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# Cardiopulmonary exercise testing in the early-phase of myocardial infarction

## Teste de exercício cardiopulmonar na fase precoce do infarto do miocárdio

Vandeni C. Kunz<sup>1</sup>, Karina B. S. Serra<sup>2</sup>, Érica N. Borges<sup>2</sup>, Paulo E. S. Serra<sup>3</sup>, Ester Silva<sup>1,2</sup>

### Abstract

**Objective:** To evaluate and to compare the cardiorespiratory and metabolic variables at the ventilatory anaerobic threshold level (AT) and at submaximal cardiopulmonary exercise testing (CPET) in both, healthy volunteers and in patients in the early phase after acute myocardial infarction (AMI). **Method:** Twenty-six volunteers underwent a submaximal or symptom-limited cardiopulmonary exercise testing (CPET) on a cycle ergometer and were divided into AMI group (AMIG=12, 56.33±8.65 years) and healthy group (CG=14, 53.33±3.28 years). The primary outcome measures were the cardiorespiratory and metabolic variables obtained at the peak workload and at the AT of the CPET. Statistical test: independent Student's *t*-test,  $\alpha=5\%$ . **Results:** The AMIG presented lower values at the AT and the peak workload of the CPET compared to the CG: power in watts (91.06±30.10 and 64.88±19.92; 154.93±34.65 and 120.40±29.60);  $\text{VO}_2 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  (17.26±2.71 and 12.19±2.51; 25.39±5.73 and 19.41±5.63);  $\text{VCO}_2 \text{ L}\cdot\text{min}^{-1}$  (1.43±0.31 and 0.93±0.23; 2.07±0.43 and 1.42±0.36);  $\text{VO}_2 \text{ L}\cdot\text{min}^{-1}$  (1.33±0.32 and 1.00±0.23; 1.97±0.39 and 1.49±0.36);  $\text{VEL}\cdot\text{min}^{-1}$  (42.13±8.32 and 27.51±5.86; 63.07±20.83 and 40.82±11.96); HR (bpm) (122.96±14.02 and 103.46±13.38; 149.67±13.77 and 127.60±10.04), double product (DP) (bpm.mmHg.min<sup>-1</sup>) (21835.86±3245.93 and 17333.25±2716.51; 27302.33±3053.08 and 21864.00±2051.48), respectively. The variable oxygen uptake efficiency slope (OUES L/min) was lower in the AMIG (1.79±0.51) than the CG (2.26±0.37). The AMIG presented neither ECG alterations nor symptoms that limited the CPET. **Conclusion:** The results suggest that patients with AMI Killip class I presented lower functional capacity and DP compared to the CG without presenting ischemic alterations. Thus, the study suggests that submaximal CPET can be applied at an early stage to evaluate cardiorespiratory status since it is both safe and highly sensitive to detect changes.

**Keywords:** oxygen consumption; myocardial infarction; physical exercise; physical therapy.

### Resumo

**Objetivo:** Avaliar e comparar as variáveis cardiorrespiratórias e metabólicas no nível do limiar de anaerobiose ventilatório (LAV) e no pico do teste de exercício cardiopulmonar (TECP) submáximo em voluntários saudáveis e em pacientes na fase precoce após o infarto agudo do miocárdio (IAM). **Método:** Vinte e seis voluntários realizaram TECP submáximo ou sintoma limitante em cicloergômetro e foram divididos em grupo IAM (G-IAM=12, 56,33±8,65 anos) e grupo saudável (GC=14, 53,33±3,28 anos). As medidas dos desfechos principais foram as variáveis cardiorrespiratórias e metabólicas obtidas no pico e no LAV do TECP. Teste estatístico: *t*-Student não pareado,  $\alpha=5\%$ . **Resultados:** O G-IAM apresentou menores valores no LAV e no pico do TECP que o GC ( $p<0,05$ ): potência em Watts (91,06±30,10 e 64,88±19,92; 154,93±34,65 e 120,40±29,60);  $\text{VO}_2 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  (17,26±2,71 e 12,19±2,51; 25,39±5,73 e 19,41±5,63);  $\text{VCO}_2 \text{ L}\cdot\text{min}^{-1}$  (1,43±0,31 e 0,93±0,23; 2,07±0,43 e 1,42±0,36);  $\text{VO}_2 \text{ L}\cdot\text{min}^{-1}$  (1,33±0,32 e 1,00±0,23; 1,97±0,39 e 1,49±0,36);  $\text{VEL}\cdot\text{min}^{-1}$  (42,13±8,32 e 27,51±5,86; 63,07±20,83 e 40,82±11,96); FC (bpm) (122,96±14,02 e 103,46±13,38; 149,67±13,77 e 127,60±10,04); duplo produto (DP) (bpm.mmHg.min<sup>-1</sup>) (21835,86±3245,93 e 17333,25±2716,51; 27302,33±3053,08 e 21864,00±2051,48), respectivamente. A variável *Oxygen Uptake Efficiency Slope* (OUES L/min) do G-IAM foi 1,79±0,51 e do GC 2,26±0,37,  $p<0,05$ . O G-IAM não apresentou alterações eletrocardiográficas ou sintomas que limitassem o TECP. **Conclusão:** Os resultados mostram que os pacientes com IAM Killip I apresentaram menor capacidade funcional e DP em relação ao GC, sem apresentar alterações isquêmicas. Assim, o estudo sugere que o TECP submáximo pode ser aplicado precocemente para a avaliação cardiorrespiratória por apresentar alta sensibilidade para detectar alterações de forma segura.

**Palavras-chave:** consumo de oxigênio; infarto do miocárdio; exercício físico; fisioterapia.

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## Introduction ::::

The recommendation for physical therapy treatment based on physical training within a cardiac rehabilitation program for patients after acute myocardial infarction (AMI) depends on its evolution based on clinical criteria and results of invasive and non-invasive exams<sup>1-3</sup>. Among the non-invasive examinations, the cardiopulmonary exercise testing (CPET) performed in an early-phase after the coronary event has become routine in several medical centers<sup>3-5</sup>. From this exam, it is possible to obtain more precise information regarding the integration among the pulmonary, cardiovascular and musculoskeletal systems and the changes of the functional aerobic capacity due to pathological conditions, such as in the AMI<sup>5-7</sup>. In addition, it is possible to evaluate the prognosis of the patient in relation to risk stratification for new cardiac events<sup>2,3</sup>.

The literature reports that the maximal oxygen consumption ( $\text{VO}_{2\text{max}}$ ) is one of the most investigated variables<sup>8,9</sup>. However, the  $\text{VO}_{2\text{max}}$  is hardly achieved by cardiac patients, whose the exercise performance is limited by peripheral muscle fatigue, dyspnea, and the presence of significant cardiac alterations<sup>10</sup>. Moreover, the exercise performance depends on the motivation and perception of the subjects. In this case, the determination of the ventilatory anaerobic threshold (AT), which is an important physiologic parameter, has been recommended since it provides information regarding the physiological changes from the aerobic to the anaerobic metabolism<sup>11</sup>. Therefore, it has been considered more objective for the prescription of aerobic physical training, demonstrating good reproducibility<sup>9,12,13</sup>.

Furthermore, in the AT level there is a balance between the supply and consumption of  $\text{O}_2$  in the working muscles, preventing acidosis; the sympathetic nervous system is not over stimulated, and thus minor changes occur in the release of the epinephrine and norepinephrine hormones, which allows that, in this exercise level, these patients become able to maintain a working frequency for a prolonged period of time<sup>14</sup>.

Additionally, from the CPET it is possible to evaluate the variables  $\text{VE}/\text{VCO}_2$  slope and the Oxygen Uptake Efficiency Slope (OUES), which indicate the ventilatory efficiency for the production of carbon dioxide and oxygen consumption, respectively. Thus, from these variables it is possible to obtain clinical information about the functional status, disease severity<sup>15-17</sup>, and also information about the prognosis of coronary diseases, without exposing the patient to maximal CPET<sup>9,18,19</sup>. Moreover, it can be used to evaluate and prescribe the intensity of physical exercise in a cardiac rehabilitation program<sup>19,20</sup>.

The submaximal CPET has been used to evaluate the variables of cardiac patients, since during this test the oxygen supply to tissues while performing the exercise is not limited. Submaximal tests are more appropriate for patients with cardiovascular disorders because they provide greater efficacy and safety for the prescription of physical training in physical therapy treatment programs<sup>14,21,22</sup>.

The hypothesis of the present study was that patients may be submitted to submaximal CPET, after hospital discharge due to AMI, to evaluate clinical, hemodynamic, metabolic and electrocardiographic responses to submaximal CPET. Therefore, the aim of this study was to evaluate and to compare the cardiorespiratory and metabolic variables at the AT level and at the peak of the submaximal CPET in healthy subjects and in patients in the early phase after the AMI.

## Method ::::

### Study design and ethic approval

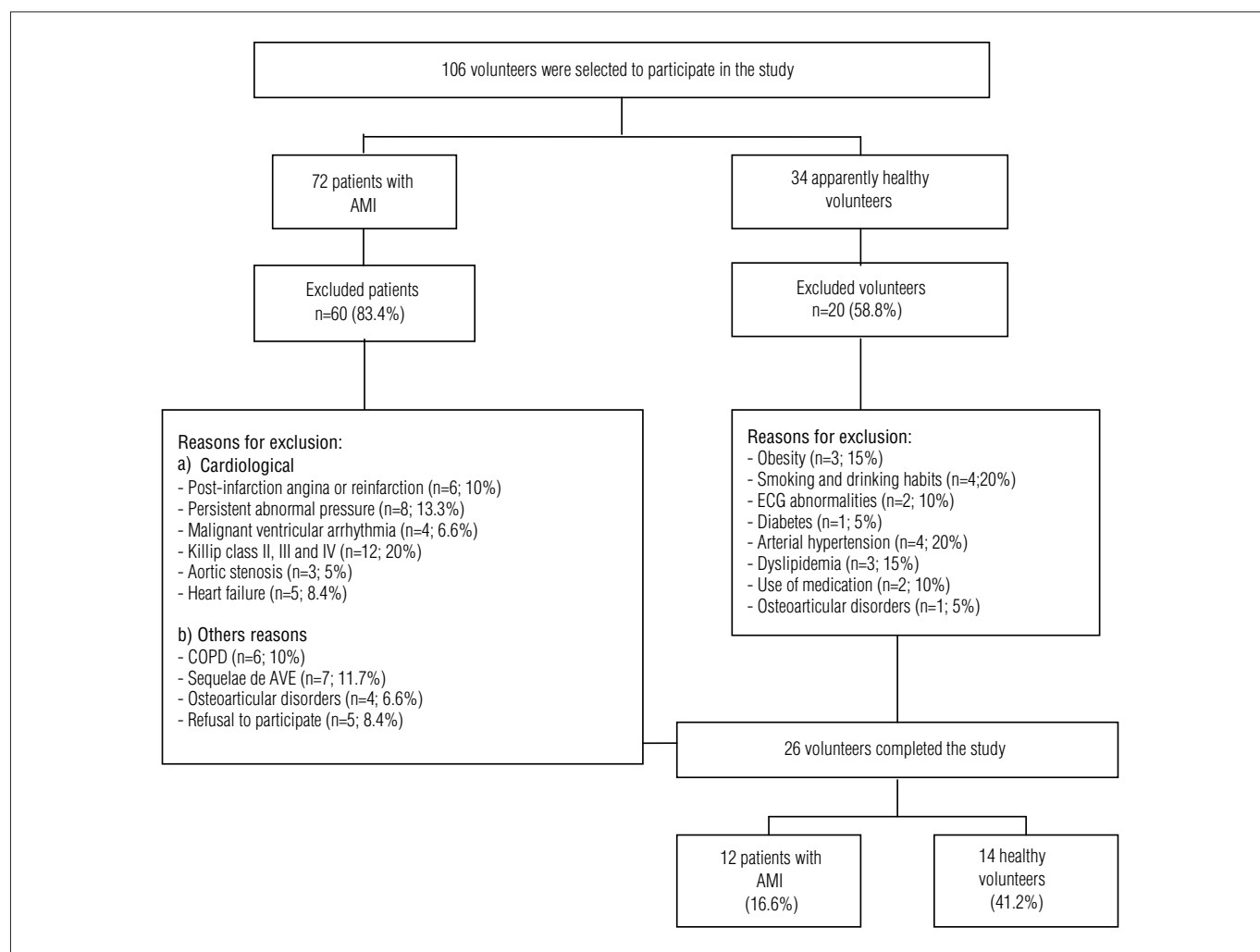
This was a cross-sectional study, with the approval of the Ethics Committee of Research of the Universidade Metodista de Piracicaba (UNIMEP), Piracicaba, SP, Brazil, n° 63/06. The participants agreed and signed an informed consent form according to the Resolution n° 196/96 of the Brazilian Health National Council.

### Sample size calculation

The sample size was calculated for the variable  $\text{VO}_2$  in  $\text{mL.kg}^{-1}.\text{min}^{-1}$ , with a 95% confidence level and statistical power of 80%, capable to detect a difference between-groups (two-tailed test) suggested a number of 12 subjects for each group, (*Graph Pad Stat Mate*, version 1.01i, 1998).

### Participants

One hundred and six subjects (72 with AMI and 34 healthy) with ages ranging between 50 and 65 years were screened for study participation. Of these, 12 patients with the diagnosis of AMI ( $56.33 \pm 8.65$  years-old) and 14 healthy subjects ( $53.33 \pm 3.28$  years-old) completed the study. The flow of the participants through the study can be observed in Figure 1.



**Figure 1.** Flow diagram of the study.

The participants of the AMI group (AMIG) were selected in the Coronary Units of the Hospital dos Fornecedores de Cana de Piracicaba, SP and Santa Casa de Misericórdia de Limeira, SP, Brazil. The patients from the AMIG underwent the doppler echocardiogram and cardiac catheterization with chemical or mechanical reperfusion in the first hours after the AMI; were taking beta-blockers (atenolol,  $46 \pm 9.4$  mg/day); with left ventricular ejection fraction (LVEF) within the limits of normality ( $0.61 \pm 0.06$ ); and with clinical classification of Killip I. To compose the healthy group (CG), 34 subjects were evaluated (CG), being included 14 subjects whom had not participated in physical training programs; presented an aerobic classification as weak<sup>23</sup>, did not have any indication of cardiovascular, respiratory, musculoskeletal and/or metabolic abnormalities, were not taken medications and were not smokers or alcohol drinkers.

Subjects from both groups underwent clinical and cardiovascular evaluation and also performed blood biochemical tests (total and fraction cholesterol (HLD, LDL) blood glucose, triglycerides, creatinine and uric acid).

The diagnosis of AMI had been confirmed by the presence of two or more criteria: 1) chest or retrosternal pain (constricting or burning pain), with or without radiation for the upper limbs, neck and upper back, lasting >30 minutes with no relief of symptoms to the vasodilator; 2) ST-segment elevation >1 mV in at least two or more contiguous electrocardiogram (ECG), 3) elevation of myocardial necrosis markers CK-MB and CPK, twice the normal values<sup>24</sup>.

## Experimental procedure

All the participants underwent clinical evaluation performed by a cardiologist before the performance of the CPET.

The experimental procedures were held in acclimatized laboratory, with temperature and relative humidity around 23°C and 60% respectively. The tests were performed in the afternoon to minimize the interferences of the circadian cycle on the cardiovascular responses. The participants were previously familiarized with the laboratory environment, with the

experimental procedures and with the equipments that were used in the experiment. All subjects were instructed not to ingest caffeine, alcoholic beverages and do not perform physical exercise on the day before and in the day of the experiments. During the experiments, the AMIG should maintain the medication in use. Before beginning the tests, the volunteers were asked about the occurrence of a normal night's sleep and, in addition, examined in order to guarantee that they were with their basal conditions within the normality limits<sup>25</sup>.

## Experimental protocol

The experiment consisted of a CPET, ramp-type continuous physical exercise, performed in a cycle ergometer with electromagnetic breaking (*QuintonCorival 400*, Seattle, WA, USA), with seat height adjusted to allow knee flexion of 5-10 degrees. The participants were instructed not to perform an isometric contraction of the upper limbs, while holding the handlebars of the bicycle, and to maintain pedaling cadence at 60 rpm.

The protocol consisted of a pre-test rest sitting on a cycle ergometer for a period of 60 seconds; starting the exercise with free load during a period of 240 seconds, followed by an increase of power on every 60 seconds, individually calculated according to the formula described by Wasserman et al.<sup>14</sup>, being of 10 watts (W) for the patients of the AMIG and 15W for the volunteers of the CG. For both groups, the CPET was submaximal, being interrupted when the submaximal heart rate (HR) was reached or in the presence of signs and/or symptom-limiting<sup>26</sup>.

The HR was captured through a heart rate monitor of one channel (*MINISCOPE II Instramed-Porto Alegre*, RS, Brazil) and processed through an analog to digital converter Lab. PC+ (*National Instruments Co.* Austin, TX, USA), which represents an interface between the heart rate monitor and a microcomputer. The signal was recorded in real time, after A/D conversion, in a sampling rate of 500 Hz<sup>27</sup>; and the blood pressure (BP) was measured using the auscultatory method based on Korotkoff sound on every 2 minutes, using a mercury sphygmomanometer (*WanMed*, São Paulo, SP, Brasil) and a stethoscope (*Littman*, St. Paul, MN, USA).

Ventilatory and metabolic variables, such as pulmonary ventilation (VE) in BTPS L/min<sup>-1</sup>, VO<sub>2</sub> mL.kg<sup>-1</sup>.min<sup>-1</sup>, and VCO<sub>2</sub> in L/min<sup>-1</sup>, respiratory exchange ratio (R) and HR were recorded simultaneously during the entire CPET, breath by breath, through a measurement system of the expired gases (CPX/D *Med Graphics - Breeze*, St. Paul, Minnesota, USA), which was calibrated before each test. These variables were subsequently processed and calculated as moving means every eight respiratory cycles for better kinetic observation of responses during physical exercise.

## Analysis of ventilatory and metabolic variables

The determination of AT was performed through the graphic visual analysis method of the responses of the metabolic and ventilatory variables, performed by three observers with previous experience in the administration of the procedures used for such purpose. The criterion for the quantification of the AT was the moment that a disproportional increase of VCO<sub>2</sub> in relation to a linear increase of VO<sub>2</sub> was observed by analyzing the graphic in the ergospirometer monitor<sup>11,27</sup>. For this analysis, it was selected the slope interval between the early response of the ventilatory and metabolic variables at increasing power until the respiratory compensation point (RCP) or until the end of the exercise, if the participant did not present the RCP. This analysis was based in the method *V-slope* described by Wasserman and McIlroy<sup>28</sup>, which is considered a gold-standard. From this, there were verified the power values in watts, HR in bpm, VO<sub>2</sub> in mL.kg<sup>-1</sup>.min<sup>-1</sup> and L/min, VCO<sub>2</sub> and L/min R, VE in L/min, respiratory exchange rate (R) and corresponding to the AT and the peak of exercise. The AT value was considered as the mean of the data obtained from the analysis of the three observers. The inter-rater reliability measured by the intraclass correlation coefficient (ICC) was of 0.96<sup>29</sup>.

The slope VE/VCO<sub>2</sub> was calculated by linear regression models, from the beginning of increase of power during the test until the peak of exercise, using the values of the increased minute ventilation in relation to the carbon dioxide production, obtained during the CPET<sup>30</sup>.

The OUES, which represents the relation between VO<sub>2</sub> and VE during the incremental exercise test, was calculated by logarithm expression of ventilation, in which OUES is defined as the regression slope "a" in  $VO_2 = a \cdot \log VE + b$ . A high or sharpened OUES represents greater efficiency of VO<sub>2</sub>, whereas a low OUES represents a greater VE in relation to VO<sub>2</sub><sup>20</sup>. For the calculation of the predicted values of OUES, we used the equation published by Hollenberg and Tanger<sup>31</sup>, in which men is represented by  $OUES (L/min) = [1320 - (26.7 \times \text{age}) + (1394 \times \text{body surface area})] / 1000$ .

## Statistical analysis

Data analysis was performed using the software SPSS, version 16. The normal distribution of all variables was verified using the Shapiro-Wilk test. Independent Student's *t*-test, with significance level of  $\alpha=5\%$ , was used for the between-group comparison. The results for age, anthropometric characteristics and cardiovascular variables during rest were expressed as means and standard-deviation. The results of the clinical



characteristics were expressed in number of volunteers and percentage. The values of cardiorespiratory variables obtained in the CPET were expressed as mean and standard deviation, mean difference and its 95% confidence intervals (CI).

## Results

### Sample characteristics

Anthropometric characteristics, age and cardiovascular variables during rest did not differ between the groups studied (Table 1). The risk factors present at AMIG were tabagism, hyperglycemia, hypercholesterolemia, hypertriglyceridemia, systemic arterial hypertension. On the other hand, the CG did not present any of the risk factors mentioned above. The clinical characteristics related to the AMIG data concerning the localization and clinical classification of the AMI, left ventricle ejection fraction (LVFE), type of myocardial reperfusion and the use of medications are presented in Table 1.

### Analysis of the ventilatory and metabolic variables

The ventilatory and metabolic variables obtained during peak exercise and the AT, concerning to power,  $\text{VO}_2$ ,  $\text{VCO}_2$ , VE, HR e DP of the AMIG were significantly lower compared to CG ( $p < 0.05$ ). The values of the variables slope  $\text{VE}/\text{VCO}_2$  and OUES predicted did not present significant between-group difference. The OUES obtained in the AMIG was lower than the CG ( $p < 0.05$ ). However, the variables R, SBP and DBP at peak exercise and at AT did not present between-group difference ( $p > 0.05$ ) (Table 2).

### Signs and symptoms during the cardiopulmonary exercise testing

The electrocardiographic data during rest and during CPET are described in Table 3. Patients presented an abnormal resting ECG related to AMI, and in the effort ECG any patient presented alterations in the ST-segment and the changes observed during resting was maintained. The data related to the symptoms of AMIG present at the peak of exercise and at the AT during the CPET is described in Table 3. In the AT, all patients reported absence of symptoms during effort

**Table 1.** Age, anthropometric characteristics, cardiovascular variables and clinical characteristics of the acute myocardial infarction group (AMIG) and the control group (CG) expressed as mean and standard deviation, number of volunteers and percentages of the sample.

	AMIG (n=12)	CG (n=14)
	mean±SD	mean±SD
Age and anthropometric characteristics		
Age (years)	56.33±8.65	53.33±3.28
Height (cm)	166.08±4.94	170±6.68
Body mass (kg)	76.25±12.45	79.46±7.96
BMI (kg/m <sup>2</sup> )	27.42±3.82	27.4±3.28
Cardiovascular variables		
HR (bpm)	66.08±10.08	69.5±9.43
SBP (mmHg)	126.67±13.03	116.25±6.44
DBP (mmHg)	78.33±11.15	76.25±6.44
	n (%)	n (%)
Clinical characteristics		
Smokers	6 (50)	0 (0)
Hypertension≥140/90 mmHg	2 (16.6)	0 (0)
Fasting hyperglycemia≥126 mg/dL	4 (33.3)	0 (0)
Hypercholesterolemia >240 mg/dL	3 (25)	0 (0)
Hypertriglyceridemia >200 mg/dL	4 (33.3)	0 (0)
AMI location		
Anterior	4 (33.3)	-
Postero-inferior	8 (66.6)	-
Killip I clinical classification	12 (100)	-
LVEF>40%	12 (100)	-
Reperfusion		
Chemical	6 (50)	-
Mechanical	6 (50)	-
Medications		
Betablockers	12 (100)	-
ACEI	2 (16.6)	-

kg/m<sup>2</sup>=kilograms per square meter; HR=heart rate; bpm=beats per minute; SBP=systolic blood pressure; DBP=diastolic blood pressure; mmHg=millimeters of mercury; n=number of volunteers; mg/dL=milligram per deciliter; LVEF=left ventricle ejection fraction; ACEI=angiotensin-converting enzyme inhibitor; Mean±SD=mean±standard deviation.

and at peak of exercise, two patients had dyspnea associated to hypertension reactive to the effort, one patient and presented dyspnea and nine patients had fatigue of the lower limbs, evaluated based on the non-maintenance of the rpm.

## Discussion

The early evaluation of the aerobic functional capacity in patients suffering from AMI using beta blockers is of fundamental importance for the risk stratification, recommendation about the limitations to perform physical activity, as well as to prescribe the appropriate physical training intensity<sup>14,32</sup>. In this

**Table 2.** Values in means and standard deviation of the ventilatory and metabolic variables obtained at the peak of the cardiopulmonary exercise test (CPET) and the anaerobic threshold (AT) of the acute myocardial infarction (AMIG) and control groups (CG).

Variables		AMIG (n=12)	CG (n=14)	Diff. b/t means	95%CI (diff. b/t means)	p-value
PEAK	Power (W)	91.06±30.10	154.93±34.65	-65.46	-90.14 to -0.79	0.00
	VO <sub>2</sub> (mL.kg <sup>-1</sup> .min <sup>-1</sup> )	17.26±2.71	25.39±5.73	-7.93	-11.29 to -4.58	0.00
	VCO <sub>2</sub> (L/min)	1.43±0.31	2.07±0.43	-0.64	-0.93 to -0.35	0.00
	VO <sub>2</sub> (L/min)	1.33±0.32	1.97±0.39	-0.65	-0.93 to -0.38	0.00
	VE (L/min)	42.13±8.32	63.07±20.83	-20.39	-32.12 to -8.65	0.00
	R	1.03±0.04	1.05±0.06	-0.01	-0.04 to 0.02	0.26
	HR (bpm)	122.96±14.02	149.67±13.77	-26.80	-37.20 to -16.40	0.00
	SBP (mmHg)	177.08±10.54	182.33±9.98	-5.19	-12.75 to 2.37	0.08
	DBP (mmHg)	95.00±9.05	90.67±7.99	4.13	-2.28 to -10.55	0.09
	DP (bpm.mmHg.min <sup>-1</sup> )	21835.86±3245.93	27302.33±3053.08	-5466.50	-7971.21 to -2961.78	0.00
AT	Potency (W)	64.88±19.92	120.40±29.60	-55.47	-74.72 to -36.23	0.00
	VO <sub>2</sub> (mL.kg <sup>-1</sup> .min <sup>-1</sup> )	12.19±2.51	19.41±5.63	-7.07	-10.32 to -3.81	0.00
	VCO <sub>2</sub> (L/min)	0.93±0.23	1.42±0.36	-0.49	-0.73 to -0.26	0.00
	VO <sub>2</sub> (L/min)	1.00±0.23	1.49±0.36	-0.50	-0.74 to -0.27	0.00
	VE (L/min)	27.51±5.86	40.82±11.96	-13.03	-20.10 to -5.96	0.00
	R	0.92±0.03	0.94±0.03	-0.01	-0.04 to 0.01	0.12
	HR (bpm)	103.46±13.38	127.60±10.04	-23.71	-32.56 to -14.87	0.00
	SBP (mmHg)	167.08±10.10	171.33±8.34	-4.56	-11.44 to 2.30	0.09
	DBP (mmHg)	88.33±7.18	85.33±5.50	2.83	-1.85 to 7.52	0.11
	DP (bpm.mmHg.min <sup>-1</sup> )	17333.25±2716.51	21864.00±2051.48	-4527.75	-6416.40 to 2639.09	0.00
VE/VCO <sub>2</sub> slope		26.89±3.54	28.21±4.79	-1.31	-4.73 to -2.09	0.21
OUES (L/min) predicted		2.38±0.35	2.53±0.23	-0.15	-0.37 to 0.07	0.09
OUES (L/min) obtained		1.79±0.51	2.26±0.37	-0.36	-0.71 to -0.01	0.02
AHA		Very weak	Weak			

W=watts; VO<sub>2</sub>=oxygen consumption; mL.kg.min<sup>-1</sup>=milliliters per kilogram per minute; VCO<sub>2</sub>=carbon dioxide production; L/min=liters per minute; R=respiratory exchange ratio; VE=pulmonary ventilation; HR=heart rate; bpm=beats per minute; SBP=systolic blood pressure; DBP=diastolic blood pressure; DP=double product; mmHg=millimeters of mercury; AT= anaerobic threshold; OUES=Oxygen uptake efficiency slope; AHA=American Heart Association.

sense, the AMIG underwent to sub-maximal CPET 22±4 days (on average) after the AMI, as well as in the studies of Tabet et al.<sup>33</sup> and Duru et al.<sup>34</sup>, which evaluated the patients at 18 and 36 days (on average) after the AMI, respectively. During the CPET, the AMIG have not presented any signs or symptoms that limited its performance.

In our study, we observed that the AMIG showed lower aerobic functional capacity both in the AT and at peak exercise compared to the CG, demonstrated by the power, HR, VO<sub>2</sub>, VCO<sub>2</sub> and VE, obtained during the CPET. The AMIG presented VO<sub>2</sub> values in the AT of 12.19±2.51 mL.kg<sup>-1</sup>.min<sup>-1</sup>, being this result lower than the findings by Tabet et al.<sup>33</sup> (15.9±5.1 mL.kg<sup>-1</sup>.min<sup>-1</sup>) which have evaluated sedentary infarction patients using atenolol (69±4 mg). At peak exercise, the values obtained from VO<sub>2</sub> were 17.27±2.71 and 25.39±5.73 mL.kg<sup>-1</sup>.min<sup>-1</sup> for the AMIG and CG, respectively, being these values similar to those found in studies of Giallauria et al.<sup>30</sup> and Tabet et al.<sup>33</sup>.

The lowest functional capacity values presented by AMIG, in both at the AT and at peak exercise, can be attributed to two

distinct mechanisms: 1) the presence of pathology and 2) to the use of betablocker therapy.

Intolerance to exercise in patients with AMI is a common problem. These patients usually present a reduction in the central and peripheral blood flow during exercise, since the increased peripheral vascular conduction is strongly associated to cardiac output response. Thus, after the AMI, the changes in ventricular function that compromise cardiac output may be responsible for the decline in aerobic functional capacity of these patients<sup>35-37</sup>. Therefore, the lowest values of VO<sub>2</sub> found in the AMIG, both in the AT and in the peak of the sub-maximal CPET, may be attributed to reduced cardiac output and increased peripheral vascular conductance. This condition may lead the patient, during exercise, to a situation of lactate accumulation and lower limb fatigue<sup>38-40</sup>, which contributes for lower exercise tolerance and possibly justify the findings of this study.

Another important aspect in this study is related to beta-blocker therapy used by AMIG, being these medications are routine and first choice for treatment of this pathology<sup>41</sup>.

**Table 3.** Symptoms, signs and electrocardiographic alterations presented by the AMIG during the cardiopulmonary exercise test (CPET).

AMIG patients	Symptoms presented at the AT	Signs and symptoms at CPET peak workload	Electrocardiographic alterations presented in repose	Electrocardiographic alterations presented during the CPET
1	Asymptomatic	Dyspnea and light effort-induced hypertension	Sinus rhythm, inactive area of the anteroseptal wall, diffuse alteration of ventricular repolarization	Absence of ST-segment alterations and absence of arrhythmias
2	Asymptomatic	LL fatigue	Sinus rhythm, inactive area of the inferolateral wall	Absence of ST-segment alterations and absence of arrhythmias
3	Asymptomatic	LL fatigue	Sinus rhythm, inactive area of the anterior wall	Absence of ST-segment alterations and absence of arrhythmias
4	Asymptomatic	LL fatigue	Sinus rhythm, inactive inferolateral area	Absence of ST-segment alterations and absence of arrhythmias
5	Asymptomatic	LL fatigue	Sinus rhythm, inactive area of the lower wall	Absence of ST-segment alterations and absence of arrhythmias
6	Asymptomatic	LL fatigue	Sinus rhythm, inactive area of the anteroseptal wall, diffuse alteration of ventricular repolarization	Absence of ST-segment alterations and absence of arrhythmias
7	Asymptomatic	LL fatigue	Sinus rhythm, left anterior hemiblock and alteration in ventricular regularization	Absence of ST-segment alterations and absence of arrhythmias
8	Asymptomatic	Dyspnea	Sinus rhythm, inactive inferolateral area, isolated polymorphic ventricular extrasystoles	Absence of ST-segment alterations and ventricular arrhythmias
9	Asymptomatic	LL fatigue	Sinus rhythm, inactive area of the lower wall	Absence of ST-segment alterations and absence of arrhythmias
10	Asymptomatic	Dyspnea and light-to-moderate effort-induced hypertension	Sinus rhythm, inactive inferolateral area	Absence of ST-segment alterations and absence of arrhythmias
11	Asymptomatic	LL fatigue	Sinus rhythm, inactive inferolateral area	Absence of ST-segment alterations and ventricular arrhythmias
12	Asymptomatic	LL fatigue	Sinus rhythm, inactive area of the lower wall	

AMIG=Acute myocardial infarction group; AT=Anaerobic threshold; LL=lower limb; CPET=cardiopulmonary test.

These drugs improve survival and reduce hospitalization in this group of patients, and its action on exercise tolerance is still contradictory<sup>30,33,43,42</sup>.

The beta-blockers are able to partially antagonize the sympathetic activity, which reduces HR, the myocardial oxygen consumption and increases the time of left ventricular filling, with improve myocardial perfusion<sup>44</sup>. The beta-blocker may also partially inhibit inflammatory activity, with effects on apoptosis and hypertrophy of cardiomyocytes, leading to increase left ventricular ejection fraction and, consequently, increase cardiac output. Therefore, the beta-blocker therapy may influence the hemodynamic adjustment needed to maintain the increasing needs of muscle metabolic demand<sup>44,45</sup>, although some studies suggest that these drugs improve exercise tolerance, but do not improve the performance of the exercise and the consumption of oxygen<sup>9,45</sup>. It is likely that, in our study, patients after AMI have been benefited by the use of beta-blocker therapy, however presenting lower values of oxygen consumption in relation to the CG.

Although the SBP and the DBP at the peak and at AT has not differ during the CPET, the DP, which is estimated by multiplying the HR by SBP, was significantly higher for the CG. This indicates an increased myocardial oxygen consumption, which may be explained by the fact that the CG have reached higher power (watts), indicating greater functional aerobic capacity. In addition, the AMIG was in beta-blocker therapy and showed lower HR values at peak exercise and at AT. Accordingly, it is important to concurrently measure the HR and BP to safely assess the cardiovascular stress during exercise, since high values of DP at the peak of the exercise test must be related to preserved ventricular function and absence of ischemia<sup>46</sup>.

In addition to the variables already discussed, we emphasize that the assessment of the slope  $VE/VCO_2$  and OUES is of fundamental importance, since we can obtain information from pulmonary perfusion capability and cardiac output in an indirect way. Our results show median values of  $VE/VCO_2$  of  $26.89 \pm 3.54$  for AMIG and  $28.21 \pm 4.79$  for CG, which are considered within the normal range. Previous



studies have determined values of normality for  $VE/VCO_2$  slope lower than 30 and changed values between 30 and 70, which are usually found in patients with cardiac alterations<sup>9,42</sup>. In this way, the results suggest that both groups evaluated did not present reduced pulmonary perfusion capability and cardiac output, since this variable present a significant correlation with preserved function of mecanorreceptores and ergorreceptores, thereby contributing to the normal respiratory test response to exercise. However, in the study of Giallauria et al.<sup>30</sup> in patients after 36 days of AMI, the relationship of  $VE/VCO_2$  was  $33.80 \pm 4.00$ . These results differ from those observed in our study. On the other hand, for healthy individuals aged 50-60 years-old, Sun et al.<sup>47</sup> found  $VE/VCO_2$  values of  $27.20 \pm 3.00$ , which is similar to our findings.

Addition to the evaluated parameters described above, it is also possible to estimate the cardiopulmonary functional reserve of patients with AMI through the OUES variable<sup>20</sup> without therefore submitting them to maximal exercise testing. The OUES is physiologically based on the development of metabolic acidosis, which is controlled by the redistribution of blood flow to the activate muscles. The OUES is also based on physiologic dead space, which is affected by pulmonary perfusion<sup>9</sup>. In this study, we found OUES values for AMIG below the predicted, being the obtained value of  $1.79 \pm 0.51$  L/min and the predicted values of  $2.38 \pm 0.35$  L/min. However, the results of the AMIG are similar to the findings of the studies from Van Laethem et al.<sup>9</sup>, Davies et al.<sup>20</sup> ( $1.60 \pm 0.70$  L/min) and Van de Veire et al.<sup>48</sup> ( $1.30 \pm 0.43$  L/min).

Therefore, the AMIG presents a reduction of cardiopulmonary functional reserve index in addition to the reduction of functional capacity, which perhaps may be justify by the fact that the presence of pathologies and in elderly people occur changes in the ventilatory responses to exercise due to abnormalities in the musculoskeletal system (increased ergor-reflex activity, reduced efficiency of muscle fibers of type 1) and decreased lung capacity and volumes, resulting in lower OUES values.

The results of the present study reinforce the importance of determining the functional capacity and the aerobic cardiopulmonary reserve of coronary patients, as these variables will contribute to guide the physical activity prescription for this population<sup>37</sup>.

Moreover, during the CPET, is also possible to determine clinical changes that usually include the presence of chest pain and dyspnea due to physical effort, and also muscle fatigue. During the performance of the CPET the patients from AMIG were asymptomatic at AT reporting only dyspnea and fatigue

of the lower limbs at peak exercise (Table 3). With regards to the electrocardiographic data during the CPET, no patient presented changes in the ST-segment, indicating the absence of ischemic event during the effort. There was also no changes were observed for the electrocardiogram alteration that already existent during rest. These findings demonstrate that even those patients that have presented reduced functional aerobic capacity, they have not presented clinical changes regarding the symptomatology that could limited the CPET. Therefore, these patients can be safely included in physical training programs to improve functional capacity and exercise tolerance, aiming to reduce modifiable risk factors for cardiovascular disease, to stabilize and slow down or even reverse the progression of atherosclerotic processes, reducing morbidity and mortality.

The impossibility to generalize our results can be considered a limitation of the present study, since only AMI Killip class I patients, asymptomatic, clinically stable and using beta-blockers were evaluated. More detailed studies with samples that involve patients with Killip II clinical classification, as well as patients with AMI not receiving beta-blocker therapy, would be relevant to assess whether they can perform physical activity safely without the supervision of a specialist in the area of cardiac rehabilitation.

## Conclusion ...

The results show that patients with AMI Killip I had lower functional capacity in relation to CG, without presenting ischemic changes. The results of the  $VE/VCO_2$  slope and OUES indicate that the AMIG has normal ventilatory response to exercise, however with reduced cardiorespiratory functional response. Thus, the study suggests that the sub-maximal CPET can be early administered to cardio-respiratory assessment since it offers high sensitivity to detect changes in a safely manner.

## Implications for physical therapy

For some time, the physical therapy area has sought scientific basis to guide clinical practice and subsidize the choice of interventions. Detailed analyses of the CPET may be used as a diagnostic tool for assessing the cardiopulmonary responses to physical exercise.

In addition, the relationship of the AT with heart alterations refers to the importance of the physiotherapeutic treatment

be directed to minimize the overload to the cardiovascular system, providing better exercise tolerance and reduced symptoms such as dyspnea and fatigue of the lower limbs.

Therefore, the introduction of the CPET executed by health professionals aim to encourage the use of this non-invasive technique in the cardiac rehabilitation filed and, therefore to evaluate and re-evaluate the functional capacity of the AT level before and after physiotherapy interventions.

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