

Muscle dysfunction in chronic respiratory diseases

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Muscle involvement is no longer regarded as a mere secondary consequence of chronic respiratory diseases, but rather as a central component of their pathophysiology and clinical impact. This issue of BRN Reviews focuses precisely on this systemic dimension of respiratory diseases, bringing together a series of reviews that explore the biological mechanisms, clinical manifestations, and therapeutic strategies related to skeletal muscle dysfunction across different respiratory conditions. Collectively, these articles provide an integrated and up-to-date perspective on a problem that profoundly influences functional capacity, quality of life, and prognosis in millions of patients worldwide.

For decades, clinical attention in diseases such as chronic obstructive pulmonary disease (COPD), bronchiectasis, and interstitial lung diseases primarily focused on pulmonary abnormalities. However, accumulating evidence has demonstrated that skeletal muscle is one of the organs most profoundly affected by systemic inflammation, oxidative stress, hypoxemia, physical inactivity, and metabolic disturbances associated with these conditions. Loss of muscle mass, reduced muscle strength, and oxidative capacity, together with the development of sarcopenia, are now recognized as major contributors to exercise intolerance, functional disability, and frailty in these patients.

Within this context, the review dedicated to COPD examines in depth the pathophysiological mechanisms underlying skeletal muscle dysfunction, integrating mitochondrial alterations, fiber-type shifts, and muscle wasting with their functional and clinical consequences. The article highlights how impaired oxidative

capacity and mitochondrial dysfunction translate into early fatigue and exercise limitation, while emphasizing the importance of comprehensive clinical tools capable of evaluating skeletal muscle impairment from both physiological and functional perspectives.¹

Complementing this mechanistic perspective, another review broadens the focus toward the major clinical drivers of muscle dysfunction in COPD and other chronic respiratory diseases. Readers will find a particularly valuable synthesis regarding the role of physical inactivity, lung hyperinflation, systemic inflammation, hypoxemia, corticosteroid exposure, and acute exacerbations as modulators of muscle injury and remodeling. One of the most important messages emerging from this work is that muscle dysfunction does not result from a single mechanism, but rather from the dynamic interaction between respiratory mechanical overload, peripheral deconditioning, and chronic systemic stress.²

This issue also includes a dedicated review on bronchiectasis, a disease in which sarcopenia and skeletal muscle dysfunction have traditionally received less attention. The article emphasizes that bronchiectasis should likewise be understood as a systemic disease, where persistent inflammation, recurrent infections, malnutrition, and physical inactivity contribute to clinically relevant structural and functional muscle abnormalities. Particularly noteworthy is the discussion regarding the role of oxidative stress and endoplasmic reticulum stress as biological mechanisms implicated in muscle loss, opening new avenues for future therapeutic strategies.³

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Finally, the review focused on exercise training modalities provides an essential translational perspective. In light of growing evidence that skeletal muscle dysfunction is at least partially reversible, the authors analyze the differential effects of resistance training, continuous and interval endurance training, as well as eccentric and combined exercise modalities. The message is clear: modern pulmonary rehabilitation should evolve toward individualized programs aimed not only at improving exercise tolerance but also at restoring muscle mass, strength, and mitochondrial function.⁴

Taken together, the articles assembled in this issue reflect a profound conceptual shift: chronic respiratory diseases can no longer be understood exclusively through the lens of pulmonary impairment. Skeletal muscle dysfunction represents a key systemic manifestation with major diagnostic, prognostic, and therapeutic implications. Early recognition and multidisciplinary

management of muscle involvement offer a genuine opportunity to modify disease trajectory and improve patient outcomes.

We hope this issue of BRN Reviews will stimulate further research in this evolving field and, above all, encourage the incorporation of skeletal muscle assessment and treatment as an integral component of the management of chronic respiratory diseases.

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