

Relationship between the difference of slow and forced vital capacity and physical activity in daily life in patients with Chronic Obstructive Pulmonary Disease

Correlação entre a diferença da capacidade vital lenta e forçada com a atividade física na vida diária em pacientes com Doença Pulmonar Obstrutiva Crônica

Correlación entre la diferencia en la capacidad vital lenta y forzada con la actividad física en la vida diaria de pacientes con Enfermedad Pulmonar Obstrutiva Crónica

Leila Donária¹, Ana Cristina Schnitzler Moure², Larissa Martinez³, Karina Couto Furlanetto⁴, Nidia Aparecida Hernandez⁵, Fabio Pitta⁶

ABSTRACT | The aim of this study was to correlate the difference of vital capacity (VC) and forced vital capacity (FVC) (VC-FVC) with physical activity in daily life (PADL) in patients with chronic obstructive pulmonary disease (COPD); and investigate the differences in PADL in individuals with VC smaller or greater than FVC. Twenty-eight patients with COPD (18 men, 67±8 years; FEV₁: 40±13% predicted) had their lung function assessed by spirometry and were divided into two groups: VC>FVC (n=17) and VC≤FVC (n=11). Furthermore, they had their PADL evaluated by a validated activity monitor which measures, among other variables, time spent/day walking, standing, sitting and lying. There were no correlations between VC-FVC and the variables of PADL in the general group. In the group VC>FVC there was statistically significant correlation between VC-FVC and the time spent/day standing (r=-0.56) and sitting (r=0.75). In the group VC≤FVC, VC-FVC was significantly correlated with time spent/day standing (r=0.57) and lying (r=-0.62). When comparing the groups, there was no statistically significant difference for any variable of PADL (p>0.05 for all). In conclusion, in patients with VC

greater than FVC there was high correlation with time spent/day sitting, but not with time spent/day walking. Therefore, individuals with greater airflow obstruction according to the VC-FVC difference tend to spend more time in activities of lower energy expenditure, which do not involve walking.

Keywords | Chronic Obstructive Pulmonary Disease; Exercise; Spirometry.

RESUMO | O objetivo do estudo foi correlacionar a diferença entre capacidade vital lenta (CVL) e capacidade vital forçada (CVF) (CVL-CVF) com a atividade física na vida diária (AFVD) em pacientes com doença pulmonar obstrutiva crônica (DPOC); e verificar as diferenças na AFVD entre indivíduos com CVL maior ou menor do que a CVF. Vinte e oito indivíduos com DPOC (18 homens; 67±8 anos; VEF₁: 40±13% previsto) tiveram a função pulmonar avaliada pela espirometria e foram divididos em dois grupos: CVL>CVF (n=17) e CVL≤CVF (n=11). Ademais, tiveram a AFVD avaliada objetivamente pelo monitor de atividade física DynaPort®, que quantifica na vida diária, dentre outros,

Study carried out at the Pulmonary Physical Therapy Research Laboratory (LFIP), of the Universidade Estadual de Londrina (UEL), Londrina (PR), Brazil.

¹Universidade Estadual de Londrina (UEL) - Londrina (PR), Brazil. Email: leiladonaria@hotmail.com. Orcid: 0000-0002-1733-9778

²Universidade Estadual de Londrina (UEL) - Londrina (PR), Brazil. Email: aninhac_moure@hotmail.com. Orcid: 0000-0002-5562-3286

³Universidade Estadual de Londrina (UEL) - Londrina (PR), Brazil. Email: larissa.mmartinez@hotmail.com. Orcid: 0000-0002-8610-6310

⁴Universidade Estadual de Londrina (UEL) - Londrina (PR), Brazil. Universidade do Norte do Paraná (Unopar), Londrina (PR), Brazil. Email: ka_furlanetto@hotmail.com. Orcid: 0000-0002-7496-7228

⁵Universidade Estadual de Londrina (UEL) - Londrina (PR), Brazil. Email: nyhernandes@gmail.com. Orcid: 0000-0002-5219-851X

⁶Universidade Estadual de Londrina (UEL) - Londrina (PR), Brazil. Email: fabiopitta@uol.com.br. Orcid: 0000-0002-3369-6660

Corresponding address: Fabio Pitta - Av. Robert Koch, 60 - Londrina (PR), Brazil - Zip Code: 86038-350 - Email: fabiopitta@uol.com.br - Financing source: Araucária Foundation and the Coordination for the Improvement of Higher Education Personnel (Capes). The PhD Professor Fabio Pitta is supported by a research grant from the National Council for Scientific and Technological Development (CNPq) - Conflict of interests: nothing to declare - Presentation: May 7th, 2019 - Accepted for publication: Nov. 17th, 2019 - Study approved by the Research Ethics Committee of the State University of Londrina (UEL), under opinion No. 173/2012.

o tempo gasto por dia andando, em pé, sentado e deitado. Não foram encontradas correlações significativas entre CVL-CVF e as variáveis da AFVD no grupo geral. No grupo CVL>CVF foi encontrada significância estatística na correlação entre a CVL-CVF e o tempo gasto por dia em pé ($r=-0,56$) e sentado ($r=0,75$). Já no grupo CVL≤CVF, houve correlação significativa somente com o tempo gasto por dia em pé ($r=0,57$) e deitado ($r=-0,62$). Ao comparar ambos os grupos, não houve diferença estatisticamente significativa para nenhuma das variáveis da AFVD ($p>0,05$ para todas). No grupo com CVL maior que a CVF houve correlação alta com o tempo gasto sentado, mas não com o tempo andando. Portanto, indivíduos com maior obstrução ao fluxo aéreo segundo a diferença CVL-CVF tendem a gastar mais tempo em atividades de menor gasto energético, que não envolvam caminhar.

Descritores | Doença Pulmonar Obstrutiva Crônica; Exercício; Espirometria.

RESUMEN | El presente estudio tuvo el objetivo de correlacionar la diferencia entre la capacidad vital lenta (CVL) y la capacidad vital forzada (CVF) (CVL-CVF) con la actividad física en la vida diaria (AFVD) de pacientes con enfermedad pulmonar obstructiva crónica (EPOC); y verificar las diferencias de la AFVD entre individuos con CVL mayor o menor que la CVF.

Se evaluaron la función pulmonar de veintiocho personas con EPOC (18 hombres; 67 ± 8 años; $VEF_1: 40\pm 13\%$ esperado) mediante espirometría, y los dividieron en dos grupos: CVL>CVF ($n=17$) y CVL≤CVF ($n=11$). La AFVD también se evaluó objetivamente por el monitor de actividad física DynaPort®, el cual cuantifica el tiempo que se gasta en la vida diaria caminando, de pie, sentado y acostado. No se encontraron correlaciones significativas entre CVL-CVF y las variables de la AFVD en el grupo general. En el grupo CVL>CVF, se encontró una significación estadística en la correlación entre CVL-CVF y el tiempo que se gasta diariamente en pie ($r=-0,56$) y sentado ($r=0,75$). El grupo CVL≤CVF presentó una correlación significativa solo con el tiempo que se gasta diariamente en pie ($r=0,57$) y acostado ($r=-0,62$). La comparación entre ambos grupos no resultó en diferencias estadísticamente significativas en ninguna de las variables de AFVD ($p>0,05$ para todas). En el grupo con CVL mayor que la CVF, hubo una alta correlación con el tiempo que se gasta sentado, pero con el tiempo que se gasta caminando no se encontró este resultado. Se concluye que las personas con una mayor obstrucción del flujo de aire de acuerdo con la diferencia CVL-CVF tienden a gastar más tiempo en actividades con menos gasto de energía, las que no implican caminar.

Palabras clave | Enfermedad Pulmonar Obstructiva Crónica; Ejercicio; Espirometría.

INTRODUCTION

According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), chronic obstructive pulmonary disease (COPD) is defined as “a preventable and treatable disease, characterized by persistent airflow obstruction, usually progressive and associated with an abnormal chronic inflammatory response in airways and lungs to harmful particles or gases”¹. As a consequence of this limitation to airflow, dyspnea is one of the symptoms of greatest complaint among those who suffer from the disease². In an attempt to minimize or avoid this respiratory symptom, patients with the disease may reduce physical activities in daily life, maintaining a predominantly sedentary lifestyle^{3,4}. Paradoxically, airflow limitation, dyspnea and physical inactivity induce a greatest ventilatory demand for the same activity, feeding the dyspnea-physical inactivity-dyspnea cycle⁵. In addition to pulmonary involvement, extrapulmonary factors (such as muscle dysfunction,

systemic inflammation and nutritional changes, among others) also contribute to the disease progression¹.

Due to the sedentary lifestyle of patients with COPD and the negative impact of this characteristic on disease evolution, interest in objectively monitoring the level of physical activity in daily life (PADL) of this population has grown⁶. Both sedentary behavior and reduced level of physical activity are known to be independent predictors of mortality in patients with COPD^{7,8}. However, the devices cost can make this assessment difficult in clinical practice, so that monitoring of sedentary behavior and PADL is not performed in many rehabilitation and treatment centers for COPD patients.

Hernandes et al.⁹ studied the profile of PADL level for individuals with COPD in Brazil and observed they are less active when compared to healthy elderly people, spending more time lying down or sitting, in addition to walking with less intensity of movement. That study also observed there is only a weak correlation between the degree of airflow limitation, assessed by the forced

expiratory volume in the first second (FEV_1), and the level of PADL in COPD⁹, which corroborates previous findings in the literature¹⁰. Therefore, researchers have been looking for potential strategies to make these patients more physically active since low levels of physical activity have been associated with accelerated decline in lung function, exercise intolerance, peripheral muscle weakness, less muscle mass, acute exacerbation of the disease and, consequently, worse prognosis¹¹.

Vital capacity (VC), measured by a simple spirometer, is a lung volume that can be assessed using vital capacity (VC) and forced vital capacity (FVC) maneuvers. In healthy individuals there is little or no difference between VC and FVC; nonetheless, some studies have shown that, in patients with COPD, VC is greater than FVC and a more pronounced VC-FVC difference is related to a higher degree of airflow obstruction, small airway collapse and air trapping¹²⁻¹⁴. However, one does not know whether the difference between VC and FVC correlates better than FEV_1 with PADL in COPD. Such information is relevant, as it would facilitate the identification of the most physically inactive individuals (and therefore at higher risk) through simple spirometry in places where physical activity monitors are not available.

Therefore, the objectives of this study were to correlate the VC-FVC difference with PADL variables (intensity of movement, time spent walking, standing, sitting and lying down per day) in patients with COPD; and to verify differences in PADL level between individuals with VC greater or less than FVC.

METHODOLOGY

Design

This is a cross-sectional observational study, conducted with a convenience sample of patients with COPD at the Pulmonary Physiotherapy Research Laboratory (LFIP), Department of Physiotherapy at the Universidade Estadual de Londrina (UEL). All ethical principles established in Resolution 196/96 of the National Health Council were respected and all individuals signed an informed consent form.

The sample consisted of individuals with COPD who met the following inclusion criteria: confirmed diagnosis of COPD, according to GOLD¹, with no

exacerbations occurring in the last three months; absence of serious comorbidities, such as osteomioarticular and cardiovascular diseases, that could interfere with the implementation of the proposed protocol; and not having done any kind of physical exercise program regularly in the last year. Patients who for some reason were unable to carry out the assessments proposed in the protocol would be excluded from the study. The evaluated individuals did not use home oxygen or an auxiliary walking device.

Procedures

Initially, the demographic (gender and age) and anthropometric (weight, height and body mass index – BMI) data of the individuals were evaluated. Then, a spirometric evaluation was performed with a portable spirometer (SpiroBank GÖ; MIR, Italy), according to the guidelines of the American Thoracic Society (ATS)¹⁵. VC and FVC maneuvers were performed to determine VC, FEV_1 , FVC, FEV_1/FVC ratio and VC-FVC difference. The reference values used were those proposed for the Brazilian population by Pereira, Sato and Rodrigues¹⁶. Individuals were divided into two groups according to the difference between VC and FVC: one group with $VC > FVC$ and the other with $VC \leq FVC$.

For the assessment of PADL, patients used the DynaPort® physical activity monitor (McRoberts, Netherlands) for two days a week, 12 hours a day. The DynaPort® is a multiaxial accelerometer validated in COPD^{17,18} that accurately records the time spent per day in different activities and postures (walking, standing, sitting and lying), as well as the intensity of movements during walking. Specific software was used for the analysis of data recorded by Dynaport® (Dyrector 1.0.7.18, McRoberts, Netherlands).

The assessment of respiratory muscle strength was performed using the maximum inspiratory (PI_{max}) and expiratory (PE_{max}) pressures, in order to better characterize the sample, and followed the protocol established by Black and Hyatt¹⁹. The equipment used was an analog manovacuometer (Makil, Londrina, Brazil). PI_{max} and PE_{max} were expressed as a percentage of the predicted value, based on the reference values of Neder et al.²⁰.

For the assessment of functional exercise capacity, the six-minute walk test (6MWT) was performed strictly in

accordance with ATS standards²¹. The reference values used were those of Britto et al.²² for the predicted percentage calculations.

The sensation of dyspnea was assessed using the Medical Research Council (MRC) scale validated into Portuguese²³. The scale consists of only five items, among which the patient chooses the one corresponding to how much dyspnea limits his daily life. Its score varies between 1 and 5, and higher values indicate greater limitation due to dyspnea in daily life.

Statistical analysis

The analysis of data distribution was performed using the Shapiro-Wilk test. In cases where data distribution was normal, the variables were described as mean±standard deviation, with intergroup comparisons performed using the unpaired Student's t test. Otherwise, data were described as median and comparisons were made using the Mann-Whitney test. Correlations were analyzed using Pearson or Spearman coefficients, depending on the normality in data distribution. Statistical analysis was performed using the GraphPadPrism software, version 6.0. The level of statistical significance was set at $p \leq 0.05$.

The G Power[®] program was used to calculate the study's power, taking into account a bivariate correlation model. A sample of 28 individuals showed a power of 99% considering a 0.75 correlation between PADL and the difference between VC-FVC and adopting a 5% statistical significance.

RESULTS

Twenty-eight individuals were submitted to the evaluations and there were no exclusions. The general characteristics of the sample are shown in Table 1. One may notice the sample consisted of men and women who were mostly elderly, with mild overweight and moderate to very severe obstruction, according to GOLD¹ criteria. Individuals in the VC>FVC and VC≤FVC groups did not show statistically significant differences in terms of lung function, maximum respiratory pressures, exercise capacity, dyspnea in daily life and anthropometric and demographic characteristics ($p > 0.05$ for all) (Table 1).

Table 1. General characteristics of the sample

Variable	General n=28	CVL>CVF n=17	CVL≤CVF n=11
Age (years)	67±9	66±9	69±8
Gender (M/F)	18/10	12/5	6/5
BMI (kg.m ⁻²)	26±5	25±5	27±4
VEF ₁ (%pred)	41±13	40±12	43±16
GOLD (II/III/IV) (n)	6/15/7	3/10/4	3/5/3
Plmax (%pred)	74±18	77±16	73±21
PEmax (%pred)	109±32	110±36	108±33
6MWT (%pred)	74±16	73±17	75±16
MRC scale (pts)	4 [3-4]	4 [4-4]	4 [2-5]
Intensity of movement (m/s ²)	1.82±0.3	1.88±0.32	1.71±0.27
Time spent walking/day (min)	52±31	58±35	44±24
Time spent standing/day (min)	244±128	271±145	195±89
Time spent sitting/day (min)	297±103	287±126	339±69
Time spent lying down/day (min)	121 [19-176]	98±91	137±83

Results expressed as mean ± standard deviation or median [interquartile range 25%-75%]. VC: vital capacity; FVC: forced vital capacity; M: male; F: female; BMI: body mass index; kg: kilograms; m: meters; FEV₁: forced expiratory volume in the first second; GOLD: Global Initiative for Chronic Obstructive Lung Disease; n: number of individuals; Plmax: maximum inspiratory pressure; PEmax: maximum expiratory pressure; 6MWT: 6-minute walk test; % pred: percentage of predicted values; MRC: Medical Research Council; pts: points. Comparison between VC>FVC and VC≤FVC groups: $p > 0.05$ for all.

Results of the correlation between VC-FVC difference and the PADL variables in the general group are shown in Table 2. There were no statistically significant correlations between the VC-FVC difference and any of the variables ($p > 0.05$ for all).

When the VC>FVC group (greater airflow obstruction) was analyzed in isolation, a statistically significant, moderate and negative correlation was observed between the VC-FVC difference and the time spent standing/day ($r = -0.56$, $p = 0.02$) and also a strong and positive correlation with the time spent sitting per day ($r = 0.75$, $p = 0.0008$) (Figure 1).

Table 2. Correlations of the VC-FVC difference with PADL variables in the general group

Variable	r	p
Intensity of movement (m/s ²)	0.13	0.51
Time spent walking (min/day)	0.10	0.60
Time spent standing (min/day)	0.12	0.53
Time spent sitting (min/day)	-0.05	0.81
Time spent lying down (min/day)	-0.24	0.51

r: correlation coefficient.

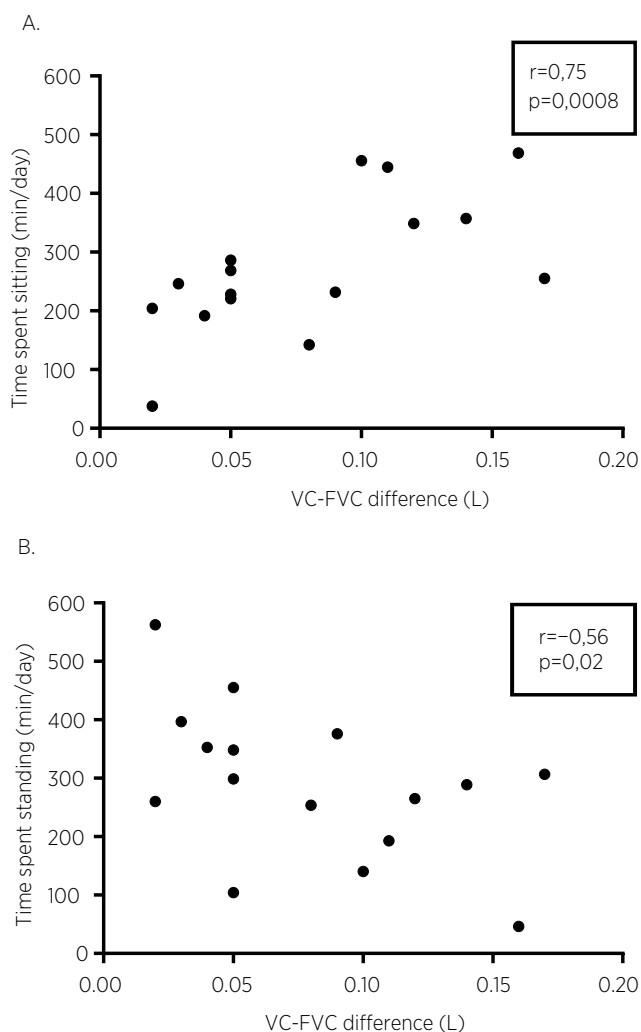


Figure 1. Correlation between the VC-FVC index and time sitting/day (A) and time standing/day (B) in the VC>FVC group

For the other PADL variables, no statistically significant correlations were observed ($p \leq 0.05$ for all).

Regarding the group with $VC \leq FVC$ (less airflow obstruction), one can also only observe a positive correlation between the VC-FVC difference and the time spent standing per day ($r=0.57$, $p=0.07$), as well as a negative one with the time spent lying down ($r=-0.62$, $p=0.04$).

When comparing the PADL variables between the VC>FVC and $VC \leq FVC$ groups, there were no statistically significant differences ($p \leq 0.05$ for all) (Table 1).

DISCUSSION

This study did not observe a correlation between the difference in VC and FVC with the PADL variables in the general group. However, when individuals were separated into two groups: greater air trapping ($CVL > FVC$) and less

trapping ($CVL \leq FVC$), the results revealed a moderate and negative correlation between the greatest obstruction and the activity that requires the greatest energy expenditure (standing), and a moderate and positive correlation with sedentary activity (sitting position). In the group with the lowest obstruction, moderate and positive correlations were observed with activity that requires greater energy expenditure (standing position), and moderate and negative correlations with sedentary activity (lying position). However, there was no statistically significant difference in physical activity or in sedentary behavior between groups.

As far as the authors could verify after a thorough search in the literature, the relationship between the VC-FVC difference and PADL in individuals with COPD had not yet been studied. Therefore, this study is a pioneer in this relationship. Similar studies involving any other population were also not found in the literature.

In the study by Pitta et al.¹⁰, a correlation between pulmonary function and PADL was also observed in patients with COPD, corroborating our findings. However, the correlation found by the authors was weak ($r=0.29$) and the pulmonary function variable studied was FEV_1 , unlike this study. FEV_1 represents only airflow obstruction, while the difference between VC and FVC is also related to air trapping. This fact is explained by the following mechanism: during the VC maneuver there is less compression of the thoracic gases, which allows a greater volume of air to be exhaled; in turn, during the FVC maneuver a great compression of the airways happens and a smaller volume of air is exhaled. In healthy individuals this tendency to collapse is minimized by the alveolar structures; however, in individuals with COPD the alveolar walls are altered, causing the airways to tend to collapse during a forced maneuver, causing air trapping^{12,13}. For this reason, it is plausible to raise the hypothesis this fact explains the greater correlation between the VC-FVC difference and PADL found in this study.

Yuan et al.²⁴ studied the relationship between the VC-FVC difference and exercise tolerance in patients with COPD. This study showed an inverse and significant correlation between VC>FVC and peak VO_2 during a maximum exercise test; in addition, the VC>FVC difference proved to be an independent predictor of exercise capacity in these patients. The authors attributed these results to the fact that VC>FVC suggests airway collapse and air trapping, contributing to the development of dynamic hyperinflation, which would influence a worse performance during exercise. Despite the work of Yuan

et al.²⁴ having included variables in their analyses that differ from those of this study, one can say the results corroborate with each other, considering that exercise capacity is correlated with the PADL in COPD.

Recently, the literature has shown that not only PADL is associated with a worse disease prognosis, but also sedentary behavior^{7,8}. These results indicate there is a relationship between sedentary behavior and air trapping, i.e., the greater the air trapping, the greater the time spent sitting per day.

Regarding the limitations of this study, patients with mild disease (i.e., GOLD I) were not included in the sample. Most were classified as GOLD III (severe disease), which limits the external validity of the results. The difficulty in including patients with mild disease is in the fact they are generally asymptomatic and, thus, hardly seek medical attention, which ends up delaying the diagnosis and limiting participation in research.

The results of this study clarify the relationship between the difference between VC-FVC and PADL in individuals with COPD, which contributes to clinical practice at the time of assessment to track the possibility of physical inactivity in these patients. Thus, a better treatment plan can be designed for those who are sedentary, encouraging physical activity for these patients.

CONCLUSION

The results of this study indicate that individuals with COPD who present greater obstruction to airflow, according to the VC-FVC difference, tend to spend more time in sedentary behavior. VC-FVC correlates moderately with the time spent on these activities and can be used to infer physical inactivity in this population.

REFERENCES

- Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of Chronic Obstructive Pulmonary Disease (2018 report) [Internet]. Fontana: GOLD; 2018 [cited 18 Feb 2020]. Available from: https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf
- Lareau SC, Meek PM, Roos PJ. Development and testing of the modified version of the pulmonary functional status and dyspnea questionnaire (PFSDQ-M). *Heart Lung*. 1998;27(3):159-68. doi: 10.1016/s0147-9563(98)90003-6
- Pitta F, Troosters T, Spruit MA, Probst VS, Decramer M, Gosselink R. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2005;171(9):972-7. doi: 10.1164/rccm.200407-8550C
- Troosters T, Sciurba F, Battaglia S, Langer D, Valluri SR, Martino L, et al. Physical inactivity in patients with COPD, a controlled multi-center pilot-study. *Respir Med*. 2010;104(7):1005-11. doi: 10.1016/j.rmed.2010.01.012
- Pessoa IMBS, Costa D, Velloso M, Mancuzo E, Reis MAS, Parreira VF. Effects of noninvasive ventilation on dynamic hyperinflation of patients with COPD during activities of daily living with upper limbs. *Rev Bras Fisioter*. 2012;16(1):61-7. doi: S1413-35552012000100011
- Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Quantifying physical activity in daily life with questionnaires and motion sensors in COPD. *Eur Respir J*. 2006;27:1040-55. doi: 10.1183/09031936.06.00064105
- Furlanetto KC, Donária L, Schneider LP, Lopes JR, Ribeiro M, Fernandes KB, et al. Sedentary Behavior Is an Independent Predictor of Mortality in Subjects With COPD. *Respir Care*. 2017;62(5):579-87. doi: 10.4187/respcare.05306
- Waschki B, Kirsten A, Holz O, Müller KC, Meyer T, Watz H, Magnussen H. Physical activity is the strongest predictor of all-cause mortality in patients with COPD: a prospective cohort study. *Chest*. 2011;140(2):331-42. doi: 10.1378/chest.10-2521
- Hernandes NA, Teixeira DC, Probst VS, Brunetto AF, Ramo EMC, Pitta F. Perfil do nível de atividade física na vida diária de pacientes portadores de DPOC no Brasil. *J Bras Pneumol*. 2009;35(10):949-56. doi: 10.1590/S1806-37132009001000002
- Pitta F, Takaki MY, Oliveira NH, Sant'anna TJ, Fontana AD, Kovelis D, et al. Relationship between pulmonary function and physical activity in daily life in patients with COPD. *Respir Med*. 2008;102(8):1203-7. doi: 10.1016/j.rmed.2008.03.004
- Vaes AW, Garcia-Aymerich J, Marott JL, Benet M, Groenen MT, Schnohr P, et al. Changes in physical activity and all-cause mortality in COPD. *Eur Respir J*. 2014;44(5):1199-209. doi: 10.1183/09031936.00023214
- Chhabra SK. Forced vital capacity, slow vital capacity, or inspiratory vital capacity: which is the best measure of vital capacity. *J Asthma*. 1998;35(4):361-5. doi: 10.3109/02770909809075669
- Brusasco V, Pellegrino R, Rodarte JR. Vital capacities in acute and chronic airway obstruction: dependence on flow and volum histories. *Eur Respir J*. 1997;10:1316-20. doi: 10.1183/09031936.97.10061316
- Martinez L, Rodrigues D, Donária L, Furlanetto KC, Machado FVC, Schneider LP, et al. Difference Between Slow and Forced Vital Capacity and Its Relationship with Dynamic Hyperinflation in Patients with Chronic Obstructive Pulmonary Disease. *Lung*. 2019;197(1):9-13. doi: 10.1007/s00408-018-0174-y
- Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. ATS/ERS task force. Standardization of lung function testing. *Eur Respir J*. 2005;26(2):319-38. doi: 10.1183/09031936.05.00034805
- Pereira CAC, Sato T, Rodrigues SC. Novos valores de referência para espirometria forçada em brasileiros adultos de raça branca. *J Bras Pneumol*. 2007;33(4):397-406. doi: 10.1590/S1806-37132007000400008

17. Rabinovich RA, Louvaris Z, Raste Y, Langer D, Van Remoortel H, Giavedoni S, et al. Validity of physical activity monitors during daily life in patients with COPD. *Eur Respir J*. 2013;42(5):1205-15. doi: 10.1183/09031936.00134312
18. Van Remoortel H, Raste Y, Louvaris Z, Giavedoni S, Burtin C, Langer D, et al. Validity of six activity monitors in chronic obstructive pulmonary disease: a comparison with indirect calorimetry. *PLoS One*. 2012;7(6):391-8. doi: 10.1371/journal.pone.0039198
19. Black LF, Hyatt RE. Maximal respiratory pressures: normal values and relationship to age and sex. *Am Rev Respir Dis*. 1969;99(5):696-702. doi: 10.1164/arrd.1969.99.5.696
20. Neder JA, Andreoni S, Lerario MC, Nery LE. Reference values for lung function tests. II. Maximal respiratory pressures and voluntary ventilation. *Braz J Med Biol Res*. 1999;32(6):719-27. doi: S0100-879X1999000600007
21. American Thoracic Society. ATS Statement: Guidelines for the Six-Minute Walk Test. *Am J Respir Crit Care Med*. 2002;166(1):111-7. doi: 10.1164/ajrccm.166.1.at1102
22. Britto RR, Probst VS, Andrade AF, Samora GA, Hernandez NA, Marinho PE, et al. Reference equations for the six-minute walk distance based on a Brazilian multicenter study. *Braz J Phys Ther*. 2013;17(6):556-63. doi: 10.1590/S1413-35552012005000122
23. Kovelis D, Segretti NO, Probst VS, Lareau SC, Brunetto AF, Pitta F. Validation of the Modified Pulmonary Functional Status and Dyspnea Questionnaire and the Medical Research Council scale for use in Brazilian patients with chronic obstructive pulmonary disease. *J Bras Pneumol*. 2008;34(12):1008-18. doi: S1806-37132008001200005
24. Yuan W, He X, Xu QF, Wang HY, Casaburi R. Increased difference between slow and forced vital capacity is associated with reduced exercise tolerance in COPD patients. *BMC Pulm Med*. 2014;14:16. doi: 10.1186/1471-2466-14-16