Original Research

In-hospital mobilization after cardiac surgery: investigation of a dose-effect of once- and twice-daily exercise on cardiac autonomic modulation

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Abstract

Background: Coronary artery bypass surgery (CABG) implies in impairment of cardiac autonomic modulation (CAM). In-hospital mobilization positively affects CAM; however, it is not known whether higher exercise dosage would provide the same benefits in CAM as lower dosage in patients post-CABG. **Aims:** To investigate the dose-effect of an exercise inpatient program performed once or twice-daily on cardiac autonomic modulation post-CABG. **Design:** Prospective trial with a quasi-experimental design. **Methods:** Thirty patients of both sexes with a diagnosis of coronary heart disease and first-time post-CABG were allocated in a non-random manner into GEX1 (n = 10) and GEX2 (n = 10), composed of patients engaged in one and two daily exercise sessions plus usual care (breathing exercises, education with no systematized mobilization exercise program), respectively; and control group (CG, n = 10), composed of those who only received usual care. Patients underwent a mobilization protocol until discharge, which included a progressive five steps of active-assistive exercises of lower/upper limbs. Heart rate (HR) and R-wave intervals (RRi) were recorded by heart rate monitor at basal condition and discharge time. CAM was assessed by heart rate variability (HRV). **Results:** At discharge, the higher-dose group (GEX2) showed significant higher values of: parasympathetic (RMSSD: 7.9±1.3 ms vs 4.6±0.4 ms) and overall CAM indexes (STD RR: 7.5±1.1 ms vs 4.8±0.5 ms and TINN (38±6.4 ms vs 23±2.8 ms) compared with CG, respectively. In addition, mean HR (GEX2: 88.1 ±12.3 bpm; GEX1: 79.4±5.7 bpm, CG: 100.4±10.1 bpm) and mean RR (GEX2: 694.0±101.8 bpm; GEX1: 759.1±57.0 bpm, CG: 602.8±59.1 bpm) were different to exercise groups compared to controls regardless dosage. However, there was no significant difference between the exercise groups (GEX1 and GEX2). **Conclusions:** Regardless dosage, post-CABG patients who engaged in a mobilization-exercise program demonstrated better cardiac autonomic modulation at discharge compared with the control group. The results are encouraging further investigation in the field of in-hospital exercise rehabilitation dosage on cardiac autonomic modulation in a more comprehensive sample to strengthen the findings.

Keywords: Autonomic Nervous System; Coronary Artery Disease; Exercise; Rehabilitation; Cardiac Rehabilitation.

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How can the results of this study be used in clinical practice?

- Inpatient exercise-based rehabilitation improves cardiac autonomic control in post-CABG.
- Once or twice daily exercise rehabilitation post-CABG results in heart rate variability benefits.
- The results strengthen the importance of inpatient exercise-based rehabilitation focusing on an important outcome that is the cardiac autonomic control.

Introduction

Cardiac rehabilitation (CR) is strongly recommended for patients after coronary artery bypass grafting (CABG) surgery[1]. Early mobilization as part of an inpatient physical program is encouraged after cardiac surgery in order to counteract surgical and hospitalization negative effects[2]. Several benefits of exercise-based rehabilitation have been demonstrated, including improvement of functional capacity and reduction of postoperative complications, length of hospital stay[3], and health care costs[4].

Previously, our research group has already demonstrated beneficial effects of an early mobilization program, performed once-daily on cardiac autonomic modulation (CAM) in post CABG patients[5,6]. Interestingly, the dysfunction of the autonomic nervous system seems to be associated with increased risk of morbidity and mortality in these patients[7,8]; therefore, CR represents a powerful tool to improve clinical care and patients' outcomes.

Although early mobilization has been recommended, studies on the optimal dose effect of exercise in a hospital setting on different outcomes has not yielded conclusive results. A Swedish survey indicates that physiotherapy-supervised mobilization and exercise following cardiac surgery are prescribed ranging from one to three times a day during hospital stay[9]. However, there is no information on the benefits of different dosages of mobilization.

A cumulative effect of exercise or a dose-response relationship between physical exercises and health outcomes was previously reported and greater benefit has been linked with higher amounts of exercise[10]. Conversely, a low dose-response relationship between dose-exercise therapy and improvements was also reported[11]. Nevertheless, the effect of different exercise dosage on CAM early after CABG has not been explored before. Therefore, to contribute to an adequate post-CABG rehabilitation management, the current study aimed to investigate the dose-effect of an exercise inpatient program performed once or twice-daily on cardiac autonomic modulation post-CABG. It was hypothesized a dose-dependent adaptation on CAM with greater benefit in the twice-daily exercise group.

Methods

Population

This study is a prospective trial with a blinded outcome assessment and a quasi-experimental design, conducted within the coronary unit and cardiovascular ward of a tertiary hospital in Araraquara- SP-Brazil. All methods were carried out in accordance with relevant guidelines and regulations (Declaration of Helsinki). Patients awaiting first-time CABG were invited to participate in the study, after giving written informed consent. The protocol was approved by the local Ethics Committee (numbers 197/2005 CAAE 0095.0.135.000-05; 109/2010 CAAE 0191.0.135.000-09).

Thirty patients undergoing elective CABG surgery were enrolled in three different groups: GEX1 (n = 10) and GEX2 (n = 10), were composed of patients who performed a physical exercise protocol (mobilization exercise program) once and twice-daily, respectively plus usual care (breathing exercises, education instruction and no systematized mobilization exercise program); and CG, n = 10, performed only the usual care. This study was defined as a quasi-experimental design in which participants were assigned to either control group or experimental groups in a non-random manner. Eligibility criteria for participants included patients of both sexes who undergone an elective and first CABG carried out with cardiopulmonary bypass. Exclusion criteria comprised: emergent, concomitant surgery or other types of cardiac surgery, with recent myocardial infarction (less than six months), implanted pacemaker, unstable angina, chronic disturbances in heart rhythm, significant acute arrhythmias, valvular heart disease, chronic obstructive pulmonary disease, severe non-cardiac diseases, surgical complications, clinical instability, use of vasoactive drugs and inability to perform rehabilitation according to the proposed protocol.

Pre-operatively, patients' age, gender, weight, height, body mass index (BMI), cardiac risk factors and other relevant medical history were documented. Additionally, education about the effects of surgery on cardiorespiratory function, post-operative routines and the CR program were provided. Post-operatively, surgical and hospital data were recorded.

Interventions

During the inpatient phase, a daily-supervised usual care was applied to all patients. It consisted of respiratory exercises as: standard voluntary deep-breathing exercises from functional residual capacity to total lung capacity (40 deep breaths in four sets of 10, each breath included a 5 s hold at end of inspiration) followed by coughs or huffs (with wound support) for approximately 15 min. Patients were also instructed to perform these breathing and coughing exercises independently every waking hour. Patients of control group received the usual care intervention.

Patients allocated to the exercise groups were engaged to one (GEX1) or two daily exercise sessions (GEX2) plus usual care. Exercise protocol was similar for both groups and initiated on the first post-operative day until discharge[5]. Heart rate (HR) was monitored and maintained around 20 beats per minute above resting value as described previously[12], using a Polar S810i telemetry system (Polar Electro Oy, Kempele, Finland).

Mobilization exercise program: The protocol was organized in steps. Each step corresponded to one day of post-operative intervention. STEP 1: Active-assistive exercises of the lower/upper extremities - ankles and wrists, 5 sets of 10 repetitions; bed inclined at 45°; STEP 2: Active exercises of upper and lower limbs in sitting position (90º) - flexion-

extension of the bilateral shoulder, elbow, wrist, knee and ankle; adduction-abduction of the hips (2 sets of 15 for each) and orthostatic position/walking on spot (5 min) as tolerated; STEP 3: Active exercises, as in step 2, in 3 sets of 15 in the sitting position and ambulation within the inpatient ward (5 min) (approximate time spent = 50 min); STEP 4: Exercises similar in step 3 in sitting position; ambulation within the inpatient ward (10 min); STEP 5: Exercises similar to step 3 in orthostatic position, ambulation (10 min) and flight of stairs (four steps). STEP 5 was remained to those hospitalized beyond five days.

Interventions were undertaken by physiotherapists, specifically trained in the methods used in the study; the hospital staff were asked to avoid discussing issues of physiotherapy with patients, and to refer any questions regarding the study or physiotherapy treatments to the research team.

Outcomes

The main outcome of this study was the CAM measured by heart rate variability (HRV), which is a considerable potential tool to assess the autonomic nervous system in patients with cardiovascular disorders[13,14]. According to Task Force, inference is that therapeutic interventions that increase HRV may be protective against cardiac mortality and sudden cardiac death[14].

HR and RR interval (RRi) recording

HR and RRi were recorded for posterior analysis of HRV at: 1) pre-operative day, for autonomic basal function characterization and 2) at discharge time. All recordings were obtained during the afternoon, at rest and, in a sitting position for 10 min. Care was taken to avoid any manipulations during recording and no patient consumed caffeinated drinks/foods or smoked on the morning of assessments or during the procedure. Each patient rested for 10 min before the initiation of data collection to ensure the stabilization of HR.

HRV analysis

HR data were transferred to the computer and the RRi series were reviewed by visual inspection. Data were analyzed using Kubios HRV analysis software (MATLAB, version 2 beta, Kuopio, Finland). Series of 300 stable sequential RRi were considered for analysis.

Linear traditional measures in the time domain HRV analysis were evaluated by calculating the following, widely accepted parameters: Standard deviation of RRi (STD RR) in ms which represents a global index of HRV (overall HRV) and reflects all the cyclic components responsible for variability in the recording period; square root of the mean squared difference of successive RRi (RMSSD) in ms reflecting alterations in autonomic tone that are predominantly vagally mediated; and geometrical forms as the integral of the RRi histogram divided by the height of the histogram (RR tri

index) and the baseline width of the RRi histogram (TINN) in ms, that provides an estimate of the overall HRV[14-16].

Statistical analysis

Data are expressed as mean (standard deviation) unless otherwise specified. Between-group difference in continuous variables (pre-operative and discharge time) were examined by analysis of variance (ANOVA) or Kruskal-Wallis according to normality and/or equal variance, followed by Tukey's or Dunn's test. Fisher's Exact Test was applied for non-continuous variables. All the statistical analyses were two-tailed and P values ≤ 0.05 were considered significant. Statistical analyses were conducted using the SigmaPlot Software for Windows, version 11.0.

Results

Thirty patients were enrolled, and baseline characteristics are summarized in Table 1. No differences were observed among groups initially regarding clinical or demographic data, including age, height, gender and BMI. The surgical procedure data were comparable between groups, demonstrated by similar aortic cross clamping time, total surgery time and number of graft anastomoses. In addition, length of coronary care unit stay and post-operative hospital stay was also similar among groups. Usual medications prescribed after CABG were antiplatelet drug, statins, B-blockers, calcium antagonists, angiotensin converting enzyme inhibitors (ACEI) and analgesics. However, cardiopulmonary bypass time was different among the three groups with lower values in GEX2 compared to GEX1 and CG.

Compliance with trial methodology

All patients allocated in exercise groups, GEX1 and GEX2, participated in a once daily or twice-daily supervised postoperative exercise protocol, respectively, initiating on the first post-operative day until discharge (approximately five days). No clinically relevant adverse events occurred throughout the study. Vital signs remained within the range of normality in all patients.

Heart rate variability

There was no statistically significant difference among groups to HRV pre-operative condition (Table 2), although trends favoring GEX1 were observed (STD RR, RRtri, TINN, RMSSD). Postoperatively, at discharge, after rehabilitation completion program, HRV data demonstrated significant difference among the groups. Parasympathetic RMSSD HRV index and indexes of overall variability of RRi (STD RR, TINN) were significantly higher in GEX2 compared to the controls. In addition, mean HR was lower and mean RR was higher to exercise groups (GEX1 and GEX2), regardless dosage compared to CG as shown in Figure 1. However, there was no difference at discharge between the exercise groups (GEX1 and GEX2).

Table 1. Basic clinical, risk factors and surgical data.

	CG n = 10	GEX1 n = 10	GEX2 n = 10
Age, years	56.8 (10.8)	59.3 (7.9)	58.1 (4.9)
Male, number [%]	9 [90]	8 [80]	8 [80]
Weight, kg	72.8 (11.1)	71.9 (14.7)	70.6 (9.6)
Height, m	1.63 (0.06)	1.66 (0.07)	1.65 (0.09)
Body mass index, kg/m²	27.8 (4.2)	25.9 (4.9)	25.8 (2.9)
Respiratory rate, ipm	18.1 (4.2)	18.2 (1.5)	19.7 (3.0)
Risk factors			
Smoking history, number [%]	10 [100]	7 [70]	7 [70]
Arterial hypertension, number [%]	8 [80]	8 [80]	9 [90]
Diabetes mellitus, number [%]	5 [50]	6 [60]	6 [60]
Pharmacological treatment, number [%]			
β-blockers	9 [90]	7 [70]	10 [100]
Calcium antagonists	–	–	1 [10]
Antiplatelet	10 [100]	10 [100]	10 [100]
Pre and post-operative data			
Cardiopulmonary bypass, min	77.5 (11.3)	72.0 (25.8)	49.2 (17.7) [†] [‡]
Aortic cross clamping time, min	41.2 (8.0)	40.6 (18.9)	29.1 (13.2)
Distal anastomoses, number	2.5 (0.8)	2.6 (0.8)	2.1 (0.6)
Coronary care unit stay, days	2.2 (0.8)	2.0 (0.0)	2.5 (1.3)
Post-operative hospital stay, days	4.9 (1.7)	4.9 (0.3)	5.0 (1.1)

Data presented as mean (standard deviation, SD) or number (percentage) of subjects; CG = Control Group; GEX1 = one exercise daily session; GEX2 = two exercise daily sessions; †statistical difference between CG and GEX2; ‡statistical difference between GEX1 and GEX2.

Table 2. Heart rate variability indexes at baseline and discharge.

	CG n = 10	GEX1 n = 10	GEX2 n = 10	*P*-value
Mean RR, ms				
Baseline	810.3 (153.9)	939.21 (86.4)	904.8 (110.9)	0.14
Discharge	602.8 (59.1)	759.1 (57.0)*	694.0 (101.8)*	0.0004
Mean HR, bpm				
Baseline	76.7 (15.0)	64.4 (6.0)	67.1 (7.4)	0.14
Discharge	100.4 (10.1)	79.4 (5.7)*	88.1 (12.3)*	0.0002
STD RR, ms				
Baseline	17.5 (7.2)	20.1 (6.3)	13.5 (2.6)	0.07
Discharge	4.8 (2.1)	7.0 (1.6)	7.6 (3.9)*	0.05
RMSSD, ms				
Baseline	12.0 (4.4)	20.4 (9.2)	13.1 (5.6)	0.06
Discharge	4.6 (1.8)	6.9 (1.2)	7.9 (4.6)*	0.04
RR Tri				
Baseline	5.1 (1.9)	6.1 (1.9)	4.2 (0.7)	0.07
Discharge	1.9 (0.3)	2.3 (0.4)	2.6 (0.4)	0.13
TINN, ms				
Baseline	84.0 (35.6)	96.5 (30.2)	65.5 (15.5)	0.06
Discharge	23 (10.6)	35 (7.4)	38 (21.2)*	0.04

Data presented as mean (standard deviation, SD); CG = Control Group; GEX1 = one exercise daily session; GEX2 = two exercise daily sessions; RR = R-R intervals; STD RR = standard deviation of all RR; HR = heart rate; RMSSD = square root of the mean squared difference of successive RR; RRTRI = triangular index; TINN = triangular interpolation of RR intervals.

Discussion

This study aimed to investigate a potential dose-response of an exercise-based impatient program after cardiac CABG surgery on CAM. Our results suggest that regardless the doses of exercise (once or twice a day) there was significant cardiac autonomic benefit compared to controls.

Dose-response of physical activity and health benefits has been demonstrated for overall mortality, risk of coronary heart disease and numerous health outcomes including cardiorespiratory fitness, body composition and high-density lipoprotein cholesterol (HDL-C) in diverse populations[17-21]. In postmenopausal women, Friedenreich et al.[19] observed
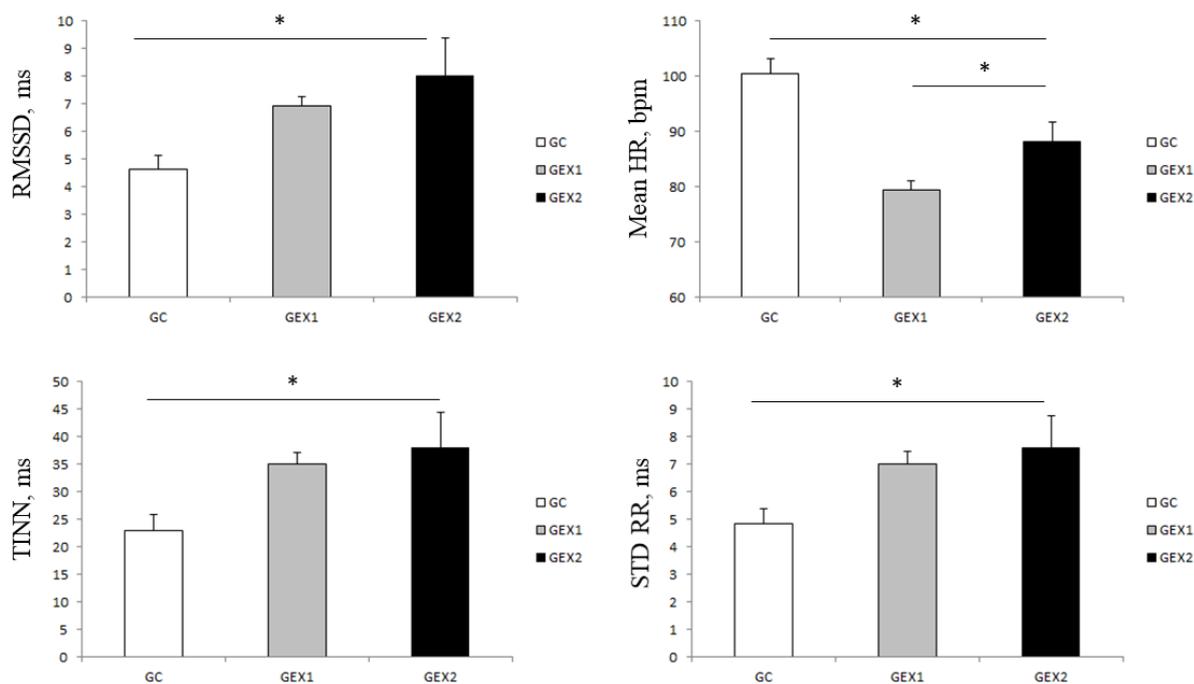
Figure 1. HRV indexes at discharge. Abbreviations: STD RR: standard deviation of the mean of all inter-beat intervals; RRtri: triangular index; TI NN: triangular interpolation of NN interval histogram; RMSSD: square root of the mean squared difference of successive RR intervals, ms: milliseconds; HR = heart rate; CG = Control Group; GEX1 = one exercise daily session; GEX2 = two exercise daily sessions. *Different from CG.

an additional benefit of higher-volume aerobic exercise (300 versus 150 minutes/week) for adiposity outcomes and risk of postmenopausal breast cancer, while Lee et al.[21] showed that elderly men who exercised once or twice per week had a lower risk of all-cause mortality compared with sedentary.

Although these studies have supported the dose-response relationship with largest health improvements among training programs of greater duration and/or intensity[22,23], there is no study involving patients after cardiac surgery, more specifically in CABG surgery, and exercise programs performed during the hospitalization phase (CR phase I).

Early mobilization and exercise-based inpatient rehabilitation after cardiac surgery has gained wide acceptance and evidence[2]. A multifactorial positive effect value has been proved, including effects on postoperative respiratory complications, functional capacity and CAM[2,5,6,9,24-26]. Previously, our group was able to demonstrate a positive cardiac autonomic effect of an early mobilization program performed once a day[5,6]. At hospital discharge, patients that engaged in an early mobilization protocol presented higher values of parasympathetic and overall HRV indexes compared to a control group[5].

Although some effect of early mobilization on HRV has already been demonstrated, no information about the dosage of exercise intervention is available at this early stage of

rehabilitation. The current study is the first to focus directly on the influence of different dosages of an inpatient exercise program on HRV parameters in patients who underwent cardiac surgery.

For this purpose, in a comparison of once or twice a day and no systematic rehabilitation, the group enrolled to physical exercise twice-daily demonstrated significantly higher values of overall variability indexes of RRi (STD RR and TINN) and parasympathetic status (as shown by greater HRV RMSSD index) compared to control group. On the other hand, mean HR presented lower values at discharge regardless of the volume of exercise imposed with significant difference for both groups (once and twice a day) in comparison to control group. Therefore, our current results suggest that both doses of exercise provided cardiac autonomic benefits without advantage.

To highlight the clinical importance of these findings, it is relevant to point out the role of the autonomic nervous system in the regulation of the cardiovascular system in order to match cardiac output with the body's need during various exogenic stimuli[14]. Moreover, cardiac autonomic nervous system has a significant impact on cardiac electrophysiology and arrhythmogenesis, which is an important clinical aspect mainly after a surgical procedure[27,28].

The finding of high resting heart rate of this study was proved to be associated with ventricular arrhythmogenesis

(positive ventricular late potentials) by factors as premature ventricular complexes and depressed HRV[29]. It was also previously demonstrated that a decreased HRV may be indicative of an electrically unstable myocardium[28], myocardial vulnerability and occurrence of malignant arrhythmias[14]. Besides that, it has been demonstrated that CABG patients with postoperative decreased HRV have a higher incidence of adverse coronary events, such as new myocardial infarction or sudden death[8,30]. In this study, longitudinal follow-up was not performed to investigate these outcomes, which would be interesting in future studies.

Inpatient and outpatient exercise-based programs have been shown to increase HRV and consequently the cardiac autonomic regulation in a variety of clinical populations[31-33]. A similar hospital-based exercise program was carried out post-acute myocardium infarction once a day and resulted in increased vagal and decreased sympathetic cardiac modulation; however, exercise dosage was not the focus of that study[34].

In the outpatient field, some evidence suggests that at least two mediators, angiotensin II and nitric oxide, may play roles in mechanisms contributing to beneficial modifications of HRV[33]. Nitric oxide has a direct effect on vagal tone[35] and angiotensin is an inhibitor of cardiac vagal activity[36]. However, there is no studies available in which the mechanisms responsible to improve cardiac regulation after CABG facing early mobilization were investigated.

Previous studies showed that surgical procedure per se leads to an impairment of cardiac autonomic regulation attributed to several factors such as direct surgical manipulation of the heart and adjacent structures, duration of surgery, anesthesia, aortic clamping, cardioplegic arrest and cardiopulmonary bypass extracorporeal circulation (CPB)[37,38]. In the current study, although CPB time was shorter in GEX2, authors conducted an additional association analysis between HRV indexes versus CPB time and there was no relationship between them, suggesting there are no effects of this surgical factor on the studied sample.

A strength of this study was to show an import and practical aspect regarding one and two exercises daily sessions and no influence of inpatient exercise dosage on cardiac autonomic adaptation after CABG. Importantly, the terminus dose can be referred to different components of exercise training such as frequency, intensity, and duration. In the present study, distinct dosage was considered by adjusting frequency of exercise, adding a complete exercise session in another period of the day. Thus, there are several possibilities to change and test dose–response in exercise rehabilitation programs which deserves attention in results' comparisons.

Despite its strength, the study has limitations. The small sample, which may have contributed to the absence of difference between groups due to a Type II error. The study design did not consider an intention to treat analysis and only those who actually performed all the proposed steps were considered to be part of the final analysis. The quasi-experimental design with non-random allocation is liable to

bias; however, it was the only way to develop the study due to logistical factors. In addition, HRV assessments did not consider the effects of respiratory rate and daily medications. Furthermore, due to the harmful potential of surgical procedure to autonomic system, baseline parameters should ideally be considered in the period after the surgery. Finally, we have to assume a potential influence of cardiopulmonary bypass time on cardiac autonomic modulation, although sub-analysis in the present study have not pointed that out.

In conclusion, our results suggest that regardless dosage, post-CABG patients who engaged in a mobilization-exercise program demonstrated significant better cardiac autonomic modulation at discharge compared with the control group. The results are encouraging further investigation in a more comprehensive sample to reinforce the findings in the field of in-hospital exercise rehabilitation investigation.

Conflict of interest

None

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