ISSN: 2577 - 8005

Research Article

Medical & Clinical Research

Impact of Chronic Obstructive Pulmonary Disease on the Quadriceps

Amine Meridj*, Redouan Belala, Khaled Tlili and Yacine Djeghri

University Constantine 3, Algéria

***Corresponding Author**

A. Meridj, Pulmonology Service, Constantine Regional Military University Hospital, Algéria.

Submitted: 20 Jan 2025; **Accepted**: 29 Jan 2025; **Published**: 25 Feb 2025

Citation: Meridj, A., Belala, R., Tlili, K., & Djeghri, Y. (2025). Impact of Chronic Obstructive Pulmonary Disease on the Quadriceps. *Med Clin Res, 10*(2), 01-04.

Summary

COPD is à major public health challenge and major source of chronic disease and death across the globe. Estimating the prevalence of COPD is complex, as it requires cohorts of patients representative of the population using spirometric measurements.

COPD is associated with many comorbidities, including lung cancer, cardiovascular disease, osteoporosis, cachexia and muscle weakness are the most serious and common. COPD is à known complication of peripheral muscle dysfunction, which is associated with exercise intolerance and a darker prognosis. It is interesting to evaluate the peripheral muscle integrity in patients with COPD.

Usually, the doctors pulmonologists who manage patients with COPD, neglect the comorbidities and especially the muscular damage often associated with this systemic pathology. Despite the fact that the recommendations of the learned societies continue to encourage research and management of all comorbidities associated with COPD the efforts of treating physicians should not only focus on the medical treatment of COPD patients. But they should also look into all comorbidities and try to assess the overall impact of COPD on body musculature. Comparing different muscle groups and studying the potential benefits of targeted muscle rehabilitation. This could include specific exercises to strengthen not only the respiratory muscles (diaphragm), but also locomotor muscles such as the quadriceps.

Keywords: COPD, Public health, Chronic disease, Smoking, Systemic inflammation, Chronic obstructive pulmonary disease

1. Introduction

COPD is a major public health challenge and a major source of chronic disease and death across the globe. The estimation of the prevalence of COPD is complex, as it requires cohorts of patient's representative of the population using spirometric measurements [1]. There is a wide geographic disparity in the prevalence of COPD [2]. This situation can be explained by the disparities between survey methods, diagnostic criteria, and target populations.

Over the next 30 years, the prevalence of smoking in developing countries and population aging in developed countries will lead to an increase in COPD prevalence [3]. The prevalence of COPD is estimated at 4.5 million deaths per year by 2030 [3].

COPD is associated with many comorbidities, including lung cancer, cardiovascular disease, and osteoporosis. Cachexia and muscle weakness are the most serious and common [4]. Locomotor muscle dysfunction is a major systemic manifestation of chronic obstructive pulmonary disease. Muscle weakness has many causes, the most important being physical inactivity [5] and systemic inflammation [6]. Systemic corticosteroid treatment, hypoxemia, hypercapnia, undernutrition, electrolyte disorders, heart failure, and hypogonadism are also implicated [7].

Depending on the severity of the disease and the population studied, it is estimated that 4 to 35% of COPD patients experience a decrease in muscle mass [8, 9]. A recent study found that 32% of patients with COPD had lower than normal quadriceps strength. About 25% of patients in stage GOLD I and II and 38% of patients in stage GOLD IV had muscle weakness [10].

This muscle weakness has several serious effects, including

intolerance to exercise [11, 12], reduced quality of life, and increased mortality [13]. In patients with a significant decrease in airflow, the decrease in the transverse area of the mid-thigh is associated with a relative risk of mortality 13 times higher than that observed in patients with good muscle mass [14].

Although atrophy can affect all types of quadriceps fibers [15], type IIx fibers appear to be the most affected [16]. This phenomenon can occur even in the absence of severe airflow obstruction [10].
The balance between hypertrophy and atrophy in the quadriceps of COPD patients involves signaling pathways similar to those observed in the diaphragm. In addition, physical activity may cause quadriceps hypertrophy in these patients by increasing IGF-1 mRNA expression [17]. Increased apoptosis was noted in the quadriceps of patients with a reduced body mass index [18], suggesting a potential involvement of this normal cellular process in muscle atrophy. Although the idea of a role for apoptosis in skeletal muscle atrophy is attractive in itself, there is no consensus that apoptosis plays a role in the development of muscular dysfunction in COPD.

Compared to healthy controls, the proportion of oxidative type I fibers decreases, while that of glycolytic type II fibers increases in patients with COPD [15, 19, 20]. This is distinct from normal aging, which is associated with a decrease in type II fibers [21]. The proportion of type I fibers is negatively correlated with disease severity [15, 19].

The typographical changes in muscle fibers observed in the quadriceps do not affect muscles of the upper limbs, such as the biceps and deltoid [22, 23]. The idea that only some peripheral muscles have variations in the percentage of fiber types suggests that local factors (inflammation, oxidative stress, etc.) are responsible for these variations.

Regarding contractility, patients with COPD have a decrease in muscle strength due to quadriceps atrophy and decreased muscle fiber size [11, 24, 25]. In these patients, the decrease in quadriceps strength is proportional to muscle mass, suggesting that the contractile device has been preserved [23]. In addition, in vitro experiments on the contractility of isolated quadriceps muscle bundles from COPD patients and healthy controls confirm this hypothesis [26].

Muscle capillaries, essential for oxygen transport, allow a homogeneous distribution in the muscle tissue, thus optimizing the use of oxygen by cellular components, including mitochondria, and maximizing muscle performance. A reduction in capillarization, resulting in insufficient oxygen transport, is considered to be a contributing factor to stress intolerance in COPD. Decreased capillary contact with oxidative fibers type I and IIa was observed in the context of COPD [15].

Vascular endothelium growth factors play a crucial role in angiogenesis, and Barreiro et al. [27] showed that the levels of these factors are reduced in the quadriceps muscles of COPD patients compared to healthy controls.

In addition, Gosker et al. [28] reported a decrease in mitochondrial density in the lateral broad muscle of COPD patients compared to controls, while Picard et al. [29] noted the retention of respiratory function in individual mitochondria. However, the latter produce more oxidative stress than the controls [29, 30]. An increase in reactive oxygen species may promote the degradation of muscle proteins via the ubiquitin-proteasome pathway [31, 32].

Finally, concerning the changes in energy metabolism at the quadriceps level in COPD, several studies noted a decrease in oxidative enzymes (3-hydroxyacyl-CoA dehydrogenase, citrate synthase) [33-35] and the enzyme ratio of oxidative to glycolytic enzymes [34]. Reduced physical activity was also observed, even in COPD patients at stage I of the GOLD classification [36].

Muscle mass can be measured using different imaging methods: computed tomography (CT), magnetic resonance imaging (MRI), and dual-energy X-ray absorptiometry (DEXA). Previous research has suggested that CT, MRI, and DEXA could all identify changes in the muscle mass of the lower limbs after training [11, 37, 38].

However, the equipment required for these measurements is large and expensive. It may require special expertise to interpret images, and in the case of CT and DEXA, subjects are sensitive to ionizing radiation. The value of these imaging methods as a measure of results, when repeated testing is involved, is therefore limited. Ultrasound is an imaging method that assesses the thickness and transverse areas of superficial muscles such as the rectus femoris.
Chronic obstructive pulmonary disease (COPD) is associated with numerous comorbidities, including muscle involvement, which consists of changes in the structure and function of peripheral and respiratory muscles. Ultrasound can provide a non-invasive assessment of muscle damage [39]. It has the advantage of being portable and contains no ionizing radiation. The reliability of this method for measuring healthy quadriceps size has been confirmed by numerous studies [40, 41], but data is limited to COPD. Many studies have confirmed that ultrasound is a reliable method for measuring quadriceps muscle size [40-42]. This technique allows for precise visualization and measurement of the different muscles constituting the quadriceps (rectus femoris, vastus medialis, vastus lateralis, and vastus intermedius). It is assumed that in the future, the use of ultrasound for diaphragmatic and quadriceps assessment by pulmonologists, intensivists, and rehabilitation doctors will be widespread and will have new applications in the diagnosis and follow-up of patients with COPD [43].

2. Conclusion

Quadriceps weakness and fatigue are the most important disabling symptom in many patients with COPD and have a significant impact on their quality of life. In addition, systemic factors such as inflammation, oxidative stress, corticosteroid use, hormonal disturbances and nutritional deficits are involved in the

development of muscle weakness.

The doctors in charge of the management of patients with COPD should not be associated with a major extra-pulmonary manifestation of chronic respiratory diseases (Quadriceps atrophy). Several methods are available to doctors to assess the mass Skeletal muscle in COPD, such as bioelectrical impedance, dual energy X-ray absorptiometry (D-XA) and imaging technologies such as ultrasound, computed tomography, magnetic imaging and spectroscopy Unlike other more invasive methods, ultrasound allows for a real-time and repeated evaluation without risk to the patient, while providing remarkable accuracy in measuring the thickness and kinetics of the quadriceps.

In addition, the quadriceps ultrasound is a relatively simple examination to perform and its increasing accessibility, particularly with the use of wearable devices, allows its integration into daily clinical practice. Eventually, it could become a standardized tool in the assessment of patients with COPD, not only to assess the severity of the disease but also to monitor the evolution of respiratory function over time.

References

1. Chabot, F., Zysman, M., Guillaumot, A., Gomez, E., Kheir, A., & Chaouat, A. (2019). La bronchopneumopathie chronique obstructive. *Bulletin de l'Académie Nationale de Médecine, 203*(1–2), 63–71.
2. Raherison, C., & Girodet, P. (2009). Epidemiology of COPD. *European Respiratory Review, 18*(114), 213–221.
3. Halpin, D., Celli, B., Criner, G., Frith, P., Varela, L., Salvi, S., et al. (2019). The GOLD summit on chronic obstructive pulmonary disease in low-and middle-income countries. *The International Journal of Tuberculosis and Lung Disease, 23*(11), 1131–1141.
4. Decramer, M., & Janssens, W. (2013). Chronic obstructive pulmonary disease and comorbidities. *The Lancet Respiratory Medicine, 1*(1), 73–83.
5. Waschki, B., Kirsten, A., Holz, O., Müller, K.-C., Meyer, T., Watz, H., et al. (2011). Physical activity is the strongest predictor of all-cause mortality in patients with COPD: A prospective cohort study. *Chest, 140*(2), 331–342.
6. Spruit, M. A., Gosselink, R., Troosters, T., Kasran, A., Gayan-Ramirez, G., Bogaerts, P., et al. (2003). Muscle force during an acute exacerbation in hospitalised patients with COPD and its relationship with CXCL8 and IGF-I. *Thorax, 58*(9), 752–756.
7. Van Vliet, M., Spruit, M. A., Verleden, G., Kasran, A., Van Herck, E., Pitta, F., et al. (2005). Hypogonadism, quadriceps weakness, and exercise intolerance in chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine, 172*(9), 1105–1111.
8. Coronell, C., Orozco-Levi, M., Mendez, R., Ramírez-Sarmiento, A., Galdiz, J., & Gea, J. (2004). Relevance of assessing quadriceps endurance in patients with COPD. *European Respiratory Journal, 24*(1), 129–136.
9. Vestbo, J., Prescott, E., Almdal, T., Dahl, M., Nordestgaard, B. G., Andersen, T., et al. (2006). Body mass, fat-free body mass, and prognosis in patients with chronic obstructive pulmonary disease from a random population sample: Findings from the Copenhagen City Heart Study. *American Journal of Respiratory and Critical Care Medicine, 173*(1), 79–83.
10. Seymour, J., Spruit, M., Hopkinson, N., Natanek, S., Man, W.-C., Jackson, A., et al. (2010). The prevalence of quadriceps weakness in COPD and the relationship with disease severity. *European Respiratory Journal, 36*(1), 81–88.
11. Bernard, S., LeBlanc, P., Whittom, F., Carrier, G., Jobin, J., Belleau, R., et al. (1998). Peripheral muscle weakness in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine, 158*(2), 629–634.
12. Nici, L., Donner, C., Wouters, E., Zuwallack, R., Ambrosino, N., Bourbeau, J., et al. (2006). American Thoracic Society/ European Respiratory Society statement on pulmonary rehabilitation. *American Journal of Respiratory and Critical Care Medicine, 173*(12), 1390–1413.
13. Pitta, F., Troosters, T., Spruit, M. A., Probst, V. S., Decramer, M., & Gosselink, R. (2005). Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine, 171*(9), 972–977.
14. Marquis, K., Debigaré, R., Lacasse, Y., LeBlanc, P., Jobin, J., Carrier, G., et al. (2002). Midthigh muscle cross-sectional area is a better predictor of mortality than body mass index in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine, 166*(6), 809–813.
15. Whittom, F., Jobin, J., Simard, P.-M., Leblanc, P., Simard, C., Bernard, S., et al. (1998). Histochemical and morphological characteristics of the vastus lateralis muscle in patients with chronic obstructive pulmonary disease. *Medicine and Science in Sports and Exercise, 30*(10), 1467–1474.
16. Gosker, H. R., Engelen, M. P., van Mameren, H., van Dijk, P. J., van der Vusse, G. J., Wouters, E. F., et al. (2002). Muscle fiber type IIX atrophy is involved in the loss of fat-free mass in chronic obstructive pulmonary disease. *The American Journal of Clinical Nutrition, 76*(1), 113–119.
17. Vogiatzis, I., Stratakos, G., Simoes, D. C., Terzis, G., Georgiadou, O., Roussos, C., et al. (2007). Effects of rehabilitative exercise on peripheral muscle TNFα, IL-6, IGF-I, and MyoD expression in patients with COPD. *Thorax, 62*(11), 950–956.
18. Agustí, A. G., Sauleda, J., Miralles, C., Gomez, C., Togores, B., Sala, E., et al. (2002). Skeletal muscle apoptosis and weight loss in chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine, 166*(4), 485–489.
19. Gosker, H. R., Zeegers, M. P., Wouters, E. F., & Schols, A. M. (2007). Muscle fibre type shifting in the vastus lateralis of patients with COPD is associated with disease severity: A systematic review and meta-analysis. *Thorax, 62*(11), 944–

949.
20. Jobin, J., Maltais, F., Doyon, J.-F., LeBlanc, P., Simard, P.-M., Simard, A.-A., et al. (1998). Chronic obstructive pulmonary disease: Capillarity and fiber-type characteristics of skeletal muscle. *Journal of Cardiopulmonary Rehabilitation and Prevention, 18*(6), 432–437.
21. Larsson, L. (1983). Histochemical characteristics of human skeletal muscle during aging. *Acta Physiologica Scandinavica, 117*(3), 469–471.
22. Sato, Y., Asoh, T., Honda, Y., & Fujimatsu, Y. (1997). Morphologic and histochemical evaluation of muscle in patients with chronic pulmonary emphysema manifesting generalized emaciation. *European Neurology, 37*(2), 116.
23. Gea, J., Pasto, M., Carmona, M., Orozco-Levi, M., Palomeque, J., & Broquetas, J. (2001). Metabolic characteristics of the deltoid muscle in patients with chronic obstructive pulmonary disease. *European Respiratory Journal, 17*(5), 939–945.
24. Gosselink, R., Troosters, T., & Decramer, M. (1996). Peripheral muscle weakness contributes to exercise limitation in COPD. *American Journal of Respiratory and Critical Care Medicine, 153*(3), 976–980.
25. Hamilton, A. L., Killian, K. J., Summers, E., & Jones, N. L. (1995). Muscle strength, symptom intensity, and exercise capacity in patients with cardiorespiratory disorders. *American Journal of Respiratory and Critical Care Medicine, 152*(6), 2021–2031.
26. Debigaré, R., Cote, C., Hould, F., LeBlanc, P., & Maltais, F. (2003). In vitro and in vivo contractile properties of the vastus lateralis muscle in males with COPD. *European Respiratory Journal, 21*(2), 273–278.
27. Barreiro, E., Schols, A. M., Polkey, M. I., Galdiz, J. B., Gosker, H. R., Swallow, E. B., et al. (2008). Cytokine profile in quadriceps muscles of patients with severe COPD. *Thorax, 63*(2), 100–107.
28. Gosker, H., Hesselink, M., Duimel, H., Ward, K., & Schols, A. (2007). Reduced mitochondrial density in the vastus lateralis muscle of patients with COPD. *European Respiratory Journal, 30*(1), 73–79.
29. Picard, M., Godin, R., Sinnreich, M., Baril, J., Bourbeau, J., Perrault, H., et al. (2008). The mitochondrial phenotype of peripheral muscle in chronic obstructive pulmonary disease: Disuse or dysfunction? *American Journal of Respiratory and Critical Care Medicine, 178*(10), 1040–1047.
30. Puente-Maestu, L., Pérez-Parra, J., Godoy, R., Moreno, N., Tejedor, A., González-Aragoneses, F., et al. (2009). Abnormal mitochondrial function in locomotor and respiratory muscles of COPD patients. *European Respiratory Journal, 33*(5), 1045–1052.
31. Crul, T., Testelmans, D., Spruit, M. A., Troosters, T., Gosselink, R., Geeraerts, I., et al. (2010). Gene expression profiling in vastus lateralis muscle during an acute exacerbation of COPD. *Cellular Physiology and Biochemistry, 25*(4–5), 491–500.
32. Gomes-Marcondes, M. C. C., & Tisdale, M. J. (2002). Induction of protein catabolism and the ubiquitin-proteasome pathway by mild oxidative stress. *Cancer Letters, 180*(1), 69–74.
33. Maltais, F., LeBlanc, P., Whittom, F., Simard, C., Marquis, K., Bélanger, M., et al. (2000). Oxidative enzyme activities of the vastus lateralis muscle and the functional status in patients with COPD. *Thorax, 55*(10), 848–853.
34. Green, H. J., Bombardier, E., Burnett, M., Iqbal, S., D'Arsigny, C. L., O'Donnell, D. E., et al. (2008). Organization of metabolic pathways in vastus lateralis of patients with chronic obstructive pulmonary disease. *Am J Physiol Regul Integr Comp Physiol, 295*(3), R935–R941.
35. Maltais, F., Simard, A.-A., Simard, C., Jobin, J., Desgagnés, P., & LeBlanc, P. (1996). Oxidative capacity of the skeletal muscle and lactic acid kinetics during exercise in normal subjects and in patients with COPD. *Am J Respir Crit Care Med, 153*(1), 288–293.
36. Watz, H., Waschki, B., Meyer, T., & Magnussen, H. (2009). Physical activity in patients with COPD. *European Respiratory Journal, 33*(2), 262–272.
37. Kongsgaard, M., Backer, V., Jørgensen, K., Kjaer, M., & Beyer, N. (2004). Heavy resistance training increases muscle size, strength and physical function in elderly male COPD-patients—A pilot study. *Respiratory Medicine, 98*(10), 1000–1007.
38. Casaburi, R., Bhasin, S., Cosentino, L., Porszasz, J., Somfay, A., Lewis, M. I., et al. (2004). Effects of testosterone and resistance training in men with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med, 170*(8), 870–878.
39. Meridj, A., Belaala, R., & Djeghri, Y. (2024). Role of ultrasound in predicting diaphragm and quadriceps involvement in COPD patients. *Radiology and Imaging Technology, 10*(127).
40. Bemben, M. G. (2002). Use of diagnostic ultrasound for assessing muscle size. *The Journal of Strength & Conditioning Research, 16*(1), 103–108.
41. Gruther, W., Benesch, T., Zorn, C., Paternostro-Sluga, T., Quittan, M., Fialka-Moser, V., et al. (2008). Muscle wasting in intensive care patients: Ultrasound observation of the M. quadriceps femoris muscle layer. *J Rehabil Med, 40*(3), 185–189.
42. Sipila, S., & Suominen, H. (1991). Ultrasound imaging of the quadriceps muscle in elderly athletes and untrained men. *Muscle & Nerve, 14*(6), 527–533.
43. Meridj, A., Belaala, R., Djeghri, Y. (2024). Influence of COPD on the Diaphragm and Muscles of the Lower Limbs. *J Pulmonol Respir Res, 8*(2), 056-059