

Aspects of skeletal muscles in chronic respiratory disease

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Keywords

Skeletal muscle, COPD, diaphragm, pulmonary rehabilitation, anabolic

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This review series examines current aspects in the aetiology, assessment and management of skeletal muscle dysfunction in chronic respiratory disease. The reader may wonder why this is of interest in disorders where the lung is the primary organ of impairment. First, skeletal muscle dysfunction is one of the commonest extra-pulmonary manifestations in chronic respiratory disease. Previous cross-sectional studies have estimated that approximately a third of individuals with chronic obstructive pulmonary disease (COPD) have significant quadriceps muscle weakness,¹ while 15% have evidence of sarcopenia.² The prevalence of skeletal muscle dysfunction increases with worsening disease severity.^{1,2} Second, the skeletal muscles play a vital role in life, providing the mechanical basis for breathing and movement.³ Peripheral and respiratory muscle dysfunction is a significant contributor to breathlessness and functional capacity.^{4–6} This is illustrated elegantly by the observation that considerable exercise limitation persists despite lung transplantation and restoration of lung function.⁷ Third, skeletal muscle dysfunction not only contributes to symptoms and functional impairment in chronic respiratory disease, but influences prognosis. Reductions in peripheral muscle strength^{8,9} and mass,¹⁰ as well as whole body fat-free mass¹¹ are associated with increased mortality in COPD. Most importantly, unlike the lungs, skeletal muscle dysfunction is potentially remedial with relatively simple interventions such as exercise-training.¹² This provides an opportunity to significantly improve the symptoms and functional performance of individuals with chronic respiratory disease who often have limited pharmacological options for their lung disease. This is reflected by the increasing prominence of pulmonary rehabilitation in respiratory disease guidelines.^{13,14}

Through the deeper understanding of the cellular mechanisms of muscle wasting, there have been

notable advances in the development of potential therapeutic anabolic and anti-catabolic drugs, which are described in detail by Evans (REF Evans review). Although these drugs will eventually be used more broadly for muscle dysfunction in non-respiratory populations (e.g. cancer cachexia, older individuals with sarcopenia), there is potential that these agents may have an important therapeutic role in selected individuals with chronic respiratory disease and skeletal muscle dysfunction. Spruit and colleagues remind us that there is already a strong evidence base for non-pharmacological interventions such as exercise-training (REF SPRUIT review). Whereas efficacy is established, implementation may be more challenging.^{15,16} Physical inactivity and systemic inflammation are often cited as important aetiological factors for skeletal muscle dysfunction in chronic respiratory disease,³ but muscle loss is also a phenomenon associated with ageing. In the gerontology literature, the sarcopenia and frailty phenotypes are well described and associated with skeletal muscle weakness and loss. Maddocks and colleagues review recent work assessing whether these phenotypes are relevant in chronic respiratory disease populations (REF MADDOCKS review). The final review series article from Supinski and Callahan focuses on the diaphragm, particularly in the catabolic milieu of the critical care setting (REF SUPINSKI REF). Over the past two decades there has been a dramatic increase in the number of patients undergoing mechanical

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ventilation. Diaphragm weakness is highly prevalent and this may have deleterious consequences, such as duration of ventilation/weaning difficulties and increased mortality.

The series is kick-started by Barreiro and Gea who provide a comprehensive and eloquent review of the aetiology of skeletal muscle dysfunction in COPD and outline the current knowledge regarding relevant molecular and biological pathways (REF Barreiro review).

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