

## Cachexia and Chronic Respiratory Failure: Lessons From Ventilatory Support

Patients with chronic obstructive pulmonary disease (COPD) who suffer from chronic respiratory failure pose a challenging problem in daily clinical practice. Particularly in the final phase of the disease, COPD is characterized by a range of pathological changes that contribute to a highly variable clinical picture. Particularly in the last decade, various studies have stressed the important role of nutritional status, even in patients suffering from chronic respiratory failure.

Survival studies in selected groups of patients with COPD and in population-based studies have consistently shown higher COPD-related mortality rates in underweight and normal-weight patients than in overweight and even obese patients.<sup>1-3</sup> Particularly, wasting of the metabolically and functionally active fat-free mass has been reported as an independent predictor of survival<sup>4,5</sup>

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In this issue of *RESPIRATORY CARE*, Budweiser et al reported their findings about body-weight changes in cachectic patients receiving noninvasive positive-pressure ventilation.<sup>6</sup> The prevalence of malnutrition, as indicated by a body mass index (BMI) < 20 kg/m<sup>2</sup> was 20.6% of the patients. It has to be realized that the prevalence of muscle wasting probably will be much higher, because loss of fat-free mass—either as a consequence of cachexia or muscle atrophy—is frequently masked by an increase in fat mass, resulting in an adequate BMI, particularly in females.<sup>4</sup> Assessment of fat-free mass therefore has to be considered in the routine assessment of COPD patients, as a systemic marker of disease severity.

In this selected group of patients the data from Budweiser et al may contribute to better understanding disturbances in energy balance. Indeed, weight loss, and particularly loss of fat mass, occurs if energy expenditure exceeds dietary intake. Besides these impairments in total energy balance, an imbalance between protein synthesis and protein breakdown has to be considered to explain processes of muscle wasting.

Total daily energy expenditure is usually divided into 3 components: resting energy expenditure, diet-induced thermogenesis, and physical-activity-induced thermogenesis. Different reports have focused on resting energy expendi-

ture measurements in COPD. Besides the established role of systemic inflammation, the work of breathing is evaluated as a possible factor to increase resting energy expenditure. Studies investigating this issue, however, have demonstrated conflicting results<sup>7-10</sup> Part of this controversy can be explained by methodological pitfalls, such as variability in the technique to measure the oxygen cost of ventilation. In a study that compared resting energy expenditure before and after nasal intermittent positive-pressure ventilation, eliminating diaphragmatic and intercostals activity, no reduction in resting energy expenditure was observed, which suggests that the elevated resting energy expenditure was not attributable to increased respiratory muscle work<sup>11</sup> The reported correlation between BMI and the severity of respiratory impairment, especially with hyperinflation, in the present study does not conflict with these data. First of all, BMI is a reflection of the overall energy balance. Furthermore, static hyperinflation and particularly dynamic hyperinflation has to be considered as one of the determining factors explaining the reported increase in activity-related energy expenditure in COPD patients.<sup>12</sup>

Budweiser et al, in this issue of *RESPIRATORY CARE*,<sup>6</sup> report a significant increase in body weight after 6 and 12 months intervention with NPPV. No correlation between changes in BMI and changes in blood gases, lung function, or inspiratory muscle function could be detected in this subgroup of malnourished patients. Lacking information about energy intake, body composition, changes in activity level, or number of exacerbations, one can only conclude that in this subgroup of patients the disturbances in energy balance are reversed by institution of NPPV. Similar observations, particularly increases in fat mass, are reported after lung-volume-reduction surgery. Further controlled studies including body composition assessment and energy balance evaluation will be important to better understand the underlying mechanisms after NPPV. Important to consider is the selection procedure applied by Budweiser et al. Indeed, only stable COPD patients in the absence of signs of systemic inflammation were included. Previous studies indeed indicate that non-response after nutritional supplementation in COPD is associated with relative anorexia and an elevated systemic inflammatory response.<sup>13</sup> Based on the data reported by Budweiser et al,

it also would be very important to better understand the possible consequences of NPPV on restoration or improvement of dietary intake in these patients, as studies have pointed toward the existence of altered regulation of appetite; levels of leptin, the adipocyte-derived hormone involved in the afferent hormonal signaling to the brain in a feedback mechanism that regulates appetite, are influenced by systemic inflammation and hypoxemia.<sup>14,15</sup> Based on careful clinical observations, as reported in this issue of *RESPIRATORY CARE*, further prospective studies can be designed in order to improve health status and prognosis of these very disabled COPD patients. Optimal medical therapy has to focus attention not only on attenuation of progression of the disease, but also on overcoming the heterogeneous and complex pathology in the end phase of the disease!

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