



## Exacerbation and functional capacity of patients with COPD undergoing an exercise training program: longitudinal study

*Exacerbação e capacidade funcional de pacientes com DPOC submetidos ao treinamento físico: estudo longitudinal*

Diego Marmorato Marino<sup>[a]</sup>, Kamilla Tays Marrara<sup>[a, b]</sup>, Juliano Ferreira Arcuri<sup>[a]</sup>, Cecília Candolo<sup>[a]</sup>, Maurício Jamami<sup>[a]</sup>, Valéria Amorim Pires Di Lorenzo<sup>[a]\*</sup>

<sup>[a]</sup> Universidade Federal de São Carlos (UFSCar), São Carlos, SP, Brazil

<sup>[b]</sup> Centro Universitário Central Paulista (Unicep), São Carlos, SP, Brazil

---

### Abstract

**Objective:** To analyze if there is influence of body weight, body mass index (BMI), body composition, dyspnoea, grip strength and tolerance to exertion in the occurrence of exacerbation during a 12-month follow up of patients with COPD who underwent a physical training program. **Material and methods:** Sixty three patients were distributed in two groups, (Exacerbation Group — EG, n = 29; Non-Exacerbated Group — NEG, n = 34). The Mann Whitney test was used for the comparison between groups, the Friedman test

---

\* DMM: PhD student, e-mail: [diego\\_marmorato@hotmail.com](mailto:diego_marmorato@hotmail.com)

KTM: PhD, e-mail: [kmarrara@hotmail.com](mailto:kmarrara@hotmail.com)

JFA: PhD student, e-mail: [julianoarcuri@gmail.com](mailto:julianoarcuri@gmail.com)

CC: PhD, e-mail: [cecilia@ufscar.br](mailto:cecilia@ufscar.br)

MJ: PhD, e-mail: [jamami@ufscar.br](mailto:jamami@ufscar.br)

VAPL: PhD, e-mail: [vallorenzo@ufscar.br](mailto:vallorenzo@ufscar.br)

(posthoc Dunn) to compare the assessments and the logistic regression analysis, with a significance level of  $p < 0.05$ . **Results:** There is a significant difference between the groups in age and walked distance (WD) in the sixminute walk test (6MWT). The WD was reduced in 6<sup>th</sup>, 9<sup>th</sup> and 12<sup>th</sup> month reevaluation compared to baseline and 3 months for the EG. Logistic regression analysis showed a significant interaction between the lean body mass and the WD, BMI with the lean body mass and the BMI with the WD, this and the isolated dyspnoea, and lean body mass with body weight. **Conclusion:** Involving several variables along the follow up of patients with COPD in physical therapy programs is important, since it may prevent or reduce the chance of the occurrence of exacerbations. In addition, older patients with less tolerance to physical activity had a higher number of episodes of exacerbation, even when participating in a physiotherapy program associated to exercise training.

**Keywords:** Exercise therapy. Physical therapy modalities. COPD.

### Resumo

**Objetivos:** Analisar se há influência do peso corporal, índice de massa corpórea (IMC), composição corporal, dispneia, força de preensão palmar (FPP) e tolerância ao esforço na ocorrência de exacerbação ao longo de 12 meses de acompanhamento de pacientes com DPOC submetidos a um programa de treinamento físico que desenvolveram ou não a exacerbação. **Métodos:** Sessenta e três pacientes foram distribuídos em dois grupos (Grupo Exacerbação — GE,  $n = 29$ ; Grupo Não Exacerbação — GNE,  $n = 34$ ). O teste Mann-Whitney foi utilizado para a comparação entre os grupos, teste de Friedman (post-hoc e Dunn) para comparação das avaliações e a análise de regressão logística, com nível de significância  $p < 0,05$ . **Resultados:** Há diferença significativa entre os grupos quanto à idade e distância percorrida (DP) no teste de caminhada de seis minutos (TC6). A DP apresentou-se reduzida no 6<sup>o</sup>, no 9<sup>o</sup> e no 12<sup>o</sup> mês de reavaliação comparados a avaliação e ao 3<sup>o</sup> mês para o GE. Na análise de regressão logística observou-se interação significativa entre a MM e a DP, IMC com a MM, bem como do IMC com a DP, desta e da dispneia isoladas e da MM com o peso corporal. **Conclusão:** Conclui-se a importância de envolver diversas variáveis ao longo do acompanhamento de pacientes com DPOC em programas fisioterapêuticos na tentativa de prevenir a ocorrência de exacerbações ou reduzir sua chance de ocorrência. Além disso, pacientes mais idosos e com menor tolerância à atividade física tiveram maior número de episódios de exacerbação, mesmos estando inseridos em um programa fisioterapêutico de treinamento físico.

**Palavras-chave:** Exercício. Fisioterapia. DPOC.

### Introduction

Exacerbation is defined as an acute increase in respiratory symptoms, which exceed the usual daily variation and lead to a change in the regular medication, characterizing an exacerbation of the chronic obstructive pulmonary disease (COPD) (1). An exacerbation is a natural event on the COPD history (2), associated with a worsening in dyspnoea (3), which implies in impaired exercise capacity, reducing not only physical activities but also quality of life and life expectancy (4, 5, 6).

The reduction in physical activities is related to a higher probability of a new exacerbation episode, hospitalization and mortality (7, 8). Therefore, a

relevant strategy in the treatment of patients with COPD is their inclusion in an exercise program, since they improve their overall health and functional capacity. Furthermore, those programs may reduce the frequency of hospitalizations (9).

According to Vilaró et al. (10) and Wehrmeister et al. (11), several researches have studied the relationship between the exacerbation risk factors and the number and duration of hospitalizations in patients with COPD. Nevertheless, there is a lack of studies with a longitudinal 12-month follow up of patient's functional capacity and its influence on exacerbations in ambulatory patients, who are participating in exercise programs, which justifies the present study.

The hypothesis of the present study is the existence of an association between dyspnoea, handgrip force and exercise tolerance and a reduced number of exacerbations during a 12-month follow up, since patients were included in an exercise training program associated with respiratory physiotherapy.

Therefore, the aim of the present study was to analyse if weight, body-mass index, body composition, dyspnoea, handgrip force and the exercise tolerance influence the occurrence of exacerbations during a 12-month follow-up in patients with COPD undergoing a exercise training program.

The research question was: Which variables are associated with exacerbation episodes in patients with COPD, compared with those who did not exacerbate, included in an exercise training program associated with respiratory physiotherapy?

## Materials and methods

The present study was a prospective longitudinal study, which enrolled patients with clinical diagnosis of COPD. The period of the study was from January 2010 to September 2011, and each patient was followed during 12 months in which they underwent a physiotherapy program. All patients were assessed, and reassessed after three, six, nine and 12 months.

This study was conducted in the Respiratory Physiotherapy Special Unity and in the Health-School Unity of the institution, where 51 patients (men and women) with clinical diagnosis of COPD (GOLD stages II and III) (1) were assessed.

At the end of the 12-month follow up, the included patients were distributed in two groups, according to the presence of exacerbations (Exacerbated Group — EG) or not (Non-Exacerbated Group — NEG). This distribution was realized to analyse the variables in both groups during the follow up, and there was no difference in the physiotherapy treatment each group received; moreover, even after an exacerbation episode, the patients resumed the physiotherapy treatment.

The inclusion criteria were men or women with clinical diagnosis of COPD, with a forced expiratory volume in the first second ( $FEV_{1}$ ) and forced vital capacity (FVC) ratio ( $FEV_{1}/FVC$ ) < 70% and with moderate to severe obstruction (1); former smokers; clinically stable in the moment of the initial contact, and participation in no more than three months in the physiotherapy program.

The exclusion criteria were patients with pulmonary infections in the first assessment and other comorbidities such as heart, rheumatic and orthopaedic diseases that could prevent the conduction of one of the assessments due to exercise limitation.

The study was approved by the Ethics Committee of the Institution (432/2008) and patients signed a consent form, in order to comply with the 196/96 resolution of the Brazilian National Health Council.

## Experimental procedures

All patients underwent to following assessments: Anthropometric and demographic data collection, fat-free mass (FFM) by a body composition analysis, airway obstruction using  $FEV_{1}$ , dyspnoea using the modified Medical Research Council scale (mMRC), handgrip force and exercise tolerance using the walked distance (WD) in a six-minute walk test (6MWT).

The assessments were performed in five moments (each three months); however, prior to the first assessment, there was an initial contact during a physiotherapy session in one of the locations where the study was conducted, and during this contact the patient was invited to participate after an explanation regarding the aims of the study.

The included patients were participating in a physiotherapy program, consisting in an aerobic physical training in treadmill or stationary bicycle, with duration of at least 20 minutes, and an intensity defined as 80% of the maximum speed and inclination reached in a prior symptom-limited cardiopulmonary test (CPT). The intensity was constantly adjusted to maintain the dyspnoea in values of 4-6 in the Borg Scale (0-10), but always under the 85% of the predicted maximum heart rate. Furthermore, the program also included respiratory, upper and lower limbs exercises, and neck, back and limbs stretching (1). Manoeuvres to promote clearance of respiratory secretions were performed only when patients required.

## Exacerbation

Exacerbations were carefully assessed in the present study, according to the appearance or worsening of two or more signs and symptoms (dyspnoea, purulent mucous, increase in mucous volume, cough and wheezing) for more than two consecutive days.

Furthermore, an exacerbation was also characterized as a sustained worsening of the health condition of the patients that demanded a non-scheduled visit to a health service, such as emergency services, primary care facilities or the responsible pneumologist. The number of exacerbations was identified in each reassessment that occurred in the third, sixth, ninth and twelfth month after the baseline assessment.

#### Anthropometric data

The measurements of weight and height were assessed using a scale (Welmy™, model 110FF, São Paulo – SP, Brazil) and patients were instructed to stand over the scale, without their shoes and using light clothes, which allowed the calculation of the body mass index (BMI), according to Willett (12).

#### Body composition

The body composition analysis was carried out using a bioimpedance analyser and FFM was obtained (Ironman, Tanita™). All patients were instructed to do not eat or drink for a period of 3 hours prior to the analysis, and the patient stood over the scale with light clothes, no shoes, and with its feet aligned with the electrodes; following the instructions of the manufacturer.

#### Dyspnoea

The assessment of the dyspnoea was conducted using the mMRC scale (13). This scale is based in the difficulty of each activity that could lead to dyspnoea. It varies from “0” (the individual is not disturbed with breathlessness, unless when practicing vigorous exercise) to “4” (the individual presents breathlessness while leaving home or changing clothes). The scale was applied as an interview by the assessor.

#### Pulmonary function

The pre and post-bronchodilators pulmonary function test was realized to assess the severity of the obstruction, considering the  $FEV_1/FVC < 70\%$  and  $FEV_1$ , classifying the patients according to the

GOLD criteria as stage II ( $50\% \leq FEV_1 < 80\%$  of the predicted value) and stage III ( $30\% \leq FEV_1 < 50\%$  of the predicted value) (1).

#### Handgrip force

The assessment of handgrip force was realized in the dominant upper limb, using a dynamometer Jamar™ (Jackson, MI 49203 USA), in kilograms-force (kgf) (14), adjusted in the second position. The patients were seated and they were instructed to maintain the elbow in 90° of flexion, the forearm and fist in neutral position, following the standardization of the American Society of Hand Therapists (ASHT).

Patients realized three maximum voluntary contractions, with a 30 seconds rest period between them. To the analysis, the mean value was used, and a maximum of 5% of difference among the contractions was considered reliable.

#### Exercise tolerance

The exercise tolerance was assessed by the WD of the 6MWT. This test was realized in a 30-meters length corridor, according to the standardization of the ATS (15). The WD was recorded in meters and compared with predicted values, calculated using the Formula: Predicted  $WD_m = 622.461 - (1.846 \times age_{years}) + (61.503 \times Gender_{men = 1, women = 0})$  (16).

#### Statistical analysis

The results of the present study were expressed in median and inter-quartile range, presented in tables. For the comparison between groups and the five assessments, the applicative GraphPad InStat for Windows was used. Data distribution verification was performed using the Shapiro-Wilk test. Mann-Whitney test was carried out to compare both groups, and Friedman test was used to compare all five assessments, using the Post-hoc of Dunn, considering a significance level of  $p < 0.05$ .

Moreover, a logistic regression analysis was carried out (17) using the statistical software R and SAS 9.3 (SAS/STAT, Version 9.3 of SAS System for Windows); and presented in estimated odds ratio and its 95% confidence interval.

The logistic regression model was adjusted using the variables: weight, BMI, FFM, dyspnoea, handgrip force, WD in the 6MWT; and for each moment of assessment the best model was selected. To the best model, the odds ratio were calculated using the minimum, first quartile, median, mean, third quartile and maximum value for each variable. Nevertheless, the presentation of these values was determined according to the significance of the obtained results of the corresponding variable in each moment of assessment in the study.

## Results

A total of 63 patients (four women) met the inclusion criteria and based in the occurrence or not of an exacerbation after the period of the 12-month follow up, two groups were formed, the exacerbation group (EG, n = 29) and non-exacerbated group (NEG, n = 34). All patients received the same treatment, and they were separated only for the analysis of the data from this study (Figure 1).

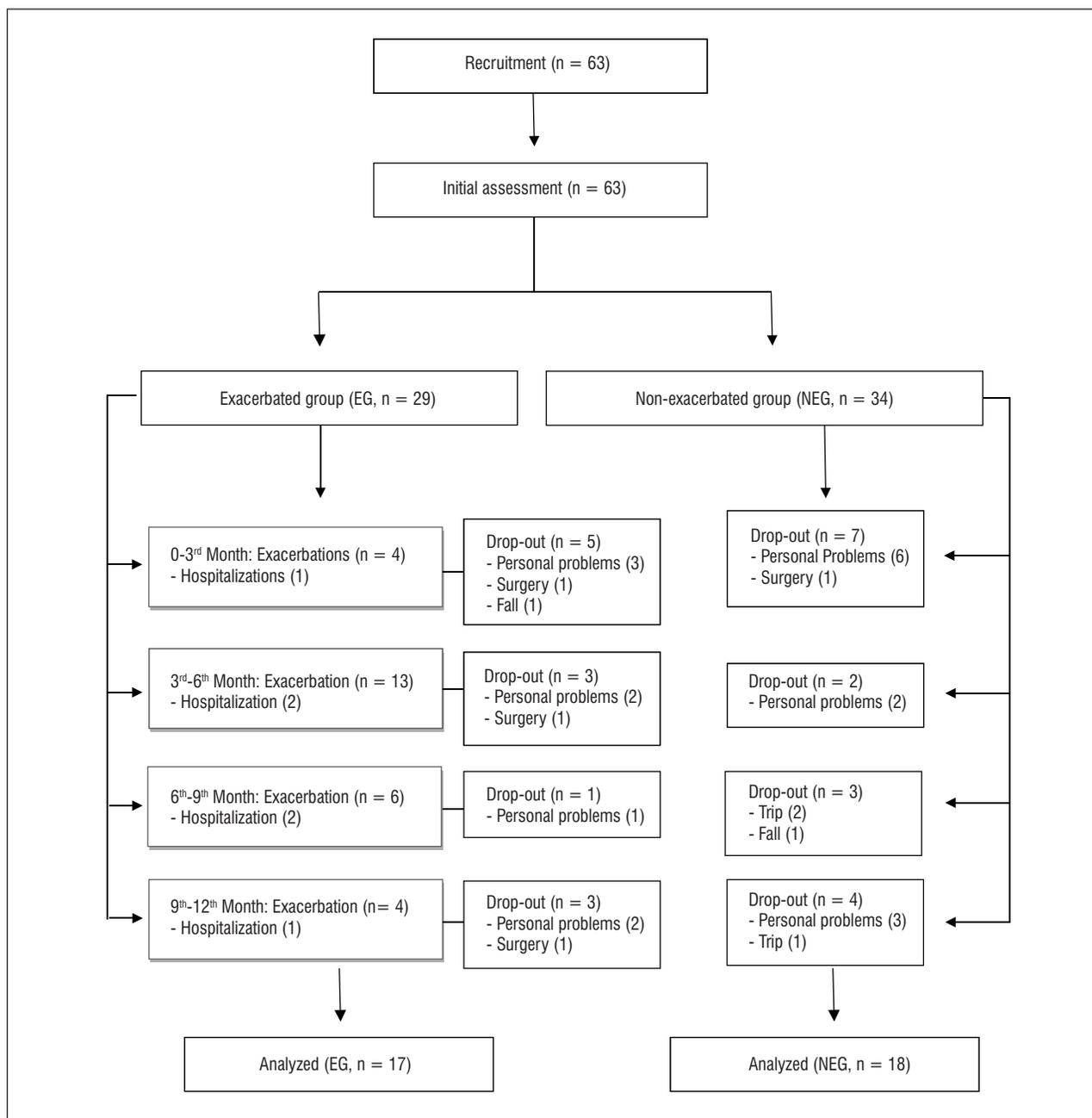


Figure 1 - Study flowchart

Figure 1 displays the number of patients that exacerbated in each period of assessment throughout the 12-month follow-up, the patients who were hospitalized and the number of patients who dropped out the study.

Regarding the occurrence of exacerbations, all patients from EG presented two or more episodes throughout the 12-month follow up, which mostly were characterized as an increase of the dyspnoea with the need of a visit in a health service. However, some patients required a hospitalization due to the exacerbation in this period (Figure 1).

Table 1 displays the variables regarding the anthropometric, spirometric, body composition analysis, as well as the dyspnoea, handgrip force and WD in the 6MWT for both groups. A significant intergroup difference was found for age ( $p = 0.02$ ) and WD in the 6MWT ( $p = 0.04$ ).

Table 2 shows the variables weight, BMI, FFM, dyspnoea, handgrip force, WD in the 6MWT in the 12-month follow up of EG and NEG, which demonstrate statistical difference for the 6MWT, which was reduced in the 6<sup>th</sup>, 9<sup>th</sup> and 12<sup>th</sup> months reassessment, compared to the baseline and third month assessment in the EG.

Regarding the logistic regression analysis, there was a significant interaction between the FFM and the WD in the 6MWT in the probability of an exacerbation in the follow-up period. Depending on which level FFM is (minimum, first quartile, median and third quartile) there is a change of the WD power of exacerbation prediction (Table 3). Therefore, in a patient with a FFM of 37.9 kg, each one unit increase in the WD on the 6MWT may reduce in 7% the exacerbation chance. Nevertheless, in a patient with a FFM of 41.2 kg, each one unit increase in the WD on the 6MWT may reduce in 5% the chance of an exacerbation. A patient with a higher value of FFM, such as 46.2 or 45.9, has a smaller influence of the WD to predict an exacerbation, an increase in one unit in the WD may reduce only 3% the chance of an exacerbation.

Depending on each level of WD in the 6MWT (minimum, first quartile, mean), there is a change on the influence of the FFM to predict an exacerbation. In patients with a WD of 242m, the chance of exacerbation is reduced in 72% with a one unit change of the FFM, while in a patient with a WD of 338 m or 426 m, the chance is reduced in 52% and 21%, respectively (Table 3).

Considering the reassessment after 3 months of the baseline, a significant interaction was found between the BMI with the FFM, as well as between the BMI with the WD in the 6MWT (Table 3). The presented values are the first quartile, mean and third quartile. In a patient with a BMI of 23.6 kg/m<sup>2</sup> (third quartile), an increase in one unit of the FFM led to a 60% reduction in the chance of an exacerbation and a one unit increase in the WD led to a 11% reduction. However, the prediction power of the WD is reduced when the BMI is lower, as an example, when the patients presents a BMI of 23.6 (mean), the chance of an exacerbation is reduced in 6% with a one unit increase in the WD.

The results presented in Table 4 also demonstrated the interaction between the BMI with the FFM and the WD in the 6MWT. In a patient with a FFM of 43.3 kg (first quartile) and a WD of 507 m (third quartile), the chance of an exacerbation is reduced in 88% when the BMI is one unit higher. With a FFM of 45.8 (mean) and a WD of 434 (mean) the chance is reduced in 83% and when increasing the WD to 507 m, the same reduction in the BMI led to a 96% of reduction in this chance. If the patient presents a FFM of 49.4 kg (third quartile) and a WD of 354 (first quartile), the chance of an exacerbation is reduced in 81%, but if the patient has a higher WD, such as 434 m, the chance is reduce in 96%, in each one unit increase in the BMI.

The reassessment six months after the baseline presented a significant prediction power of the WD in the 6MWT, but without interactions. Consequently, when the WD is one unit higher, there is a reduction of 2% in the chance of exacerbation. Moreover, there was a significant interaction between the FFM and the weight (Table 4). In a patient with a FFM of 48.6 kg (third quartile), each increase of one unit in the weight led to a reduction of 30% in the chance of an exacerbation. Nevertheless, if the patient presents a FFM of 54.9 kg (maximum), this chance is reduced in 57% (Table 4).

Considering the reassessment nine months after the baseline, a significant influence on the number of exacerbations was observed for the WD in the 6MWT and also for the dyspnoea, measured by the mMRC. The chance of a patient to exacerbate is reduced in 2% each increase of one unit in the WD and in 92% each increase in one unit of the mMRC (Table 4).

**Table 1** - Anthropometric, spirometric, body composition characteristics and baseline values of dyspnoea, handgrip force, walked distance and predicted distance in the 6MWT of both groups

Variables	Exacerbated Group n = 29	Non-Exacerbated Group n = 34
Age (years)	72 (70.8–75.3)	63.5 (60–73.5) *
Weight (kg)	68.9 (55.4–74)	65.2 (56.1–74)
Height (cm)	169 (168–171.8)	164 (154.3–170)
BMI (kg/m <sup>2</sup> )	24 (19.8–25)	24.6 (20.4–26)
FEV <sub>1</sub> (% predicted)	50 (36–58.4)	47.8 (32.1–55.8)
FVC (% predicted)	76.5 (66.5–85)	71 (58.6–90.2)
FEV <sub>1</sub> /FVC (%)	55.6 (49–68.1)	53.1 (40.5–64.5)
Fat-Free Mass (kg)	45.8 (43.7–50.7)	46.3 (40–51.2)
Dyspnoea (mMRC)	2 (2–2)	2 (2–2)
Handgrip Force (kgf)	38 (30.7–38.4)	38 (33.3–39.9)
Walked Distance in the 6MWT (m)	404 (314–468.5)	480 (421–536)*
Predicted distance in the 6MWT (m)	551.1 (545.5–552.9)	566.7 (549.2–573.2)

Note: BMI = Body-mass index; FEV<sub>1</sub> = Forced expiratory volume in the first second; FVC = Forced vital capacity; 6MWT = Six-minute walk test. \*Mann-Whitney, p < 0.05.

**Table 2** - Body Composition, dyspnoea, handgrip force of both groups over the 12-month follow up

(To be continued)

	Exacerbated group				
	Baseline (n = 29)	3 months (n = 24)	6 months (n = 21)	9 months (n = 20)	12 months (n = 17)
Weight (kg)	68.9 (55.4–74)	65.3 (56.4–76.1)	67.3 (58–76.2)	67.5 (58–76)	63.8 (58.4–74.9)
Body Mass Index (kg/m <sup>2</sup> )	24 (19.8–25)	22.5 (20.3–24.9)	22.2 (21–26)	22.2 (20.8–26.9)	21.2 (20.7–24.2)
Fat-free mass (kg)	45.8 (43.7–50.7)	47.3 (44.1–49.6)	46.6 (45.5–48.8)	47.1 (46.7–49)	48.5 (46.7–49.2)
Dyspnoea (mMRC)	2 (2–2)	2 (1–2)	2 (1–2)	2 (1–2)	2 (1–2)
Handgrip Force (kgf)	38 (30.7–38.4)	37.8 (33.9–38.4)	37.3 (32.3–39.4)	36.4 (30.3–39)	36.4 (34.7–38.1)
Walked Distance in the 6MWT (m)	404 (314–468.5)	406 (298–501.3)	290 (229–465)**	314 (288.3–404)**	354 (260–393)**
	Non-exacerbated group				
	Baseline (n = 34)	3 months (n = 27)	6 months (n = 25)	9 months (n = 22)	12 months (n = 18)
Weight (kg)	65.2 (56.1–74)	64.2 (57.6–75.1)	64.6 (58–77)	64.4 (58.1–68.6)	66.5 (58.4–68.8)
Body Mass Index (kg/m <sup>2</sup> )	24.6 (20.4–26)	24.4 (20.6–26.1)	24.1 (20.7–26)	23.8 (21.1–25.5)	23.9 (20.5–25.5)
Fat-free mass (kg)	46.3 (40–51.2)	45.1 (41–47.3)	44.9 (41.1–46.2)	44.5 (40.9–49.4)	46.1 (41.4–53.1)

**Table 2** - Body Composition, dyspnoea, handgrip force of both groups over the 12-month follow up

(Conclusion)

	Non-exacerbated group				
	Baseline (n = 34)	3 months (n = 27)	6 months (n = 25)	9 months (n = 22)	12 months (n = 18)
Dyspnoea (mMRC)	2 (2-2)	2 (2-2)	2 (2-2)	2 (1-2)	2 (1-2)
Handgrip Force (kgf)	38 (33.3-39.9)	37.7 (35.8-39.1)	37.7 (33.8-40.1)	37.8 (33.8-39.5)	37.6 (33.4-37.9)
Walked Distance in the 6MWT (m)	480 (421-536)	477 (372-540)	482 (378-548)	470 (366-526)	496 (368-522)

Note: Friedman Test and Dunn *post-hoc*. \*Statistical difference when compared to the baseline; #Statistical difference when compared to the third month.

**Table 3** - Interaction of the walked distance in the 6MWT with the FFM presented in estimated *odds ratio* and its 95% confidence interval in the assessment and interaction of the body mass index with the fat-free mass, as well as the walked distance in the 6MWT after a three-month follow-up

<i>Walked Distance in the 6MWT - BASELINE</i>		
	<i>Estimated Odds Ratio</i>	<i>95% CI</i>
FFM = 37.9kg	0.93	0.88-0.97
FFM = 41.2kg	0.95	0.91-0.98
FFM = 46.2kg	0.97	0.96-0.99
FFM = 45.9kg	0.97	0.95-0.99
<i>Fat-free mass - BASELINE</i>		
	<i>Estimated Odds Ratio</i>	<i>95% CI</i>
WD in the 6MWT = 242 m	0.28	0.12-0.69
WD in the 6MWT = 338 m	0.48	0.29-0.81
WD in the 6MWT = 426 m	0.79	0.64-0.97
<i>Fat-free mass - THIRD MONTH</i>		
	<i>Estimated Odds Ratio</i>	<i>95% CI</i>
BMI = 26.1 kg/m <sup>2</sup>	0.40	0.18-0.91
<i>Walked distance in the 6MWT - THIRD MONTH</i>		
	<i>Estimated Odds Ratio</i>	<i>95% CI</i>
BMI = 23.6 kg/m <sup>2</sup>	0.94	0.90-0.98
BMI = 26.1 kg/m <sup>2</sup>	0.89	0.83-0.97
<i>Body mass index - THIRD MONTH</i>		
	<i>Estimated Odds Ratio</i>	<i>95% CI</i>
FFM = 43.3 kg and WD in the 6MWT = 507m	0.12	0.03-0.49
FFM = 45.8 kg and WD in the 6MWT = 434m	0.17	0.05-0.57
FFM = 45.8 kg and WD in the 6MWT = 507m	0.04	0.004-0.39
FFM = 49.4 kg and WD in the 6MWT = 354m	0.19	0.05-0.73
FFM = 49.4 kg and WD in the 6MWT = 434m	0.04	0.003-0.48

Note: 6MWT = Six-minute walk test; CI = Confidence Interval; FFM = Fat-free mass; WD = Walked Distance.

**Table 4** - Walked distance in the 6MWT, and the interaction of the Fat-free mass with the body weight, presented in estimated *odds ratio* and its 95% Confidence interval after six month follow-up; Walked distance in the 6MWT and dyspnoea after nine months of follow up

<i>Walked distance in the 6MWT – SIXTH MONTH</i>		
	<i>Estimated Odds Ratio</i>	<i>95% CI</i>
<b>WD in the 6MWT</b>	0.98	0.96–0.99
<i>Weight – SIXTH MONTH</i>		
	<i>Estimated Odds Ratio</i>	<i>95% CI</i>
<b>FFM = 48.6 kg</b>	0.7	0.54–0.91
<b>FFM = 54.9 kg</b>	0.43	0.22–0.84
<i>Walked distance in the 6MWT – NINITH MONTH</i>		
	<i>Estimated Odds Ratio</i>	<i>95% CI</i>
<b>WD in the 6MWT</b>	0.98	0.97–0.99
<i>Dyspnoea – NINITH MONTH</i>		
	<i>Estimated Odds Ratio</i>	<i>95% CI</i>
<b>Dyspnoea</b>	0.08	0.008–0.49

Note: 6MWT = six-minute walk test; CI = confidence interval; FFM = Fat-free mass; WD = Walked Distance.

The reassessment after twelve months led to data without any conclusive results, probably due to the small amount of data in this period.

## Discussion

### Main findings

The present study demonstrated as its main finding that there is an interaction of some variables, which may determinate the chance of the occurrence of an exacerbation in patients with COPD (stages II and III), in a twelve-month follow up. Furthermore, the exercise tolerance was reduced throughout the 12-month follow up in the EG. Moreover the patients from the exacerbation group presented older age and less exercise tolerance.

Nevertheless, the body composition, dyspnoea and handgrip were similar during all reassessments for both groups, as well as the exercise tolerance on the NEG.

### Study relevance

The present study contributes with the understanding of the behaviour of the exercise tolerance over a long-term follow up and its influence in exacerbation episodes in patients with COPD who are undergoing an exercise training of moderate intensity and high frequency. These characteristics pointed out the finding that older patients and with lower functional capacity were the ones who exacerbated, which led to a reduction in the exercise capacity throughout the months, even when included in a physiotherapy treatment associated with a aerobic training.

Other relevant finding is that the chance of exacerbation may be influenced by the interaction between the FFM and weight or BMI, and also by the interaction between BMI with the WD in the 6MWT. In addition, some isolated variables, such as WD in the 6MWT and the dyspnoea, influence the chance of an exacerbation in patients with COPD stages II and III.

Older age and low FEV<sub>1</sub> are some factors related to the occurrence of exacerbation episodes (18, 19),

and in the present study, patients included in the EG were older, however they presented similar FEV<sub>1</sub> when compared to the NEG.

#### Exacerbation Episodes, functional capacity and physiotherapy treatment associated with aerobic training

Soler-Cataluña et al. (20) assessed the impact of an exacerbation on mortality in COPD patients, and they observed that patients who needed a hospitalization due to an exacerbation has worse prognosis. This suggests that intensity, alongside the frequency, also plays a role in the consequences of an exacerbation. In the present study, six patients needed hospitalization over the period of 12 months, and some of them were hospitalized more than once.

Pamplona and Morais (21) pointed out that in the period of an exacerbation, and even after it, a significant reduction in the activities level is observed. Moreover, approximately 25% of the patients who suffered an exacerbation do not recover their functional capacity even after three months.

In addition, although EG and NEG realized the same protocol of physiotherapy, the patients from the first presented exacerbation episodes due to a lower exercise tolerance in the baseline, with a difference between means of 77m in the 6MWT.

The exercise intolerance is a common manifestation in patients with COPD (22), caused by multiple factors, such as respiratory, cardiovascular and muscle impairment, which may lead to dyspnoea and fatigue that limits the activities of daily living (23).

Some authors (24, 25) suggests that exercise tolerance, assessed by a 6MWT may be a good mortality predictor, since it reflects not only the respiratory function, but also the cardiopulmonary and skeletal muscle functions. Moreover, it is related to other important outcomes in patients with COPD, such as dyspnoea (24). Therefore, an increase in the dyspnoea, which characterize most of the exacerbation episodes, and the skeletal muscle impairment favours this intolerance (26, 27).

Exercise training seeks to reduce the intolerance in patients with COPD, and its benefits are clear in the literature regarding in the increase in the WD in the 6MWT and in relieving of exercise intolerance (28). Consequently, the inclusion of exercise training in the respiratory physiotherapy programs is essential.

However, some patients who were undergoing the exercise training program still presented exacerbations, but it is important to highlight the fact that these patients maintained a similar body composition, dyspnoea and handgrip force during the period of the study. Moreover, the majority of the exacerbation episodes occurred during the winter months (May, June and July), when the temperature and air humidity are altered and contributes to the occurrence of an exacerbation.

According to Spencer et al. (29), respiratory rehabilitation programs including exercise training for at least eight weeks may show benefits in the exercise capacity, reduction of dyspnoea and health care visits, which may be maintained for 12 months if the patient realize the exercises at home, five times a week.

Nevertheless, his study has some limitations, such as being conducted in a single health centre, and enrolling a convenience sample. Moreover, there was a small amount of data after 12 months of follow up, which prevented some analysis in this period. However, the results of the present study presented that older patients with COPD and with more exercise intolerance need to receive more attention regarding the strategies of the supervised physiotherapy treatment and the weekly training frequency. As a result, a better control of the occurrence of exacerbations is expected, since these patients receive pharmacological treatment by the pneumologist.

## Conclusion

According to the obtained results, it is important to encompass several variables in the assessment of patients with COPD who are undergoing a physiotherapy program in an attempt to prevent the occurrence of exacerbations or reduce their chance. This may be possible due to the interaction between the variables. In addition, the frequent reassessment of the exercise tolerance and dyspnoea is necessary, which are also related to the occurrence of episodes of exacerbation.

Furthermore, non-exacerbated patients presented maintenance of the exercise tolerance level during the period of the study, and older patients with lower exercise capacity presented more exacerbation episodes, leading to a more sever impairment of their functional capacity. This may cause a higher risk of complications, even when they are

included in a physiotherapy program associated to exercise training.

Other consideration is the reduction of the functional capacity which was not recovered even with the exercise training, since the prejudice was maintained along the 12-month follow up.

## References

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Bethesda: Global Initiative for Chronic Obstructive Lung Disease; 2011.
2. Kon SSC, Canavan JL, Man WDC. Pulmonary rehabilitation and acute exacerbations of COPD. *Expert Rev Respir Med.* 2012;6(5):523-31.
3. Mackay AJ, Hurst JR. COPD Exacerbations: causes, prevention, and treatment. *Immunol Allergy Clin North Am.* 2013;33(1):95-115.
4. Connors AF, Dawson NV, Thomas C, Harel Jr FE, Desbiens N, Fulkerson Wj, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. *Am J Respir Crit Care Med.* 1996;154(4):959-67.
5. Langer D, Probst VS, Pitta F, Burtin C, Hendriks E, Schans CPVD, et al. Guia para prática clínica: fisioterapia em pacientes com Doença Pulmonar Obstrutiva Crônica (DPOC). *Rev Bras Fisioter.* 2009;13(3):183-204.
6. Rizzi M, Grassi M, Pecis M, Andreoli A, Taurino AE, Sergi M, et al. A specific home care program improves the survival of patients with chronic obstructive pulmonary disease receiving long term oxygen therapy. *Arch Phys Med Rehabil.* 2009;90(3):395-401.
7. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. *Thorax.* 2006;61(9):772-8.
8. Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Physical activity and hospitalization for exacerbation of COPD. *Chest.* 2006;129(3):536-44.
9. Casaburi R, ZuWallack R. Pulmonary rehabilitation for management of chronic obstructive pulmonary disease. *N Engl J Med.* 2009;360(13):1329-35.
10. Vilaró J, Ramirez-Sarmiento A, Martínez-Llorens JM, Mendoza T, Alvarez M, Sánchez-Cayado N, et al. Global muscle dysfunction as a risk factor of readmission to hospital due to COPD exacerbations. *Respir Med.* 2010;104(12):1896-902.
11. Wehrmeister FC, Knorst M, Jardim JR, Macedo SEC, Noal RB, Martínez-Mesa J, et al. Programas de reabilitação pulmonar em pacientes com DPOC. *J Bras Pneumol.* 2011;37(4):544-55.
12. Willett W. *Nutritional epidemiology.* 2nd ed. Oxford: Oxford University Press; 1998.
13. Mahler D, Wells C. Evaluation of clinical methods for rating dyspnea. *Chest.* 1988;93(3):580-6.
14. Figueiredo IM, Sampaio RF, Mancini MC, Silva FCM, Souza MAP. Teste de força de prensão utilizando dinamômetro Jamar. *Acta Fisiatr.* 2007;14(2):104-10.
15. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS Statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med.* 2002;166(1):111-7.
16. 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(11):1080-5.
17. Hosmer DW, Lemeshow S. *Applied Logistic Regression.* 2nd ed. New York: John Wiley & Sons; 2000.
18. García-Aymerich J, Farrero E, Felez MA, Izquierdo J, Marrades RM, Antó JM. Risk factors of readmission to hospital for a COPD exacerbation: a prospective study. *Thorax.* 2003;58(2):100-5.
19. Spencer S, Calverley PMA, Burge PS, Jones PW. Impact of preventing exacerbations on deterioration of health status in COPD. *Eur Respir J.* 2004;23(5):698-702.
20. Soler-Cataluña JJ, Martínez-García MA, Román-Sánchez P, Salcedo E, Navarro M, Ochoa R. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax.* 2005;60(11):925-31.
21. Pamplona P, Morais L. Treino de exercício na doença pulmonar crônica. *Rev Port Pneumol.* 2007;13(1):101-28.

22. Debigaré R, Côté CH, Maltais F. Peripheral muscle wasting in chronic obstructive pulmonary disease – Clinical relevance and mechanisms. *Am J Respir Crit Care Med.* 2001;164(9):1712-7.
23. Ferreira EVM. Teste cardiopulmonar de exercício na DPOC: indo além do consumo máximo de oxigênio. *J Bras Pneumol.* 2012;38(5):539-40.
24. Enright PL, McBurnie MA, Bittner V, Tracy RP, McNamara R, Arnold A, et al. The 6-min walk test: a quick measure of functional status in elderly adults. *Chest.* 2003;123(2):387-98.
25. Pinto-Plata VM, Cote C, Cabral H, Taylor J, Celli BR. The 6-min walk distance: change over time and value as a predictor of survival in severe COPD. *Eur Respir J.* 2004;23(1):28-33.
26. Gosselink R, Troosters T, Decramer M. Distribution of muscle weakness in patients with stable chronic obstructive pulmonary disease. *J Cardiopulm Rehabil.* 2000;20(6):353-60.
27. Nici L, Donner C, Wouters E, Zuwallack R, Ambrosino N, Bourbeau J, et al. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med.* 2006;173(12):1390-413.
28. American Thoracic Society-European Respiratory Society. Skeletal muscle dysfunction in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 1999;159:S1-28.
29. Spencer L, Alison J, McKeough Z. Maintaining benefits following pulmonary rehabilitation: a randomised controlled trial. *Eur Resp J.* 2010;35(3):571-7.

Received: 08/30/2013

Recebido: 30/08/2013

Approved: 12/01/2014

Aprovado: 01/12/2014