Revista Brasileira de Fisioterapia
ISSN: 1413-3555
rbfisio@ufscar.br
Associação Brasileira de Pesquisa e Pós-Graduação em Fisioterapia
Brasil

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Revista Brasileira de Fisioterapia, vol. 17, núm. 2, marzo-abril, 2013, pp. 152-162
Associação Brasileira de Pesquisa e Pós-Graduação em Fisioterapia
São Carlos, Brasil

original article

BJPT Brazilian Journal of Physical Therapy

COPD patients' oxygen uptake and heart rate on-kinetics at cycle-ergometer: correlation with their predictors of severity

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ABSTRACT | Objectives: To assess whether there is a correlation between oxygen uptake (VO_2) and heart rate (HR) on-kinetics in the constant-load cycle-ergometer test (CLT) and the BODE index and its isolated variables in patients with chronic obstructive pulmonary disease (COPD). **Method**: Fourteen male patients between 55 and 78 years of age with moderate to severe COPD were evaluated. Each patient underwent spirometry, the six-minute walk test (6MWT), the cycle-ergometer incremental test (IT) and CLT on alternate days. The exhaled gases were collected, and the VO_2 and HR on-kinetics were analyzed. The BODE index was calculated. **Results:** It was noted that the VO_2 *tau* (τ) and mean response time (MRT) were significantly higher than HR τ and MRT. Moderate and strong correlations between τ and MRT of the VO_2 and HR and the BODE index was noted (r=0.75 and r=0.78; r=0.62 and r=0.63, respectively), and there were correlations between the VO_2 τ and MRT and the forced expiratory volume in one second (FEV_1) (r=–0.60; r=–0.53) and the distance traveled at 6MWT (DT-6MWT) (r=–0.61; r=–0.44) and DT-6MWT % predicted (r=–0.62; r=–0.46). The HR τ and MRT were correlated with DT-6MWT (r=–0.59; r=–0.58) and DT-6MWT % predicted (r=–0.62; r=–0.62). **Conclusion:** The slowing of cycle-ergometer VO_2, and especially of HR on-kinetics, may be key markers of disease severity. Furthermore, airflow obstruction and reduced exercise capacity are associated with the slowing of patients' VO_2 and HR on-kinetics.

Keywords: COPD; oxygen uptake; kinetics; heart rate; physical therapy; disease severity index.
This study was registered at ClinicalTrials.gov (NCT01529489).

HOW TO CITE THIS ARTICLE

Pessoa BV, Beltrame T, Pires Di Lorenzo VA, Catai AM, Borghi-Silva A, Jamami M. COPD patients' oxygen uptake and heart rate on-kinetics at cycle-ergometer: correlation with their predictors of severity. Braz J Phys Ther. 2013 Mar-Apr; 17(2):152-162. http://dx.doi.org/10.1590/S1413-35552012005000073

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by ventilatory, metabolic and peripheral muscle limitations and reduced exercise capacity. These limitations are associated with significant loss of body mass, reduced strength and endurance of the respiratory and peripheral muscles[1] and high mortality risk[2]. Additionally, exercise intolerance may be marked by the slowing of oxygen uptake (VO_2) and heart rate (HR) kinetics at exercise onset[3,4] when compared to age-matched healthy elderly adults[4,5].

The slowing of VO_2 and HR kinetics in COPD patients is associated with hypoxemia, larger pulmonary ventilation volume, disorders of respiratory mechanics, inefficient oxygen supply across the rest-exercise transition, biomechanical breakdown of reactions stimulating peripheral mitochondrial oxygen consumption (QO_2)[4-8], autonomic imbalance and redistribution of blood flow to peripheral and respiratory muscles[4]. Early recruitment of type IIb fibers and accumulation of metabolites, which increases peripheral muscle fatigue, are also part of this condition[4,7].

Reduced exercise capacity has been linked to COPD patients' reduced survival. Considering the severity of the above-mentioned alterations, Celli et al.[2] developed the BODE [Body Mass Index, Obstruction, Dyspnea, Exercise Capacity] index. This multidimensional index has gained ground and relevance in the scientific literature because it provides prognostic information on COPD severity, further reflecting the functional disability induced by the disease. The BODE index comprises body mass index (BMI; B), airflow obstruction (O), dyspnea (D) and exercise capacity (E). Therefore, it measures the

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Received 02/07/2012 Revised 29/10/2012 Accepted 20/11/2012

primary changes found in COPD patients and has been considered their best predictor of survival[2]. Its isolated variables [BMI, dyspnea, forced expiratory volume in one second (FEV_1) and distance traveled in the six-minute walk test (6MWT)] are also considered evaluation parameters but fail to assess the systemic repercussions of the disease.

VO_2 and HR kinetics have been studied using moderate-to-high intensity cycle-ergometer or treadmill constant-load tests (CLT)[9]. It is known that the posture adopted during exercise and the effects of gravity may affect VO_2[10-13] and HR[9,14,15] kinetics. The slowed VO_2 on-kinetics of COPD patients was recently associated with the BODE index in constant-speed treadmill tests[16]. However, interestingly, the slowing of VO_2 on-kinetics was associated with functional limitation by 6MWT and showed no correlation with airflow obstruction[16]. Considering that VO_2 on-kinetics is a key index of aerobic capacity and exercise tolerance evaluation[4,6,8,9] associated with the BODE index mortality predictor[16], the present study aims to correlate COPD patients' VO_2 and HR on-kinetics with the BODE index and its isolated variables at CLT. The hypothesis of the present study is that COPD patients' VO_2 and HR on-kinetics are associated with the BODE index, exercise capacity and disease severity.

Method

Study subjects

Fourteen men from 55 to 78 years of age with clinical and functional diagnosis of COPD participated in this study. All of the patients had FEV_1/forced vital capacity (FVC) < 0.7 and post-bronchodilator FEV_1 < 80% predicted[17] and were referred for treatment in the Special Unit Respiratory Physical Therapy of the Federal University of São Carlos (Unidade Especial de Fisioterapia Respiratória, Universidade Federal de São Carlos, UFSCar), São Carlos, SP, Brazil. Clinical and spirometric diagnosis of COPD at stages II, III and IV[17] confirmed by pre- and post-bronchodilator spirometry performed under the supervision of a pulmonologist[17], prior tobacco smoking history, no history of infections or disease exacerbation in the last month or change in medications in the four weeks preceding the survey were adopted as study inclusion criteria. Furthermore, all patients were considered sedentary for at least six months and were classified as sedentary or insufficiently active according to the International Physical Activity Questionnaire - short version (IPAQ) classification[18].

Tobacco smokers, drinkers, and patients with pulmonary hypertension (mean pulmonary artery pressure ≥ 25 mmHg detected by echocardiography), uncontrolled hypertension, hypoxemia (peripheral oxygen saturation, SpO_2, below 80% at rest), or cardiovascular, metabolic, neurological, rheumatic and/or musculoskeletal disorders that would preclude participation in the study were excluded. The study was approved by the Research Ethics Committee (Comitê de Ética em Pesquisa) of UFSCar (Opinion No. 163/2010), and all patients freely signed an informed consent form according to Resolution 196/96 of the Brazilian National Health Council (Conselho Nacional de Saúde).

Experimental procedures

The study participants were subjected to a general physical examination, pulmonary function test, body composition assessment, 6MWT, symptom-limited cycle-ergometer incremental test (IT) and CLT. Data were collected from each patient on alternate days, and the tests were performed at intervals of two to four days[19] to avoid negative interference with performance (presence of pain, circulating catecholamines, peripheral muscle fatigue). The tests were conducted in a room in which the temperature was controlled at 18° to 22°C and the relative air humidity was controlled at 50 to 70%; all measurements were performed at the same time of day for each patient. The patients were familiarized with the tests and the equipment on the first day of evaluation. All patients received instructions prior to performing the tests regarding the type of food to be prepared and the type of clothing and footwear to be worn for the tests; they were also instructed to avoid physical activity on the day before the tests. The patients remained at rest for approximately 15 minutes prior to performing any experimental procedure.

Pulmonary function test: This test was performed using a portable spirometer (COSMED microQuark PC - based Spirometer®, Pavona di Albano, Rome, Italy), according to the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines[20]. The values obtained were compared with the values predicted by Knudson et al.[21].

Body composition assessment: This assessment was performed by bioelectrical impedance using bipolar foot-electrodes (Tanita®, model BC-553, Illinois, USA). After the and muscle mass (MM)[22] analyses were performed, the BMI = body mass (Kg)/height^2 (m) and lean muscle mass index (LMMI) = MM(Kg)/height^2(m)[23] were calculated.

Patients with LMMI < 16.0 Kg/m^2 were considered nutritionally depleted[23].

BODE index: All COPD patients underwent all of the necessary measurements to calculate the BODE index. This multidimensional index comprises the BMI, the degree of airway obstruction (predicted post-bronchodilator FEV_1%)[17] and dyspnea (Medical Research Council dyspnea scale)[24] and the distance traveled at 6MWT. Patients were scored according to the results obtained for the four variables (0-1 for the BMI and 0-3 for FEV_1, dyspnea and distance traveled at 6MWT)[2]. The BODE index can be divided into quartiles: quartile 1 includes scores of 0-2, quartile 2 includes scores of 3-4, quartile 3 includes scores of 5-6, and quartile 4 includes scores of 7-10[2]; the higher the score, the greater the patient's likelihood of mortality.

Functional capacity evaluation

Six-minute walk test (6MWT): This test was performed according to the ATS guidelines[25]. It was performed on a 30-meter-long flat hallway twice daily with a 30-minute interval between each session; the largest value of distance traveled was selected for analysis. The patients were instructed and encouraged to walk as fast as possible for 6 minutes, using standardized phrases every minute of the self-paced tests[25]. The distance traveled in the 6MWT was compared to the distance predicted using the equation of Iwama et al.[26]. The percentage of distance traveled was calculated using the following equation: [(distance traveled at 6MWT/predicted distance[26])*100].

Symptom-limited cycle ergometer incremental test (IT): All patients underwent IT in which exhaled gases were collected (VO_{2000} MedGraphics Corp.®, St Paul, MN, USA) to assess the workload peak. IT was performed using a cycle ergometer with electromagnetic brakes (Ergo-FIT®, model Ergo 167 Cycle, Pirmasens, Germany) and a protocol with increasing steps[27]. The patients were instructed to pedal at 60 rpm with standard vocal encouragements from the same rater every two minutes. The test began with a 1-minute warm-up period at minimal cycle ergometer load (15 W), with 5- to 10-W increases every 2 minutes that were individually selected to maintain the period of load increase in the 8-to-12-minute range[27]. A 1-minute active recovery using minimal cycle ergometer load followed the peak load interruption and was followed by a 6-minute passive recovery. The patients were monitored by pulse oximetry throughout the entire test (Nonin®, model 2500, Minneapolis, MN, USA). HR was measured using a heart rate monitor (Polar® FS2c™ Kempele, Finland), and dyspnea and lower limb fatigue were assessed using the CR [Category Ratio]-10 modified Borg scale[28]. Those measurements were combined with the blood pressure (BP) measurement. The electrocardiographic tracing was continuously recorded using an Ecafix® heart monitor (Model Active "E", São Paulo, São Paulo, Brazil).

The criteria for IT interruption were very intense dyspnea or lower limb fatigue (Borg > 7)[28], SpO_2 < 80%, reaching the maximum HR predicted for the patient's age and inability to sustain the pace previously set at 60 rpm.

The calculation of chronotropic reserve (HR:HRR reserve) was performed indirectly using the equation HRmax – HR reached in the test[27], with HRmax = 220 – age. The ventilatory demand was assessed by the ratio minute ventilation (V_E)/ maximum voluntary ventilation (MVV)[27].

Cycle-ergometer constant load test (CLT): The patients were instructed to pedal at 60 rpm and given standard vocal encouragements every minute. A protocol with a constant workload of 70% of the maximum intensity found in the IT[27] was used to assess the patient's maximum tolerated time (tolerance limit: Tlim) and subsequent analysis of VO_2 and HR on-kinetics. A cycle ergometer initial minimal load of 15 W was used for 1 minute during the warm-up and cool-down phases and in the post-test 6-minute passive recovery period. Values of SpO_2, HR, BP, feelings of dyspnea and lower limb fatigue[28] at rest and peak exercise were recorded. The electrocardiographic tracing was monitored throughout the entire test. The physical performance and maximum tolerance reached in the test (Tlim) were recorded in addition to HRR[27] and V_E/MVV[27] calculation.

Gas analysis

During the tests, the exhaled gases were collected using a *MedGraphics® VO_{2000}* model gas analyzer (St Paul, MN, USA) with a face mask coupled to a medium-flow bidirectional pneumotachograph. This system measures microsamples of exhaled gases by averaging every three breaths[29]. The equipment was calibrated automatically according to the manufacturer's specifications prior to each test. The data used for the analysis were V_E (L min^{-1}), VO_2 (in mL min^{-1} and mL kg^{-1} min^{-1}), carbon dioxide output (VCO_2), respiratory rate (RR) and tidal volume (TV)[27]. The acceptable interday reliability for V_E (VC 7.3 – 8.8%), VO_2, and VCO_2 (VC: 5.3 – 6.0%) has been evaluated in previous studies[29]. The highest

and most consistent value of the last 30 seconds of the stage was used to assess the value of metabolic, ventilatory and cardiovascular variables, dyspnea and lower limb fatigue at peak IT or CLT Tlim.

On-kinetics analysis

The VO_2 and HR raw data were transferred into SigmaPlot 11.0 software (Systat Software, San Jose, CA, USA) for analysis. Phase I kinetics (cardiodynamic) were not excluded because there was a previous warm-up that, combined with the ergospirometer used, reduced the possibility of that phase affecting the kinetic evaluation[30]. The rest-to-exercise transition response (first 180 seconds) was subjected to a monoexponential fit, $f_{(t)} = a_0 + a (1 - e^{-(t-TD)/\tau})$, where $f_{(t)}$ represents VO_2 or HR at any time $_{(t)}$; a_0 is the basal value corresponding to the mean value of the final minute of the warm-up period; "a" is the amplitude, that is, the magnitude of the steady-state response; τ is the curve time constant, which is the time required to reach 63% of the steady-state response (that is, the adaptation rate); and TD is the time delay for the onset of the VO_2 or HR response. The mean response time was also calculated (MRT, $\tau + TD$)[31].

A nonlinear algorithm using least squares to assess the best-fit parameters was used for the kinetics study[32,33]. The a_0 and a_1 parameters describe the parameters related to the Y-axis main component (VO_2 and HR), while τ and TD describe the parameters related to the X-axis (time). Only functions with $r > 95\%$ were included in the final analysis to ensure the quality of the regressions[34].

Statistical analysis

The statistical software SPSS 18.0 was used for data analysis. Data normality was assessed by applying the Shapiro-Wilk test, which indicated that the study sample had normal distribution. The values were expressed as the mean and standard deviation or median (interquartile range). The paired t-test was used to analyze the parameters of VO_2 and HR on-kinetics at CLT, and Pearson and Spearman's correlation coefficients was used. The significance level was set at $p < 0.05$.

Results

Study subjects

Table 1 shows the studied patients' demographic, anthropometric, spirometric, 6MWT, dyspnea, and BODE index characteristics. Eight COPD patients were graded as GOLD stage II[17], five patients were considered GOLD stage III[17], and one was considered GOLD stage IV[17]. Four of the 14 patients with COPD used short-acting bronchodilators, and eight used long-acting bronchodilators. Two patients from that sample combined the used of oral corticosteroids, and two others combined short- and long-acting bronchodilators. The patients with bronchodilators used the medication during the evening prior to the test, so most of them performed the tests after more than eight post-bronchodilator hours.

The study patient's metabolic, ventilatory and cardiovascular responses, the maximum power output (watts) at IT and the maximum tolerance reached (minutes) at CLT are shown in Table 2.

Oxygen uptake and heart rate on-kinetics

Table 3 shows the studied patients' values of VO_2 and HR on-kinetics at CLT. The VO_2 τ and MRT were significantly higher than the HR τ and MRT.

Correlations

Figures 1A, 1B, 1C, 1D, 1E and 1F show the correlations between the COPD patients' VO_2 τ and MRT and the BODE index, FEV_1 and distance traveled at 6MWT. Figures 2A, 2B, 2C and 2D show the correlations between the COPD patients' HR τ and MRT and the BODE index and distance traveled at 6MWT.

Strongly significant positive correlations were found in the CLT between the BODE index and the VO_2 τ and MRT ($r = 0.75$ and $r = 0.78$, respectively), and moderately negative correlations were found between the VO_2 τ and MRT and the FEV_1 ($r = –0.60$ and $r = –0.53$, respectively), the distance traveled at 6MWT ($r = –0.61$ and $r = –0.44$, respectively) and the predicted % distance traveled ($r = –0.62$ and $r = –0.46$, respectively). Furthermore, moderately statistically significant positive correlations were found in the CLT between the BODE index and the HR τ and MRT ($r = 0.62$ and $r = 0.63$, respectively), while moderately significant negative correlations of the HR τ and MRT with the distance traveled at 6MWT ($r = –0.59$ and $r = –0.58$, respectively) and the predicted % distance traveled ($r = –0.62$ and $r = –0.62$, respectively) were found.

Discussion

The main results of this study show positive correlations between the τ and MRT of the VO_2 and HR at CLT and the BODE index and negative

Table 1. COPD patients' demographic, anthropometric, spirometric, six-minute walk test, MRC scale and BODE index characteristics.

Variables	COPD Patients (n = 14)
Demographic and Anthropometric	
Age (years)	68.0 ± 6.5
Body Mass (kg)	69.5 ± 11.7
Height (cm)	167.1 ± 7.7
BMI (kg/m^2)	24.7 ± 2.7
Lean Muscle Mass (kg)	47.5 ± 7.4
LMMI (kg/m^2)	16.9 ± 1.6
Spirometric	
FEV_1 (L)	1.7 ± 0.7
FEV_1 (%pred)	58.7 ± 17.4
FVC (L)	3.0 ± 1.0
FVC (%pred)	87.9 ± 24.5
FEV_1/FVC (%)	54.5 ± 12.7
FEV_1/FVC (%pred)	61.7 ± 11.4
MVV (L/min)	57.0 ± 26.1
MVV (%pred)	65.2 ± 32.8
Six-minute walk test (6MWT)	
Distance Traveled (m)	435.0 ± 85.7
Distance Traveled (%predicted)	77.9 ± 15.5
MRC – 1	1 patient
MRC – 2	13 patients
BODE Index	2.0 (1.0 – 3.0)
BODE Index - Quartile 1	9 patients
BODE Index - Quartile 2	4 patients
BODE Index - Quartile 3	1 patient

Data are expressed as the mean ± standard deviation; median (interquartile range). COPD = chronic obstructive pulmonary disease; BMI = body mass index; LMMI = lean muscle mass index; FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity; MVV = maximum voluntary ventilation; MRC = Medical Research Council scale.

correlations between the VO_2 τ and MRT at CLT and the FEV_1 and exercise capacity at 6MWT. Regarding HR on-kinetics, only moderately negative correlations were found between τ and MRT and exercise capacity at 6MWT.

Oxygen uptake and heart rate on-kinetics

The COPD patients' VO_2 τ and MRT were significantly slower than the HR τ and MRT at CLT, most likely indicating the presence of peripheral limitation in the study population. A faster rise in HR on-kinetics may show a better fit of that physiological variable to physical activity in COPD patients.

VO_2 and HR on-kinetics and its relationship to the BODE index and its determinants

The BODE index has been suggested as a key mortality-predictive index in COPD and may indicate the degree of systemic and functional impairment caused by the disease[2]. It is known that the on-kinetics of VO_2 and, as was more recently shown, of HR are slowed in the presence of COPD[3-7,16,35] and that these variables enable the inference of such patients'

compromised exercise performance[3,4]. It was recently suggested that the BODE index is associated with COPD patients' slowed VO_2 on-kinetics[16]. However, the authors infer that one of the limitations underlying the lack of results regarding HR on-kinetics could be the type of ergometer used (treadmill), which unlike the present study, in which a cycle ergometer was used, did not allow precise control of the external load during the physical exercise. It is also noteworthy that exercises performed on a treadmill[9,11-14] provide greater recruitment of muscle mass, show distinct patterns of motor unit recruitment and result in changes in perfusion pressure[9] and muscle blood flow compared to exercises performed on a cycle ergometer. It is noteworthy that the results of the current study showed moderate to strong correlations between VO_2 and HR on-kinetics in tests performed on a cycle ergometer after assessing the BODE index, including only COPD patients in the sample and using the first 180 seconds of the rest-to-exercise transition response, unlike the study by Borghi-Silva et al.[16], which used 360 seconds of exercise performed on a treadmill.

Based on the discussion presented above, the slowed VO_2 and HR on-kinetics at cycle-ergometer, especially the latter, may be key markers of COPD severity. Studies have shown that the BODE index accurately reflects patients' limitations in the

Table 2. Study subjects' metabolic, ventilatory, cardiovascular and subjective responses and physical capacity at the symptom-limited incremental exercise test (IT) and constant-load cycle-ergometer test (CLT).

COPD Patients (n = 14)	Symptom-limited incremental exercise test (TI)	Constant-load cycle- ergometer test (CLT)
Physical capacity	58.6 ±18.4	17.0 ± 9.7
Metabolic Variables		
VO_2 peak (L/min)	1.23 ± 0.41	1.08 ± 0.40
VO_2 peak (%pred)	72.2 ± 21.1	62.7 ± 19.9
Ventilatory Variable		
V_E peak (L/min)	39.1 ± 7.9	36.5 ± 20.3
V_E/MVV	0.70 ± 0.17	0.67 ± 0.14
SpO_2 (%)	93.3 ± 2.8	93.6 ± 1.9
Cardiovascular Variables		
HR peak (beats.min^{-1})	123.1 ± 15.4	124.4 ± 14.9
HRR (beats.min^{-1})	31.1 ± 17.0	34.5 ± 16.5
Subjective Variables		
Dyspnea peak	4 (1 – 6)	2 (1 – 6)
LL fatigue peak	4 (1 – 7)	2 (0.5 –6)

VO_2 = oxygen uptake; VE = pulmonary ventilation; V_E/MVV = airflow demand; HR = heart rate; HRR = heart rate reserve; SpO_2 = peripheral oxygen saturation; LL = lower limbs. Physical Capacity refers to the maximum power output (watts) at IT and limit of tolerance (Tlim; minutes) reached at CLT.

Table 3. Study patients' oxygen uptake (VO_2) and heart rate (HR) on-kinetics parameters at the constant-load cycle-ergometer test (CLT).

CLT	VO_2 on-kinetics	HR on-kinetics
Baseline (BL)	392.4 ±265.3	86.6 ±11.9
Amplitude (a)	558.9 ±175.3	14.1 ±4.3
Tau (τ, s)	60.6 ±14.4	38.5 ±20.6*
Time Delay (TD, s)	2.8 ±6.1	0.6 ±1.4
MRT (τ + TD, s)	63.4 ±14.1	39.1 ±20.4*

Data are expressed as the mean ± standard deviation. Baseline and Amplitude: L/min for VO_2 and beats.min^{-1} for HR, respectively. Paired t-test ($p < 0.001$): * = τ and MRT of $VO_2 \neq \tau$ and MRT of HR. VO_2 = oxygen uptake; HR = heart rate; a = steady-state response magnitude; τ = curve time constant, that is, time required to reach 63% of the steady-state response (adaptation rate); TD = response onset time delay; MRT = mean response time (τ + TD).

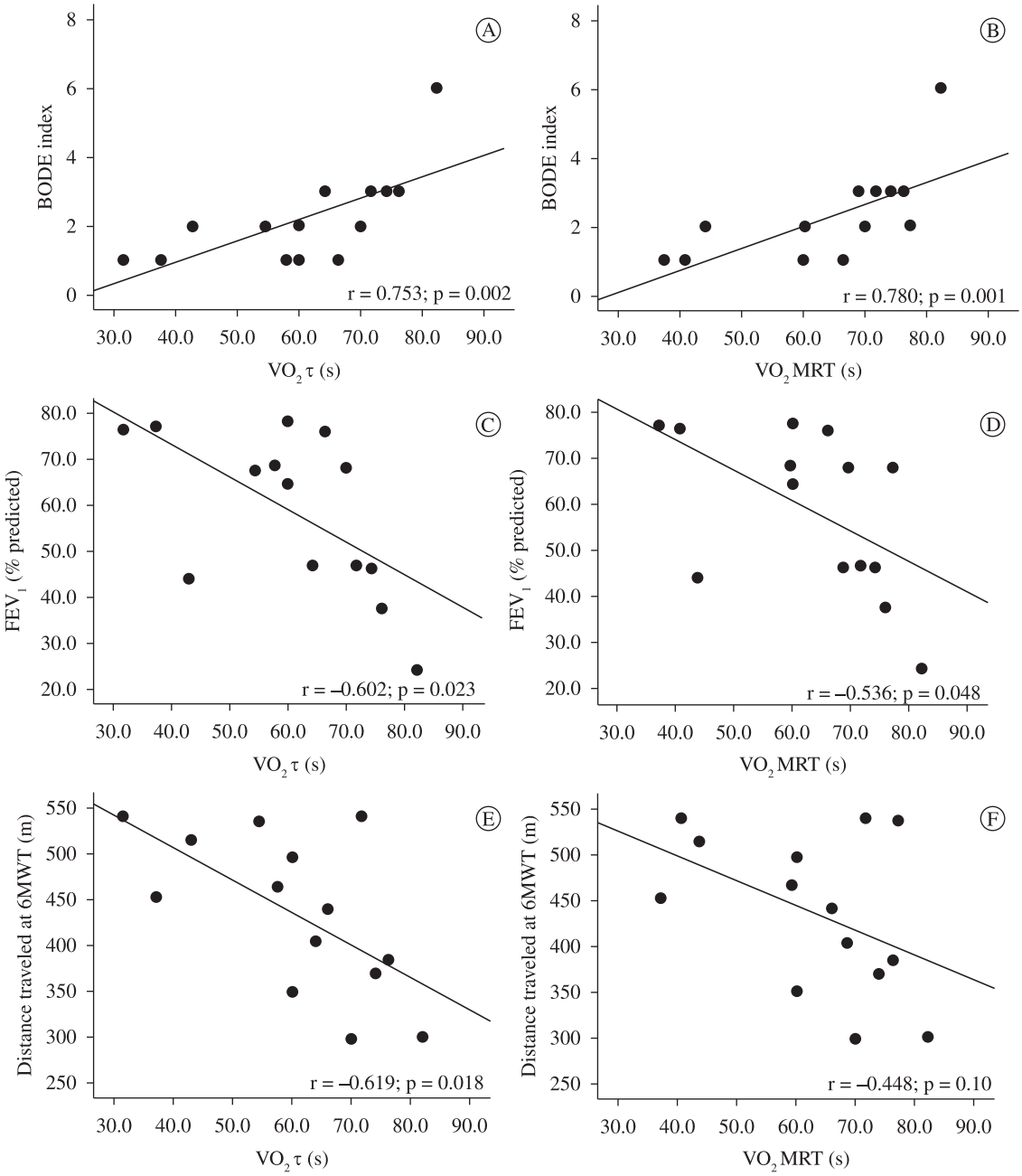

Figure 1. Correlation between oxygen uptake (VO_2) time constant (τ) and mean response time (MRT) and the BODE [Body Mass Index, Obstruction, Dyspnea, Exercise Capacity] Index, forced expiratory volume in one second (FEV_1) and distance traveled at the six-minute walk test (6MWT) of chronic obstructive pulmonary disease (COPD) patients.

activities of daily life according to the London Chest Activity Daily Living Score[36]. Furthermore, it reflects upper-limb peripheral muscle weakness evaluated by the manual dynamometer[37] and exercise capacity assessed by the 2-minute Sit-to-Stand Test test and the 6MWT on a treadmill[37], measures that may also reflect the level of limitation of the physical activities of daily life according to the time spent per day in various activities and body positions, including walking, standing, and the intensity of movement measured when the patient is walking[38].

Additionally, there are moderate correlations between FEV_1 and distance traveled at 6MWT with VO_2 on-kinetics, unlike the results of the study by Borghi-Silva et al.[16], in which only correlations with the 6MWT were found. The differences in the results

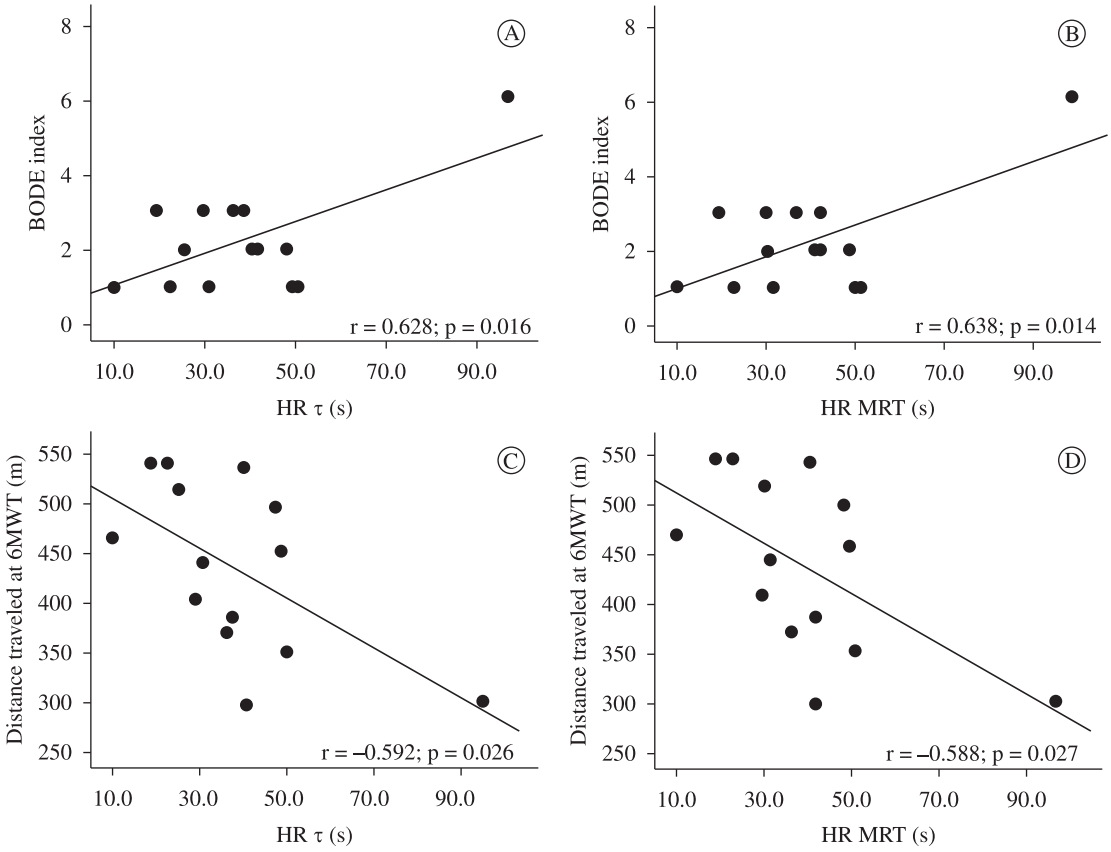

Figure 2. Correlation between the heart rate (HR) time constant (τ) and mean response time (MRT) and the HR BODE [Body Mass Index, Obstruction, Dyspnea, Exercise Capacity] Index and distance traveled at the six-minute walk test (6MWT) of chronic obstructive pulmonary disease (COPD) patients.

can most likely be explained by the use of different types of ergometers in the two studies[9,11-14].

Moderate negative correlations were found between VO_2 τ and MRT and FEV_1, suggesting that the slowing of VO_2 on-kinetics is reflected by the level of airway obstruction, although the same cannot be said regarding HR on-kinetics. FEV_1 is one of the variables composing the BODE index and has been considered a key prognostic marker of mortality in COPD[39], although studies show that FEV_1 alone does not represent systemic manifestations of the disease[40,41].

The COPD patients' VO_2 and HR τ and MRT showed moderate negative correlation with distance traveled (m) and predicted (%) at 6MWT. These results provide further data on exercise performance assessed by on-kinetics as a prognostic marker in COPD patients. In contrast, there were no statistically significant correlations between VO_2 and HR τ and MRT with BMI and BMI, suggesting that this parameter do not quantify the slowing of VO_2 and HR on-kinetics. Other authors also claim to have found no relationship between BMI and peripheral muscle impairment, exercise capacity, muscle mass, level of physical activity in daily life or limitations in daily-life activities[36,42-46]. The absence of correlation can be attributed to the low levels of disease severity in the COPD patients studied (nine patients in quartile 1, four patients in quartile 2 and only one patient in quartile 3).

Study limitations

One of the limitations of this study is the small number of participants; a larger number of participants would strengthen the results. However, despite the relatively small sample number, moderate-to-strong correlations were found in the present study. The method of HR (mean taken every three beats) and VO_2 (mean taken every three breaths) data collection also represents a study limitation. However, some authors[47-49] report that HR and VO_2 data obtained using ergospirometric systems like the system used in the present study are similar to those obtained using the breath-to-breath systems

that are currently in use. Finally, a monoexponential model was applied in the present study to analyze the moderate-to-high intensity exercise on-kinetics, even at 70% VO_2 peak exercise. However, the time used in the present study (3 minutes) excluded the possibility of slow component onset, which was also used in previous studies[4,7].

Conclusions

The observed slowed-ergometer on-kinetics of VO_2, and especially of HR, in COPD patients may be key markers of disease severity. Furthermore, the airflow obstruction and reduced exercise capacity observed in COPD patients are associated with the slowing of VO_2 and HR on-kinetics. Further studies evaluating kinetic effects as markers of systemic damage in COPD patient populations, the effects of different treatments and the use of different ergometers are required.

Acknowledgments

Grateful acknowledgement is made of our colleagues in the Laboratory of Spirometry and Respiratory Physical Therapy (Laboratório de Espirometria e Fisioterapia Respiratória) and the Cardiopulmonary physical therapy Laboratory (Laboratório de Fisioterapia Cardiopulmonar) for their friendly cooperation and of the study patients for their effort and cooperation during this research. We would also like to acknowledge the São Paulo Research Foundation (Fundação de Amparo à Pesquisa do Estado de São Paulo, FAPESP), which provided funding (2009/01842-0), and the Capes [Higher Education Coordination Agency] and CNPq [National Council for Scientific and Technological Development] for granting a scholarship.

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