Respiratory Medicine (2005) **99**, S3–S10

respiratoryMEDICINE

Systemic effects of COPD

Marc Decramer[a,*], Fernando De Benedetto[b], Adriana Del Ponte[c], Stefano Marinari[b]

[a]*Respiratory Division, Katholieke Universiteit, University Hospital, Leuven, Belgium*
[b]*Department of Pneumology, Ospedale San Camillo de Lellis, Chieti, Italy*
[c]*Medicine and Ageing Science Department, Colle dell'Ara Hospital, Chieti, Italy*

Received 5 August 2005; accepted 7 September 2005

KEYWORDS
COPD;
Systemic effects;
Nutritional depletion;
Muscle weakness

Summary Chronic obstructive pulmonary disease (COPD) is characterised by a range of pathological changes of the respiratory system, including airflow limitation secondary to structural changes of the small airways and loss of alveolar attachments, inflammation, ciliary dysfunction, and increased mucous production. COPD also has significant systemic consequences. The relationships between these pulmonary and nonpulmonary morbidities are not fully understood, and this further complicates the assessment of disease severity and prognosis. Although improving lung function and disease symptoms have been the main focus of COPD management, these parameters alone do not reflect the full burden of disease. More recent endeavours have highlighted the potential role of addressing physical limitations imposed by systemic alterations.

It is evident that systemic manifestations are common in COPD. Indeed, many patients demonstrate a gradual and significant weight loss that exacerbates the course and prognosis of disease. This weight loss is often accompanied by peripheral muscle dysfunction and weakness, which markedly contribute to exercise limitation and impaired quality of life. Weight loss has been postulated to be the result of a high metabolic rate that is not compensated for by increased dietary intake. The cause of this elevated metabolism is a matter of much debate, and several factors have been implicated. Similarly, the processes underlying depletion of muscle mass and function have not been fully delineated.

The impact of the systemic manifestations of COPD is substantial, and although many attempts have been made to elucidate the mechanisms underlying these manifestations, there are important questions, which remain to be answered. An

Abbreviations: BCM, body cellular mass; BIA, bioelectrical impedance analysis; COPD, chronic obstructive pulmonary disease; CXCL-8, CXC chemokine ligand-8; FEV_1, forced expiratory volume in 1 s; HRQoL, health-related quality of life; IGF-1, insulin-like growth factor-1; IL-6, interleukin-6; LBM, lean body mass; OCB, oxygen cost of breathing; QF, quadriceps force; QoL, quality of life; 6MWD, 6-min walk distance; SGRQ, St. George's respiratory questionnaire; TNF-α, tumour necrosis factor-alpha

*Corresponding author. Tel.: +32 16 346807; fax: +32 16 347126.
E-mail address: marc.decramer@uz.kuleuven.ac.be (M. Decramer).

0954-6111/$ - see front matter
doi:10.1016/j.rmed.2005.09.010

increase in our understanding in this field will doubtless highlight potential therapeutic targets, and assist in guiding future therapeutic development.

Introduction

Chronic obstructive pulmonary disease (COPD) is a debilitating multicomponent respiratory condition. The pathogenesis and clinical manifestations of COPD are not confined solely to pulmonary inflammation and structural remodelling, but extend to and encompass a variety of systemic alterations.[1] These extrapulmonary effects include systemic inflammation, nutritional abnormalities and weight loss, skeletal muscle dysfunction and additional organ effects. The high burden of COPD resulting from respiratory symptoms, such as breathlessness and exacerbations, is further contributed to by systemic effects, leading to a pronounced deterioration in health status and a diminished quality of life (QoL). Recently, there has been a much greater appreciation of the clinical importance of the systemic manifestations of COPD.[1] This article will focus primarily on the systemic nutritional and muscular components of COPD, discussing aetiology, diagnosis and treatment approaches.

Nutritional abnormalities in pulmonary disease: evidence from epidemiological studies

The most obvious clinical expression of nutritional abnormalities is unexplained weight loss.[1] Evidence of a relationship between body weight and COPD first emerged from a study investigating metabolic imbalances in severe bronchial obstruction.[2] The authors detected a meaningful correlation between low body weight and reduced survival rates in the participants, highlighting for the first time the role of nutritional depletion in COPD. This observation was later confirmed and extended, in a large population study, in which body weight was found to be directly related to severity of lung function determined by the forced expiratory volume in 1 s (FEV_1).[3] This study also provided additional information on the role of body weight on survival—mortality was found to increase as patient body weight decreased, regardless of lung function impairment. Low body weight therefore appears to be an independent marker of poor disease outcome.[4]

Aetiology of nutritional depletion: what, why and how?

Several studies have shown that malnutrition or reduced body weight is common in individuals with COPD, affecting approximately 10–15% of patients with mild-to-moderate disease, and 50% of patients with advanced-stage disease and chronic respiratory failure.[5–8] The pathophysiological basis of weight loss is not very well understood, although a high metabolic rate that is not compensated for by a corresponding increase in caloric intake is thought to play an important role.[9,10] The cause of the increased basal metabolic rate, however, is a matter of much debate and several hypotheses have been proposed (Fig. 1).

One hypothesis implicates increased energy expenditure, with the increased oxygen consumption by respiratory muscles that results from the increased workload required to overcome airway obstruction—the hallmark of COPD.[11] More recently, however, other studies have demonstrated that increased oxygen consumption is also evident in skeletal, non-respiratory muscle in COPD patients. Furthermore, breathing efficiency is comparable between patients with COPD, and healthy volunteers.[12] The role of the oxygen cost of breathing in the hypermetabolic state of COPD, therefore, remains uncertain.

Other factors implicated in raising basal metabolic rate include medications commonly used in the treatment of COPD (e.g. β_2-agonists and the phosphodiesterase inhibitor theophylline) and catecholamines (e.g. noradrenaline), although studies investigating the role of these hormones in hypermetabolism are limited. In addition, inflammatory mediators, such as tumour necrosis factor-alpha (TNF-α), C-reactive protein and lipopolysaccharide-binding protein are thought to play a role.[13] Finally, the increased thermic effect of patient activity has also been reported to contribute to the increased metabolism observed in COPD patients.[14]

Assessing nutritional status: methods of evaluation

Depletion in fat-free mass (including skeletal muscle) accounts for much of the observed weight loss in COPD, although cases have been reported in which alterations in body composition occurred even in the absence of any obvious weight loss.[8,15,16] Several methods are employed for measuring body composition. Anthropometry is a simple and widely used approach for assessing fat mass through skinfold thickness, body circumference, body mass