Sarcopaenia in chronic obstructive pulmonary disease
Michael C Steiner

Lower limb muscle strength may be a predictor of mortality in patients with chronic obstructive pulmonary disease

Human beings are designed to move. Despite changes in modern lifestyles that have led to a reduction in habitual physical activity in the developed world, this remains an important human biological function. The skeletal muscles, forming one of the largest tissue compartments of the body, are dedicated to this end. The ability to move in the form of athletic performance peaks in the third and fourth decades of life and then progressively declines. Skeletal muscle mass declines by around 30% by the seventh and eighth decades and further in the third and fourth decades of life and then form of athletic performance peaks in the third and fourth decades of life and then

The cellular and molecular mechanisms underlying muscle wasting remain largely unexplored in COPD. However, recognition of the importance of muscle wasting and the clinical significance of muscle wasting in COPD have led to the development of strategies to prevent and treat muscle wasting. These strategies include exercise interventions, nutritional support, and the use of specific therapies such as corticosteroids. The effects of these interventions on muscle mass and function in COPD have been evaluated in several studies, and the results have been inconsistent. However, the evidence suggests that exercise interventions and nutritional support are effective in maintaining muscle mass and function in COPD, and the use of specific therapies such as corticosteroids may be beneficial in selected cases. Overall, the prevention and treatment of muscle wasting in COPD is an important area of research, and further studies are needed to fully understand the mechanisms and factors involved in muscle wasting in this disease.
to disability and frailty in the elderly has focused recent attention on these mechanisms in sarcopenia. Muscle mass is determined by the relative balance of muscle protein synthesis and breakdown. These are in turn influenced by a number of factors, including exercise, dietary protein intake and the action of anabolic hormones such as testosterone, growth hormone and insulin. It is uncertain whether sarcopenia is due to gradual changes in the relative rates of muscle protein synthesis and breakdown in the basal state. Moreover, the magnitude of any such changes may be too small to detect, given the slow pace of muscle loss during healthy ageing. More important may be the responses of ageing muscle to diet and physical activity, which themselves change with age.

The responsiveness of ageing muscle to physical activity appears to be preserved, as there are numerous studies that have confirmed that resistance training can produce similar increments in muscle mass in the young and the old. More recent data, however, suggest that older people are less able to use dietary protein for muscle protein synthesis. These changes were associated with alterations in intracellular anabolic signalling pathways that may also be linked to inflammation-mediated proteolysis via the ubiquitin–proteosome system. These pathways could therefore represent a common mechanism by which muscle protein synthesis and breakdown are uncoupled, leading to rapid loss of muscle mass such as that seen in cachectic individuals with COPD.

Muscle wasting in COPD may occur in some patients in a progressive linear manner, but the inability to build muscle effectively using dietary protein also suggests that ageing muscle may be more vulnerable to short-lived illnesses such as exacerbations where muscle breakdown is accelerated. Exacerbations are associated with extended periods during which patients are inflamed and inactive (particularly if hospitalised), and may be treated with therapy such as high-dose corticosteroids that have a potentially negative effect on muscle mass. In some patients therefore, muscle wasting could be more “events driven”, where exacerbations cause brief but rapid losses of muscle protein from which the muscle fails to adequately recover. Support for this concept comes from studies showing that patients with COPD who have been hospitalised for an exacerbation may lose muscle strength rapidly (up to 5% in a few days) and that the effects of an exacerbation on physical activity and performance may be prolonged. In addition, recent trials exploring the role of early rehabilitation after hospitalisation in COPD showed that patients allocated to standard care showed very little improvement in exercise performance after discharge. This suggests that losses of fitness and muscle function after exacerbation are prolonged and may indeed not fully recover to the pre-exacerbation baseline. These trials did confirm the effectiveness of exercise training in this setting, providing hope that the damaging effects of exacerbations can be overcome by an effective rehabilitation strategy. Interestingly, the study of Swallow et al found that mortality was not increased in those who had been admitted for an exacerbation, suggesting that these events were less important in their cohort. However, the study may have lacked statistical power to examine this question and other studies have indicated that hospital admission in COPD is associated with a higher mortality. Longitudinal studies measuring decline in muscle mass and function are needed to disentangle the effects of these multiple potential influences on the aetiology and progression of skeletal muscle disease in COPD.

The implication of the link between muscle strength and prognosis is that we may be able to reduce mortality in COPD by interventions to improve muscle function. Indeed the skeletal muscles are a potential therapeutic target in a disease where the primary pulmonary pathology is largely irreversible. The benefit of this approach is illustrated by the success of pulmonary rehabilitation in improving symptoms and reducing disability. The mechanism of this improvement is largely through skeletal muscle adaptation to physical training. There is circumstantial evidence that rehabilitation also improves survival, although this has not been conclusively demonstrated in adequately powered clinical trials. It is unlikely that such trials will now be conducted, as this would involve withholding pulmonary rehabilitation from patients who would clearly benefit from it on grounds of symptoms and quality of life.

Pharmacological interventions targeted at skeletal muscles such as anabolic and sex hormone supplementation are at an early stage of evaluation, but show promise and may have a place in selected patients. Nutritional support for patients with weight loss has proved disappointing when applied across the board, but may benefit selected patients when combined with an appropriate anabolic stimulus such as exercise.

Muscle wasting is clearly of functional and prognostic importance in COPD, but we have much to learn about the natural history and underlying mechanisms of this aspect of the disease. The situation is complex because muscle atrophy in COPD occurs on a background of age-related sarcopenia. The application of advances in our understanding of the biology of muscle growth in young and old humans may help us unravel these issues and direct us to new therapies aimed at reversing muscle wasting. Such developments are likely to have a wide application, given the importance of disabling chronic diseases in an ageing population.

doi: 10.1136/thx.2006.076009

Correspondence to: Dr M C Steiner, Department of Respiratory Medicine, Institute for Lung Health, University Hospitals of Leicester NHS Trust, Glenfield Hospital, Groby Road, Leicester LE3 9QP, UK; michael.steiner@uhl-tr.nhs.uk

REFERENCES

COPD exacerbation

Chronic obstructive pulmonary disease exacerbation and risk of pulmonary embolism

J A Wedzicha, J R Hurst

Pulmonary embolism is not a common feature in patients with chronic obstructive pulmonary disease with uncomplicated exacerbations

Exacerbations of chronic obstructive pulmonary disease (COPD) are episodic of acute deterioration in respiratory symptoms that are accompanied by physiological changes and associated with increases in airway and systemic inflammation. These episodes are responsible for considerable morbidity and mortality, especially in patients with more severe COPD. There is consequently much interest in understanding the underlying pathophysiology of exacerbations and determining their triggers, so that appropriate interventions can be designed to prevent these events, reduce their severity and thus improve health status.

We now recognise that respiratory infections are important triggers of exacerbation. Respiratory viral infections, especially with human rhinovirus (the cause of the common cold), influenza and respiratory syncytial virus may be isolated from up to 60% of exacerbations. Exacerbations where a virus is isolated have increased airway and systemic inflammatory changes. The role of bacteria at exacerbation has been more difficult to determine as airway bacteria are also found in stable patients with COPD, especially those with more severe COPD. However, we now know that bacterial strain change may play a part in triggering exacerbation. Airway bacteria may be present in up to 70% of COPD exacerbations, and their isolation is accompanied by increased airway inflammatory changes.

Viruses and bacteria may also be co-isolated from the same exacerbation, and recent studies have suggested that the presence of both pathogens may have a synergistic effect on the degree of airway inflammation, especially when exacerbations are severe. Thus, airway infection can be implicated as a trigger in most COPD exacerbations, even taking into account difficulties in sampling these patients that can lead to underestimating the significance of airway infection.

There is also interest in other causes of COPD exacerbation. Air pollution has been associated with an increase in hospital admissions in patients with COPD, although these effects are relatively small. As COPD exacerbations are closely linked to respiratory infections, the hypothesis has been put forward that pollutants can increase susceptibility to viral infection. One study has suggested that with higher personal nitrogen dioxide exposure, there is a greater risk of an asthmatic exacerbation after respiratory infection.

Similar mechanisms might be operating in patients with COPD and further studies investigating the associations between pollution and infection are required. Exacerbations therefore result from further insult to the COPD airway, but a number of conditions may mimic exacerbation by causing worsening dyspnoea in patients with underlying COPD. One such condition is pulmonary embolism, a disorder of the vasculature rather than the airway. Although pulmonary embolism is not thought to predispose to exacerbation, there have been a number of reports suggesting that the prevalence of deep venous thrombosis and pulmonary
Sarcopaenia in chronic obstructive pulmonary disease

Michael C Steiner

*Thorax* 2007 62: 101-103
doi: 10.1136/thx.2006.067009

Updated information and services can be found at:
http://thorax.bmj.com/content/62/2/101.1

These include:

**References**
This article cites 39 articles, 13 of which you can access for free at:
http://thorax.bmj.com/content/62/2/101.1#BIBL

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections

Epidemiologic studies (1829)

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/