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RESEARCH ARTICLE

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Physical activity and its clinical correlates in chronic thromboembolic pulmonary hypertension

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Abstract

Limited data are available on physical activity (PhA) levels in chronic thromboembolic pulmonary hypertension (CTEPH) patients, as well as on the clinical utility of PhA measurements using questionnaires and accelerometers. We aimed to study PhA levels of CTEPH patients and their clinical correlates, and to compare PhA levels measured by the International Physical Activity Questionnaire (IPAQ) with measures from accelerometers. This is a cross-sectional study ($n = 50$). PhA levels were measured using accelerometers and questionnaires (IPAQ). Clinical parameters evaluated were walked distance on the 6-min-walking test (6MWT), pulmonary vascular resistance, N-terminal brain natriuretic peptide and quality of life (HRQoL) (Cambridge Pulmonary Hypertension Outcome Review questionnaire). Time spent in sedentary behavior was lower in self-reported measurement (279 ± 165 min/day) compared with accelerometry (446 ± 117 min/day, $p < 0.000$). Accelerometer-derived data showed that CTEPH patients spent 60% of the recorded time in sedentary behaviors and 2% in moderate-to-vigorous PhA (MVPA). Correlation analysis showed that MVPA was significantly correlated with 6MWT ($p = 0.023$) and symptom domain of HRQoL ($p = 0.044$). Self-reported MVPA was significantly higher than the one registered by the accelerometer (411 ± 569 vs. 131 ± 108 min/week, $p = 0.027$). Bland–Altman analysis indicated poor agreement between the two methods. Our results showed that CTEPH patients spend most of their days in sedentary behaviors and only a small amount of time in MVPA. Only MVPA was associated with HRQoL and CTEPH severity. In addition, we showed a poor agreement between self-reported and accelerometer-derived PhA in CTEPH patients, with the former overestimating the overall PhA.

KEYWORDS
accelerometry, chronic thromboembolic pulmonary hypertension, physical activity, questionnaire

INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a subtype of pulmonary hypertension (PH)[1] characterized by the presence of chronic organized residual thrombi in the pulmonary circulation, which can lead to a progressive vasculopathy and, eventually, right-sided heart failure.[2] The predominant symptoms of CTEPH patients are dyspnea, fatigue, and exercise intolerance,[3] which impacts on health-related quality of life (HRQoL).

Physical activity (PhA) levels in heart failure patients were associated with mortality in several studies and stood as a sensitive surrogate marker to treatments with established prognostic impact.[4] Despite the fewer evidence in PH, reduced PhA levels have been associated with poor HRQoL, increased disease severity, and poor survival in pulmonary arterial hypertension (PAH) patients.[5,6] PhA levels (number of steps per day) correlated with exercise capacity in PAH patients,[7] which is an established benchmark for disease severity, prognosis, and response to therapy.[8] In addition, PhA levels are a continuous metric closely aligned with the treatment goals of most cardiovascular diseases such as relieving exertional symptoms and improving functional status. These unique characteristics make PhA an increasingly valued outcome to be measured in both clinical trials and in daily clinical practice settings. In fact, telemonitoring PhA levels may provide a method to continuously assess patients for clinical change over a prolonged duration of time.[7]

There are several instruments to measure PhA levels, including questionnaires and portable devices. Questionnaires are simple and easy to use, are cost-effective, and allow identification of the context in which PhA is performed (e.g., occupational, recreational).[9] Accelerometers are devices sensitive to motion that provide accurate information about total PhA but are more expensive and require expertise to manage and analyze its output data.[10] There is a lack of empirical data on how these tools measure PhA levels in PH.

Scarce data are available regarding the impact of PhA levels in CTEPH patients, as well as on the clinical utility of PhA measurements using questionnaires and accelerometers. Our study aimed: (i) to describe PhA levels of CTEPH patients and examine its clinical correlates; and (ii) to compare PhA levels measured by the International Physical Activity Questionnaire (IPAQ) with objective measures from triaxial accelerometers in CTEPH patients.

METHODS

Study design and participants

We conducted a cross-sectional study in a Portuguese pulmonary hypertension expert center (Pulmonary Vascular Disease Unit, Centro Hospitalar Universitário do Porto). Inclusion criteria were a diagnosis of CTEPH according to international guidelines[11] and the ability to understand the requirements for valid accelerometry. Patients were excluded if they were unable to walk independently. We included both prevalent and incident CTEPH patients. Demographic and disease-specific clinical measures were retrieved from electronic health records (PAH Tool; Inovultus). Right ventricle systolic dysfunction was defined as tricuspid annular plane systolic excursion (TAPSE) < 17 mm or fractional area change (FAC) < 35%.

The study was approved by the Ethics Committee of our University (N/REF.a 2018.160 (137-DEFI/136-CES)). All procedures were conducted according to the Declaration of Helsinki, and patients signed informed consent to participate.

Clinical parameters evaluation

Blood sample collection

All subjects underwent venous blood sampling drawn from an antecubital vein. Samples were processed immediately and N-terminal brain natriuretic peptide (NT-proBNP) was measured on the day of blood sampling using the standard protocol of our hospital laboratory (Roche NT-proBNP assay).

Hemodynamic assessment

Hemodynamic assessment was performed by right heart catheterization using the right femoral vein. Pulmonary artery, right atrial, and pulmonary capillary wedge pressures were recorded at the end of a quiet respiratory cycle. Cardiac output was obtained using thermodilution. Pulmonary vascular resistance (PVR) was calculated using the standard formulas.

Six-minute walking test

The 6-min walk test (6MWT) was performed in a 30-m-long corridor under the same environmental conditions and at approximately the same time of the day. Participants were

instructed to walk the maximal distance in 6 min time. Resting stops were allowed when patients feel to be necessary.

HRQoL

HRQoL was assessed by self-administering questionnaires. Participants were asked to complete the Portuguese validated version of the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) questionnaire, an HRQoL instrument specific to PAH patients, validated for use in clinical practice and in clinical research settings.[12]

Accelerometer-assessed PhA

PhA was objectively assessed with a triaxial accelerometer (Actigraph GT3X). Participants were instructed to wear the accelerometer over the right hip for 7 consecutive days, except while sleeping, bathing, and water-related activities. They were encouraged to participate in their routine activities while completing the study. ActiLife software (Actigraph, version 6.9) was used to process the accelerometer data. Only participants with valid PA data (≥10 h/day, at least 4 days) were included in the analysis. The average min/day spent at different categories of PhA intensity was defined as sedentary time (<200 counts/min),[13] light PhA (200−2689 counts/min), and MVPA (≥2690counts/min).[14] Meeting international PhA guidelines was defined as ≥150 min/week of MVPA.[15]

The International Physical Activity Questionnaire-Short Form (IPAQ-SF)

Self-reported PhA was assessed with the short form of IPAQ (IPAQ-SF),[16] through personal interview. The IPAQ-SF estimates PhA frequency and duration during the previous 7 days. It focuses on moderate, vigorous, and walking physical activities and time spent sitting. The scoring protocol assigns the values of 3.3 METs to "walking," 4.0 METs to "moderate," and 8.0 METs to "vigorous" activity.[17] Meeting international PhA guidelines was defined as ≥150 min/week of MVPA.[15] Thus, to estimate MVPA we merged the reported activities ≥3 METs (walking + moderate + vigorous PhA).

Statistical analysis

Normal data distribution was examined by the Shapiro −Wilk test. Non-normal data were transformed into square root (HRQol scale, PVR and mean right atrial pressure [mRAP]) or ranks (IPAQ MVPA, ACC MVP, and NT-proBNP) for subsequent analysis and then transformed back to the original scale for the purpose of clarity. Categorical data are reported as absolute values and percentages. Between-gender comparisons was performed by independent t test. Age cut point was defined as ≥65 years as conventionally used to define older adults. Partial correlation (adjusted by gender and age) was used to assess the association between PhA variables with clinical parameters, and between the variables derived from the two methods. Sitting time and MVPA from IPAQ-SF were compared with sedentary time and MVPA derived from accelerometer using paired t test. The strength and limits of agreement between the two methods were assessed using the Bland–Altman technique.[18] Statistical analysis was performed using the IBM SPSS 24 software (SPSS), and the statistical significance was set at $p < 0.05$.

RESULTS

Studied population

A total of 50 patients accepted to participate in the study, but only 43 had accelerometer valid data ($n = 43$). The demographic and clinical characteristics of the studied CTEPH patients are displayed in Table 1. They were predominantly female (72.1%) and had a mean age of 63 ± 16 years old. Most of them were in functional class NYHA II (58.1%) and had a 6MWD of 377 ± 144 m. Echocardiography data showed that 67% presented right ventricle systolic dysfunction and the mean PVR by right heart catheterization was 6 ± 3.4 WU, despite most of them being on pulmonary vasodilators (Table 1).

PhA levels

Accelerometer was used on average 6.6 ± 0.8 days, with a mean daily wear time of 815 min (13.6 ± 1.2 h/day). The mean of total activity was 472 ± 232 counts per minute (cpm). Time spent in sedentary behaviors was 8 ± 2 h/day (Table 2). Considering PhA levels, patients spent an average of 5.6 ± 2.3 h/day in light PhA and 19 ± 17 min/day in MVPA (131 ± 108 min/week). Men spent more time in MVPA (180 ± 105 vs. 109 ± 105 min/week, respectively; $p = 0.028$) than women. Analysis by age showed that older patients spent significantly less time in MVPA (96 ± 105 vs. 171 ± 102 min/week, $p = 0.007$).

TABLE 1 Baseline demographic and clinical features of studied population

Characteristics	CTEPH ($n = 43$)
Age (years)	63 ± 16
Gender, *n* (%)	
Female	31 (72.1)
Male	12 (27.9)
BMI	27 ± 5
Disease duration (years)	3.0 ± 2.8
NYHA, *n* (%)	
I	8 (18.6)
II	25 (58.1)
III	10 (23.3)
Hypertension	25 (58.1%)
Dyslipidemia	18 (41.9%)
Diabetes mellitus	5 (11.6%)
Former smoker	6 (14%)
Heart failure	8 (18.6%)
6MWD (m)	377 ± 144
NT-proBNP (pg/ml)	296 ± 335
PASP (mmHg)	60.6 ± 23.8
TAPSE (mm)	18 ± 3
FAC (%)	31 ± 11
S' wave (cm/s)	11 ± 2
RV dysfunction, *n* (%)	24 (61.5)
mRAP (mmHg)	6 ± 3
mPAP (mmHg)	38.9 ± 14.1
CO (L/min)	5.6 ± 1.8
PVR (UW)	6.0 ± 3.4
OAC	43 (100%)
Riociguat, *n* (%)	14 (32.6)
PDE5I, *n* (%)	12 (27.9)
ERA, *n* (%)	30 (69.8)
Diuretic, *n* (%)	21 (48.8)
BPA, *n* (%)	8 (18.6)
PEA, *n* (%)	5 (11.5)
Oxygen therapy	13 (30%)

Abbreviations: 6MWD, 6-min walking distance; BMI, body mass index; BPA, balloon pulmonary angioplasty; CO, cardiac output; ERA, endothelin receptor antagonist; FAC, fractional area change; mPAP, median pulmonary artery pressure; mRAP, mean right atrial pressure; NT-proBNP, N-terminal brain natriuretic peptide; NYHA, New York Heart Association functional class; OAC, oral anticoagulant; PASP, pulmonary artery systolic pressure; PDE5I, phosphodiesterase type 5 inhibitor; PEA, pulmonary endarterectomy; PVR, pulmonary vascular resistance; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.

HRQoL levels

Overall, the CTEPH patients showed a distribution of the CAMPHOR scores that were indicative of a moderate HRQoL impairment: symptoms (11.5 ± 6.5); functioning (11.3 ± 6.3); and quality of life (8.3 ± 6.8).

Relationship between PhA variables with clinical parameters

In partial correlation analysis, accelerometer-derived MVPA (min/week) present a positive mild correlation with 6MWD ($r = 0.359$, $p = 0.023$) and a negative one with the symptom domain of CAMPHOR ($r = -0.371$, $p = 0.044$). Total activity, sedentary time, and light PhA did not correlate with any clinical parameter (Table 3). Data derived from IPAQ-SF showed that total activity (METs/week) presented a mild correlation with total HRQoL ($r = -0.337$, $p = 0.033$) and functional scale ($r = -0.342$, $p = 0.031$), and sedentary time with total HRQoL; $r = 0.338$, $p = 0.033$).

PhA levels according to NYHA class and RV dysfunction

When PhA levels were compared between NYHA class (I–II vs. III–IV), patients in class III–IV had lower total PhA (339 ± 210 vs. 516 ± 225 cpm, $p = 0.035$) and spend more time in sedentary behaviors (526 ± 105 vs. 441 ± 114 min/day; $p = 0.046$). Regarding RV dysfunction, patients with RV dysfunction spend less time in light PA (301 ± 141 vs. 408 ± 143 min/day; $p = 0.040$) and had less total PA (415 ± 200 vs. 585 ± 255 cpm; $p = 0.033$) when compared with those without RV dysfunction. Data are displayed in Table 4.

Differences between self-reported and objective measures of PhA

Time spent in sedentary behavior was lower in self-reported measurement (270 ± 164 min/day) compared with accelerometery (446 ± 117 min/day, $p < 0.001$) (Table 2). Considering time spent in MVPA per week, the mean self-reported time was significantly higher than the one registered by the accelerometer (420 ± 576 vs. 131 ± 108 min/week, $p = 0.027$). These differences persisted when we analyzed the data according to sex and age.

TABLE 2 Descriptive PA levels from accelerometer variables

	All ($n = 43$)	Women ($n = 31$)	Men ($n = 12$)	<65 years ($n = 19$)	≥65 years ($n = 24$)
Accelerometer					
Total activity (cpm/day)	472 ± 232	436 ± 227	485 ± 152	525 ± 186	392 ± 210
Sedentary time (min/day)	462 ± 117	449 ± 116	501 ± 119	455 ± 132	470 ± 109
Light PA (min/day)	336 ± 144	326 ± 144	314 ± 119	358 ± 144	297 ± 127
MVPA (min/day)	19 ± 17	16 ± 15	29 ± 18*	27 ± 16	15 ± 16*
MVPA (min/week)	131 ± 108	109 ± 105	180 ± 105*	171 ± 102	96 ± 105*
MVPA ≥ 150 min/week, *n* (%)	15 (35)	8 (26)	7 (59)	8 (42)	7 (29)
IPAQ					
Sedentary time (min/day)	270 ± 164	261 ± 171	291 ± 150	263 ± 188	275 ± 146
MVPA (min/day)	60 ± 82	39 ± 53	115 ± 115	62 ± 66	59 ± 95
MVPA (min/week)	420 ± 576	270 ± 275	807 ± 809	432 ± 462	410 ± 661
MVPA ≥ 150 min/week, *n* (%)	25 (58)	16 (51)	9 (75)	13 (68)	12 (50)

Note: Data are mean ± SD.

Abbreviations: cpm, counts per minute; min, minutes; MVPA, moderate-to-vigorous PA; PA, physical activity.

*$p < 0.05$.

TABLE 3 Partial correlation between PA variables with clinical parameters

	6 MWT	NT-proBNP	PVR	HRQOL	Functional scale	Symptoms scale
Accelerometer						
Total activity (cpm)	0.270 (0.105)	−0.171 (0.312)	−0.034 (0.847)	−0.234 (0.158)	−0.212 (0.200)	−0.282 (0.132)
Sedentary (min/day)	−0.100 (0.539)	0.089 (0.584)	−0.061 (0.717)	0.175 (0.274)	0.147 (0.358)	0.156 (0.409)
Light PA (min/day)	0.172 (0.294)	0.032 (0.847)	0.006 (0.973)	−0.149 (0.359)	−0.079 (0.627)	−0.153 (0.420)
MVPA (min/week)	**0.359 (0.023)**	−0.162 (0.317)	−0.065 (0.694)	−0.174 (0.277)	−0.261 (0.099)	**−0.371 (0.044)**
IPAQ						
Total activity (METs/week)	0.265 (0.086)	−0.103 (0.509)	−0.229 (0.157)	**−0.338 (0.033)**	**−0.342 (0.031)**	−0.268 (0.082)
Sedentary time (min/day)	−0.152 (0.330)	0.127 (0.419)	−0.070 (0.655)	**0.337 (0.033)**	0.235 (0.130)	0.244 (0.115)
MVPA (min/week)	0.259 (0.096)	−0.081 (0.605)	−0.191 (0.220)	−0.291 (0.059)	−0.300 (0.060)	−0.239 (0.122)

Note: Adjusted by gender and age. Data are *r* (*p*). Bold values represent $p < 0.05$.

Abbreviations: 6MWT, 6-min walk test; cpm, counts per minute; HRQoL, health-related quality of life; min, minutes; MVPA, moderate-to-vigorous PA; NTproNP, N-terminal brain natriuretic peptide; PA, physical activity; PVR, pulmonary vascular resistance.

Correlation and agreement between self-reported and objective measures of PhA

To compare the validity and the accuracy of self-reported and accelerometer-derived PhA were analyzed the following parameters: the validity correlation, the systematic error, the 95% limits of agreement, and the standard error of the estimate are displayed in Table 5. Correlation between self-reported and accelerometer measured was significant for sedentary time ($p = 0.004$), but not significant for MVPA ($p = 0.276$). A significant mean difference (systematic error) between self-reported and accelerometer-derived PhA data was detected in sedentary time ($p = 0.001$) but not for MVPA ($p = 0.083$). By analyzing the 95% limits of agreement, both sedentary time and MVPA presented a higher variation, ranging from −464 to 104 min/day for sedentary time, and from −630 to 840 min/week for MVPA. The standard error of the estimate was 109 min/day for sedentary time and 106 min/week for MVPA.

Separate Bland−Altman plots were built for sedentary time and MVPA (Figure 1). In both sedentary time and MVPA, the limits of agreement were wide, indicating poor agreement between the methods. Figure 1a shows

TABLE 4 Descriptive PA levels from accelerometer variables according to NHYA class and RV dysfunction

	NYHA Class		RV dysfunction	
	I– II ($n = 33$)	II–IV ($n = 10$)	Yes ($n = 24$)	No ($n = 19$)
Accelerometer				
Total activity (cpm/day)	516 ± 225	339 ± 210*	415 ± 200	585 ± 255*
Sedentary time (min/day)	441 ± 114	526 ± 105*	482 ± 126	4311 ± 99
Light PA (min/day)	361 ± 139	262 ± 139	301 ± 141	408 ± 143*
MVPA (min/day)	21 ± 15	17 ± 20	18 ± 15	25 ± 17
MVPA (min/week)	139 ± 102	104 ± 125	115 ± 96	160 ± 105
MVPA ≥ 150 min/week, *n* (%)	11 (33)	4 (40)	6 (27)	8 (38)

Abbreviations: cpm, counts per minute; MVPA: moderate-to-vigorous PA; NYHA, New York Heart Association functional class; PA, physical activity; RV, right ventricle.

TABLE 5 Descriptive values for self-report physical activity levels

	Self-reported (mean ± SD)	Mean difference (95% LOA)	*r* (*p*)[a]	SEE
Sedentary time (min/day)	288 ± 170	−180 (−464; 104)*	0.467 (0.004)**	109
MVPA (min/week)[a]	411 ± 568	105 (−630; 840)	0.182 (0.276)	106

Note: Mean difference: self-reported − objective measured parameter.

Abbreviations: LOA, limits of agreement (mean difference ± 1.96SD); MVPA, moderate-to-vigorous PA; *r*, Pearson correlations between self-reported and measured parameters (validation coefficient); SEE, standard error of the estimate expressed in min/day (sedentary) or min/week (MVPA).

[a]Adjusted for gender and age.

*$p < 0.05$ for comparison between self-reported and measured parameters; **$p < 0.05$ for correlations between estimated and measured sedentary time.

that most patients underestimated time spent in sedentary behavior. MVPA plot shows a linear tendency for the agreement between the two methods (Figure 1b). This plot revealed that at higher levels of PhA, the difference between self-reported data and accelerometers data becomes greater. In these cases, the self-reported levels were greater than what was measured by the accelerometer. The same patterns were observed when the data were analyzed separately by sex and age (Figures S1 and S2).

DISCUSSION

The main findings of our study are the following: (i) CTEPH patients spent most of their awake time in sedentary behavior, and only a small amount of time in moderate to vigorous PhA; (ii) MVPA correlated only to functional capacity and HRQoL and not to RV function or pulmonary hemodynamics; (iii) PhA data derived from questionnaires have a poor correlation and agreement with PhA measured by accelerometer.

To the best of our knowledge, our study represents the largest description of accelerometery-derived PhA of CTEPH patients. Previous studies mostly included subjects with prevalent PAH and had smaller sample size.[7,19–21] Using accelerometer data, we show that CTEPH patients spent 60% of the recorded time in sedentary behaviors, 38% in light PhA, and only 2% in MVPA. Overall, these patterns of PhA are similar to those described in PAH women ($n = 15$), which spent 64% of their waking time in sedentary behavior, while their daily activity was mainly comprised of light PhA (33%), and just a few minutes in moderate or more intense PhA (2%−3%).[19] In a cohort of different etiologies of PH patients, a similar pattern of sedentary time was observed, where patients spent on average 10 h per day in sedentary behavior.[20] In contrast, our patients spend more time in light PhA and less in MVPA in comparison with those described by Gonzalez-Saiz et al.[20] This may be related to differences in age (63 vs. 48 years old). The 19 min/day of MVPA observed in our CTEPH patients was similar to other cardiorespiratory diseases such as heart failure with preserved ejection fraction patients (19 ± 26 min/day)[22] and COPD patients (18 ± 17 min/day)[23] (Figure 2).

Only 35% ($n = 15$) of our patients met the international recommendations for MPVA (≥150 min/week). Similar results were found by González-Saiz et al.,[20] where less than two-thirds of PH patients met the minimum recommended level of PhA. Concordantly, two small studies also showed that time spent performing

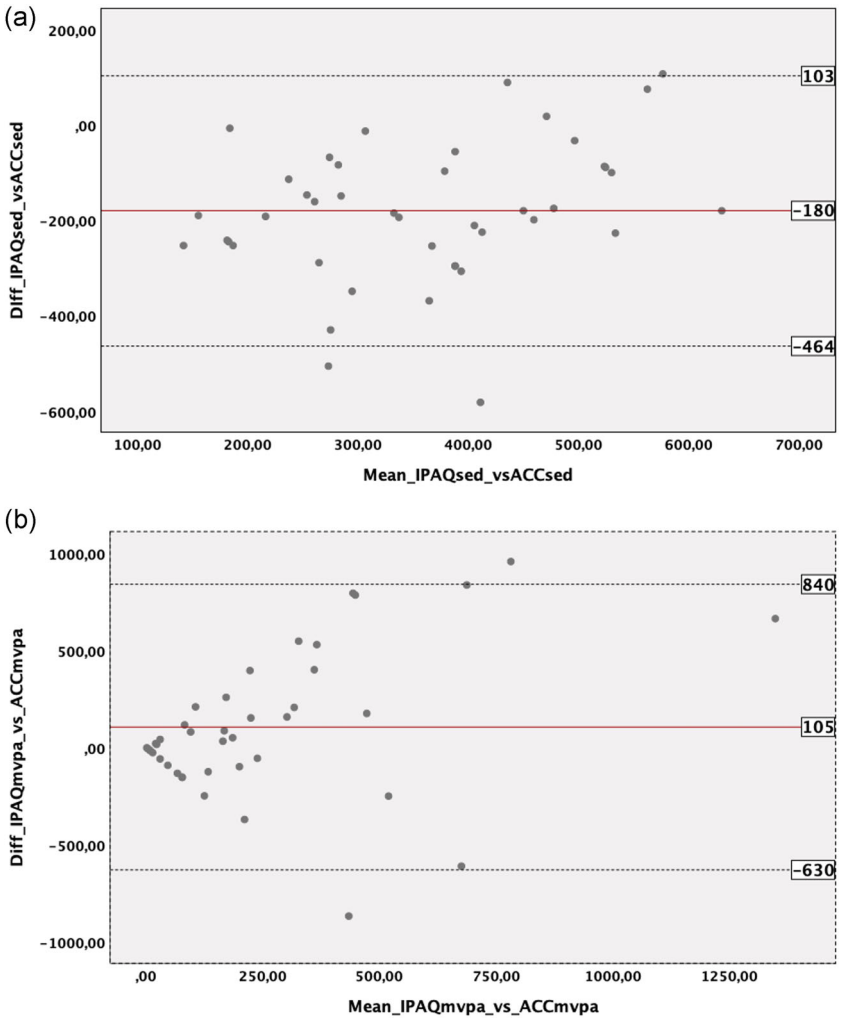

FIGURE 1 Bland–Altman plot of the mean bias and 95% limits of agreement for time spent in (a) sedentary behaviors and (b) MVPA. Red line indicates mean difference (systematic error); dotted line indicates the 95% limits of agreement (mean ± 1.96 SD). ACC, accelerometer; IPAQ, International Physical Activity Questionnaire; MVPA: moderate-to-vigorous physical activity; SD, standard deviation; SED, sedentary time

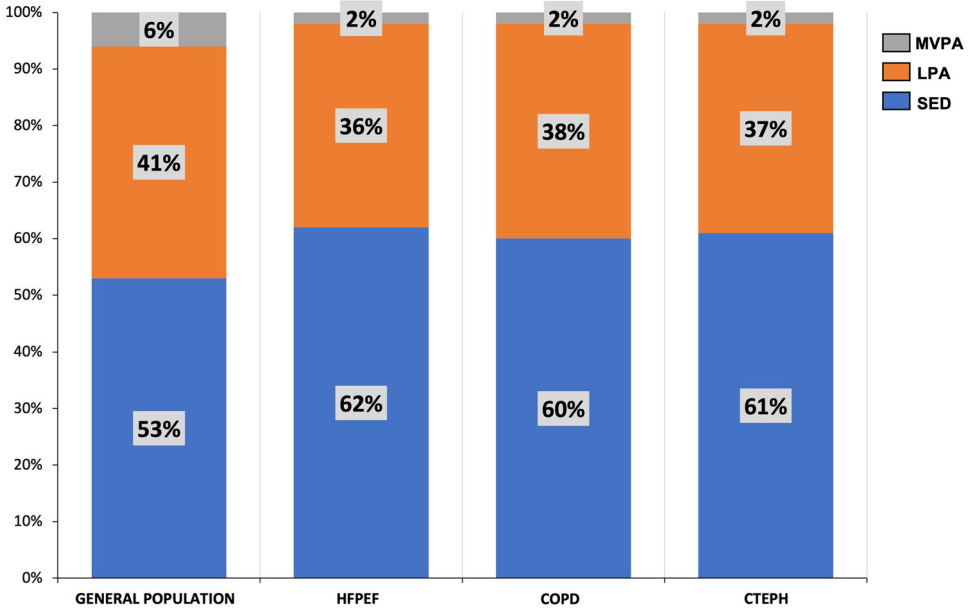

FIGURE 2 Per cent of time spend in sedentary behaviors, light PA, and MVPA in our CTEPH population, compared with general population[24] (age range from 43 to 82 years), HFpEF,[22] and COPD[23] patients. LPA, light physical activity; MVPA, moderate-to-vigorous physical activity; SED, sedentary time

MVPA is well below the recommended in PAH patients.[19,21] These results might be explained by several factors. First, CTEPH is characterized by a severe hemodynamic change in the pulmonary circulation and right ventricle dysfunction with a significant impact on exercise physiology.

The observed significant correlation between MVPA and the symptoms scale of HR-QoL supports this hypothesis. However, the mild correlation indicates that other mechanisms must be involved. Second, there is still the myth of avoiding exercise in PH patients, so patients might be afraid of increasing their PhA. In this regard, it is still unclear the impact of rehabilitation programs on PhA, but there is some evidence that aerobic exercise training can increase PhA levels.[25]

PAH symptoms directly affect patient's physical mobility and emotional state which is translated into a low level of HRQoL.[26] In this study, CAMPHOR scores indicate a moderate HRQoL impairment. Symptom and QoL scores were similar to those reported in previous studies.[27,28] Functioning score in our study was lower, which can be attributed to the different PH groups and lower disease severity of our patients (77% were in NYHA class I–II). In our study, we found that MVPA was significantly correlated with the symptom domain of CAMPHOR. A similar finding was reported by Matura et al.,[19] where increased PhA levels (total activity) were inversely associated with the symptom score in women with PAH.

Previous studies showed that exercise training can result in clinically relevant improvements of functional capacity in PAH patients.[29] In our study, only time spent in MVPA was significantly associated with functional capacity (6MWT). The mild correlation of MVPA with 6MWT, and the lack of correlation between other PhA intensity with disease severity parameters reveals that PhA may be influenced by other determinants beyond disease, such as comorbidities related (e.g., osteoarticular pathology, left heart disease, pulmonary disease) or even physical deconditioning due to sedentary lifestyle. Up to now, no recommendations about the optimal PhA level in patients with PH exist. While it is well known that any increase in the amount of PhA may translate into some health benefits,[15] CTEPH patients should be educated about the importance of reducing their sedentary time and engage in more MVPA for health-related benefits, to improve their exercise capacity and HRQoL.

Given the growing recognition of the association of PA levels with HRQoL and disease severity in many cardiopulmonary diseases, a rigorous characterization of their patterns is crucial for a better understanding of the impact of PH in the patient's lives, as well as to prescribe tailored lifestyle changes. The IPAQ-SF was validated against accelerometer measurements in 12 countries enrolling several populations.[16] However, our data show that IPAQ-SF is not reliable to assess PhA levels in CTEPH population. We found that PhA measurements obtained by IPAQ-SF compared with that obtained by accelerometer-derived data overestimates MVPA and underestimates sedentary/sitting time. We also verified the absence of agreement between self-reported and accelerometer-derived sedentary time and MVPA. This means that measuring PhA levels in the same person with these instruments leads to important variations in magnitude and concordance of the measured outcome. The lack of agreement between methods is probably related to the different constructs measured by the two instruments. While the accelerometer measures the motion through the acceleration of body mass, the questionnaires measure the time spent in specific behaviors.[30] Although IPAQ-SF data agreed and correlated poorly with accelerometer-derived PhA, it was significantly correlated with HRQOL scales. However, it is important to note that only accelerometer data correlate with objective measurements of disease severity (6MWT). Therefore, the use of objective measures of PhA seems to have particular importance to prescribe tailored lifestyle changes and avoid bias in populations with limited physical function and limited past knowledge and experience on regular PhA.

The study has some limitations. The observational nature of our study limits the ability to assess the establishment of causal inferences. The cross-sectional design precludes the study of the impact of the improvement of the disease on PhA measures. The single-center and the small sample size limit the generalizability of our results.

Taken together, our results showed that CTEPH patients spend most of their days in sedentary behavior and only a small amount of time in MVPA. Only MVPA was positively and negatively associated with HRQoL and CTEPH severity, respectively. In addition, we showed a poor agreement between self-reported and accelerometer-derived PhA in CTEPH patients, with the former overestimating the overall PhA. Future studies are needed to explore the utility of accelerometers to provide additional information to other known prognostic factors, and to understand the causes of sedentarism and its response to interventions with established prognostic value.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ETHICS STATEMENT

The study was approved by the Ethics Committee of Centro Hospitalar Universitário do Porto (N/REF.a 2018.160 (137-DEFI/136-CES)).

AUTHOR CONTRIBUTIONS

Cristine Schmidt, Miguel Monteiro, and Mário Santos contributed to the conception and design, data acquisition, analysis, interpretation of data, drafted the article, and critically revised the manuscript. Inês Furtado, Luísa Carvalho, Fabienne Gonçalves, and Abílio Reis contributed to data acquisition, analysis and interpretation of data, and critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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