

Combined Physical Training Improves Exercise Tolerance and Prognosis in Individuals with COPD

Treinamento Físico Combinado Melhora a Tolerância ao Exercício e o Prognóstico em Indivíduos com DPOC

El entrenamiento físico combinado mejora la tolerancia al ejercicio y el pronóstico en individuos con EPOC

Victor Fernando Couto¹, Cilso Dias Paes², Bruna Varanda Pessoa³, Marcos Rassi Fernandes⁴, Mauricio Jamami⁵, Marcos Rassi Fernandes Filho⁶, Valéria Amorim Pires Di Lorenzo⁷

How to cite: Couto VF, Paes CD, Pessoa BV, Fernandes MR, Jamami M, Fernandes Filho MR, Lorenzo VAPD. Combined Physical Training Improves Exercise Tolerance and Prognosis in Individuals with COPD. REVISA.2020;9(2): 282-90. Doi: <https://doi.org/10.36239/revisa.v9.n2.p282a290>

REVISA

1. Centro Universitário de Goiatuba, Physiotherapy Department. Goiatuba, Goias, Brazil.

2. Hospital Estadual de Sumaré. Sumare, Sao Paulo, Brazil

3. Universidade do Sagrado Coração. Graduate Program in Physiotherapy. Sao Carlos, Sao Paulo, Brazil.

4. Universidade Federal de Goiás, Faculdade de Medicina, Graduate Program in Health Sciences. Goiania, Goias, Brazil,

5. Universidade Federal de São Carlos, Graduate Program in Physiotherapy. Sao Carlos, Sao Paulo, Brazil.

6. Universidade Federal de Goiás. Goiania, Goias, Brazil,

7. Universidade Federal de São Carlos, Graduate Program in Physiotherapy. Sao Carlos, Sao Paulo, Brazil.

Received: 28/02/2020
Accepted: 14/03/2020

RESUMO

Objetivo: Avaliar o efeito deste treinamento sobre a tolerância ao exercício em pessoas com DPOC e sobre o prognóstico da doença. **Método:** Nove idosos com DPOC (GDPOC) e nove idosos saudáveis (GS) foram avaliados antes e após TFC por Teste de caminhada de seis minutos (TC6'), teste incremental no cicloergômetro (TIC), composição corporal e teste de 1 repetição máxima (1RM). O GDPOC foi avaliado também pelo índice BODE. O TFC constou de trinta minutos de treinamento aeróbio e três séries de quinze repetições de treinamento resistido em leg press horizontal com carga de 40-60% do teste de 1 repetição máxima, com intervalo de cinco minutos para recuperação. Foram realizadas três sessões semanais durante seis semanas. **Resultados:** No GDPOC, houve aumento significativo na distância percorrida e melhora no índice BODE. **Conclusão:** O TFC de seis semanas evidencia ser efetivo para melhora da tolerância ao exercício em indivíduos idosos com DPOC e do prognóstico de indivíduos da doença.

Descritores: Doença pulmonar obstrutiva crônica; Educação física e treinamento; Tolerância ao exercício; Idoso.

ABSTRACT

Objective: To identify the effect of this training on exercise tolerance in people with COPD and on the prognosis of the disease. **Method:** Nine elderly patients with COPD (COPDG) and nine healthy elderly (HG), were evaluated before and after physical training to: six-minute walk test (6MWT), incremental test on cycle ergometer (ICT), body composition and test 1 repetition maximum (1MR), it was evaluated also in COPDG the BODE index. The training consisted of thirty minutes of aerobic training and three sets of fifteen repetitions of resistance training in leg press horizontal with 40-60% of 1MR, with an interval of five minutes for recovery. Three weekly sessions were held for six weeks.

Results: In COPDG, there was a significant increase in the distance covered and an improvement in the BODE index. **Conclusion:** The 6-week CPT evidence to be effective in improving exercise tolerance in both elderly COPD subjects and the prognosis of disease.

Descriptors: Pulmonary disease chronic obstructive; Physical education and training; Exercise tolerance; Elderly.

RESUMEN

Objetivo: evaluar el efecto de esta capacitación sobre la tolerancia al ejercicio en personas con EPOC y sobre el pronóstico de la enfermedad. **Métodos:** Nueve personas mayores con EPOC (GEPOC) y nueve personas mayores sanas (GS) fueron evaluadas antes y después de TFC mediante una prueba de caminata de seis minutos (6MWT), prueba incremental en el cicloergómetro (ICT), composición corporal y una prueba de 1 repetición máxima (1RM). El GEPOC también se evaluó utilizando el índice BODE. El TFC consistió en treinta minutos de entrenamiento aeróbico y tres series de quince repeticiones de entrenamiento de resistencia en press de piernas horizontal con una carga del 40-60% de la prueba de 1 repetición máxima, con un intervalo de cinco minutos para la recuperación. Se realizaron tres sesiones semanales durante seis semanas. **Resultados:** En GEPOC, hubo un aumento significativo en la distancia recorrida y una mejora en el índice BODE. **Conclusión:** El TFC de seis semanas demuestra ser efectivo para mejorar la tolerancia al ejercicio en personas mayores con EPOC y el pronóstico de las personas con la enfermedad.

Descriptores: Enfermedad Pulmonar Obstrutiva Crónica; Educación Física Y Entrenamiento; Tolerancia Al Ejercicio; Anciano.

ORIGINAL

Introduction

The combined physical training (CPT) that constitutes the combination of aerobic and resistance training has been shown to be beneficial in improving exercise tolerance, strength, peripheral muscle endurance of the lower limbs, in addition to being more tolerable in healthy elderly and elderly people affected by chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD).¹⁻³ This training has two different types, the long duration, in which strength training is added to the existing aerobic training, increasing the duration of the sessions⁴⁻⁵ and the short duration, in which the duration of the aerobic training session is reduced to half and the other half of the session is dedicated to strength training.⁶

We consider that aging provides a natural process of declining strength of skeletal muscles, respiratory muscles and body mass index, which interferes with functional capacity leading to exercise intolerance. Functional losses are accentuated when these elderly people develop COPD, due to the systemic manifestations that the disease causes.⁷

Systemic manifestations related to COPD, such as an increase in the inflammatory process due to a higher concentration of circulating cytokines and oxidative stress, lead to the development of hypermetabolism⁸, which contributes to weight loss, associated with the reduction of lean body mass. This results in dysfunction of the peripheral skeletal musculature, especially of the lower limbs, compromising the ability to perform physical exercises.⁹

Such manifestations lead to an increase in the ventilatory demand and sensation of dyspnea, which contributes to the limitation of activities of daily living and to the compromised quality of life of the affected. These individuals may still have recurrent exacerbations, depending on the disease progression, which is an important risk factor for hospitalization, in addition to indicating a worse prognosis in their survival.⁹⁻¹⁰ The COPD prognostic predictor index, called BODE, was created based on these manifestations in which of the four variables evaluated, three can be modified by physical training.⁹

CPT has been identified as the best training strategy for muscle purposes, as it presents a 15% increase in the amount of capillaries per fiber and a 38% increase in the activity of citrate synthase, an important enzyme that participates in oxidative metabolism.^{6,11} We hypothesize that short-term combined physical training is able to improve exercise tolerance and reduce the total score of the BODE index in individuals with COPD.

Thus, the objective of this study was to evaluate whether short-term combined physical training interferes with exercise tolerance and prognosis in individuals with COPD.

Method

Participants and study design

This is a prospective controlled study conducted at the Federal University of São Carlos during the period from March to August 2010. The subjects of the COPD research were referred to the special respiratory physiotherapy laboratory (LEFIR), through pulmonologists in the city of São Carlos. Male individuals were recruited to compose the group of healthy individuals (GS) through the university open to seniors.

Inclusion and Exclusion Criteria

Inclusion criteria were clinical and spirometric diagnosis of moderate to very severe COPD (post-bronchodilator spirometry with forced expiratory volume in the first second (FEV1) / forced vital capacity (FVC) <0.7 and FEV1 <80%), age equal and older than 60 years, male, ex-smokers and clinically stable for at least one month.

Individuals with orthopedic and neurological diseases that made it impossible to perform the tests (assessment of body composition and tolerance to physical exercise), as well as those with pulmonary exacerbations during the performance of CPT, were excluded from the study.

Independent Variables

- Avaliação da Composição Corporal

This evaluation was carried out using the bioelectrical impedance scale (Tanita®, model BC-553), with the individuals in the orthostatic position, allowing the analysis of weight (Kg), % body fat (%BF), % muscle mass (%MM) and body mass index (BMI).¹² All performed a fast of at least four hours to standardize liquid intake.

Dependent Variables

- Tolerance to physical exercise

Evaluated by the distance covered, which was measured by the six-minute walk test (6MWT). This test was carried out in a flat corridor 30 meters long and 1.5 meters wide.

Rest was allowed, in an orthostatic position, with the chronometer on, if the individual had a sensation of dyspnea ≥ 7 , tiredness of the lower limbs ≥ 7 , assessed using the borg scale (EB) - CR10, SpO₂ below 85% and / or reached submaximal heart rate (HR).¹³ He was instructed to continue as soon as he had SpO₂ $\geq 90\%$, submaximal HR below the predicted value and EB-CR10 ≤ 3 until the end of the sixth minute.¹⁴⁻¹⁵

- COPD prognosis

Evaluated by the BODE index, before and after CPT of short duration. For this assessment of this prognosis, four variables were considered, according to Celli et al.¹⁶

Intervention

•Short-term Combined Physical Training Program

The intensity of the aerobic training of the short duration CPT was determined by the incremental symptom limiting test (ICT) in a cycle ergometer, using the modified BALKE protocol. (17) Before performing this test, each individual performed three minutes of warm-up on the exercise bike (Ergo 167 Cycle), using a minimum load of 15 watts.

This program consisted of aerobic training associated with resistance exercises of the lower limbs, which was performed three times a week for six weeks. The aerobic training of each individual was performed on an exercise bike for 30 minutes maintaining a load of 40% of the ICT, being increased 10% after three weeks of training.^{6,18} This training was interrupted if the individual had signs and symptoms, according to the guidelines of the Brazilian Society of Cardiology.¹⁹

Resistance training of lower limbs consisted of three sets of fifteen repetitions, in a horizontal leg press (Righetto PR1070). At the end of each series, individuals had two minutes of rest.²⁰

The intensity of this training was between 40-60% of the maximum load tolerated in the test of 1 maximum repetition (1MR), being increased 10% every two weeks of training. The 1MR test consisted of determining the load for resistance training.²⁰

All individuals were initially evaluated and reevaluated after a six-week period of short-term CBT, in terms of body composition, lung function and distance covered. The BODE index assessment was applied only to the COPD group.

Data Analysis

The median and interquartile intervals were calculated because the data had a non-normal distribution.

The Wilcoxon and Mann-Whitney tests were used for intra-group and inter-group analysis, respectively, comparing scores (medians). The significance level was $p < 0.05$.

Ethical Aspects

This study was approved by the Ethics and Research Committee of UFSCar, under opinion No. 272/2010.

Results

This study was initially composed of 11 individuals with COPD and 09 healthy individuals. Of these, two from GDPOC were excluded because they had pulmonary exacerbations during the practice of CFT. The baseline characteristics of the groups included in the study are described in table 1.

Table 1 - Characteristics of the study sample.

Variables	GDPOC	GS
	Median (Interquartile)	Median (Interquartile)
Sex	9 homens	9 homens
Age	71 (68-75,3)	66 (59,8-70,7)
Height (cm)	167 (163,7-170,3)	175 (168,7-177,9)
Weight (Kg)	71 (61,8-78,1)	72 (65,4-85,9)
BMI (kg/m ²)	24,5 (21,6-26,9)	24,9 (21,7-27,9)
BF (%)	27 (22,4-31,6)	22,3 (18,9-32,3)
LM (%)	49 (43,3-51,9)	51,2 (48,3-55,7)
FEV ₁ % (L)	46,6 (37,3-64)	108,6 (97,8-116,9)
Wpeak (watts)	30 (26,6-42,2)	60 (42,5-67,5)
basal SpO ₂ (%)	93 (92-95)	97 (95-98)
1MR(Kg)	60 (49,9-70,5)	80 (68,7-87,4)
TD (% prev)	88,2	99,2
TD (m)	486 (371-530,7)	560 (493,8-646,2)
BODE	3 (2,1-4,1)	-

Legend: BMI= Body mass index; BF= Body Fat; LM= Lean Mass; FEV₁= Forced Expiratory Volume in the first second; Wpeak= Peak load in incremental test on cycle ergometer; SpO₂= Peripheral oxygen saturation; 1MR= Maximum repetition test; TD= Travelled distance; BODE= Body Mass Index, Obstruction of Airway, Dyspnea and Exercise Capacity Index.

There was no significant difference in age, weight and height between individuals from GDPOC and GS. The FEV₁ of the GDPOC was significantly lower when compared to the GS, characterizing airway obstruction.

There was no significant difference before and after six weeks of short-term CPT in body composition and spirometry variables, except BMI (Table 2).

Table 2 - Effect of short-term CPT on body composition and spirometric components.

Variables	GDPOC (n=9)		GS (n=9)	
	Median (Interquartile)		Median (Interquartile)	
	Pre	Post	Pre	Post
Weight	71 (61,8-78,1)	71,2 (62-79,1)	71,5 (64,2-85)	73 (64,8-84,7)
BF (%)	27 (22,4-31,6)	25,8 (22,4-32)	22,3 (19-32,3)	22,7 (18,6-31,4)
LM (%)	49 (43,4-51,8)	51 (44,7-52,6)	51,2 (48,3-55,3)	51,3 (48,4-56,3)
BMI (%)	24,6 (21,6-26,9)	26,2 (22,8-27,7)*	24,9 (21,7-27,8)	25 (21,8-27,7)**
FEV ₁ % (L)	46,6 (37,3-63,9)	47,5 (39,1-67,3)	108,2 (101-112,4)	108,6 (102-114)

Legend: CPT= Combined Physical Training; BF= Body Fat percentage; LM=Lean mass percentage; BMI= Body mass index; FEV₁= Forced Expiratory Volume in the first second. *Statistically significant difference between groups (Wilcoxon test)/ ** Statistically significant difference between groups (Mann Whitney test).

The distance covered in the 6MWT 'was significantly shorter in the GDPOC when compared to the GS. Both groups showed a significant increase in PD in the post-CFT situation. After the short-term CPT period, the total score of the BODE index decreased significantly from pre to post-training in GDPOC subjects (table 3).

Table 3 - Effects of short-term CPT on exercise tolerance and the BODE prognostic index

Variables	GDPOC		GS	
	Median (Interquartile)		Median (Interquartile)	
	Pre	Post	Pre	Post
TD (m)	486 (371-530)	558 (457-606)*	560 (493-646)	642 (541-684)*/**
Δ TD (m)	72 (65-78)		82 (74-84)	
BODE Index	3 (2,1-4)	2 (1,4-3)*	-	-

Legend: CPT= Combined Physical Training; TD= Traveled distance; ΔTD= Delta de ganho na distância percorrida após o CPT de curta duração; BODE= Índice de Massa Corporal, Obstrução de Vias Aéreas, Dispneia e índice de capacidade ao exercício. *Diferença estatisticamente significativa intra-grupo (teste de Wilcoxon). / ** Diferença estatisticamente significativa intergrupos (Teste de Mann Whitney).

At GDPOC, two individuals interrupted the incremental test on the cycle ergometer during the evaluation period, as they reached submaximal HR.

Discussion

We observed that the combination of aerobic and short-term resistance training improved exercise tolerance and prognosis in individuals with COPD. The variable distance covered by the 6MWT ', in those belonging to the GDPOC, showed shorter distances when compared to individuals from the GS. Both showed an increase of Δ72m vs Δ82m, respectively, and in individuals with COPD, a minimum difference of 35 m from the baseline value is considered a minimal clinically important diffe.²¹

Therefore, GDPOC improved exercise tolerance by measuring TD in the 6MWT '. This test is applied in pulmonary rehabilitation programs in order to monitor the effectiveness of the instituted procedure.²² The predicted values were obtained through the median and it was observed that individuals with COPD initially had poor aerobic conditions, which changed after six weeks.

Short-term CPT improved "exercise tolerance" in individuals with COPD, benefiting them from their greater systemic and pulmonary impairment, due to the previously installed disease. This can be explained by the aerobic training intensity of 60-70% of the ICT which may have resulted in an increase in the concentration of capillaries, oxidative enzymes, mitochondrial density, in addition to a reduction in glycolytic enzymes.^{4,23}

Although the intensity of physical training have been considered low, the functional performance of GDPOC was increased.^{6,18} The combination of resistance training from lower limbs to aerobic may also have contributed to improving exercise tolerance, as peripheral muscle limitation is one of the factors that lead to intolerance to exercise.⁴

Wanke et al., In two months of protocol / 4 times a week, observed that the combination of aerobic training on the cycle ergometer and inspiratory muscle training significantly increased the performance of inspiratory muscles, maximum oxygen consumption (VO₂ max) and peak ventilation, when

compared to the group that performed only aerobic training on the cycle ergometer.²⁴ However, no resistance training of lower limbs was performed, which makes it impossible to compare results.

Wang et al. observed an increase in the distance covered in the group of individuals with COPD who underwent TEC only, as well as in the group of individuals who underwent TEC in association with inspiratory muscle training, after eight weeks of training.²⁵⁻²⁶

It was observed that, after the six-week period of short-term CPT, there was a reduction in the BODE index score in GDPOC, which was associated with the disease prognosis.^{16,27} Nasis et al. also pointed out a reduction of one point in the BODE index, after the same CPT, but compared the interval combined training with the continuous combined training for 12 weeks²⁸, whereas in the present study such reduction was already possible in just six weeks of training.

It suggests that the combination of aerobic and low-intensity resistance training, in the same session, lasting one hour, may also be indicated in individuals with COPD. A possible explanation for the reduction in this index may have been an increase in the percentage of lean mass (% LM) and a decrease in BMI in the research subjects of this group.

BMI and % LM were used to assess changes in nutritional status before and after CPT. After short-term CFT, these rates improved, reflecting the nutritional status of patients with COPD. This shows us that physical training, when performed correctly and respecting the systemic manifestations of the disease, can improve the nutritional status of patients with COPD.²⁹

The fact that patients with this condition have systemic limitations that compromise, especially the cardiorespiratory and skeletal muscle systems, justifies the use of short-term CFT to improve the disease prognosis.

The study has as limitations the non-probabilistic sampling, small number of individuals in the groups and the absence of a comparative group of CPT with a longer duration. On the other hand, the fact that it is prospective, with the presence of a control group, constitutes forces of the research.

Thus, we suggest that for future studies, randomized interventions with short and long-term CFTs are carried out, as well as long-term evaluation of the post-training effect.

Conclusion

Short-term CPT improves exercise tolerance, evidenced by the greater distance covered in the 6MWT in GDPOC. In addition, the reduction of the BODE index in codes with COPD indicates a better prognosis of the disease.

Acknowledgment

To the entire team of the Special Laboratory of Respiratory Physiotherapy (LEFIR), especially those who contributed directly to the execution of this study.

References

1. American College of Sports Medicine. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Med Sci Sports Exerc.* 2011; 43: 1334-59.
2. Libardi CA, De Souza GV, Cavaglieri CR, Madruga VA, Chacon-Mikahil MP. Effect of resistance, endurance and concurrent training on TNF-alpha, IL-6 and CRP. *Med Sci Sports Exerc.* 2012; 44: 50-6.
3. Markofski MM, Carrillo AE, Timmerman KL, Jennings K, Coen PM et al. Exercise training modifies ghrelin and adiponectin concentrations and is related to inflammation in older adults. *J Gerontol A Biol Sci Med Sci.* 2014; 69(9): 675-681.
4. Ortega F, Toral J, Cejudo P, Villagomez R, Sanchez H, Castilho J. Comparation of effects of strength and endurance training in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2002; 166: 669-74.
5. Ertek S, Cicero A. Impact of physical activity on inflammation: effects on cardiovascular disease risk and other inflammatory conditions. *Arch Med Sci.* 2012; 8: 794-804.
6. Bernard S, Whitton F, Lebranc P, Jobin J, Belleau R, Carrier G, et al. Aerobic and strength training in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 1999; 159: 896-901.
7. Rodrigues F. Importância de fatores extrapulmonares: depressão, fraqueza muscular, qualidade de vida - na evolução da DPOC. *Rev Port Pneumol.* 2010; 16(5): 709-15.
8. Pedersen BK, Febbraio, MA. Muscles, exercise and obesity: skeletal muscle as a secretory organ. *Nat Rev Endocrinol.* 2012; 8: 457-65.
9. Seymour JM, Spruit MA, Hopkinson NS, Natanek SA, Man WDC, Jackson A, et al. The prevalence of quadriceps weakness in COPD and the relationship with disease severity. *Eur Resp J.* 2010; 36: 81-8.
10. Cardoso AP. Exacerbação da DPOC. *Pulmão RJ.* 2013; 22: 60-4.
11. Libardi CA, Cavaglieri CR, Tricoli V, Roschel H, Vechin FC, Conceição MS et al. Effect of concurrent training with blood flow restriction in the elderly. *Int J Sports Med.* 2015; 36(5): 395-9.
12. Fontoura CSM, Cruz DO, Londero LG, Vieira RM. Avaliação nutricional de pacientes críticos. *Rev Bras Ter Intensiva.* 2006; 18: 298-306.
13. Vivacqua R, Hespanha R. Introdução - Histórico - Perspectiva. In: *Ergometria e Reabilitação em Cardiologia.* Rio de Janeiro: Medsi; 1992.
14. Soares MR, Pereira CAC. Teste de caminhada de seis minutos: Valores de referência para adultos saudáveis no Brasil. *J Bras Pneumol.* 2011; 37: 576-83.
15. Iwama AM, Andrade GN, Shima P, Tanni SE, Godoy I, Dourado VZ. The six-minute walk test and body weight-walk distance product in healthy Brazilian subjects. *Braz J Med Biol Res.* 2009; 42: 1080-5.
16. Cote CG, Celli BR. Pulmonary rehabilitation and the BODE index in COPD. *Eur Respir J.* 2005; 26: 630-6.
17. Oga T, Nishimura K, Tsukino M, Hajiro T, Ikeda A, Izumi T. The effects of oxitropium bromide on exercise performance in patients with stable chronic obstructive pulmonary disease. A comparison of three different exercise tests. *Am J Respir Crit Care Med.* 2000; 161: 1897-1901.
18. Probst VS, Troosters T, Pitta F, Decramer M, Gosselink R. Cardiopulmonary stress during exercise training in patients with COPD. *Eur Respir J.* 2006; 27: 1110-8.
19. Sociedade Brasileira de Cardiologia. II Diretrizes sobre Testes Ergométricos. *Arq Bras Cardiol.* 2002; 78(2): 1-17.
20. Casaburi R, Bhasin S, Cosentino L, Porszasz J, Sonfay A, Lewis MI. Effects of testosterone and resistance training in men with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2004; 170: 870-8.

21. Puhan MA, Mador MJ, Held U, Goldstein R, Guyatt GH, Schunemann HJ. Interpretation of treatment changes in 6-minute walk distance in patients with COPD. *Eur Respir J*. 2008; 32: 637-43.
22. Dourado VZ, Godoy I. Recondicionamento muscular na DPOC: principais intervenções e novas tendências. *Rev Bras Med Esporte*. 2004; 10(4): 331-4.
23. Egan C, Deering BM, Blake C, Fullen MB, McCormack NM, Spruit MA, et al. Short term and long term effects of pulmonary rehabilitation on physical activity in COPD. *Respir Med*. 2012; 106:1671-9.
24. Wanke T, Formanek D, Lahrmann H, Brath H, Wild M, Wagner C, et al. Effects of combined inspiratory muscle and cycle ergometer training on exercise performance in patients with COPD. *Eur Respir J*. 1994; 7(12): 2205-11.
25. Wang K, Zeng GQ, Li R, Luo YW, Wang M, Hu YH, et al. Cycle ergometer and inspiratory muscle training offer modest benefit compared with cycle ergometer alone: a comprehensive assessment in stable COPD patients. *Int J Chronic Obstr Pulm Dis*. 2017; 12: 2655-68.
26. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med*. 2013; 188(8): e13-e64.
27. Puhan MA, Schunemann HJ, Frey M, Scharplatz M, Bachmann LM. How should COPD patients exercise during respiratory rehabilitation. Comparison of exercise modalities and intensities to treat skeletal muscle dysfunction. *Thorax*. 2005; 60: 367-75.
28. Nasis IJ, Vogiatzis I, Stratakos G, Athanasopoulos D, Koutsoukou A, Daskalakis A, et al. Effects of interval-load versus constant-load training on the BODE index in COPD patients. *Respir Med*. 2009; 103: 1392-8.
29. Luo Y, Zhou L, Li Y, et al. Fat-free mass index for evaluating the nutritional status and disease severity in COPD. *Respir Care*. 2016; 61(5):680-8.

Correspondent Author

Victor Fernando Couto
2360 Mato Grosso St. Setor alto da serra.
ZIP: 75600-000. Goiatuba, Goias, Brazil.
victorfcouto@gmail.com