

Functional capacity, health impact, and risk of sarcopenia in individuals with chronic obstructive pulmonary disease.

Janine Bosi Tonel^{1*}, Maitê Mendes Pellenz², Maria Elaine Trevisan³, Ariovaldo Leal Fagundes¹ and Luciane Flores Jacobi⁴

¹Hospital Universitário de Santa Maria, Avenida Roraima, número 1000, Prédio 22, Bairro Camobi, 97105-900, Santa Maria, Rio Grande do Sul, Brazil.

²Universidade Federal de Santa Maria, Santa Maria, Rio Grande do Sul, Brazil. ³Departamento de Fisioterapia, Centro de Ciências da Saúde, Universidade Federal de Santa Maria, Santa Maria, Rio Grande do Sul, Brazil. ⁴Departamento de Estatística do Centro de Ciências Naturais e Exatas, Universidade Federal de Santa Maria, Santa Maria, Rio Grande do Sul, Brazil. *Author for correspondence E-mail: janine.btonel@gmail.com

ABSTRACT. This study aimed to verify the functional capacity of individuals with chronic obstructive pulmonary disease (COPD) and its associated factors. This study is a cross-sectional, observational study with quantitative data analysis. It was performed with patients previously diagnosed with any degree of COPD: I (mild), II (moderate), III (severe), and IV (very severe). Functional capacity was assessed using the six-minute step test (6MST), the risk for sarcopenia was identified using the SARC-F + CC questionnaire, and the clinical impact of COPD was quantified using the COPD Assessment Test (CAT) questionnaire. Moreover, primary data were collected from the patients to identify associated factors. The results of the 37 patients evaluated (59.5% female; 81.1% elderly), 30 (81.1%) had reduced functional capacity. Out of these, 53.3% were at risk for sarcopenia and 93.3 % were somehow clinically impacted by COPD. Their impact was classified into mild to moderate (53.3%) and severe and very severe (40%). Furthermore, most patients (60%) had a recent diagnosis and almost all of them (96.7%) were smokers or former smokers. In conclusion, most patients had reduced functional capacity which was significantly associated with dyspnea and risk of sarcopenia.

Keywords: Chronic disease; exercise; dyspnea; respiratory system.

Received on November 7, 2023.

Accepted on March 18, 2025.

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the three main causes of death worldwide, seen in considerable numbers in emergencies and hospital admissions. Studies have also shown that its morbidity is associated with age and the development of other comorbidities (GOLD, 2022). It is characterized by airflow limitation due to changes in the airways and/or lung parenchyma, and its main symptoms are dyspnea and chronic cough, while its main cause is smoking (GOLD, 2022). Moreover, it has significant extrapulmonary effects that can contribute to its severity and the increase in mortality rates (Spruit et al., 2017; Park et al., 2019; Machado et al., 2020).

Functional capacity changes as a of COPD, resulting from a systemic inflammatory process caused by the disease. Among these changes are the dysfunction of ventilatory and peripheral skeletal muscles, a direct relationship with osteoporosis, and exercise intolerance, which together promote a reduction in the quality of life of individuals affected by the disease (Dourado et al., 2006; Yoshimura et al. 2017).

A crucial alteration for understanding COPD and its relationship with functional capacity is that, in these patients, there is a change in the diaphragmatic muscles, with an increase in type I fibers and a decrease in type 2 fibers. These adaptations in the face of the disease promote a reduction in strength and muscular endurance, when compared to healthy individuals (Dourado et al., 2006).

Functional capacity is defined as resistance to physical exercise (Dourado et al., 2006) and, in addition to being altered by COPD, it is also affected by sarcopenia. Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength and is present in 15% of the population diagnosed with COPD, affecting even more the daily activities of these patients (Jones et al., 2015; Byun et al., 2017; Cruz-Jentoft et al., 2018; Sepúlveda-Loyola et al., 2020; GOLD, 2022).

Therefore, this study aimed to verify the functional capacity of individuals with chronic obstructive pulmonary disease and the associated factors in patients followed up at a pulmonology outpatient clinic of a University Hospital in the southern region of Brazil.

Materials and methods

This is an observational, cross-sectional study with quantitative data analysis carried out with patients previously diagnosed with COPD and treated at a pulmonology outpatient clinic of a university hospital in the southern region of Brazil, which is certified as an educational institution (Castro et al., 2021). The study included adults of both sexes who had a clinical and spirometric diagnosis of COPD at any severity degree and were clinically stable.

Patients who had a history of COPD exacerbation at the time of evaluation or in the three previous months; had another pulmonary disease; had decompensated cardiovascular diseases; had neuromuscular and orthopedic diseases that prevented the evaluations; performed strenuous activities in the 12 hours previous to the study procedures; were feverish and/or in a flu-like state on the day of the evaluation; had peripheral oxygen saturation lower than or equal to 90% at the time of the evaluation; or were unable to understand and perform the activities proposed by the study, were excluded.

Eligible individuals were evaluated from March 2021 to January 2022. Collections were performed via electronic medical records, and primary data were collected directly from the research participants.

Based on the results of spirometry, previously collected from the patients' electronic medical records, they were classified according to their COPD severity using the GOLD criteria (2022) as follows: mild (GOLD I), $FEV_1 \geq 80\%$ predicted; moderate (GOLD II), $50.0\% \leq FEV_1 < 80.0\%$ predicted; severe (GOLD III), $30\% \leq FEV_1 < 50\%$ predicted; and very severe (GOLD IV), $FEV_1 < 30\%$ predicted.

Primary data were collected through an evaluation form that included gender, age, body mass index (BMI), measurement of waist circumference (Arcuri et al., 2015), vital signs, time of diagnosis, lifestyle habits such as smoking, and associated comorbidities. The sensation of dyspnea was evaluated by the modified Medical Research Council (mMRC) scale (Kovelis et al., 2008).

Functional capacity was assessed using the six-minute step test (6MST), which is a tolerable and reproducible test to evaluate individuals with COPD (Ribeiro et al., 2022). The 6MST was performed using a 20-cm-high step with a non-slip rubber surface for patient safety, following the principles of the American Thoracic Society's six-minute walk test (6MWT) (American Thoracic Society [ATS], 2002).

Patients were instructed to step up and down the step as quickly as possible for six minutes, aiming at the maximum number of repetitions. They should be able to alternate the lower limbs while their upper limbs remained at rest along the body. Before starting the test, the patients were asked about the sensation of dyspnea and the perception of tiredness, both evaluated by the BORG Scale (Borg, 1982). Their heart rate (HR) and peripheral oxygen saturation (SpO_2) were verified using a portable digital oximeter (G-TECH LED®, São Paulo, Brazil).

During the test, this evaluation was repeated every two minutes and in the first and fifth minutes of recovery after the test was performed. The number of steps climbed in six minutes was recorded and expressed as a numeral and percentage of the predicted value. Based on Arcuri's equation (Kovelis et al., 2008), (Equations 1) and (Equations 2) were used for male and female patients, respectively.

$$6MST_M = 263.17 - 0.876I - 0.585WC \quad (1)$$

$$6MST_F = 222.09 - 0.876I - 0.585WC \quad (2)$$

Where: $6MST_M$ = Six-Minute Walk Test for Males; $6MST_F$ = Six-Minute Walk Test for Females; I = Age (in years); WC = Waist Circumference (in centimeters)

From the predicted value resulting from the equations, it could be inferred that individuals who climbed the step thirty times less than the predicted value in the 6MST presented reduced functional capacity (Kovelis et al., 2008). The *Simple questionnaire to rapidly diagnose sarcopenia and calf circumference* (SARC-F + CC) (Barbosa-Silva et al., 2016), composed of closed questions and applied directly to the individuals participating in the research, was used to assess sarcopenia. In addition to measuring calf circumference in centimeters, this questionnaire evaluates five components: muscle strength; the need for assistance to walk; the ability to get up from a chair; the ability to climb stairs; and the frequency of falls. Each item is given a score from 0 to 2 points, and their sum may reach 0 to 10 points. Calf circumference scores from 0 to 10. Scores greater than or equal to 11 in this questionnaire are suggestive of sarcopenia (Malmstrom et al., 2013; Barbosa-Silva et al. 2016).

To assess the impact of COPD symptoms on the well-being of individuals with this disease, the *COPD Assessment Test* (CAT) was used, which is a simple instrument used to quantify the clinical impact of COPD

and to help in the assessment of the patients' health status (Silva et al., 2013; Ferrari et al., 2016). The CAT instrument is a questionnaire composed of eight items: cough, phlegm, chest tightness, shortness of breath, limitation in household activities, confidence in leaving home, sleep, and energy. For each item, the patient may choose only one answer, whose score varies from 0 to 5. At the end of the test, the scores of all answers are added, and the results vary according to the range of scores obtained. The clinical impact is then classified into mild, 6 to 10 points; moderate, 11 to 20 points; severe, 21 to 30 points; and very severe, 31 to 40 points (Silva et al., 2013).

This study protocol was approved by the Human Research Ethics Committee of a public higher education institution under CAEE protocol number 43018821.9.0000.5346, following the guidelines of Resolution No. 466/12 by the Brazilian National Health Council (CNS). All participants signed a written informed consent form.

Data analysis was performed using the Statistica software, and p-values lower than 0.05 were considered significant. A simple crossing of qualitative variables was performed and their association with reduced functional capacity was verified by Fisher's exact test or by the G test. These tests were used because the sample size was small due to the fact that consultations in the pneumology outpatient department decreased by approximately 45% during the pandemic period.

Results and discussion

A total of 37 patients were evaluated. Most of the participants were female (59.5%) and elderly (81.1%, ≥ 60 years), had normal BMI weight (48.6%), and were former smokers (54.1%). The only variable that was significantly associated with reduced functional capacity was dyspnea. Other characteristics that could be associated or not with reduced functional capacity are presented in (Table 1).

Table 1. Characterization of the sample in relation to reduced functional capacity.

Characteristics	Total sample n(%)	Reduced functional capacity		p-value
		Yes n(%)	No n(%)	
Gender				
Female	22 (59.5)	18 (60.0)	4 (57.1)	0.9994†
Male	15 (40.5)	12 (40.0)	3 (42.9)	
Age group				
≤60 years	7 (18.9)	6 (20.0)	1 (14.3)	1.0000†
>60 years	30 (81.1)	24 (80.0)	6 (85.7)	
BMI				
Underweight	5 (13.5)	5 (16.7)	0 (0.0)	0.2321††
Normal	18 (48.6)	15 (50.0)	3 (42.9)	
Overweight	14 (37.8)	10 (33.3)	4 (57.1)	
Diagnosis time				
≤5 years	23 (62.2)	18 (60.0)	5 (71.4)	0.6869†
>5 years	14 (37.8)	12 (40.0)	2 (28.6)	
Smoker				
Yes	16 (43.2)	11 (36.7)	5 (71.4)	0.2214††
No	1 (2.7)	1 (3.3)	0 (0.0)	
Former smoker	20 (54.1)	18 (60.0)	2 (28.6)	
Dyspnea (MRC)				
0	4 (10.8)	1 (3.3)	3 (42.8)	0.0267††
1	11 (29.7)	9 (30.0)	2 (28.6)	
2	2 (5.4)	1 (3.3)	1 (14.3)	
3	6 (16.2)	6 (20.0)	0 (0.0)	
4	14 (37.8)	13 (43.3)	1 (14.3)	
GOLD*				
1	7 (18.9)	4 (13.3)	3 (42.9)	0.2254††
2	12 (32.4)	10 (33.3)	2 (28.6)	
3	13 (35.1)	11 (36.7)	2 (28.6)	
4	5 (13.5)	5 (16.7)	0 (0.0)	

†Fisher's Exact Test. ††G Test. * GOLD = Global Initiative for Chronic Obstructive Lung Disease [GOLD]. BMI = body mass index. MRC = Medical Research Council. Significant association statistical (p<0.05).

The categorization of COPD according to airflow limitation and clinical parameters is shown in (Figure 1). Most patients were classified into GOLD groups 2B and 3B.

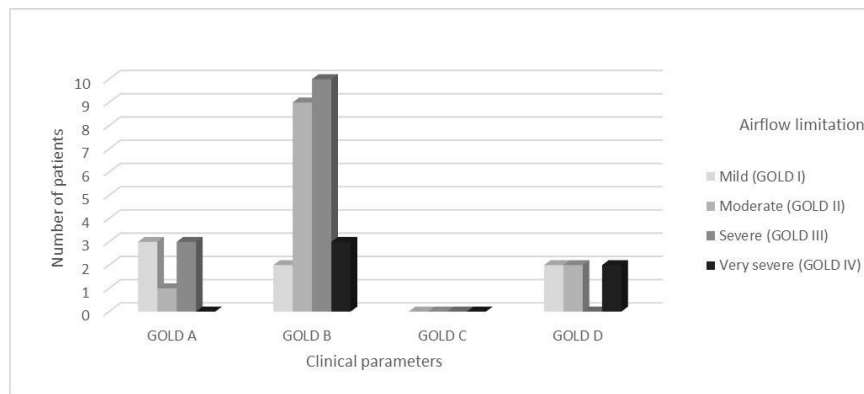


Figure 1. Sample categorization according to airflow limitation and clinical parameters established by the GOLD criteria.

Functional capacity, the main data examined in this study, presented surprising and worrisome results: 81% of the patients evaluated had reduced functional capacity. Also, individuals with reduced functional capacity had a mean percentage predicted approximately 50% lower than those with preserved functional capacity. These data are presented in (Figure 2).

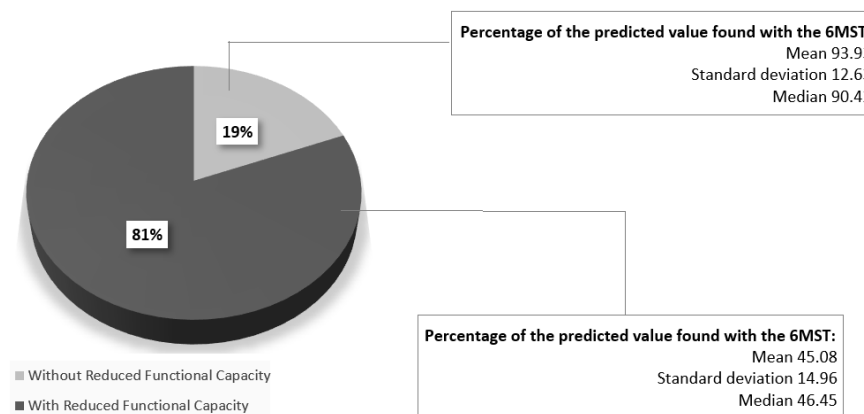


Figure 2. Functional capacity according to the six-minute step test (6MST).

The relationship between functional capacity, risk of sarcopenia, and clinical impact of COPD is shown in (Table 2). A significant association can be observed between reduced functional capacity and sarcopenia ($p < 0.05$).

Table 2. Relationship between functional capacity, risk of sarcopenia, and clinical impact of COPD.

Parameters	Reduced functional capacity		p-value
	Yes n (%)	No n (%)	
Sarcopenia (SARC-F + CC)			
Positive for sarcopenia	16 (53.3)	0 (0.0)	0.0124 [†]
Negative for sarcopenia	14 (46.7)	7 (100.0)	
Clinical impact (CAT)			
None	2 (6.7)	3 (42.9)	0.0627 ^{††}
Mild or moderate	16 (53.3)	3 (42.9)	
Severe or very severe	12 (40.0)	1 (14.3)	

[†]Fisher's Exact Test. ^{††}G Test. SARC-F + CC = Simple questionnaire to rapidly diagnose sarcopenia and calf circumference. CAT = COPD Assessment Test. Significant association statistical ($p < 0.05$).

It is known that COPD has a great effect on exercise tolerance. Patients usually present dyspnea and consequent fatigue after performing activities, even if simple ones (GOLD, 2022). In this study, 43% of patients with reduced functional capacity had a high score on the mMRC scale, reporting that they do not leave their homes due to dyspnea. This finding is explained by the low efficiency of gas exchange, which is associated with greater airway resistance that leads to air trapping in patients with COPD (Neder et al., 2021). As a way of minimizing these symptoms, a study showed that training the upper limbs with breathing exercises improved lung function, functional capacity, and quality of life in COPD patients (Tarigan et al., 2019).

This study showed that most of the patients have moderate to severe COPD, that is, their signs and symptoms are more intense. Dransfield et al. (2019), in a study on the eradication of COPD, discuss strategies to early diagnose the disease so that it does not worsen. The authors also report that the diagnosis of COPD is currently made only after the symptomatic, clinical, and functional worsening of these patients, which may explain the greater number of individuals with more severe degrees of the disease.

The results of this study show that almost all individuals with reduced functional capacity are or were smokers (96.7%). Smoking is the main etiology of COPD (Agusti et al., 2020), even though environmental pollution, occupational exposure, and passive smoking may also be causal factors that trigger the disease (Lopez-Campos et al., 2016). Thus, it is important that the risk factors of COPD are reduced and that its diagnosis and treatment are early in order to reduce the impact on health and to improve prevention, treatment, and prognosis (Agusti et al., 2020).

Reduced functional capacity, the main outcome investigated, was seen in almost all the individuals with COPD included in this study, being significantly associated with dyspnea and sarcopenia. Dyspnea reduces exercise tolerance and, together with sarcopenia, which is responsible for reducing lean mass and respiratory and peripheral muscle strength, increases energy expenditure. In turn, these individuals remain seated for longer periods and, consequently, present lower functional performance, which makes them less physically capable (Mansour et al., 2019).

Kanezaki et al. (2021) carried out a study to identify the effects of sarcopenia on ventilatory musculature in patients with COPD. It was found that patients with sarcopenia had lower tidal volume, higher respiratory rate and greater ventilatory discomfort in the Step Test, as well as increased ventilatory effort in the Walk Test. Concluding that sarcopenia significantly interferes with the sensation of dyspnea and fatigue in patients with COPD.

The sensation of dyspnea leads to a reduction in the activities of daily living of individuals with COPD, as a result of which there is a reduction in mass and progressive muscle strength, which, in turn, further reduces the physical capacity of these individuals. These routine changes can bring on symptoms of anxiety and depression. All biopsychological manifestations can exacerbate the sensation of dyspnea, increasing the severity of the disease and maintaining quality of life (O'Donnell et al., 2020).

In this study, 93.3% of individuals with reduced functional capacity were clinically impacted by COPD, be it related to respiratory changes, difficulty in performing activities of daily living (ADLs), or lack of sleep or energy in everyday life. Despite not being directly investigated in the present study, respiratory changes can also lead to changes in cognitive, emotional, and behavioral responses that have a direct impact on the functional capacity of these individuals (Schuler et al., 2018; GOLD, 2022).

This study was limited by the small number of participants, which can be explained by the fact that the collection period was in its entirety during the pandemic (COVID-19), when outpatient consultations were reduced. This reduced sample number may explain the study's few associations.

Conclusion

In conclusion, most patients had reduced functional capacity, which was significantly associated with dyspnea and the risk of sarcopenia. The importance of early diagnosis is also highlighted in order not to worsen the pulmonary disease.

References

- Agusti, A., Alcazar, B., Cosio, B., Echave, J. M., Faner, R., Izquierdo, J. L., Marin, J. M., Soler-Cataluña, J. J., & Celli, B. (2020). Time for a change: anticipating the diagnosis and treatment of COPD. *European Respiratory Journal*, 56(1), 2002104. <https://doi.org/10.1183/13993003.02104-2020>
- American Thoracic Society [ATS]. (2002). ATS Statement: Guidelines for the Six-Minute Walk Test. *American Journal of Respiratory and Critical Care Medicine*, 166(1), 111–117. <https://doi.org/10.1164/ajrccm.166.1.at1102>
- Arcuri, J. F., Borghi-Silva, A., Labadessa, I. G., Sentanin, A. C., Candolo, C., & Pires Di Lorenzo, V. A. (2016). Validity and Reliability of the 6-Minute Step Test in Healthy Individuals. *Clinical Journal of Sport Medicine*, 26(1), 69–75. <https://doi.org/10.1097/jsm.0000000000000190>
- Barbosa-Silva, T. G., Menezes, A. M. B., Bielemann, R. M., Malmstrom, T. K., Gonzalez, M. C., & Grupo de Estudos em Composição Corporal e Nutrição (COCONUT). (2016). Enhancing SARC-F: Improving

- Sarcopenia Screening in the Clinical Practice. *Journal of the American Medical Directors Association*, 17(12), 1136–1141. <https://doi.org/10.1016/j.jamda.2016.08.004>
- BORG, G. A. V. (1982). Psychophysical bases of perceived exertion. *Medicine & Science in Sports & Exercise*, 14(5), 377–381. <https://doi.org/10.1249/00005768-198205000-00012>
- Byun, M. K., Cho, E. N., Chang, J., Ahn, C. M., & Kim, H. J. (2017). Sarcopenia correlates with systemic inflammation in COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, 12, 669–675. <https://doi.org/10.2147/copd.s130790>
- Castro, F. C. M., Jobim, F. C., & Jacobi, L. F. (2021). Analysis of the waiting time of the diagnosis for the first breast cancer treatment in southern Brazil. *Women & Health*, 61(6), 542–549. <https://doi.org/10.1080/03630242.2021.1927285>
- Cruz-Jentoft, A. J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., Cooper, C., Landi, F., Rolland, Y., Sayer, A. A., Schneider, S. M., Sieber, C. C., Topinkova, E., Vandewoude, M., Visser, M., & Zamboni, M. (2018). Sarcopenia: revised European consensus on definition and diagnosis. *Age and Ageing*, 48(1), 16–31. <https://doi.org/10.1093/ageing/afy169>
- Dourado, V. Z., Tanni, S. E., Vale, S. A., Faganello, M. M., Sanchez, F. F., & Godoy, I. (2006). Manifestações sistêmicas na doença pulmonar obstrutiva crônica. *Jornal Brasileiro de Pneumologia*, 32(2), 161–171. <https://doi.org/10.1590/s1806-37132006000200012>
- Dransfield, M., Stolz, D., & Kleinert, S. (2019). Towards eradication of chronic obstructive pulmonary disease: a Lancet Commission. *The Lancet*, 393(10183), 1786–1788. [https://doi.org/10.1016/s0140-6736\(19\)30950-x](https://doi.org/10.1016/s0140-6736(19)30950-x)
- Ferrari, R., Coneglian, L. B., & Godoy, I. (2016). Diagnóstico e classificação da DPOC – Quais foram as últimas mudanças do GOLD? *Pneumologia Paulista*, 29(3), 14–18.
- Global Initiative for Chronic Obstructive Lung Disease [GOLD]. (2022). *Global strategy for the diagnosis, management, and prevention of COPD report*. Retrieved from https://goldcopd.org/wp-content/uploads/2021/12/GOLD-REPORT-2022-v1.1-22Nov2021_WMV.pdf
- Jones, S. E., Maddocks, M., Kon, S. S. C., Canavan, J. L., Nolan, C. M., Clark, A. L., Polkey, M. I., & Man, W. D.-C. (2015). Sarcopenia in COPD: prevalence, clinical correlates and response to pulmonary rehabilitation. *Thorax*, 70(3), 213–218. <https://doi.org/10.1136/thoraxjnl-2014-206440>
- Kanezaki, M., Terada, K., Tanabe, N., Shima, H., Hamakawa, Y., & Sato, S. (2021). Effects of Sarcopenia on Ventilatory Behavior and the Multidimensional Nature of Dyspnea in Patients with Chronic Obstructive Pulmonary Disease. *Journal of the American Medical Directors Association*, 22(4), 827–833. ¹ <https://doi.org/10.1016/j.jamda.2021.01.081>
- Kovelis, D., Segretti, N. O., Probst, V. S., Lareau, S. C., Brunetto, A. F., & Pitta, F. (2008). Validação do Modified Pulmonary Functional Status and Dyspnea Questionnaire e da escala do Medical Research Council para o uso em pacientes com doença pulmonar obstrutiva crônica no Brasil. *Jornal Brasileiro de Pneumologia*, 34(12), 1008–1018. <https://doi.org/10.1590/s1806-37132008001200005>
- Lopez-Campos, J. L., Márquez-Martín, E., & Soriano, J. B. (2016). The role of air pollution in COPD and implications for therapy. *Expert Review of Respiratory Medicine*, 10(8), 849–859. <https://doi.org/10.1080/17476348.2016.1191356>
- Machado, A., Marques, A., & Burtin, C. (2020). Extra-pulmonary manifestations of COPD and the role of pulmonary rehabilitation: a symptom-centered approach. *Expert Review of Respiratory Medicine*, 15(1). <https://doi.org/10.1080/17476348.2021.1854737>
- Malmstrom, T. K., & Morley, J. E. (2013). SARC-F: A Simple Questionnaire to Rapidly Diagnose Sarcopenia. *Journal of the American Medical Directors Association*, 14(8), 531–532. <https://doi.org/10.1016/j.jamda.2013.05.018>
- Mansour, K. M. K., Goulart, C. da L., Carvalho-Junior, L. C. S. de, Trimer, R., Borghi-Silva, A., & Silva, A. L. G. da. (2019). Pontos de corte da função pulmonar e capacidade funcional determinantes para sarcopenia e dinapenia em pacientes com DPOC. *Jornal Brasileiro de Pneumologia*, 45(6). <https://doi.org/10.1590/1806-3713/e20180252>
- Neder, J. A., de Torres, J. P., & O'Donnell, D. E. (2021). Recent Advances in the Physiological Assessment of Dyspneic Patients with Mild COPD. *COPD: Journal of Chronic Obstructive Pulmonary Disease*, 18(3), 374–384. <https://doi.org/10.1080/15412555.2021.1913110>

- O'Donnell, D. E., Milne, K. M., James, M. D., de Torres, J. P., & Neder, J. A. (2019). Dyspnea in COPD: New Mechanistic Insights and Management Implications. *Advances in Therapy*, 37(1), 41–60. <https://doi.org/10.1007/s12325-019-01128-9>
- Park, H. Y., Kang, D., Lee, S., Shin, S. H., Kang, M. S., Kong, S., Kook, C. R., Cho, J., & Yoo, K. W. (2019). Impact of chronic obstructive pulmonary disease on mortality: A large national cohort study. *Respirology*, 25(7), 726–734. <https://doi.org/10.1111/resp.13678>
- Ribeiro, D. B., Terrazas, A. C., & Yamaguti, W. P. (2022). The Six-Minute Stepper Test Is Valid to Evaluate Functional Capacity in Hospitalized Patients with Exacerbated COPD. *Frontiers in Physiology*, 13. <https://doi.org/10.3389/fphys.2022.853434>
- Schuler, M., Wittmann, M., Faller, H., & Schultz, K. (2018). The interrelations among aspects of dyspnea and symptoms of depression in COPD patients – a network analysis. *Journal of Affective Disorders*, 240, 33–40. <https://doi.org/10.1016/j.jad.2018.07.021>
- Sepúlveda-Loyola, W., Osadnik, C., Phu, S., Morita, A. A., Duque, G., & Probst, V. S. (2020). Diagnosis, prevalence, and clinical impact of sarcopenia in COPD: a systematic review and meta-analysis. *Journal of Cachexia, Sarcopenia and Muscle*, 11(5), 1164–1176. <https://doi.org/10.1002/jcsm.12600>
- Silva, G. P. F. da, Morano, M. T. A. P., Viana, C. M. S., Magalhaes, C. B. de A., & Pereira, E. D. B. (2013). Portuguese-language version of the COPD Assessment Test: validation for use in Brazil. *Jornal Brasileiro de Pneumologia*, 39(4), 402–408. <https://doi.org/10.1590/s1806-37132013000400002>
- Spruit, M. A., Vercoulen, J. H., Sprangers, M. A. G., & Wouters, E. F. M. (2017). Fatigue in COPD: an important yet ignored symptom. *The Lancet Respiratory Medicine*, 5(7), 542–544. [https://doi.org/10.1016/s2213-2600\(17\)30158-3](https://doi.org/10.1016/s2213-2600(17)30158-3)
- Tarigan, A. P., Ananda, F. R., Pandia, P., Sinaga, B. Y., Maryaningsih, M., & Anggriani, A. (2019). The Impact of Upper Limb Training with Breathing Maneuver in Lung Function, Functional Capacity, Dyspnea Scale, and Quality of Life in Patient with Stable Chronic Obstructive of Lung Disease. *Open Access Macedonian Journal of Medical Sciences*, 7(4), 567–572. <https://doi.org/10.3889/oamjms.2019.113>
- Yoshimura, K., Sato, S., Muro, S., Yamada, M., Hasegawa, K., Kiyokawa, H., Mishima, M., & Aoyama, T. (2017). Interdependence of physical inactivity, loss of muscle mass and low dietary intake: Extrapulmonary manifestations in older chronic obstructive pulmonary disease patients. *Geriatrics & Gerontology International*, 18(1), 88–94. <https://doi.org/10.1111/ggi.13146>