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Chronic Obstructive Pulmonary Disease (COPD) and Sarcopenia: A Bidirectional Pathway

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Chronic diseases increase their prevalence as the population pyramid inverses [1], and respiratory diseases are among the most frequent conditions in elderly individuals [2]. For instance, chronic obstructive pulmonary disease (COPD) is a multi factorial entity with a wide range of clinical manifestations, and a leading cause of morbidity and mortality worldwide [3]. The pathophysiology of COPD is as wide as its clinical presentation. However, chronic inflammation is an essential component. Also, increased inflammation is associated with a higher rate of exacerbations and a faster decline in lung function [3], while systemic inflammation contributes to the extra-pulmonary manifestations of COPD.

On the other hand, sarcopenia, the age-associated decrease in muscle mass and function [4], has a prevalence of around 50% in patients above 80 years of age [5], and is particularly common in elderly individuals with COPD. It has also been associated to chronic inflammation [3,6]. The combination of pro-inflammatory cytokines has shown to reduce protein synthesis and increase proteolysis [7]. However, this is not the only factor associated to both conditions. Muscle wasting is closely related to lower survival and higher rates of exacerbation in patients with COPD [3,8]. Thus, it seems relevant to consider the association between sarcopenia and COPD.

Following are some of the various patho-physiologic mechanisms associating sarcopenia and COPD. To begin with, even short-term disuse of muscle can lead to a diminished muscle mass [7]. The functional capacity decrease associated to chronic respiratory diseases by itself is enough to cause muscle mass loss, particularly during exacerbations. Byun [3] found that patients with sarcopenia had more severe symptoms of dyspnea and higher modified medical research council dyspnea scale (mMRC) scores than those without muscle wasting [3]. Nevertheless, it seems some factors may further exacerbate muscle loss. For instance, during exacerbations, energy intake seems to lower, further decreasing amino acid availability for muscular protein synthesis [9].

Also, hypoxemia, as found in chronic respiratory diseases has been associated to proteolysis and decreased protein synthesis [7]. Hypoxia decreases the efficiency of mitochondrial electron transport chain generating reactive oxygen species. Interleukins 1 and 6 and C-reactive protein are also found in higher quantities in hypoxic patients, and these are factors that have been associated to sarcopenia [10].

Additionally, tumor necrosis factor alpha is a cytokine usually found in cachexia and other catabolic processes which may account for unexplained weight loss in a variety of diseases, including COPD [11]. This becomes relevant given that low body weight has been associated to mortality in this group of patients [7]. Also, plasma concentrations of glutamine and glutamate seem to be normal in ambulatory COPD patients with normal weight, while they decrease in low-weight patients with emphysema [7].

In older adults, sarcopenia has proven to be a useful tool for risk stratification, since its presence is associated to a variety of deleterious outcomes. Furthermore, even if muscle mass decrease is more frequent during COPD exacerbations, a prevalence of 15% of sarcopenia has been reported in patients with stable COPD [5]. Also, sarcopenia can be approached through anthropometry and dynamometry, tools that might be available in an outpatient consultation context. Even if these tools were not available, a complete interrogation may lead to discoveries such as decreased grip strength (e.g the patient keeps dropping objects involuntarily), low gait speed (e.g decreased mobility or slowness for walking), low muscle mass (e.g loss of weight), all of which are diagnostic criteria for pre-sarcopenia and sarcopenia [4].

In addition to early diagnosis of sarcopenia, pulmonary rehabilitation seems to not only improve symptoms in patients with chronic respiratory disease [12], but has also proved to "reverse" sarcopenia by decreasing the quantity of diagnostic criteria met in order to diagnose this entity in terms of the European Working Group on Sarcopenia in Older People diagnostic algorithm. Aerobic training is useful for expanding inspiratory volume, leading to

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reduced dyspnea on exertion, while increasing exercise tolerance and improving muscle function [12].

In summary, it is paramount to understand the relevance of assessing sarcopenia in patients with chronic respiratory diseases in order to allow timely diagnosis and management of both conditions, increasing quality of life for our patients.

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