

## Association Between Hemodynamic Profile, Physical Capacity and Quality of Life in Pulmonary Hypertension

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### Abstract

**Background:** No studies have described and evaluated the association between hemodynamics, physical limitations and quality of life in patients with pulmonary hypertension (PH) without concomitant cardiovascular or respiratory disease.

**Objective:** To describe the hemodynamic profile, quality of life and physical capacity of patients with PH from groups I and IV and to study the association between these outcomes.

**Methods:** Cross-sectional study of patients with PH from clinical groups I and IV and functional classes II and III undergoing the following assessments: hemodynamics, exercise tolerance and quality of life.

**Results:** This study assessed 20 patients with a mean age of  $46.8 \pm 14.3$  years. They had pulmonary capillary wedge pressure of  $10.5 \pm 3.7$  mm Hg, 6-minute walk distance test (6MWD) of  $463 \pm 78$  m, oxygen consumption at peak exercise of  $12.9 \pm 4.3$  mL O<sub>2</sub>.kg<sup>-1</sup>.min<sup>-1</sup> and scores of quality of life domains < 60%. There were associations between cardiac index (CI) and ventilatory equivalent for CO<sub>2</sub> ( $r = -0.59$ ,  $p < 0.01$ ), IC and ventilatory equivalent for oxygen ( $r = -0.49$ ,  $p < 0.05$ ), right atrial pressure (RAP) and 'general health perception' domain ( $r = -0.61$ ,  $p < 0.01$ ), RAP and 6MWD ( $r = -0.49$ ,  $p < 0.05$ ), pulmonary vascular resistance (PVR) and 'physical functioning' domain ( $r = -0.56$ ,  $p < 0.01$ ), PVR and 6MWD ( $r = -0.49$ ,  $p < 0.05$ ) and PVR index and physical capacity ( $r = -0.51$ ,  $p < 0.01$ ).

**Conclusion:** Patients with PH from groups I and IV and functional classes II and III exhibit a reduction in physical capacity and in the physical and mental components of quality of life. The hemodynamic variables CI, diastolic pulmonary arterial pressure, RAP, PVR and PVR index are associated with exercise tolerance and quality of life domains. (Arq Bras Cardiol. 2015; 104(5):387-393)

**Keywords:** Hypertension, Pulmonary; Pulmonary Heart Disease; Quality of Life; Hemodynamics / physiopathology.

### Introduction

In the follow-up of patients with pulmonary hypertension (PH), several aspects guide therapeutic decisions and prognostic determinants, such as clinical evidence of right heart failure, progression of signs and symptoms, occurrence of syncope, changes in functional class, in physical capacity and in quality of life (QOL), echocardiographic findings and hemodynamic changes<sup>1-4</sup>.

Physical limitation in PH is the cause of great clinical and investigative interest, being a marker of disease progression in the presence of a certain treatment or specific management<sup>5-9</sup>. In addition, physical capacity has been shown to be one determinant of the QOL of patients with PH. Because QOL is influenced by several aspects related to the disease, its assessment has been recommended for the follow-up of patients with PH. In addition to being considered one of the most important outcomes to assess the impact of drug therapy, the QOL assessment indicates the self-perception of treatment, assessed within the sociocultural context, considering objectives, expectations and individual behaviors<sup>4</sup>.

Considering that few studies have assessed the association of physical capacity and QOL of patients with PH and that the clinical findings of those patients can vary according to the etiology and severity of disease, the present study is justified by the need to deepen the knowledge on those aspects in specific groups and functional classes. That has prevented the influence of other diseases that cause PH and the interference

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of extremes of functional classes with physical capacity and QOL. Thus, this study was aimed at assessing the associations between hemodynamics, physical capacity and QOL in patients with PH of clinical groups I and IV<sup>10</sup> and functional classes II and III (WHO/PH), followed up at a reference outpatient clinic in the Rio de Janeiro state.

## Methods

### Study Design and Sample

This is a cross-sectional observational study, with a convenience sample of patients recruited from the outpatient clinic of Pulmonary Hypertension of the Pulmonology Service of the Clementino Fraga Filho university-affiliated Hospital, according to the following inclusion criteria: patients diagnosed with PH, with neither cardiovascular nor pulmonary disease (belonging to groups I or IV)<sup>10</sup>, functional class II and III (WHO/PH), and clinical and hemodynamic stability. In addition, the patients should be on drug treatment for PH (specific or not) for at least three consecutive months with the same drug and be at least 17 years of age.

The exclusion criteria were as follows: patients with history of unstable angina and myocardial infarction within the last month before assessment; musculoskeletal lesion limiting the practice of physical assessment tests; comorbidities that could cause dyspnea on exertion; stable angina, severe arrhythmias or acute right ventricular failure with changes in the following variables at rest: heart rate (HR)  $\geq$  120 bpm, systolic blood pressure (SBP)  $\geq$  180 mmHg; diastolic blood pressure (DBP)  $\geq$  110 mmHg.

This study was approved by the Committee on Ethics and Research of the Hospital Clementino Fraga Filho (HUCFF) of the Rio de Janeiro Federal University, under the protocol number 033/2011. All participants provided written informed consent prior to beginning their participation in the study.

### Protocols and Measurements

All patients underwent right cardiac catheterization in the Catheterization Laboratory of the HUCFF. The following data were obtained: systolic pulmonary artery pressure (sPAP), diastolic pulmonary artery pressure (dPAP), right atrial pressure (RAP), cardiac index (CI), cardiac output (CO), pulmonary vascular resistance (PVR), pulmonary vascular resistance index (PVRI), mean pulmonary artery pressure (mPAP). Systemic blood pressure was measured according to the recommendations of the Brazilian Society of Cardiology<sup>11</sup>.

The 6-minute walk distance test (6MWD) was performed at the Physical Therapy Service of the HUCFF, under blood pressure and HR monitoring, with modified BORG scale and oxygen saturation (SpO<sub>2</sub>), on a 50-meter flat corridor, with length marked every meter, according to the recommendations of the American Thoracic Society<sup>12</sup>. The previously collected data regarding age, sex, height and weight were used to calculate the predicted distance walked during the test<sup>13</sup>. At least two 6MWT were performed, respecting a minimum 30-minute interval between them, until returning to baseline measures at rest, and the best result was considered for analysis<sup>12</sup>. The data used were as follows: walked distance;

SpO<sub>2</sub> at rest and at 6 minutes; oxygen desaturation during the test; HR; systolic and diastolic blood pressure at rest and at 6 minutes; and dyspnea grade at rest and at 6 minutes.

The cardiopulmonary exercise test (ergospirometry) was performed at the Ergospirometry and Cineanthropometry Laboratory of the School of Physical Education and Sports of the Rio de Janeiro Federal University, on a treadmill (ECAFIX EG700.2 - Brazil), using the Naughton protocol and analysis of the expired gases with the VO2000 device (Inbrasport Ltda, RS, Brazil). The following criteria were considered for test interruption: significant chest pain; paleness and cold sweating; disorientation and coordination loss; vertigo and pre-lipothymia; intolerable dyspnea; cyanosis; significant ST-segment depression; T-wave inversion and appearance of Q wave; progressive and multifocal ventricular ectopy; appearance of R wave on T wave; salvos of three or more ventricular extrasystoles; ventricular paroxysmal tachycardia; second- or third-degree atrioventricular block; SBP > 250 mmHg; DBP > 120 mmHg; left bundle branch block; intense chronotropic incompetence; sustained supraventricular tachycardia; SpO<sub>2</sub> < 80%; symptomatic claudication; and on patient's request<sup>14</sup>. The results were interpreted by using the equations for the Brazilian predicted values described by Neder et al.<sup>15</sup>. The following data were assessed: peak oxygen consumption (VO<sub>2</sub> peak); peak HR and blood pressure during the test; oxygen pulse (VO<sub>2</sub> peak/HR); minute ventilation (VE); ventilatory reserve (VR); HR reserve (HRR); ventilatory equivalent for carbon dioxide (VE/VO<sub>2</sub>); ventilatory equivalent for oxygen (VE/VO<sub>2</sub>) and respiratory coefficient (RQ).

Quality of life was assessed by using a QOL questionnaire, the Short-Form 36 Health Survey (SF-36)<sup>16</sup>, comprising 36 items that assess eight domains (physical functioning, physical role, bodily pain, general health perceptions, vitality, social functioning, emotional role and mental health) and two components (physical and mental). The results of each item vary from 0 to 100, a score of 0 being equivalent to maximum disability and a score of 100 being equivalent to no disability. The participants were duly instructed by the interviewer, responding to 11 questions related to eight different QOL domains, and were scored according to the scale defined in each question. The scores and analysis of results followed the guidelines for SF-36 scoring and its score calculation<sup>16</sup>. The questionnaire was applied to the patients included in the study on the same day and prior to the 6MWT.

Data were collected on two non-consecutive days, within two weeks. On the first day, the patient's history was collected, the written informed consent provided, the SF-36 applied and 6MWT performed. The cardiopulmonary exercise test was performed on the second day of assessment.

### Statistical Treatment

All analyses were performed using the Sigmasat 3.1 software (SYSTAT Software Inc., Point Richmond, CA, USA). The distribution of the variables was assessed by using the Shapiro-Wilk test, and the results were presented as mean and standard deviation or median and maximum-minimum. The measures of association between the variables were

assessed by using Spearman or Pearson correlation tests. The significance level adopted was  $p < 0.05$ .

## Results

This study assessed 20 patients (13 women) with a mean age of  $46.8 \pm 14.3$  years, mean height of  $162 \pm 69$  cm, mean weight of  $73.4 \pm 15.0$  kg and mean body mass index (BMI) of  $27.7 \pm 5.2$  kg/m<sup>2</sup>. Table 1 shows the hemodynamic characterization of the sample.

The patients on specific drug treatment for PH for more than three months comprised 55% of the sample (11 patients), of whom 35% (6 patients) were on sildenafil (type 5 phosphodiesterase inhibitor) and 25% (5 patients) were on bosentan (endothelin receptor antagonist). Regarding the functional classification (WHO/PH), 80% of the patients were class II (6 men and 11 women) and 20% were class III (2 men and 2 women). Considering clinical characterization, 65% belonged to group I (3 men and 10 women) and 35% to group IV (4 men and 3 women).

Table 2 shows the mean values obtained in the physical capacity assessment related to cardiopulmonary exercise test and 6MWT, and the mean predicted values<sup>17,18</sup>.

Table 3 shows the scores obtained in QOL assessment.

Figure 1 shows the only associations found when assessing the physical capacity and QOL measurements in the group studied. Table 4 shows the correlations between the hemodynamic variables, the physical capacity measurements and the QOL domains and components.

## Discussion

The group of patients with PH showed a physical capacity limitation, mainly evidenced by the reduced  $VO_{2peak}$  (52.7% of the predicted value) and impact on QOL, in both physical and mental components (Table 3). Differently from other cross-sectional studies including patients with PH, the individuals assessed in the present study were restricted to the diagnostic groups I and IV, and to the functional classes II and III, avoiding the influence of other diseases that also cause PH, as well as the interference of the extremes of functional classes with physical capacity and QOL.

### Associations with hemodynamics

Taichman et al.<sup>6</sup> have found no association between QOL, 6MWT and the hemodynamic variables, which differs from our findings and might have resulted from the absence of group IV patients in their sample, in addition to having included a small number of patients with functional class I.

In 2008, Zlupko et al.<sup>24</sup> reported a correlation between RAP and the physical component ( $p = 0.05$ ;  $r = 0.29$ ) and the total value of QOL ( $p = 0.01$ ;  $r = 0.36$ ). Halank et al.<sup>5</sup> have reported associations between RAP and the domains 'physical functioning' ( $p < 0.01$ ;  $r = -0.40$ ), 'role limitations due to physical health' ( $p < 0.05$ ;  $r = -0.27$ ) and 'general health perceptions' ( $p < 0.05$ ;  $r = -0.29$ ). Both studies have supported our results, confirming the important association between elevated RAP and a reduction in the physical component of QOL.

**Table 1 - Hemodynamic characterization**

Hemodynamic characteristics	Mean (SD)
mPAP (mm Hg)	51 ± 9.11
sPAP (mm Hg)	82.4 ± 19.9
dPAP (mm Hg)	30.5 ± 7.44
RAP (mm Hg)	10.1 ± 5.21
CO (L/min)	4.1 ± 1.18
PVR (dyn.s/cm <sup>5</sup> )	839.9 ± 327.6
PCWP (mm Hg)	10.5 ± 3.72
CI (L/min/m <sup>2</sup> )	2.31 ± 0.52
PVRI (dyn.s/cm <sup>5</sup> .m <sup>2</sup> )	1568.2 ± 639.0
HR at rest (bpm)	76.6 ± 12.6
SBP (mm Hg)	115 ± 17.6
DBP (mm Hg)	75.7 ± 9.21

SD: standard deviation; mPAP: mean pulmonary artery pressure; sPAP: systolic pulmonary artery pressure; dPAP: diastolic pulmonary artery pressure; RAP: right atrial pressure; CO: cardiac output; PVR: pulmonary vascular resistance; PCWP: pulmonary capillary wedge pressure; CI: cardiac index; PVRI: pulmonary vascular resistance index; HR: heart rate; SBP: systolic blood pressure at rest; DBP: diastolic blood pressure at rest.

**Table 2 – Physical capacity assessment**

Characteristics	Mean ± SD of the values obtained	Mean ± SD of the predicted values %
6MWDt (m)	463 ± 78	83 ± 11
$VO_{2peak}$ (mL O <sub>2</sub> .kg <sup>-1</sup> .min <sup>-1</sup> )	12.9 ± 4.30	52.7 ± 22.5
VE/VCO <sub>2</sub>	41.5 ± 10	88.1 ± 23.6
VE/VO <sub>2</sub>	43.7 ± 16	80.5 ± 34.6
VO <sub>2</sub> /HR	13.8 ± 3.6	77.3 ± 17.6
HRR (bpm)	43.8 ± 26.1	47.2 ± 14.3
VR (L)	54.1 ± 25.6	41.3 ± 16.6
RQ	1.07 ± 0.31	**
SBP (mm Hg)	148.7 ± 15.3	**

SD: standard deviation; 6MWDt: 6-minute walk distance test (prediction: Pereira, 2011);  $VO_{2peak}$ : peak oxygen consumption; VE/VCO<sub>2</sub>: ventilatory equivalent for carbon dioxide; VE/VO<sub>2</sub>: ventilatory equivalent for oxygen; HR: heart rate; VO<sub>2</sub>/HR: oxygen pulse; HRR: heart rate reserve; VR: ventilatory reserve (prediction: Neder, 1999); RQ: respiratory coefficient; SBP: maximum systolic blood pressure during cardiopulmonary exercise testing; \*\*no predicted values described.

The associations observed in our study between 6MWT and the hemodynamic variables (RAP and PVR,  $p < 0.05$ ;  $r = -0.49$ ) are similar to the results found by Miyamoto et al.<sup>19</sup> in patients with idiopathic PH, in which 6MWT correlated significantly with CO, RAP and PVR ( $p < 0.001$ ), but not with mPAP.

**Table 3 – Health domains and components of the quality of life questionnaire (SF-36)\***

Domains	Median (Max – Min)
Physical functioning	30 (80 – 5)
Role limitations due to physical health	0 (100 – 0)
Bodily pain	43.5 (100 – 20)
General health perceptions	53.5 (95 – 15)
Vitality	45 (75 – 10)
Social functioning	50 (100 -12.5)
Role limitations due to emotional problems	0 (100 – 0)
Mental health	48 (100 – 20)
Physical component	39.6 (76.2 – 19.2)
Mental component	40.7 (78 – 19.6)

\*The domains and components are assessed in a percentage scale ranging from 0 to 100.

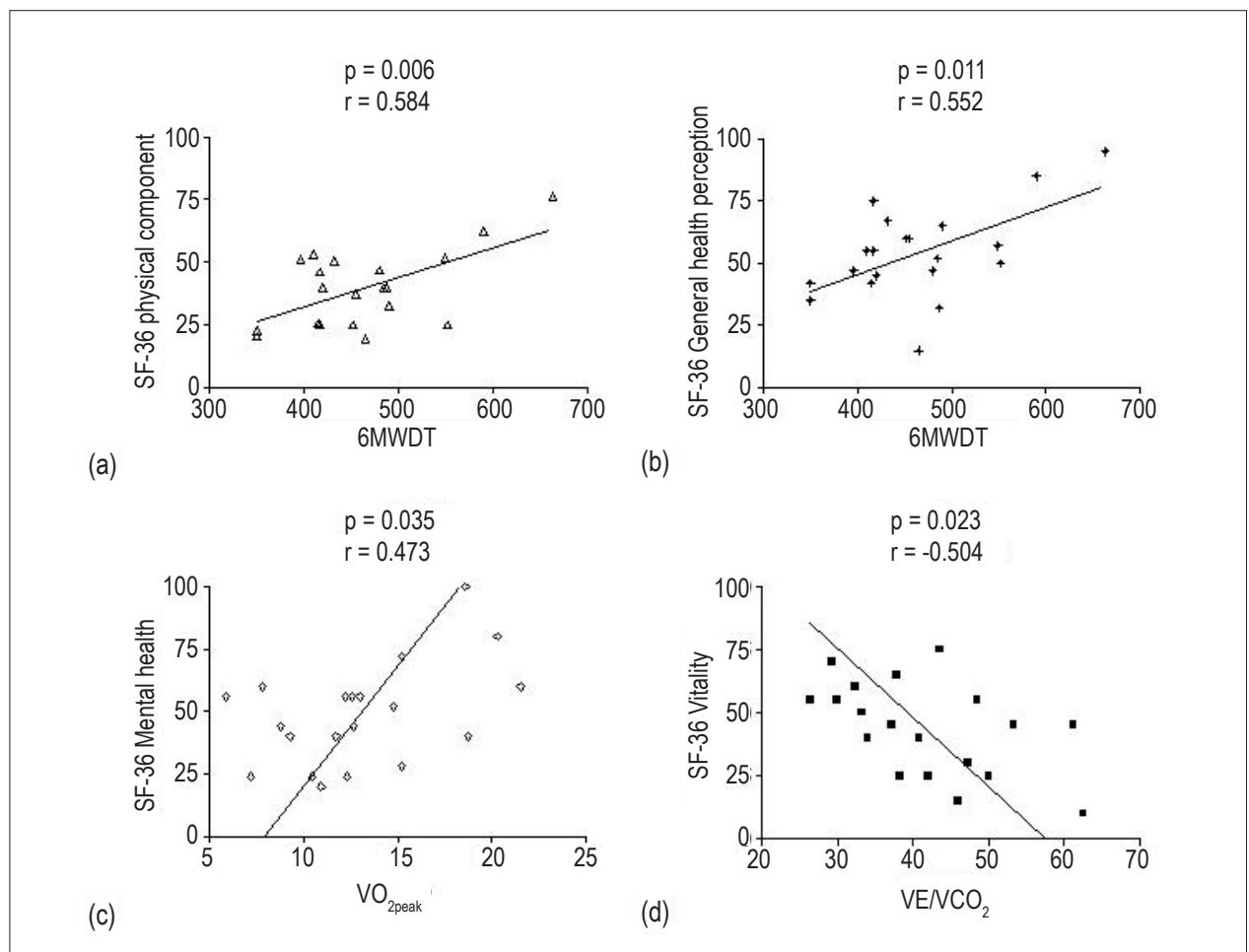
We report new correlations obtained between hemodynamic and physical variables, such as IC versus  $V'E/V'CO_2$  and  $V'E/V'O_2$  ( $p < 0.01$ ;  $r = -0.59$  and  $p < 0.05$ ;  $r = -0.49$ ) and PVRI versus  $V'E/V'CO_2$  ( $p < 0.01$ ;  $r = -0.51$ ), indicating impaired physical capacity caused by PH.

In addition, the unpublished association between PVR and the physical component of QOL ( $p < 0.01$ ;  $r = -0.56$ ) was observed, suggesting that patients with lower PVR have better QOL regarding the physical component. This can justify the use of vasodilating therapy to improve the symptoms of patients with PH.

**Physical capacity**

Walked distances shorter than 332 m<sup>19</sup> or 250 m<sup>17</sup> and desaturation greater than 10% have been reported as indicative of a worse prognosis associated with PH. Absolute values greater than 380 m during the three months of prostanoid treatment have been correlated with longer survival<sup>1</sup>.

In our study, the mean walked distance in the 6MWT was higher than the threshold indicated in the literature as having the worst prognosis ( $463 \pm 78$  m).



**Figure 1 – Associations between the SF-36 quality of life questionnaire domains and the functional variables of patients with pulmonary hypertension. 6MWD (m): 6-minute walk distance test;  $VO_{2peak}$ : oxygen consumption at peak exercise;  $VE/CO_2$ : ventilatory equivalent for carbon dioxide.**

**Table 4 – Correlation between the hemodynamic variables, the physical capacity measurements and the QOL domains and components of patients with pulmonary hypertension**

	Quality of life			Physical capacity		
	PhC	MC	GHP	6MWDT	VE/VCO <sub>2</sub>	VE/VO <sub>2</sub>
CI	0.28	0.34	0.008	0.12	-0.59**	-0.49*
dPAP	-0.06	-0.54	-0.26	-0.02	0.15	0.15
RAP	-0.33	-0.16	-0.61**	-0.49*	0.11	0.13
PVR	-0.56**	-0.30	-0.12	-0.49*	0.35	0.02
PVRI	-0.42	-0.43	-0.37	-0.40	-0.51**	0.20

CI: cardiac index; dPAP: diastolic pulmonary artery pressure; RAP: right atrial pressure; PVR: pulmonary vascular resistance; PVRI: pulmonary vascular resistance index; PhC: physical component; MC: mental component; GHP: general health perceptions; 6MWDT: 6-minute walk distance test; VE/VCO<sub>2</sub>: ventilatory equivalent for carbon dioxide; VE/VO<sub>2</sub>: ventilatory equivalent for oxygen. The associations were tested by using Pearson or Spearman correlation test. \*p < 0.05; \*\*p < 0.01.

Grünig et al.<sup>20</sup> have reported a mean walked distance in the 6MWT of 440 ± 90 m during the initial assessment of 58 patients, four of whom belonged to functional class IV. Similarly, Halank et al.<sup>5</sup> have reported a mean distance walked in the 6MWT of 343.8 ± 114 m for a group including four patients in that functional class.

Cicero et al.<sup>18</sup> have assessed 34 patients in functional classes II and III, whose initial median walked distance was 399 (117-564) m. However, the group studied included no group IV patient.

According to Sun et al.<sup>21</sup>, patients with PH can safely undergo cardiopulmonary exercise testing, and the results obtained enlarge the possibilities of prognostic analysis. The group studied had a VO<sub>2peak</sub> < 60% during exercise, ventilatory equivalents (V'E/V'O<sub>2</sub> and V'E/V'CO<sub>2</sub>) < 55 L/L and extremely variable cardiopulmonary reserve parameters (HRR and VR), with no association with other hemodynamic or QOL variables.

Five patients studied did not reach the anaerobic threshold, and those who did showed low VO<sub>2peak</sub> and VO<sub>2peak</sub>/HR values, with no significant oximetry change, but with substantial VR. Thus, physical unfitnes was the major factor for physical limitation in the group studied (18 patients). In the two remaining patients, a cardiogenic origin (VO<sub>2peak</sub>/HR < 50%) was identified, and in the other, a pulmonary origin (VR < 11L). Those results suggest that our sample patients could benefit from a physical conditioning program to improve their physical capacity.

Wensel et al.<sup>22</sup> have reported that the physical capacity of patients with PH decreased according to the severity of the disease, and they have identified VO<sub>2peak</sub> < 10.4 mL O<sub>2</sub>.kg<sup>-1</sup>.min<sup>-1</sup> and peak SBP during exercise < 120 mm Hg as predictors of poor prognosis in PH.

Considering the limits reported by Wensel et al.<sup>22</sup> and the results by Sun et al.<sup>21</sup>, seven of our patients had VO<sub>2peak</sub> lower than the value associated with worse prognosis (mean of 12.9 ± 4.3 mL O<sub>2</sub>.kg<sup>-1</sup>.min<sup>-1</sup>) and only one patient had a peak SBP during exercise of 120 mm Hg (mean of 148.7 ± 15.3 mm Hg).

The patients studied by Grünig et al.<sup>20</sup> and Halank et al.<sup>5</sup> have also undergone cardiopulmonary exercise testing, and had mean VO<sub>2peak</sub> values of 12.5 ± 3.0 and 13.0 ± 4.2 mL O<sub>2</sub>.kg<sup>-1</sup>.min<sup>-1</sup>, respectively. They have provided neither data that could assess prognosis, such as peak SBP during exercise, nor detailed cardiopulmonary exercise test data that allowed the identification of the cause of physical limitation.

Because VE/VCO<sub>2</sub> has been used as an indicator of ventilatory efficiency, its increase is associated with worsening of dyspnea and pulmonary hemodynamics<sup>14,23</sup>. According to the results obtained, the group studied had mean VE/VCO<sub>2</sub> > 30, indicating greater severity of the chronic disease, such as PH, and showed association with hemodynamic variables (CI and IPVR) and QOL (vitality domain).

#### Quality of life

When assessing QOL, we observed that the patients perceived reduced values, and we used a generic questionnaire (SF-36) because of the lack of a specific questionnaire for PH validated in Portuguese<sup>18</sup>.

Zlupko et al.<sup>24</sup> have reported a significant association between SF-36 and the Minnesota Living with Heart Failure Questionnaire (MLHFQ) adapted to PH (MLHF-PH), despite the considerations of Rubenfire et al.<sup>9</sup> in a literature review, indicating that non-specific questionnaires could reflect neither clinical state nor prognosis in PH.

Chen et al.<sup>8</sup> have assessed QOL at 6, 12 and 24 months of clinical follow-up, using three different questionnaires: SF-36, Airways Questionnaire 20 (AQ 20) and MLHFQ. Those authors have reported a significant correlation between the questionnaires (p < 0.01) and of them with functional class (p < 0.001), 6MWT (p < 0.002) and Borg scale (p < 0.001), considering them appropriate tools to assess QOL in PH.

In 2013, Twiss et al.<sup>3</sup> identified appropriate psychometric criteria of the domains 'physical functioning' and 'general health perceptions' of the SF-36 when correlated with a specific questionnaire for PH (Cambridge Pulmonary Hypertension Outcome Review - CAMPHOR).

In this study, the individuals who achieved the best performance in the 6MWT were those with the best results in the physical component assessment ( $p = 0.006$ ;  $r = 0.58$ ) and the domain 'general health perceptions' of the SF-36 ( $p = 0.011$ ;  $r = 0.552$ ). In addition, those with the worst assessment in the 'mental health' domain had the lowest  $VO_{2peak}$  ( $p = 0.035$ ;  $r = 0.473$ ), indicating a possible psychic effect in patients with lower physical capacity.

Similar results have been reported by Taichman<sup>6</sup>, who have shown an association between the 6MWT and the SF-36 physical component ( $p < 0.001$ ;  $r = 0.62$ ). In addition, Halank et al.<sup>5</sup> have reported that all domains of the questionnaire associated with the walked distance, mainly the 'general health perceptions' ( $p < 0.01$ ;  $r = 0.47$ ) and 'physical functioning' ( $p < 0.01$ ;  $r = 0.73$ ).

In the last study, except for the 'mental health' domain ( $p = 0.207$ ), all others associated with  $VO_{2peak}$  ( $p < 0.01$ ), exactly the opposite to our findings, probably due to the different characteristic of the sample, with 80% of patients in functional class III and IV.

Cicero et al.<sup>18</sup> have also identified an association between the 'physical functioning' domain and the distance walked in the 6MWT in the initial assessment ( $p = 0.01$ ;  $r = 0.44$ ) of a group of patients on a 12-month clinical follow-up.

### Study Recommendations and Limitations

This study had some limitations. The patients' daily life physical activity levels were not assessed, hindering the determination to which extent physical capacity influences daily life activities and vice-versa. Assessing gas exchange variables during the tests, by analyzing arterial blood, would also add important information to this study. In addition, despite the careful selection, the reduced size of the sample (20 patients) and the lack of a control group should be considered, mainly when assessing very heterogeneous results of some variables.

Studies with a greater number of patients and maintaining each group specificities should complement the data obtained,

in addition to the development and application of specific methods for the QOL assessment of patients with PH, comprising the particularities inherent in that disease.

### Conclusion

Patients with PH of groups I and IV and functional classes II and III have a reduction in physical capacity and in the physical and mental components of QOL. The hemodynamic variables CI, dPAP, RAP, PVR and PVRI are associated with exercise tolerance and the QOL domains.

### Author contributions

Conception and design of the research: Torres DFM, Zin WA, Guimarães FS. Acquisition of data: Torres DFM, Lopes AJ, Vigário PS, Garcia MI, Waetge D, Bandeira MLS, Bessa LGP. Analysis and interpretation of the data: Torres DFM, Zin WA, Lopes AJ, Vigário PS, Garcia MI, Waetge D, Bandeira MLS, Bessa LGP, Guimarães FS. Statistical analysis: Torres DFM, Guimarães FS. Obtaining financing: Zin WA. Writing of the manuscript: Torres DFM, Guimarães FS. Critical revision of the manuscript for intellectual content: Zin WA, Lopes AJ, Vigário PS, Garcia MI, Waetge D, Bandeira MLS, Bessa LGP, Guimarães FS.

### Potential Conflict of Interest

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

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### Study Association

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