

## Study with a Portable Gas Analyzer of the 6-Minute Walk Test in Heart Failure with Normal Ejection Fraction

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### Abstract

**Background:** Few studies have used portable gas analyzers during the 6-minute walk test (6MWT) in patients with heart failure and normal ejection fraction (HFNEF).

**Objectives:** To analyze the kinetics of hemodynamic, ventilatory, and metabolic variables in patients with HFNEF during the T6m using a portable gas analyzer.

**Methods:** Prospective, analytical study with an intentional, non-probabilistic, convenience sample. In total, 24 patients with HFNEF and past hospital admissions due to a clinical diagnosis of heart failure (HF) were included using the 2007 criteria established by the European Society of Cardiology. Three assessments were performed: 6MWT familiarization, 6MWT with the portable gas analyzer, and cardiopulmonary exercise test (CPET).

**Results:** The heart rates (HRs) and the peak  $\text{VO}_2$  at the end of the 6MWT corresponded to 85.7% and 86.45% of the values obtained during the CPET. The final HRs after the T6m were equivalent to those obtained at the CPET anaerobic threshold (AT), with relative  $\text{VO}_2$  values at the end of the 6MWT above the  $\text{VO}_2$  of the CPET AT. There was no difference between the maximum respiratory quotient (RQ) values in these two tests, which were both above 1.0. The  $\text{VE}/\text{VO}_2$  slope descended initially and then ascended significantly after the fifth minute of the test, estimating the identification of the AT.

**Conclusions:** In patients with HFNEF, the 6MWT represents an almost maximum effort, and is performed above the CPET AT and 85% above the maximum HR and the CPET peak  $\text{VO}_2$ , with a maximum RQ similar to that in the CPET. (Int J Cardiovasc Sci. 2018;31(2)143-151)

**Keywords:** Heart Failure; Blood Gas Analysis; Stroke Volume; Exercise; Walk Test.

### Introduction

Heart failure (HF) evokes the image of a dilated heart with reduced systolic function and ejection fraction (HF with reduced ejection fraction, HFREF). However, the study by Burkhoof et al.<sup>1</sup> has shown that a large proportion of patients with HF symptoms has an ejection fraction within the normal range, and are then classified as having HF with normal ejection fraction (HFNEF).<sup>2,3</sup> The limited tolerance to physical effort in

HF is often the first and main clinical characteristic of the disease.<sup>4</sup> In the identification of this exercise intolerance, the 6-minute walk test (6MWT) has been used as an instrument to evaluate the progression after different interventions.<sup>5</sup>

Only a few studies have been conducted using portable gas analyzers to describe and analyze the behavior of variables in the 6MWT and possible characteristics or markers that may help guide the therapy and improve the prognosis in HF,<sup>6-10</sup> particularly in patients with HFNEF.

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The aim of this study was to describe and analyze the kinetic behavior at each minute of hemodynamic, ventilatory, and metabolic variables in patients with HFNEF during the 6MWT using a portable gas analyzer, and to compare the findings with those obtained during a cardiopulmonary exercise test (CPET).

## Methods

Prospective, analytical study with a non-probabilistic, intentional, and convenience sample, as set by the adopted criteria, carried out at the *Hospital Universitário Antônio Pedro* (HUAP) of the *Universidade Federal Fluminense* (UFF) between March 2010 and July 2013. The study project was approved by the Ethics Research Committee at HUAP under the number 152A/2010, and all participants signed an informed consent form.

The inclusion criteria adopted to characterize HFNEF were those described by Paulus et al.,<sup>11</sup> in addition to the following factors: (A) complaints suggestive of HF (dyspnea, fatigue, and/or edema); (B) report of prior hospitalization due to decompensated heart disease, but at the moment of the test presenting with a functional class II to III according to the New York Heart Association (NYHA); (c) age > 18 years; (d) disease duration greater than 6 months; (e) use of medication; and (F) stable disease.

The exclusion criteria adopted were: (A) chronic obstructive pulmonary disease (COPD) based on clinical criteria, (B) functional class IV or other criteria contraindicating the CPET,<sup>12</sup> and (C) participation in supervised cardiac rehabilitation programs.

The patients were instructed to maintain the current medications. The tests comprised three moments: conventional 6MWT (6MWT1), 6MWT coupled to a portable gas analyzer (6MWT2), and CPET on a treadmill. Due to a matter related to the hospital's flow, some patients were first assigned randomly to the 6MWT and others to the CPET.

The 6MWT was performed in a hallway with an extension of 30 meters. The first 6MWT (6MWT1) had a learning effect as objective, as recommended in the literature.<sup>6</sup> The second 6MWT (6MWT2) was performed at least 3 days and no more than 3 weeks after the first, when the patients repeated the 6MWT, but this time they were connected to a portable gas analyzer. The maximum interval between the 6MWT and the CPET was also 3 weeks. Both the 6MWT and the CPET were scheduled by the same evaluator and applied by the same team to avoid application variability.

We used for the assessments the metabolic analyzer MedGraphics (MGC) VO2000 (Imbrasport, Porto Alegre, RS, Brazil), the system Ergo PC Elite 13, and the treadmill Centurion 300 (MicroMed, Brasília, DF, Brazil). The gas analyzer was calibrated before each test by the autocalibration system in a ventilated environment. The biological control of the calibration was performed monthly and the control by the equipment's representative (CAEL, Rio de Janeiro, RJ, Brazil) was conducted every 3 months.

In the CPET, each patient underwent a 2-minute baseline collection followed by a 1-minute warm-up at 1 km/h and 0° slope before starting the ramp protocol. In order to analyze and assess the CPET variables, we used the software ErgoPCElite for Windows 13W (MicroMed, Brasília, DF, Brazil). The perceived exertion (PE), assessed by the Borg scale (variation 0-10), and the hemodynamic and electrocardiographic variables were recorded at every minute. During the recovery phase, the patient remained seated. Two referees analyzed the report of the test to obtain the following information: VE/VCO<sub>2</sub> slope value, presence of oscillatory breathing (OB), and establishment of the ventilatory threshold I, referred from now on as the anaerobic threshold (AT). In order to determine the AT, we used the curves of the ventilatory equivalents of the VO<sub>2</sub> and VCO<sub>2</sub>, in addition to the curves of VO<sub>2</sub> and VCO<sub>2</sub> expired fractions, as recommended by the CPET guideline of the American Heart Association (AHA).<sup>13</sup>

The evaluations were performed while the patients maintained the use of their usual medications, during the same time of the day, and at least 2 hours after the last meal. Peak VO<sub>2</sub> was defined as the highest VO<sub>2</sub> value obtained up to the final 30 seconds or 10 seconds into the immediate recovery. In order to determine the occurrence of OB and the value of the VE/VCO<sub>2</sub> slope, we followed the AHA guideline<sup>13</sup> and the recommendations by Guazzi et al.<sup>14</sup> Since spirometry was not performed, the ventilatory reserve was not considered in the analysis. Only one CPET was performed, as recommended by Scott et al.<sup>15</sup>

The maximum estimated heart rate (HR) was obtained using the formula by Tanaka et al.<sup>16</sup> and was used to calculate the chronotropic index.

During the 6MWT, we recorded the HR (Polar monitor, model T31, Oulu, Finland) at each minute, along with the PE according to the Borg scale and the capillary O<sub>2</sub> saturation using a pulse oximeter (Onyx, Minneapolis, MN, USA).

In order to analyze the gases expired during the 6MWT and obtain the values of the variables, we used the same VO2000 in a portable mode connected wirelessly to a computer. We used the software Aerograph, version 4.3 (Imbrasport, Porto Alegre, RS, Brazil), which organized the data for later analysis.

During the 6MWT, the patient connected to the gas analyzer remained seated for 4 minutes and 30 seconds. After the values of the variables were collected during this resting period, the patient stood up for 30 seconds before initiating the 6MWT, which was performed according to the guidelines of the American Thoracic Society (ATS).<sup>5</sup>

All patients completed the 6 minutes of walk. The gas analysis ended after the fifth minute of recovery. The maximum blood pressure (BP) considered in the analysis was the one obtained immediately after the effort, *i.e.*, after the sixth minute of the walk when the patient sat down and the BP was then measured between 30-40 seconds during recovery.

### Statistical analysis

The numerical data are expressed as mean  $\pm$  standard deviation (SD) since all the variables included had an approximately normal distribution (p value of the Kolmogorov-Smirnov test  $> 0.05$ ). Categorical data are expressed as frequency (n) and percentage (%).

The variation of the hemodynamic, metabolic, and ventilatory measurements between the tests (assessments) CPET and 6MWT were analyzed by Student's *t* test for paired samples.

A descriptive graphic analysis was performed, presenting the mean and SD values of the measurements obtained at each minute of the variables HR and  $VO_{2r}$ , indicating, for each one of these variables, the maximum CPET values and values equivalent to the AT.

In order to evaluate the correlation levels between the 6MWT distance and the peak  $VO_{2r}$  and CPET peak  $VO_{2r}$ , we used Pearson's correlation coefficient (*r*).

We adopted a significance level of 5%. The statistical analysis was performed using the software SAS 6.11 (SAS Institute, Inc., Cary, NC, USA).

### Results

A total of 24 patients were evaluated. Of these, 22 underwent both tests (CPET and 6MWT) while two underwent only the CPET; thus, the comparison between the CPET and 6MWT included only data of 22 patients. Table 1 shows the baseline characteristics of the study population. There was a predominance of the female gender (70.8%) and obesity (58.3%). Hypertension was present in 100.0% of the patients.

**Table 1 – Clinical characteristics of the study population**

Variables	n = 24	%	
Sex	male	7	29.2
	female	17	70.8
	Mean	SD	
EF (%)	64.7	8.2	
Weight (kg)	84.3	16.6	
Height (cm)	160.2	7.4	
BMI	32.9	6.7	
Waist (cm)	104.4	13.3	
Hip (cm)	110.8	11.6	
W/H	0.944	0.086	
Age (years)	59.6	10.2	

Abbreviations: EF: ejection fraction; BMI: body mass index; W/H: waist-to-hip ratio; SD: standard deviation.

Most patients (70.8%) used beta-blockers. The profile of the medications used by the patients showed the usual therapeutic approach for hypertension: beta-blockers, angiotensin-converting enzyme inhibitors (25.0%) or angiotensin receptor blockers (54.1%), calcium channel blockers (37.5%), thiazides (29.1%), and vasodilators (48.5%).

A stratification of the patients according to the results of the CEPT and following the classification by Weber<sup>17</sup> showed a higher percentage of patients categorized as class B (30.4%).

The patients had a mean E/E' of  $15.9 \pm 4.3$ , which fulfilled one of the criteria for diagnosis of HFNEF.<sup>11</sup>

The mean walked distance was  $419.2 \pm 76.5$  meters during the 6MWT1 and  $446.2 \pm 67.7$  meters during the 6MWT2, with a significant difference between both groups ( $p = 0.002$ ).

Table 2 shows the maximum values of the variables obtained in the 6MWT2 and in the CPET. There was no difference between the maximum respiratory quotient (RQ) values of the two tests, and their maximum values were greater than 1.0. The results showed increased values at the end of the 6MWT2 (1.04), and of 22 patients who underwent the 6MWT2, 11 had an  $RQ \geq 1.0$  (50% of the group). Of these 11 patients, 7 obtained an  $RQ \geq 1.10$  (31.8% of the sample).

Since BP measurement during the 6MWT was not feasible, BP was only measured in the baseline condition and immediately after the 6MWT. Considering that prior spirometry was not performed, other ventilatory parameters were not assessed.

The longitudinal analysis of the HR during the 6MWT2 showed that the group reached stable HR values after the second minute of the 6MWT2 (T3). The maximum HR

**Table 2 – Maximum variables obtained in the 6-minute walk test (6MWT) and the cardiopulmonary exercise test (CPET) (n = 22)**

Mean values - 6MWT versus CPET					
	6MWT	SD	CPET	SD	p < 0.05
Max SBP	187.04	26.60	215.3	27.4	0.002
Max DBP	97.80	13.7	104.1	16.0	0.09
Max DP	20951	5497	27524	6130	0.0004
CircPot	2533	957	3462	1266	0.002
Max HR	110.9	18.1	125.4	19.6	0.004
HR1Rec	23.1	10.1	17.2	10.1	0.035
ChronI	0.42	0.2	0.57	0.1	0.002
O <sub>2</sub> pulse	10.5	3.6	10.5	3.5	0.95
Max RQ	1.06	0.24	1.08	0.09	0.47
VE/VCO <sub>2</sub> slope	22.3	4.8	23.2	4.4	0.10
VP	8.31	1.92	9.59	2.11	0.0002
Peak VO <sub>2</sub> (mL.kg <sup>-1</sup> .min <sup>-1</sup> )	13.8	4.1	15.9	5.4	0.025
T1/2	61.4	16.5	111.2	25.7	0.0001
OUES	1.26	0.74	1.34	0.59	0.10
AT VO <sub>2</sub>			11.76	3.79	

Max SBP: maximum systolic blood pressure; Max DBP: maximum diastolic blood pressure; Max DP: maximum double product; CircPot: circulatory power; Max HR: maximum heart rate; HR1Rec: heart rate in the first minute of recovery; ChronI: chronotropic index; O<sub>2</sub> pulse: oxygen pulse (mL.kg<sup>-1</sup>.min<sup>-1</sup>/bpm); Max RQ: maximum respiratory quotient; VE/VCO<sub>2</sub> slope: ventilation minute to carbon dioxide production ratio; VP: ventilatory power; peak VO<sub>2</sub> (mL.kg<sup>-1</sup>.min<sup>-1</sup>): oxygen consumption peak; T1/2: time (in seconds) of the recovery kinetics of oxygen consumption up to half of the value of peak effort; OUES: oxygen uptake efficiency slope; AT: anaerobic threshold; 6MWT2: second 6-minute walk test; CPET: cardiopulmonary exercise test; SD: standard deviation. All heart rate values are represented in beats per minute.

during the 6MWT2 (108.9 bpm) was similar to the HR at the CPET AT (108 bpm), shown by the dashed line (Figure 1), and 85.7% compared with the CPET maximum HR (126 bpm), highlighted in the Figure.

The longitudinal progression of the relative  $\text{VO}_2$  ( $\text{mL.kg}^{-1}.\text{min}^{-1}$ ) during the 6MWT2 in the study participants is shown in Figure 2. Note in the dashed line the  $\text{VO}_2$  value of the CPET AT ( $11.76 \text{ mL.kg}^{-1}.\text{min}^{-1}$ ) and in the highlighted area, the value of  $15.9 \text{ mL.kg}^{-1}.\text{min}^{-1}$  of the CPET peak  $\text{VO}_2$  (Figure 2).

The longitudinal progression of the production of carbon dioxide ( $\text{VCO}_2$ ) during the 6MWT2 occurred in a similar way to that of the  $\text{VO}_2$ , reaching maximum values in the 6MWT2 of  $11.5 \text{ mL.kg}^{-1}.\text{min}^{-1}$  (not displayed).

Pearson's correlation ( $r$ ) levels found between the maximum walked distance in the 6MWT2 with the peak  $\text{VO}_2$  obtained in the same test and between the walked distance with the CPET peak  $\text{VO}_2$  were  $r = 0.528$  ( $p = 0.014$ ) and  $r = 0.532$  ( $p = 0.013$ ), respectively.

## Discussion

A review of the literature on the subject of this study – 6MWT and HFNEF – has shown that most studies in this area are focused on HFREF. Therefore, it became difficult to compare the results found in the present study, which included patients with HFNEF, with data from the literature. Due to that, the discussion below will be based on similar results found in studies with HFREF.

Riley et al.,<sup>6</sup> Foray et al.,<sup>7</sup> Faggiano et al.,<sup>8</sup> and Kervio et al.<sup>10</sup> analyzed the kinetics of variables using a

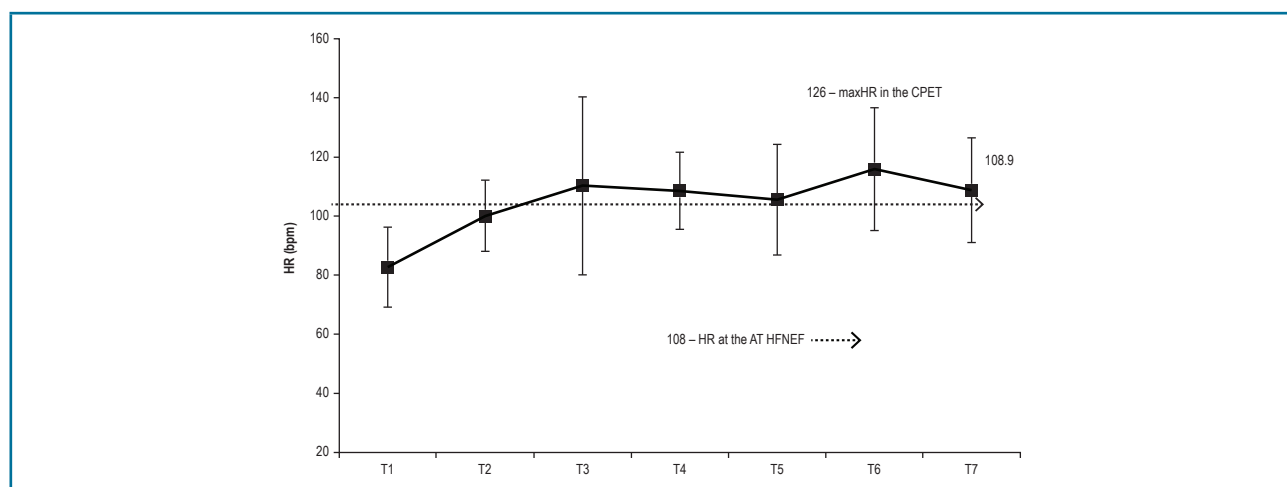
portable gas analyzer and demonstrated that the kinetics and other cardiovascular parameters are decreased in HFREF in response to the effort imposed by the 6MWT. However, no studies have described how the kinetics of patients with HFREF respond during this test.

Among the study patients, there was a predominance of patients of the female gender, with hypertension, and with an increased body mass index (BMI),<sup>3,11</sup> characteristics that confirm the typical clinical profile of patients with HFNEF.

The average distance walked is within the values that indicate a good prognosis, *i.e.*, above 300 meters.<sup>5,18</sup> A significant percentage (81.81%) equaled or increased in the 6MWT2 the distance walked during the 6MWT1 but did not obtain values of clinical significance, *i.e.*, above 50 meters.<sup>5</sup> This reinforces the importance of conducting at least one learning and familiarization test due to a potential influence on the results of the 6MWT.<sup>6,19</sup>

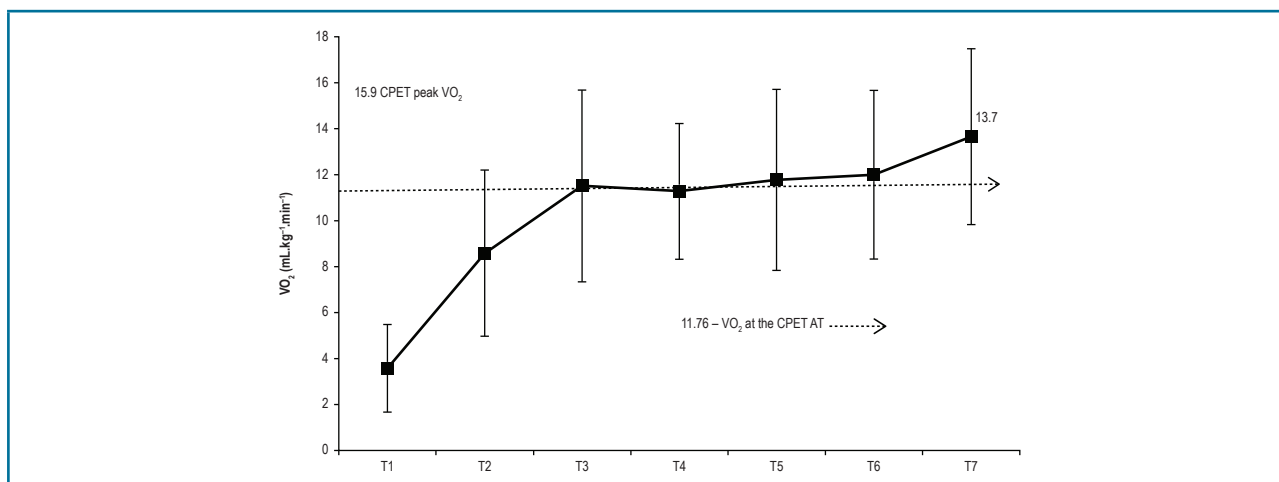
The distances obtained are aligned with the average values found in studies with patients with HFREF, such as those by Kervio et al.<sup>10</sup> ( $452.6 \pm 18.7$  meters), Faggiano et al.<sup>8</sup> ( $419 \pm 120$  meters), and Guimarães et al.<sup>9</sup> ( $470 \pm 48$  meters).

The correlation levels found between the 6MWT2 and the peak  $\text{VO}_2$  in the 6MWT1 and with the CPET peak  $\text{VO}_2$  are aligned with findings in the literature, despite some discrepancies. Some authors report a good correlation between the distance of the 6MWT and the peak  $\text{VO}_2$ , with an average of 0.73 in patients with HF<sup>6,19</sup> (all with HFREF). Riley et al.<sup>6</sup> found a high correlation ( $r = 0.63$ ), whereas Lucas et al.<sup>20</sup> and Roul et al.<sup>21</sup> found a



**Figure 1** – Longitudinal progression of the heart rate (HR) during the second 6-minute walk test (6MWT2) in the study participants. HFNEF: heart failure with normal ejection fraction; CPET: cardiopulmonary exercise test; maxHR: maximum heart rate; AT: CPET anaerobic threshold; T1: time zero of the 6MWT (baseline conditions); T2, T3, T4, T5, T6, T7: first, second, third, fourth, fifth, and sixth minutes of the 6MWT, respectively.





**Figure 2** – Longitudinal progression of the relative  $VO_2$  ( $mL/kg/min^{-1}$ ) during the 6MWT. HFNEF: heart failure with normal ejection fraction; CPET: cardiopulmonary exercise test;  $VO_2$ : oxygen consumption ( $mL \cdot kg^{-1} \cdot min^{-1}$ ); T1: time zero of the 6MWT (baseline conditions); T2, T3, T4, T5, T6, T7: first, second, third, fourth, fifth, and sixth minutes of the 6MWT, respectively, AT: anaerobic threshold.

low correlation with the walked distance in the 6MWT ( $r = 0.28$  and  $r = 0.24$ , respectively). Such discrepancies could be attributed to different methodologies of the 6MWT and the type of ergometers used.

The HFREF studies found in the literature assessing the 6MWT with portable gas analyzers and performed in a hallway were: Riley et al.,<sup>6</sup> Foray et al.,<sup>7</sup> Faggiano et al.,<sup>8</sup> and Kervio et al.<sup>10</sup> Guimarães et al.<sup>9</sup>, in turn, used the gas analyzer during two 6MWT tests performed on a treadmill, also in patients with HFREF.

In regards to HR parameters, the study group showed more stable values after the second minute of the 6MWT (T3). Kervio et al.<sup>10</sup> highlight that earlier achievement of a stable state reflect better clinical conditions and, therefore, less severe ones.

The HR at the end of the 6MWT was 85.7% of the CPET maximum HR, which is similar to the percentage values of the peak  $VO_2$  in the 6MWT in relation to the CPET peak  $VO_2$ .

It is noteworthy that the final HR in the 6MWT was similar to the HR in the CPET AT, reinforcing that the 6MWT represents an intense effort, carried out at the level of or above the CPET AT in patients with HF.<sup>6-8,10</sup>

Despite the authors' claim that patients with HFNEF present HR alterations in the first minute of recovery (HR1Rec)<sup>22</sup> and the fact that there are no data in the literature related to the 6MWT, if we consider the recommended value of 12 bpm, this value was within the normal limits both in the T6M as well as in the CPET.<sup>23</sup>

The chronotropic index analysis demonstrated a chronotropic incompetence, even if we consider the use of beta-blockers (normal  $> 0.60$ ), both in relation to the 6MWT as well as to the CPET, as found in the literature.<sup>24</sup>

The maximum  $O_2$  pulse in the 6MWT and the CPET showed no difference between the two tests, yielding reduced pulse  $O_2$  values in relation to the predicted one ( $< 85\%$ ), around 70%, and with absolute values below  $12 mL \cdot kg^{-1} \cdot min^{-1}/bpm$ , which is considered of poor prognosis.<sup>25</sup>

In relation to the two ventilatory variables analyzed, no difference in the  $VE/VCO_2$  slope was observed. The  $VE/VCO_2$  slope values are within the values cited as indicative of good prognosis ( $< 30$ ),<sup>13</sup> and this fact associated with the lack of difference between the two tests can reinforce the prognostic ability of the 6MWT. The ventilatory power (VP) analysis also showed a difference between the two tests, with higher values for the CPET. The VP, which combines the response of the SBP with the  $VE/VCO_2$  slope ( $VP = SBP \times VE/VCO_2$  slope)<sup>26</sup> showed a difference probably due to the higher SBP in the CPET. However, good prognosis values ( $> 3.5$ ) were observed for both tests.<sup>26</sup>

The RQ is a criterion to obtain intense ( $> 1.0$ ) or maximum effort in exercises of increasing intensity ( $> 1.15$ ).<sup>13</sup> There was no difference between the maximum RQ values between the two tests. The data found here are in agreement with those found by Kervio et al.,<sup>10</sup> who consider the RQ in the 6MWT as reflecting intense effort. Both in the population with HFREF<sup>10</sup> and in patients with HFNEF in the study, 50% of each sample obtained an

RQ > 1.0. Other authors agree and claim that the greater the functional deficiency of the studied cohort, the more the 6MWT would be executed close to the maximum.<sup>6-8</sup>

In the analysis of the VE/VO<sub>2</sub>, the curve first descended and then ascended, which became significant after the fifth minute of the test (T6 and T7). Such progression is one of the criteria used to identify the CPET AT.<sup>13,24</sup> When this concept is transferred to the 6MWT, it confirms that it represents an effort similar to or slightly above the AT.

In regards to the VE/VCO<sub>2</sub>, the values stabilized after the second minute of effort (T3), with peak values slightly above those of the CPET AT (24.5 ± 3.1 in the 6MWT versus 23.6 of the CPET AT). The VE/VCO<sub>2</sub> stabilized in values that do not reflect ventilatory inefficiency.

The relative VO<sub>2</sub> in the 6MWT showed stable values and its progression in patients with HFNEF did not differ from that found in similar studies in patients with HFREF, both in terms of progression during the 6MWT as well as in regards to the percentages obtained in relation to the CPET.<sup>6-8,10</sup> It reached values above the VO<sub>2</sub> corresponding to the CPET AT and of significant percentages of the CPET peak VO<sub>2</sub> (86.45%).

The variable VCO<sub>2</sub> tended to stabilize after T5 (the fourth minute of the 6MWT), which contrasts with the data presented by Kervio et al.,<sup>10</sup> in which this variable did not reach a stable state until the end of the 6MWT in patients with HFREF.

The patients with HFREF in the study by Kervio et al.<sup>10</sup> performed their 6MWT above the relative VO<sub>2</sub> of the CPET AT, which is aligned with findings in patients with HFNEF in this study. The VO<sub>2</sub> at the CPET AT obtained by Kervio et al.<sup>10</sup> (11.7 ± 0.6 mL.kg<sup>-1</sup>.min<sup>-1</sup>) is also very similar to that found in this study (11.76 mL.kg<sup>-1</sup>.min<sup>-1</sup>).

It is interesting to note that 7 out of 22 patients in the present study had peak VO<sub>2</sub> in the 6MWT equal to or greater than the CPET peak VO<sub>2</sub>, representing 31.8% of the total sample. This percentage value is aligned and supersedes those by Faggiano et al.<sup>8</sup> (27.0%) in a HFREF population.

The high intensity of the 6MWT for patients with HF is reinforced by findings from the study by Kervio et al.,<sup>10</sup> Faggiano et al.,<sup>8</sup> and Foray et al.,<sup>7</sup> which demonstrated that the 6MWT leads to a demand above 85% of the values of the CPET relative peak VO<sub>2</sub>.

Faggiano et al.<sup>8</sup> found a peak VO<sub>2</sub> at 86% of the CPET, which represented 73.0% of the VO<sub>2</sub> of the CPET AT. The present study showed similar percentages in

relation to the CPET, but the VO<sub>2</sub> at the CPET AT presented higher percentages, corresponding to 85.03% of the peak VO<sub>2</sub> in the 6MWT in patients with HFNEF. Guimarães et al.<sup>9</sup> analyzed the results of a single CPET and 6MWT on a treadmill, with the participants connected to a gas analyzer and, using an incentive, found a peak VO<sub>2</sub> at 90% of the CPET.

The values of the CPET relative peak VO<sub>2</sub> are aligned with the findings by Guazzi et al.<sup>27</sup> These authors found CPET peak VO<sub>2</sub> values of 15 mL.kg<sup>-1</sup>.min<sup>-1</sup> in HFNEF patients.

The oxygen uptake efficiency slope (OUES) showed lower values in the 6MWT, but no difference in values was observed between the 6MWT and the CPET. Although the literature indicates that reduced values in both HFREF and HFNEF,<sup>13</sup> the HFNEF patients evaluated obtained values above 1.2, which are considered to be of poor prognosis.<sup>28</sup>

The metabolic variable with the most difference was the kinetics of oxygen consumption during recovery (T1/2), which showed a significantly greater recovery time in the CPET. The T1/2 values in the 6MWT did not fulfill the criteria of poor prognosis.<sup>13,24,29</sup> Considering that the value of 90 seconds<sup>29</sup> in the CPET, the study participants exceeded this value.

## Conclusion

There is an actual possibility of patients with HFNEF to be able to perform a 6MWT at maximum or almost maximum intensity. This estimate is based on the following observations: high percentages obtained in peak values in the 6MWT in relation to the maximum value of the variables HR (85.7%) and relative VO<sub>2</sub> (86.4%) in the CPET, similar RQ values, similar peak VO<sub>2</sub> values in the 6MWT and at the CPET AT, and the progression of the VE/VO<sub>2</sub>, which after reaching a nadir, showed a trend to curve upward.

It should be noted that in relation to the reviewed studies, all conducted in patients with HFREF, the assessed variables in HFNEF showed, on average, an equal profile during the 6MWT.

## Study limitations

Some limitations in this study are identified:

- Reduced size of the study sample. Further studies with an increased number of patients are suggested to validate some of the conclusions.

- The predominance of the female gender and overweight/obesity, characteristic of HFNEF, may have influenced the variables related to functional capacity in both 6MWT and CPET.
- The peripheral determinants of peak  $\dot{V}O_2$ , such as the oxygen transportation system or changes in peripheral muscles, were not considered in the functional assessment.
- The use of beta-blockers and other medications may have influenced the interpretation of variables that integrate HR or BP in their calculation.

### Author contributions

Conception and design of the research: Teixeira JAC, Nobrega ACL, Araujo DV. Acquisition of data: Teixeira JAC, Messias LR, Dias KP, Costa WLB, Cascon RM, Miranda SMR, Teixeira PS, Jorge JG. Analysis and interpretation of the data: Teixeira JAC, Messias LR, Dias KP, Costa WLB, Teixeira PS, Nobrega ACL, Araujo DV. Writing of the manuscript: Teixeira JAC, Teixeira PS, Jorge JG. Critical revision of the manuscript

for intellectual content: Teixeira JAC, Nobrega ACL, Araujo DV. Bibliographic Survey: Teixeira JAC, Messias LR, Miranda SMR. Bibliographic Review: Costa WLB, Cascon RM.

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No potential conflict of interest relevant to this article was reported.

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### Study Association

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### Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

### References

- Burkhoff D, Maurer MS, Packer M. Heart failure with a normal ejection fraction. is it really a disorder of diastolic function? *Circulation*. 2003;107(5):656-8. PMID: 12578861.
- Vasan RS, Benjamin EJ, Levy D. Prevalence, clinical features and prognosis of diastolic heart failure: an epidemiologic perspective. *J Am Coll Cardiol*. 1995;26(7):1565-74. doi: 10.1016/0735-1097(95)00381-9.
- Zile MR, Kjellstrom B, Bennett T, Cho Y, Baicu CF, Aaron MF, et al. Effects of exercise on left ventricular systolic and diastolic properties in patients with heart failure and a preserved ejection fraction versus heart failure and a reduced ejection fraction. *Circ Heart Fail*. 2013;6(3):508-16. doi: 10.1161/CIRCHEARTFAILURE.112.000216.
- Downing J, Balady GJ. The role of exercise training in heart failure. *J Am Coll Cardiol*. 2011;58(6):561-9. doi: 10.1016/j.jacc.2011.04.020.
- ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med*. 2002;166(1):111-7. doi: 10.1164/ajrccm.166.1.at1102.
- Riley M, McParland J, Stanford CF, Nicholls DP. Oxygen consumption during corridor walk testing in chronic cardiac failure. *Eur Heart J*. 1992;13(6):789-93. PMID: 1623869.
- Foray A, Williams D, Reemtsma K, Oz M, Mancini D. Assessment of submaximal exercise capacity in patients with left ventricular assist devices. *Circulation*. 1996;94(9 Suppl):II-222-6. PMID: 8901750.
- Faggiano P, D'Aloia A, Gualeni A, Lavatelli A, Giordano A. Assessment of oxygen uptake during the 6-minute walking test in patients with heart failure: preliminary experience with a portable device. *Am Heart J*. 1997;134(2 Pt 1):203-6. PMID: 9313598.
- Guimarães GV, Bellotti G, Bacal F, Mocelin A, Bocchi EA. Can the cardiopulmonary 6-minute walk test reproduce the usual activities of patients with heart failure? *Arq Bras Cardiol*. 2002;78(6):553-60. http://dx.doi.org/10.1590/S0066-782X2002000600003.
- Kervio G, Ville NS, Leclercq C, Daubert JC, Carre F. Cardiorespiratory adaptations during the six-minute walk test in chronic heart failure patients. *Eur J Cardiovasc Prev Rehabil*. 2004;11(2):171-7. PMID: 15187823.
- Paulus WJ, Tschöpe C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. *Eur Heart J*. 2007;28(20):2539-50. doi: 10.1093/eurheartj/ehm037.
- Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GF, Bittner VA, et al; American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology, Council on Nutrition, Physical Activity and Metabolism, Council on Cardiovascular and Stroke Nursing, and Council on Epidemiology and Prevention. Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation*. 2013;128(8):873-934. doi: 10.1161/CIR.0b013e31829b5b44.
- Balady GJ, Arena R, Sietsema K, Myers J, Coke L, Fletcher, GF, et al; American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council on Peripheral Vascular Disease; Interdisciplinary Council on Quality of Care and Outcomes Research. Clinician's Guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association. *Circulation*. 2010;122(2):191-225. doi: 10.1161/CIR.0b013e3181e52e69.
- Guazzi M, Raimondo R, Vicenzi M, Arena R, Proserpio C, Sarzi Braga S, et al. Exercise oscillatory ventilation may predict sudden cardiac death in heart failure patients. *J Am Coll Cardiol*. 2007;50(4):299-308. doi: 10.1016/j.jacc.2007.03.042.



15. Scott JM, Haykowsky MJ, Eggebeen J, Morgan TM, Brubaker PH, Kitzman DW. Reliability of peak exercise testing in patients with heart failure with preserved ejection fraction. *Am J Cardiol.* 2012;110(12):1809-13. doi: 10.1016/j.amjcard.2012.08.015.
16. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. *J Am Coll Cardiol.* 2001;37(1):153-6. PMID: 11153730.
17. Task Force of the Italian Working Group on Cardiac Rehabilitation and Prevention (Gruppo Italiano di Cardiologia Riabilitativa e Prevenzione, GICR), Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology. Statement on cardiopulmonary exercise testing in chronic heart failure due to left ventricular dysfunction: recommendations for performance and interpretation. Part III: Interpretation of cardiopulmonary exercise testing in chronic heart failure and future applications. *Eur J Cardiovasc Prev Rehabil.* 2006;13(4):485-94. doi: 10.1097/01.hjr.0000201518.43837.bc.
18. Arslan S, Erol MK, Gundogdu F, Sevimli S, Aksakal E, Senocak H, et al. Prognostic value of 6-minute walk test in stable outpatients with heart failure. *Tex Heart Inst J.* 2007;34(2):166-9. PMID: 17622362.
19. Faggiano P, D'Aloia A, Gualeni A, Brentana L, Dei Cas L. The 6 minute walking test in chronic heart failure: indications, interpretation and limitations from a review of the literature. *Eur J Heart Fail.* 2004;6(6):687-91. doi: 10.1016/j.ejheart.2003.11.024.
20. Lucas C, Stevenson LW, Johnson W, Hartley H, Hamilton MA, Walden J, et al. The 6-min walk and peak oxygen consumption in advanced heart failure: aerobic capacity and survival. *Am Heart J.* 1999;138(4 Pt 1):618-24. PMID: 10502205.
21. Roul G, Germain P, Bareiss P. Does the 6-min walk test predict the prognosis in patients with NYHA class II or III chronic heart failure? *Am Heart J.* 1998;136(3):449-57. PMID: 9736136.
22. Guazzi M, Myers J, Peberdy MA, Bensimhon D, Chase P, Arena R. Cardiopulmonary exercise testing variables reflect the degree of diastolic dysfunction in patients with heart failure-normal ejection fraction. *J Cardiopulm Rehabil Prev.* 2010;30(3):165-72. doi: 10.1097/HCR.0b013e3181d0c1ad.
23. Cole CR, Foody JM, Blackstone EH, Lauer MS. Heart rate recovery after submaximal exercise testing as a predictor of mortality in a cardiovascularly healthy cohort. *Ann Intern Med.* 2000;132(7):552-5. PMID: 10744592.
24. Meneghelo RS, Araújo CG, Stein R, Mastrocolla LE, Albuquerque PF, Serra SM, et al; Sociedade Brasileira de Cardiologia. [III Guidelines of Sociedade Brasileira de Cardiologia on the exercise test]. *Arq Bras Cardiol.* 2010;95(5 suppl. 1):1-26. doi: http://dx.doi.org/10.1590/S0066-782X2010000800001.
25. Oliveira RB, Myers J, Araújo CG, Abella J, Mandic S, Froelicher V. Maximal exercise oxygen pulse as a predictor of mortality among male veterans referred for exercise testing. *Eur J Cardiovasc Prev Rehab.* 2009;16(3):358-64. doi: 10.1097/HJR.0b013e3283292fe8.
26. Forman DE, Guazzi M, Myers J, Chase P, Bensimhon D, Cahalin LP, et al. Ventilatory power: a novel index that enhances prognostic assessment of patients with heart failure. *Circ Heart Fail.* 2012;5(5):621-6. doi: 10.1161/CIRCHEARTFAILURE.112.968529.
27. Guazzi M, Dickstein K, Vicenzi M, Arena R. Six-minute walk test and cardiopulmonary exercise testing in patients with chronic heart failure: a comparative analysis on clinical and prognostic insights. *Circ Heart Fail.* 2009;2(6):549-55. doi: 10.1161/CIRCHEARTFAILURE.109.881326.
28. Hollenberg M, Tager IB. Oxygen uptake efficiency slope: an index of exercise performance and cardiopulmonary reserve requiring only submaximal exercise. *J Am Coll Cardiol.* 2000;36(1):194-201. PMID: 10898434.
29. Cohen-Solal A, Tabot JY, Logeart D, Bourgoin P, Tokmakova M, Dahan M. A non-invasively determined surrogate of cardiac power ('circulatory power') at peak exercise is a powerful prognostic factor in chronic heart failure. *Eur Heart J.* 2002;23(10):806-14. doi: 10.1053/euhj.2001.2966.

