ORIGINAL ARTICLE

Rev Bras Cir Cardiovasc 2010; 25(3): 333-340

Assessment and medium-term follow up of heart transplant candidates undergoing low-intensity exercise

Avaliação e seguimento em médio prazo em candidatos a transplante cardíaco submetidos a exercício de baixa intensidade

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RBCCV 44205-1195

Abstract

Objectives: **To study cardiovascular behavior and safety regarding a low-intensity exercise program for heart transplant candidates with severe heart failure.**

Methods: **Twenty-one patients with severe heart failure on the transplant list of the UNIFESP university hospital (Brazil) were studied. Following evaluation, the patients were monitored during an exercise program with six progressive phases (1 - upper limbs; 2 - lower limbs; 3 - walking; 4 - ½ flight of stairs; 5 - walking 200 m; and 6 - whole flight of stairs), with the intensity estimated at two to six metabolic equivalents (1 MET = 3.5 ml of O_2/kg/min.). The patients were prospectively followed up for approximately 17 months for the occurrence of clinical complications and death.**

Results: **Three patients were unable to perform the complete program; BMI, maximal respiratory pressure (Pimax and Pemax, cmH_2O) and number of previous hospitalizations were considered predictors for this subgroup. Heart rate (HR, bpm), double product (DP, bpm x mmHg) and Borg perceived exertion scale (PE) underwent the greatest oscillation during exercise, especially in phase 5 (H"METS), and are considered the best markers related to exertion. Blood pressure (BP, mmHg) oscillated little. There was no increase in the incidence of arrhythmia (Kappa=0.552) during exercise. There was a moderate positive correlation between PE and BP (r=0.4; *P*=0.02) in phase 5 (walking 200 m). The patients who died had low Pimax values upon the initial evaluation. During the exercise program, there was a reduction in BP response and an increase in HR response.**

Conclusion: **Regarding cardiovascular behavior, the exercise program proved safe and well tolerated, but there is a need for monitoring. Information obtained upon the initial evaluation and during exercise program is associated to decompensation and death. Such information could assist in determining the stage of the disease.**

Descriptors: **Exercise. Heart failure. Rehabilitation. Heart transplantation.**

Resumo

Objetivos: **Estudar o comportamento cardiovascular e segurança frente a protocolo de exercícios de baixa intensidade em pacientes com insuficiência cardíaca (IC) grave, candidatos a transplante cardíaco.**

Métodos: **Foram estudados 21 pacientes com IC grave, inscritos na lista de transplante cardíaco do Hospital Universitário da UNIFESP. Após avaliação, os pacientes foram**

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Article received on March 11th, 2010
Article accepted on August 24, 2010

monitorados durante a realização de protocolo de exercício com seis fases progressivas (1º membros superiores, 2º membros inferiores, 3º caminhada 35 m, 4º ½ lance de escada, 5º caminhada de 200 m e 6º 1 lance de escada), com intensidade estimada em 2 a 6 equivalentes metabólicos (1 MET = 3,5 ml de O_2/kg/min.). Os pacientes foram acompanhados prospectivamente por aproximadamente 17 meses quanto à ocorrência de complicações clínicas e óbito.

Resultados: **Dentre os pacientes estudados, três não foram capazes de realizar o protocolo completo, sendo as variáveis índice de massa corporal (IMC), pressão respiratória máxima (Pimáx e Pemáx, cmH_2O) e número de internações prévias, consideradas preditivas neste subgrupo. Frente ao protocolo de exercício, a frequência cardíaca (FC, bpm), duplo produto (DP, bpm x mmHg) e escala de percepção de esforço (EP, Borg) apresentaram maior oscilação, principalmente durante a fase 5 (H"5 METS), sendo considerados os melhores marcadores relativos ao esforço. A pressão arterial (PA, mmHg) apresentou pouca oscilação. Não houve aumento da incidência de arritmias (Kappa=0,552) frente ao esforço. Observamos correlação positiva moderada entre a EP apenas na fase 6 (caminhada de 200m), com PA (r=0,4; *P*=0,02). Nos pacientes com desfecho óbito, foram observados valores reduzidos de PiMax na avaliação prévia. Durante o protocolo, redução da resposta de PA e maior elevação da resposta de FC.**

Conclusão: **O comportamento cardiovascular frente ao protocolo de exercícios foi bem tolerado e seguro, mas reforça a necessidade de monitoração. Informações obtidas na avaliação clínica inicial e durante o protocolo estão associadas com a descompensação e óbito tardio, e podem auxiliar no estadiamento destes pacientes.**

Descritores: **Exercício. Insuficiência cardíaca. Reabilitação. Transplante de coração.**

INTRODUCTION

Heart failure (HF) is highly prevalent, affecting mainly those over 65 years. Approximately 10% of HF patients progress to more severe stages of the disease. They are patients that, despite optimal medical therapy, remain symptomatic, with evidence of disease progression, unacceptable quality of life and high mortality rate in a year. For these cases, transplantation is a viable therapeutic option, which has shown good results, but the increased demand for new organs made patients wait longer on transplant waiting list. During this phase, the exercise is indicated with the aim of improving the overall condition of the patient, making the surgery safer, as well as the postoperative period [1-4]. However, the expected cardiovascular behavior toward the exercise program is not well established in these patients with severe HF.

Patients with severe HF awaiting cardiac transplantation have become severely debilitated and have a great limitation to physical activity due to the onset of symptoms such as breathlessness and fatigue during exercise, activities of daily life and even at rest. These patients often suffer from their clinical decompensation and require hospitalization, besides the death risk associated with progressive circulatory failure and sudden death while awaiting cardiac transplantation. These factors make this population more susceptible to risks during the physical activity program [5,6] and may contribute to its clinical worsening due to the restrictions on movement.

Studies have recently shown the benefits of physical exercise in patients with mild to moderate HF, which are expected to increase exercise tolerance, maximum oxygen consumption, improved quality of life, the autonomic behavior of skeletal and respiratory muscles, and reducing the number of hospitalizations. However, in patients with severe HF, especially those awaiting heart transplants, the benefits are still conflicting [7-9].

We believe that the research on the cardiovascular responses to physical exercise in patients with severe HF may produce greater benefits of current recommendations for physical activity prescription, providing greater security and reliability, encouraging indication of exercise routine in this phase. Therefore, this study aims to evaluate the behavior and cardiovascular safety protocol toward low-intensity exercises in patients with severe heart failure awaiting heart transplantation.

METHODS

Study participants

The study was conducted with 21 patients (age 54.33 ± 9.63 years) from the Heart Transplant Clinic at the University Hospital of the Federal University of São Paulo (UNIFESP). Three patients were unable to perform the entire exercise series, when two of them discontinued the protocol because of lower limb pain and arrhythmia. One patient underwent continuous ECG monitoring during the protocol, but due to technical equipment problems it was not possible to record

Table 1. Baseline characteristics, stage and clinical outcome of patients that underwent exercise protocol. (n=21)

Variables	Mean DP
Descritivas	
Age(years)	54.3±9.62
Weight(kg)	67.44±13.51
Height(m)	1.64±0.09
BMI	24.82±4.04
	N (%)
Gender	
Masculine	17 (81.0)
Feminine	4 (19.0)
Medication in use	
ACE inhibitor	15 (71.4)
Digitalis	13 (61.9)
Diuretic	20 (95.2)
Beta blocker	14 (66.7)
Vasodilator	4 (19.0)
Antiarrhythmic agents	1 (4.8)
Anticoagulant	3 (14.3)
Etiology	
schemic myocardiopathy	13 (61.9)
Idiopathic myocardiopathy	6 (28.6)
Congenital cardiopathy	2 (9.5)
Smoking	
Yes	12 (57.1)
No	9 (42.9)
Clinical staging	
LVEF(%)	29.56±12.6
Functional Classification	
II	7 (35.0)
III	8 (40.0)
IV	5 (25.0)
Comorbidities	
SAH	8 (38.1)
DM	4 (19.0)
RF	2 (9.5)
AMI	
1 event	4 (19.0)
2 events	6 (28.6)
3 events	4 (19.0)
Prior Cardiac Surgery	
1	10 (47.6)
2	4 (19.0)
Maximal respiratory pressures	
PImax	-89.5±36.4
Pimax (%predicted pressure)	-76.25±31.5
PEmax	87.3±33.6
Pemax (% predicted pressure)	75.8±24.7
Clinical Outcome	
Hospitalizations	
0	9 (42.9)
1	5 (23.8)
2	4 (19.0)
<3	3 (14.4)
Death	
Yes	6 (28.6)
No	15 (71.4)

BMI - Body Mass Index, LVEF - Left Ventricular Ejection Fraction, NYHA - New York Heart Association; Systemic Arterial Hypertension (SAH), DM - Diabetes mellitus, RF - Renal Failure, AMI - Acute Myocardial Infarction; ACE - Angiotensin-Converting Enzyme. Continuous parametric data expressed as mean ± standard deviation; non-parametric data represented as median and percentiles, categorical or continuous data represented by N

the arrhythmic events, which stopped the report preparation and the detailed analysis of arrhythmias in this patient. The study participants were diagnosed with refractory heart failure, with elective indication for heart transplantation and age between 35 to 75 years. Exclusion criteria were: decompensated HF, use of vasoactive drugs, unstable angina, fixed-frequency pacemaker or cardiac defibrillator, severe valvular insufficiency or stenosis, recent surgery (less than 60 days), morbid obesity (BMI> 40 kg/m^2), diseases that preclude the achievement of exercise protocol.

Most of the population was predominantly male (81%), the body mass index (BMI) was 24.82 ± 4.04 kg/m^2. Thirteen (65%) patients were in functional class III and IV (NYHA), the most frequent heart failure etiology was the ischemic cardiomyopathy (61.9%), 12 (57.1%) patients had a history of smoking, and ten (47.6%) had undergone previous surgery (Table 1). Maximal respiratory pressures have a mean of 76.25% ± 31.54% predicted values for MIP and 75.8 ± 24.74% for MEP values. The study was approved by the Research Ethics Committee and all participants signed the informed consent.

Design and protocol

The study was described as a prospective cohort study where clinical assessment was initially performed, with information about the clinical and cardiovascular stage, followed by exercise protocol of 2-6 metabolic equivalents (METS). After this phase, patients were followed up for an average of 17.71 ± 6.43 months, according to the frequency of hospitalization, cardiac transplantation and mortality.

Standardized assessment

Using standardized assessment form, data were collected regarding medical history, such as comorbidities, smoking history, previous cardiovascular surgery, prior ischemic events in acute coronary, current medication, heart failure etiology, functional class and ejection fraction (in %) obtained from routine echocardiography examination, as well as information regarding physical examination and tests of respiratory muscle strength [10].

Low-intensity exercise protocol

After initial evaluation, patients underwent a protocol with six stages of exercise with intensity between 2 to 6 metabolic equivalents (Mets) [11]: exercise 1 - shoulder flexion-extension (20 reps) Exercise 2 - knee flexion-extension (20 reps) Exercise 3 - 35 meters walk with a speed of approximately 3 km / h, exercise 4 - walk up and down flight of stairs, exercise 5 - 200 meters walk with a speed of approximately 3 km / h; exercise 6 - walk up and down a flight of stairs.

During the implementation of the protocol, it was performed the monitoring of the heart rate (bpm), blood

pressure (BP, mmHg), mean arterial pressure (MAP, mmHg), double product (DP, mmHg / bpm), Borg Scale of Perceived Exertion (PE), and continuous Electrocardiography (ECG) telemetry (QUARK T12 model CO9055-32-99, Cosmed ®, Italy), which offered instant information on electrocardiography.

Some factors were considered for suspension or effort interruption, as clinical features according to the Brazilian Consensus on Ergonometry of the Brazilian Society of Cardiology [12].

Statistical analysis

The data were evaluated using Kolmogorov-Smirnov Normality Test (KS) to test its Gaussian distribution, while parametric continuous data were compared along the stages of exercise by ANOVA, and the Friedman test analysed the

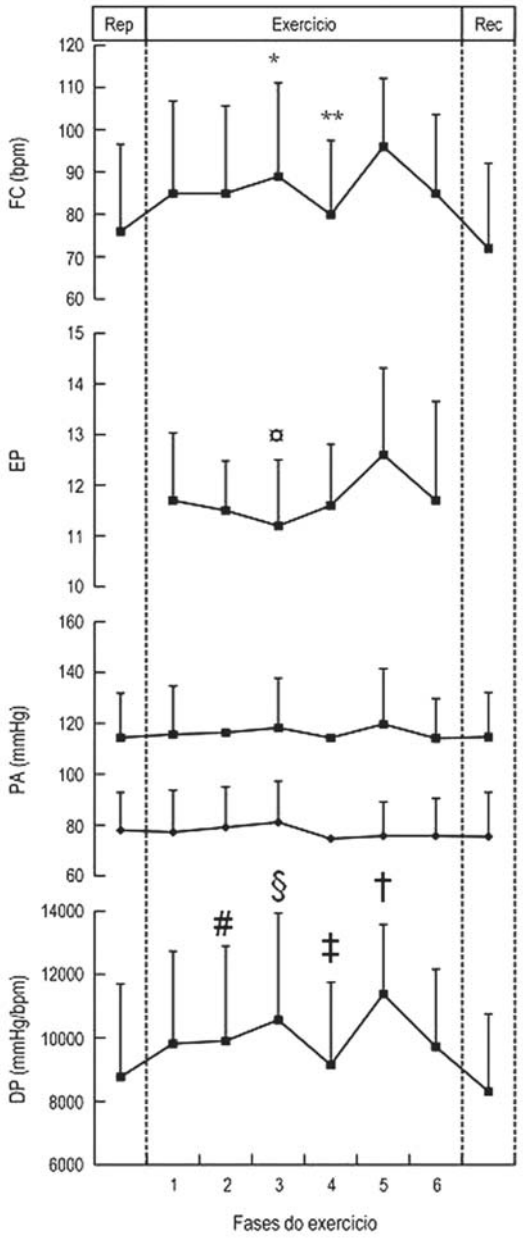

Fig. 1 - Heart rate behavior, blood pressure, perceived exertion scale and double product throughout the exercise series

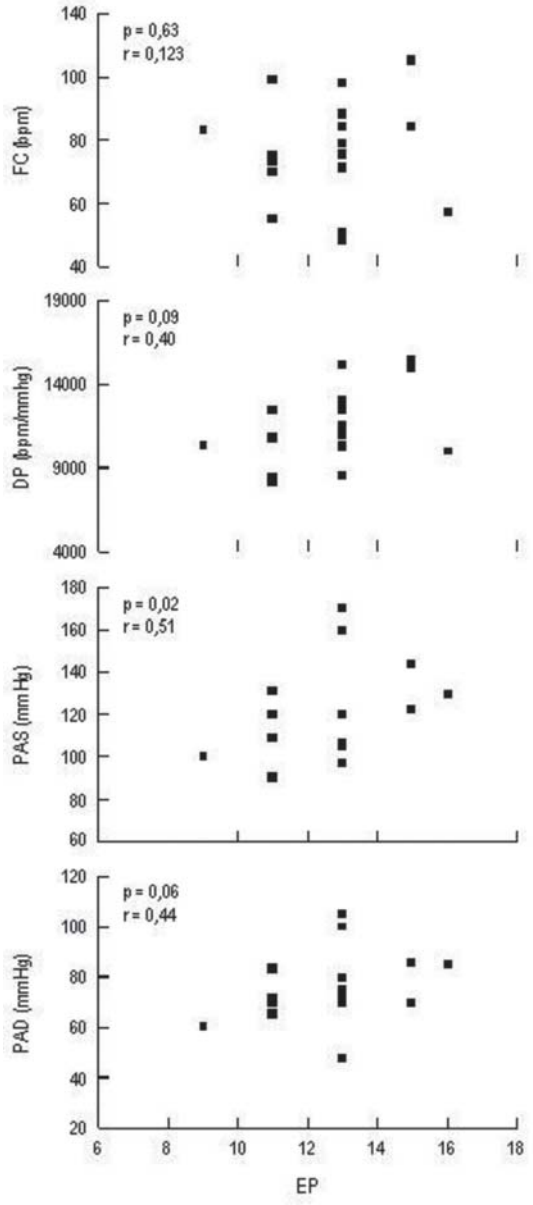

Fig. 2 - Correlation of hemodynamic variables with perceived exertion scale during 200m walk.
HR - heart rate, DP - Double product, SBP - systolic blood pressure, DBP - diastolic blood pressure; RPE – Rating of perceived exertion scale

non-parametric data. When differences were significant (*P*-value <0.05) throughout the stages of exercise, the Bonferroni method was applied for multiple comparisons. It was used Pearson's linear correlation analysis to assess the association between variables of cardiovascular performance with perceived exertion scale, which were for parametric data. Spearman's for nonparametric. When the correlation was significant, the agreement values were: > 0.75 excellent, moderate between 0.40 and 0.75 and <0.40 poor.

In order to describe if there were any difference between the amount of arrhythmic events, and also between different stages and throughout the bouts of exercise (rest, during exercise and recovery), we used the Kappa agreement analysis, which were considered reliability values <0.19 poor, moderate 0.20 to 0.40 and from 0.60 to 1 high.

RESULTS

Cardiovascular response during exercise protocol

Among 21 patients, three discontinued the protocol for lower limb pain and arrhythmia. Clinical evaluation of factors that could be associated with the interruption revealed that, the variables BMI and respiratory muscle strength were different to average values found in the population.

The average values during the rest period were 76.24 ± 20.36 bpm HR, SBP, 114.43 ± 17.50 mmHg, DBP 77.9 ± 14.88 mmHg, SD 8771 ± 2931 mmHg x bpm.

We can observe greater rise in HR, DP and RPE during the exercise 5 (200m walk), with values of 96.17 ± 16.21 bpm, 11384.11 ± 2197.7 mmHg x bpm and 13 ± 1.7, respectively. Differences in HR were found between exercises 3 and 4 (35 m 1/2 flight of stairs), where there was a reduction in HR, and between 4 and 5 (1/2 flight of stairs and 200 m) in which we observed an increase in HR. The Double Product has increased between exercises 2 and 5 (LL and 200 m) and between 3 and 5 (½ flight of stairs and 200 m), and decreased between 3 and 4 (35 m and ½ flight of stairs) and between 5 and 6 (200m and 1 flight of stairs). The RPE differs between exercises 3 and 5 (35m and 200m) where there is the greater value at 200 m.

SBP and DBP showed little change during the series of exercises. It was only found correlation among the studied variables on SBP in exercise 5 (200m) with PE, where P = 0.02 and r = 0.516 (Figure 2).

Frequency, characteristics and arrhythmia severity

During the exercises, seven different types of arrhythmia have occurred, such as: a single ventricular extrasystole, multifocal ventricular extrasystole, supraventricular extrasystole, sinus pause, atrial fibrillation and atrial fibrillation with rapid ventricular response, and the ventricular extrasystole appeared more frequently. The descriptive analysis of the type of arrhythmia revealed no increase during the exercise protocol (Kappa = 0.552). The qualitative analysis also showed no increase during the classification regarding the origin (Kappa = 0.731) or type (Kappa = 0.765).

Table 2. Comparison regarding the frequency, characteristics and arrhythmias severity, before, during and after exercise protocol.

Arrhythmia analysis	Stage								
	Rest	Exercise						Recovery	Kappa
		1	2	3	4	5	6		
All individuals analysed per stage	N=20	N=20	N=20	N=20	N=18	N=17	N=17	N=17	
Toral of patients with arrhythmia per stage	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Arrhythmia Severity									0.731
0 Degree, absent	9 (45)	11 (55)	10 (50)	10 (50)	10 (55)	8 (47)	7 (41)	9 (53)	
1st Degree, supraventricular	1 (5)	2 (10)	2 (10)	2 (10)	3 (17)	2 (12)	4 (24)	3 (18)	
2nd Degree, ventricular	10 (50)	7 (35)	8 (40)	8 (40)	5 (28)	7 (41)	6 (35)	5 (29)	
Arrhythmia Severity (low)									0.761
0 Degree, extrasystoles	9 (45)	13 (65)	12 (60)	12 (60)	13 (72)	10 (59)	11 (65)	12 (71)	
1st Degree, <30 extrasystoles/hour	6 (30)	5 (25)	5 (25)	6 (30)	3 (17)	3 (18)	2 (12)	3 (12)	
2nd Degree, >30 extrasystoles/hour	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	
3rd Degree, polymorphic extrasystoles	4 (20)	2 (10)	3 (15)	2 (10)	2 (11)	4 (24)	4 (24)	2 (24)	
4th Degree A, coupled extrasystoles	1 (5)	0 0	0 0	0 0	0 0	0 0	0 0	0 0	
4th Degree B, ventricular tachycardia	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	
5th Degree, R-on-T phenomenon	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	

1) Shoulder flexion, 2) Knee extension, 3) 35m walk, 4) Climbing ½ flight of stairs, 5) 200m walk 6) Climbing a flight of stairs. HR, SBP, DBP, RPE and DP behavior throughout the exercise series

Table 3. Comparison among survivors, deaths, hospitalized and non-hospitalized patients, during the follow-up period of 17 months.

		Death			Hospitalizations		
		No	Yes	*P*	No	Yes	*P*
Variables	n	Mean SD	Mean SD		Mean SD	Mean SD	
During clinical accessment							
PImax	20	-100.9±32.9	-63.0±31.9	0.03*	-102.2±29.8	-80.7±40.1	0.24
PEmax	20	94.9±27.9	69.7±41.8	0.13	90.9±32.4	84.4 ± 35.8	0.67
NYHA	20	2.7±0.8	3.3±0.5	0.11	2.6±0.7	3.2 ±0.8	0.07
FEVE	20	31.3±13.5	24.8±9.4	0.34	33.2±16.3	25.9 ±6.4	0.22
Number of previous surgeries	20	0.9±0.8	0.7±0.5	0.46	1.0±0.7	0.8 ±0.8	0.44
Previous AMI	20	1.7±1.1	1.0±1.3	0.25	1.5±1.2	1.5 ±1.4	0.92
During exercise HR (bpm)							
Superior limbs (SL) exercises	20	82.8±22.8	90.1±19.8	0.50	85.8±20.8	84.2 ±23.3	0.86
Inferior limbs (IL) exercises	20	83.0±22.1	90.0±17.0	0.46	84.6±20.0	85.5 ±6.3	0.92
35m walking exercise	20	87.8±24.7	±	0.67	87.6±19.1	90.5 ±24.8	0.77
½ flight of stairs exercise	19	78.1±16.8	86.8±19.4	0.36	81.2±18.2	79.9 ±17.7	0.89
200m walking exercise	17	92.3±14.9	109.7±14.4	0.05*	90.8±12.5	100.5 ±18.0	0.21
1 flight of stairs exercise	17	98.0±25.8	81.7±15.4	0.13	84.4±15.3	86.1 ±21.7	0.85
PAS (mmHg)							
Superior limbs (SL) exercises	20	121.0±19.4	102.0±10.2	0.04*	123.0±21.3	110.3 ±15.7	0.13
Inferior limbs (IL) exercises	20	122.2±18.2	101.0±12.3	0.01*	125.3±21.3	109.2 ±14.0	0.05*
35m walking exercise	20	123.0±20.7	106.6±9.3	0.02*	127.7±22.3	111.1 ±14.0	0.05*
½ flight of stairs exercise	19	121.5±19.2	97.8±10.7	0.02*	128.5±20.2	107.0 ±15.4	0.01*
200m walking exercise	17	123.6±22.6	106.2±13.5	0.17	113.1±25.1	106.2 ±13.5	0.01*
1 flight of stairs exercise	17	117.3±15.7	102.7±9.5	0.10	123.1±16.9	106.9 ±10.4	0.02*
DBP (mmHg)							
Superior limbs (SL) exercises	20	80.5±17.9	69.0±8.0	0.05*	84.0±17.3	72.0 ±14.1	0.102
Inferior limbs (IL) exercises	20	82.7±16.7	70.0±8.8	0.09	84.9±14.0	74.8 ±16.2	0.151
35m walking exercise	20	82.7±16.7	70.0±.8	0.97	84.9±14.0	74.8 ±16.2	0.151
½ flight of stairs exercise	19	79.2±18.5	66.6±9.6	0.17	84.6± 17.9	70.3 ±15.2	0.07*
200m walking exercise	17	76.7±15.0	71.7±2.3	0.25	84.3± 13.4	68.8 ±8.8	0.01*
1 flight of stairs exercise	17	77.9±16.1	67.7±4.6	0.24	84.9±16.7	68.3 ±8.2	0.01*

*MIP - maximum inspiratory pressure, MEP - maximum expiratory pressure; %pred -% of predicted pressure; NYHA - New York Heart Association, LVEF - left ventricular ejection fraction, AMI - Acute myocardial infarction * P ≤ 0.05*

Clinical outcome during follow-up period

During the average follow up of 17 months, six patients (28.5%) underwent heart transplantation, three (14.2%) died related to the transplant procedure, three (14.2%) died during the waiting time to transplant and 12 (57%) needed one or more hospitalizations due to the worsening of their clinical status.

The paired analysis of the characteristics analysed before and during the exercise protocol, revealed a significant difference between individuals that subsequently died in 17 months and the surviving group, considering the MIP, peak HR, SBP and DBP characteristics (Table 3). When the same analysis was performed for hospitalization versus no hospitalization, significant differences were found between SBP and DBP.

DISCUSSION

The current study has shown that the cardiovascular behavior toward the exercise protocol was well tolerated and safe for most analysed patients, however, it seems necessary to monitor the exercises. We also found evidence that data obtained in initial clinical evaluation may be associated with decompensation and death, and may help stratify these patients.

The exercise protocol used in this study is proposed during phase I of Cardiovascular Rehabilitation, and the advantage does not require special equipment, it is also easy to apply and does not involve additional costs. This protocol mimics the activities of daily living, unlike traditional exercise protocols with treadmills or stationary

bikes. The guideline published in 2009 [13] underscores the importance of investigating the symptoms during the activities of daily life in patients with HF, from tests of physical performance and cardiorespiratory capacity, taking into account information on plain walking, climbing stairs, bathing, performing household chores, eating, sleeping and lying constraint. Some of these activities are included in our protocol.

The study population showed the expected characteristics in patients with severe heart failure, as the presence of some comorbidities, most with functional classification III to IV, reduced cardiac function, history of disease and previous cardiac procedures with prevalence of ischemic etymology [3,8]. The maximal respiratory pressures were reduced compared to the predicted ones, as observed in other studies [14,15]. The mortality rates, during the transplantation waiting period, were lower than the 20% to 40% in the literature for this population, thus we believe this may be due to the observation period, which was not the same for all patients and not all of them were followed up until the date of transplantation [1].

Regarding the cardiovascular behavior during the exercise protocol, we observed that CF and SD showed greater variation among the variables, followed by the RPE, mainly during exercise of higher intensity and duration (200m walk). On the other hand, the other variables, such as PAS, DAP and MAP showed less variation. In the exercise recovery phase, these variables returned to resting values approximately two minutes after the exercise. Previous studies show a greater HF increase in higher intensity exercises and exercises that require greater muscle mass [16]. The cardiovascular behavior is presented as expected for this population, and we believe that patients had good tolerance to exercises.

When investigated the correlation between cardiovascular responses during the 200m walk with PE, we found a positive correlation with SBP. It is found RPE correlation reports with HR in healthy individuals in the literature, and this scale has the recommendation to be used as a form of exercise prescription in several populations. Rehabilitation Guides recommend the use of RPE to determine the intensity of exercise in patients with HF, and the value of RPE reported by the patient corresponds to a percentage of maximum HR. Physiologically, the SBP and HR rise during exercise. In spite of the fact that the classical correlation (HR) is not found, the finding demonstrates the scale compared with the effort [17,18].

To analyse the occurrence of arrhythmias, we used two classifications, one proposed by Lown & Wolf [19] to the severity of ventricular arrhythmias, and the atrioventricular classification (AV) based on the origin [20] as well as the descriptive evaluation of arrhythmic events. We observed a high incidence of arrhythmia during rest period, however, these were not exacerbated with the protocol implementation, as shown by the Kappa agreement analysis. There were not any studies showing incidence of arrhythmias during acute exercise in HF, but it is known that the incidence of arrhythmias increases depending on the type of exercise and its intensity[20,21]. Changes may occur during the exercise, and trigger arrhythmias, such as reducing the parasympathetic tone and increasing the sympathetic with higher sinus rate, and transient ischemia in areas with poor myocardial perfusion in patients with a previous history of ischemic disease. A study evaluating the continuous electrocardiography in patients with HF showed that, 90% of patients have some type of arrhythmia. Among the predisposing mechanisms, the left ventricular dysfunction, myocardial ischemia, sympathetic overactivity, elevated levels of circulating catecholamines, the Arrhythmogenic effects of inotropic agents, electrolyte disturbances, myocardial relaxation and hypotension are mentioned. [2]. Therefore, the results obtained in our study may show safety when conducting the proposed protocol.

When the comparison was made between the characteristics of survivors versus deaths, the greatest value of HR was observed during the 200m walk, and lower value of MIP in patients who died. Previous studies indicate that individuals with HF have an abnormal HR response during exercise, occurring faster rise in HR when the IC is more severe. There is also an inability to increase cardiac output in response to exercise, due to the chronotopic incompetence and reduced stroke volume, and HR is the main culprit in increasing the Q during exercise [11,20,22,23].

Some authors have found prognostic value for the maximal static respiratory evaluation in patients with HF, in which were found lower values of MIP and MEP in the absence of non-survivors, and concluded that MIP, VO2max and LVEF can be used as risk stratifiers for patients with IC [24.25]. As it was mentioned earlier, we found different values of SBP and DBP during some stages of the exercise, but not at rest. Previous studies show that the low BP at rest is considered an independent predictor of hospitalization for HF and, this may not be found in our study due to the patient's severity that showed a difference only when submitted to exercise [14].

The study had some limitations; one of them was the small patient sample, which may compromise the interpretation of partial results. However, these patients correspond to all the entries in the queue for a heart transplant, which fit the inclusion criteria of the transplantation team during the period that the study was conducted. Another limitation was that the follow-up period was not the same for all individuals. This was possibly because new patients entered the list for heart transplantation and were evaluated during the study and suffered frequent decompensation, postponing its inclusion in the study.

In summary, then, we believe that the low-intensity exercise protocol was well tolerated and safe for the majority of this population, and data obtained in the initial clinical evaluation may be associated with decompensation and death, and may help in these patients' stratification that were considered at high risk for carrying out exercise.

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