treadmill [14, 15], while other studies performed the evaluation on a cycle ergometer [16, 17]. It should be noted that all patients were trained with the same tool with which they were evaluated, both those who performed the test in ergometric bicycle and in the treadmill.

The first IAT study in HF appears to have been in 1972, when patients were asked to cycle on high work load for 60 s with 30 s of rest between intervals. Using intervals, patients could perform the exercises at least twice if they were able to perform on a continuous cycling [18]. Several years ago, most of the scientific evidence demonstrated the benefits of training in patients with HF used continuous low to moderate intensity aerobic exercise. Therefore, few were the professionals who questioned the possibility of using a method that demand greater intensity during aerobic training.

3.2. Benefits of cardiac rehabilitation in cardiac diseases: coronary disease and heart failure

The cardiovascular system response to exercise integrates systemic, cellular, and molecular signaling pathways. The benefits assign to physical training on cardiopulmonary system are improve functional capacity, lessen the intensity of breathing and muscle discomfort, improve quality of life, increase blood muscle flow, increase oxidative and metabolic capacity, attenuate or reverse skeletal muscle atrophy, improve autonomic activation, increase endothelium activation, and improve muscle performance. In this way, it believes that interval exercise training additionally prolongs exercise duration, lowers cardiovascular demand, lowers ventilator requirement, allows higher exercise intensity, and reduces symptoms of dyspnoea and leg discomfort.

A recent meta-analysis [19] from Cochrane Group in CHD concluded that exercise-based CR reduces cardiovascular mortality and provides reduction in hospital admissions and improvements in quality of life regardless of the type of strategy used to treat CHD—medicine, angioplasty, or surgery. Several trials enrolled in this meta-analysis were performed before modern techniques of myocardial revascularization, and it could affect the final results. The GOSPEL study [20] enrolled 3241 patients with recent myocardial infarction and after 3 years of follow-up showed a decreased risk of nonfatal myocardial infarction and combined end-points as cardiovascular death plus nonfatal myocardial infarction and stroke. However, the DANREHAB trial [21] showed no differences between patients with HF, CHD, or high risk heart disease randomized to rehabilitation (n = 380) versus control group (n = 390) after 12 months of follow-up in primary composite outcomes.

The last trial to determine the exercise effect on outcomes in HF patients was the HF-ACTION trial (Heart Failure and A Controlled Trial Investigating Outcomes of Exercise Training) [22, 23]. This trial enrolled 2331 stable systolic HF patients with an EF lower or equal to 35% and randomized them to aerobic training or control group in France, Canada, and United States. Study participants had CHD (51%) and EF (25%). A total of 759 patients (65%) in the exercise group died or were hospitalized compared with 796 patients (68%) in the control group (hazard ratio 0.93 [95% CI: 0.84–1.02]). So, in this sample, the primary and secondary clinical

end-points do not show difference between groups. After adjustment for highly prognostic predictors of these end-points, a modest but significant reduction for both, any cause of death or hospitalization and cardiovascular death or HF admission.

In a recent study [24], 261 patients with HF and reduced LVEF (<35%) and NYHA II-III were randomly assigned to HIIT at 90–95% of maximal HR, MCT at 60–70% of HRmax or regular exercise (RRE). In a large clinical trial study, the researchers showed that HIIT was not superior to MCT in changing left ventricular remodeling or aerobic capacity. To assess left ventricular remodeling, left ventricular end-diastolic diameter was measured at the tip of the mitral leaflet in two-dimensional parasternal long-axis view by echocardiography and, for aerobic capacity, $\text{VO}_{2\text{peak}}$ and respiratory quotient were accessed. There was also no difference between HIIT and MCT in $\text{VO}_{2\text{peak}}$, but both were superior to RRE. The researchers still reported serious adverse events during the 12 weeks intervention, though there were no statistical significant differences between groups (HIIT 39%, MCT 25%, RRE 34%, $P = 0.16$), numerically was higher in HIIT, followed by RRE and MCT: $n = 82, 76$ e 73 , respectively. Therefore, the feasibility of the IAT program remains unresolved in heart failure patients.

Other studies in patients with HF trained in IAT program evaluated variables pre and post-training such as $\text{VO}_{2\text{max}}$ [7], left ventricular ejection fraction by echocardiographic analysis [7], endothelial function by evaluation of the flow-measured dilation [7], levels of natriuretic peptide in brain plasma, myeloperoxidase, interleukin-6, quality of life by questionnaires SF-36, the Minnesota Living With Heart Failure [8], and the Hare Davis Cardiac Depression Scale [25]. These results were controversial between the group in IAT and CAT programs for some variables.

Although controversies exist for HIIAT in patients with low functional capacity, as in patients with HF, this training method is often the best tool for starting a physical activity program, preventing patients from quickly fatigue and for achieving a better progression during training. Additionally, the HIIAT has been described as feasible to be performed by elderly patients with chronic heart failure and severe alterations in LVEF.

In patients with CAD with preserved or reduced LVEF, HIIAT showed to be superior to moderate MCT to improve $\text{VO}_{2\text{peak}}$, which is closely related to long-term survival in cardiac patients [26].

3.3. Benefits of cardiac rehabilitation in patients undergone CABG, focused on interval aerobic training

There are no trials with a sample size that could be considered sufficient to assess the magnitude of effect of exercise training rehabilitation in patients undergone CABG. Regarding IAT versus CET comparisons in such patients, there are only few trials with small sample sizes. Indeed, even with more than 50 years using surgery to treat CHD The scientific evidence of effects of rehabilitation with different protocols on post-CABG management is not extensive [27].

One observational cohort study [28] with 163 survivors' patients after CABG that were followed-up for 5–6 years showed that higher levels of exercise were associated with increased functional status, after adjustment for age, sex, severity of angina, shortness of breath, and fatigue. Interestingly enough, women who did not perform exercise more than 2 times a week had significantly lower physical and social status outcomes than women who did it.

A randomized controlled trial employed to analyze whether a behavioral and educational cardiac rehabilitation program was effective in modifying cardiovascular disease risk factors in 86 patients. The results showed more aerobic capacity assessed by $\text{VO}_{2\text{max}}$ in the interventional group [29]. Quality of life tended to improve steadily over time in both groups.

In a lack of sufficient trials to evaluate the effect of IAT versus CET as rehabilitation programs on mortality or major cardiovascular events after CABG, few trials with a small sample size used surrogate end-points as hemodynamic and ventilatory parameters to test exercise performance. In this way, $\text{VO}_{2\text{peak}}$ that strongly predicts mortality and was evaluated in patients submitted to IAT versus continuous moderate training (CMT) after CABG for 4 weeks and 6 months. The $\text{VO}_{2\text{peak}}$ was measured at the baseline, 4 weeks and after 6 months, presenting similar short-term increases in both IAT and CMT groups. However, there was better long-term effect in IAT group after CABG [12]. Other clinical trial tested IAT versus CET program by 3.5 weeks in a bicycle ergometer protocol. Nine patients in each group performed the exercise 24–26 days after CABG. At the end of protocol, IAT favors increasing physical performance, lower heart rate at rest (–9 bpm versus –4 bpm), lower rate-pressure product at rest, and lower lactate. There were no differences in catecholamines between groups. The authors concluded that IAT is better suited to increase physical performance and is more effective in saving cardiac function compared to CAT [30]. Rate-pressure product were also evaluated by others, and its measures in similar sample of patients with CAD undergone CABG and then trained in either CAT or IAT programs, presented a decreasing in resting and maximal rate-pressure product more significant only in IAT group. The rate-pressure product is an indirect index of myocardial oxygen consumption of patients with CAD [31].

Flow-mediated dilatation reflect the endothelial function and serves as a prognostic marker for cardiovascular events. IAT also enhance endothelial function as observed in studies that evaluated flow-mediated dilation of brachial artery after IAT in post-infarction heart failure [7], but there is a lack of studies with patients after CABG and IAT. In patients with cardiovascular and cerebrovascular disease [32] a systematic review including 20 studies showed that HIIAT was similar to moderate CAT through improvement in endothelial function measured by flow-mediated dilatation, nitric oxide bioavailability and circulating biomarkers.

On the other hand, there is controversy whether physical activity can improve heart function among several cardiac parameters evaluated by echocardiography. One study evaluated patients after CABG [7] and failed to show improvements in systolic annular velocity, mitral annular excursion, late diastolic mitral flow velocity (A wave), early diastolic mitral velocity, late diastolic mitral velocity, deceleration time of the early diastolic mitral velocity ejection fraction, end-diastolic volume, or end-systolic volume after 4 weeks of IAT. The results were similar to baseline, except by peak early diastolic mitral flow velocity (E wave) that it showed significant fall after 4 weeks IAT. However, patients that developed heart failure after infarct, but who did not perform CABG, and undergoing physical training, the IAT showed decline in left ventricle end-diastolic and end-systolic volumes, and left ventricle ejection fraction raised from 28 ± 7.3 to $38 \pm 9.8\%$, with better results to IAT compared to CMT [7].

Regarding changes in blood markers as low-density lipoprotein (LDL)-cholesterol, HDL-cholesterol, triglycerides, glucose, and hemoglobin were not demonstrated or do not have clinical value after IAT in CABG patients [8].

The HIIAT in CABG and PCI patients has been associated with platelet activation (CD62P) and function (platelet aggregation) compared to moderate continuous exercise, showing that the risk of exercise-induced thrombosis is higher during HIIAT than moderate CAT in patients with recent revascularization. Therefore, the acute effect of HIIT on platelet activation and function in patients with recent revascularization is still on debate [33]. In 1990, some studies initiated the research about IAT in patients submitted to CABG [34], but the literature about the theme is still scarce because current researches look for to compare continuous exercise training versus control groups [19]. In this context, it should be emphasized that more clinical trials with patients after CABG are still necessary.

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