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The Impact of Obesity and Metabolic Syndrome in COPD

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1. Introduction
Obesity is becoming more and more prevalent in the world and has many recognized impacts on different body systems. Chronic obstructive pulmonary disease (COPD) is also very common and affects different systems but mainly the respiratory system. Of particular interest to us is the impact of obesity on respiratory function in general and more specifically in COPD patients.

The objectives of the chapter are to: 1) explore the different impacts of obesity on respiratory function in healthy and COPD patients; 2) to try to explain the impact of obesity on exercise tolerance and exercise dyspnea; and 3) the study the impact of obesity on the outcomes of a pulmonary rehabilitation program for COPD patients.

2. Definition of obesity
The definition of obesity is based on body mass index (BMI) which is the ratio of body mass in kilograms to the square of the height in meters. A person is overweight if BMI is between 25 and 30 kg/m² and obese if BMI is over 30 kg/m² [5]. This definition, although being simple and easily applicable to everyday clinical contexts, is somewhat simplistic in the sense that it does not take into account either body mass distribution or fat vs. fat free mass. These variables have important impact on the respiratory physiology and on the chronic obstructive pulmonary disease (COPD).

3. Epidemiology
Overweight and obesity are very prevalent in western countries. For instance, in Canada, it is estimated that, in 2004, 23.1 % of adults were obese and 36.1 % were overweight, up from 13.8 and 28.5 % respectively compared to 1979 [6]. This has led the scientific community to talk about this phenomenon in terms of “obesity epidemic”, since the condition has recently been recognized as a disease [7].

4. Effects of obesity on respiratory physiology at rest
Obesity has many different effects on respiratory physiology at rest. These effects will be explained in more detail in the following text and are summarized in table 1.
4.1 Lung volumes and respiratory mechanics

The best described effect of obesity is the reduction of the end-expiratory lung volume and functional residual capacity [2,8]. End-expiratory lung volume is the volume left in the lung at the end of a normal expiration and under most circumstances. Functional residual capacity is the resting respiratory system volume determined by the equilibrium of two opposing forces [9]; the elastic recoil of the lung which exerts a deflating effect and the elastic properties of the chest wall that tends to expand because its resting volume is higher than the functional residual capacity in healthy individuals [9]. In the obese subject, reduction of the resting respiratory system volume at functional residual capacity is caused by the extra weight of the thoracic wall and the abdomen which reduces significantly the respiratory system compliance [10]. There is an exponential relationship between BMI and both functional residual capacity and end-expiratory lung volume [2]. Total lung capacity and residual volume are relatively unaffected by obesity [11]. So, with a preserved total lung capacity and residual volume, decreased functional residual capacity has two physiologic corollaries: 1) decreased expiratory reserve volume and, 2) increased inspiratory capacity [1].

Table 1. Summary of the effects of obesity on respiratory physiology at rest and during exercise.

| At rest | Lung volumes | Reduced functional residual capacity and expiratory reserve volume exponentially with increases in BMI. Total lung capacity and residual volume within normal limits. |
| --- | --- | --- |
| Respiratory system compliance | Reduced compliance mainly due to extra upper body weight (abdomen and thorax) and breathing at lower volumes. |
| Expiratory flows | Airways narrowed and more reactive but no consistent influence of BMI on either FEV1 or FEV1/FVC ratio. |
| Oxygenation | Alveolar collapsing at the lung bases causing V/Q mismatch leading to chronic hypoxia. Worse during sleep. |
| During exercise | Oxygen consumption and ventilation | VO2, VCO2, and VE higher for any given workload due to higher metabolic cost of moving a heavier body mass and increased work of breathing. |
| Lung volumes | Dynamic hyperinflation that raises lung volumes to a more compliant zone. |
| Dyspnea | Dyspnea is increased at any given workload but is proportional to the increase of VE. |
Although airways are narrower and more reactive than normal weight subjects, both maximal ventilatory capacity and expiratory volumes are preserved in the obese subject. There is no consistent evidence of BMI influencing forced expiratory volume in 1 second (FEV1) or FEV1/forced vital capacity [12,13].
4.2 Oxygenation
As functional residual capacity gets lower, it draws near the residual volume so much that, in some subjects, each tidal volume breath results in alveolar collapsing at the lung bases. This creates ventilation perfusion mismatch and can lead to chronic hypoxemia [14]. This phenomenon is exacerbated during sleep but can also be observed during daytime [15].

4.3 Importance of body mass distribution
Fat mass distribution is of paramount importance when considering the effects of obesity on respiratory physiology. Waist size and waist-to-hip ratio is more closely related to the previously described changes than BMI alone [16,17]. Studies using dual X-ray absorptiometry (DEXA) allowed establishing that upper body fat, as opposed to lower body fat, is linked to reductions of functional residual capacity and expiratory reserve volume [18]. This association was observed for thoracic as well as abdominal fat. It thus seems that upper body mass is the main determinant of the lower lung volumes observed in the obese subject and that, because of the interdependence of the thoracic and abdominal cavity in terms of volume and pressure, the location of fat mass within the upper body is not an important determinant of lung volumes.

5. Effects of obesity on respiratory physiology during exercise

5.1 Oxygen consumption
Both oxygen consumption (VO$_2$) and carbon dioxide production (VCO$_2$) are increased for a given workload in the obese individual [3]. This higher metabolic expenditure is due to the higher energy demand caused by the extra body mass that obese subjects have to carry around. Also, decreased respiratory system compliance increases significantly the work of breathing [19]. Maximal exercise capacity in terms of VO$_2$ is not affected and is even increased [20,21]. Actually, absolute VO$_2$ tends to be higher with increasing BMI, but specific VO$_2$ expressed as VO$_2$/kg tends to be lower with increasing BMI. This effect of obesity on VO$_2$ is particularly evident in weight baring activities.

5.2 Lung volumes during exercise
As already mentioned, obese patients’ tidal volume is very close to their residual volume at rest. During exercise however, functional residual capacity increases to normal levels allowing the expansion in tidal volume to accommodate the increasing ventilatory demand in a fashion that is similar to healthy subject. In contrast to patients with obstructive lung disease, the increase in functional residual capacity is not deleterious in obese individuals as it serves to restore normal physiology and places the respiratory system in a more compliant position [22].

5.3 Ventilation and dyspnea relationship
For a given workload, obese subjects feel more dyspnea than non-obese subjects. However, the relationship between ventilation and dyspnea is unchanged [3]. Because of the increased metabolic cost associated with obesity, ventilation is higher for a given workload [3]. It thus seems that the higher perception of dyspnea in obese subjects is only a normal response to higher minute ventilation and that changes in respiratory mechanics and physiology do not really impact on subjective sensations.
6. Effects of obesity on COPD

6.1 How frequently obesity and COPD coexist in the same subject

It was traditionally thought that COPD patients were less likely to be obese. The rationale was that systemic inflammation in the more advanced stages of disease would lead to cachexia [23] rather than overweight. However, in the most recent studies looking at the association of high BMI and COPD, approximately two thirds is overweight or obese [24].

6.2 Impact of obesity on survival

A BMI below 21 kg/m² was shown to be a negative prognosis marker [25] while obesity appears to convey a survival advantage in COPD, as it is the case in other chronic disease [26]. However, data relating to this so called “obesity paradox”, whereby obesity seems beneficial on survival, is often biased because more obese patients tend to have less severe or less advanced disease.

6.3 The main physiologic changes in COPD

The main characteristics of COPD are limitation of expiratory flow and hyperinflation. At rest, FEV1 and the ratio of FEV1 to forced vital capacity are decreased while functional residual capacity, end-expiratory lung volume, total lung capacity and residual volume are elevated. The main consequence of lower expiratory flows is a limitation in maximal ventilatory capacity [27]. The consequence of higher functional residual capacity and residual volume is reduction in
the respiratory capacity (IC). The main pathophysiological reasons for these reduction in flows and elevated lung volumes are an increased airway resistance due to inflammation and mucus production and an increased lung compliance due to parenchymal destruction [28,29].

During exercise, the lower inspiratory capacity constraints the expansion in tidal volume in such a way that the increased ventilatory demand is more dependent upon the progression of the respiratory rate. This breathing pattern characterized by a rapid and shallow breathing shortens expiration, preventing full expiration to occur [4]. The increased airway resistance also contributes to this phenomenon leading to gas retention and dynamic hyperinflation [30]. Because of dynamic hyperinflation, COPD subjects breathe at higher lung volumes during exercise (closer to total lung capacity), in a less compliant portion of the volume-pressure relationship of the respiratory system. Work of breathing is increased in this situation and the resulting tidal volume for a given respiratory effort is decreased, a phenomenon being referred to as neuro-mechanical uncoupling. The final results of these physiological abnormalities for the patients is increased dyspnea perception [31].

Another important systemic consequence of COPD is limb muscle atrophy which is observed especially in the more advanced stages of the disease [23,32]. Total as well as lower limb muscle mass is decreased leading to fatigue during exercise [33]. In fact, some COPD subjects are not primarily limited by dyspnea but by leg fatigue during exercise [34]. This symptom also contributes significantly to exercise intolerance in COPD [35].

6.4 Effect of obesity on COPD at rest
Obesity and COPD have various influences on respiratory physiology, some are similar and some are opposite.

The relationship between BMI and either functional residual capacity or expiratory reserve volume are not affected by the presence of airflow obstruction [1]. However, obese COPD patients are less hyperinflated compared to their lean counterparts [1]. Moreover, for a given
FEV1, IC is higher in obese subjects [2]. These changes seem beneficial to COPD subjects, counteracting some of the deleterious effects of the disease. However, as previously mentioned, oxygen consumption is higher for a given workload for obese subjects, leading to higher ventilatory demand. This increased in ventilatory requirement further stresses the respiratory system whose capacity is already reduced by the presence of airflow limitation [35].

Fig. 4. Lung volumes of an obese and a non-obese COPD subject. A: At rest, lung volumes are reduced in the obese subject. B: During exercise, dynamic hyperinflation is reduced in the obese subject although still present. Adapted from [1].

6.5 Exercise tolerance of the obese patients with COPD
The effects of obesity on exercise tolerance in patients with COPD have not been studied extensively. In one study, obese patients with COPD had higher exercise capacity and were less dyspneic for a given ventilation during cycling exercise [1]. These effects were felt to be related to lower operating lung volumes and reduced dynamic hyperinflation [3]. Other studies have reported marked decreases in exercise tolerance during a 6-minutes walking test [36] but not during a cycling endurance test [37] in obese patients with COPD. It thus appears that obese patients with COPD perform better when cycling than in weight bearing activities such as walking [35].

7. Effects of obesity of pulmonary rehabilitation
7.1 Rehabilitation as a therapeutic intervention in COPD
Pulmonary rehabilitation is a multidisciplinary intervention focusing on exercise training and patient education and self-management [38]. The exercise component is essential if the
goal of rehabilitation is to improve exercise tolerance and reduce dyspnea [39]. It is recommended for patients experiencing persisting symptoms despite maximal pharmacologic therapy [38]. Rehabilitation can be provided in an outpatient setting or at home, with comparable benefits on exercise tolerance, dyspnea, quality of life and exacerbations [40]. It is considered the most effective therapy to improve symptoms and quality of life in COPD [41,42].

7.2 Specific exercise limitations
Obese patients with COPD entering a rehabilitation program typically have a reduced exercise tolerance. [24]. In one study, their cycling capacity was comparable to lean patients with COPD while their walking capacity was reduced. Walking is more representative of daily activities, so it is felt that patients with COPD subjects that are also obese are more limited than their non-obese counterparts. Obese patients with COPD usually show similar improvements in exercise capacity than non-obese although they are less likely to achieve clinically significant improvements during walking [24]. These observations are important because identifying obese patients as having specific exercise limitations can help tailoring the rehabilitation program to their specific needs. Although obesity is associated with more functional impairment, quality of life of obese COPD subjects is not different than their non-obese counterparts and improves to a similar extent with rehabilitation [24]. The fact that obesity does not seems to alter quality of life may be related to the subjective nature of the quality of life measures and to chronic adaptation to obesity with the progressive avoidance of certain tasks that are more challenging to obese individuals.

7.3 Good opportunity to adopt healthier lifestyles
The fact that upon entering pulmonary rehabilitation, obese COPD patients have a reduced walking capacity suggests that weight loss could be beneficial to improve their functional status. Although never formally tested, this is a legitimate assumption. Pulmonary rehabilitation could be an ideal setting to help patients with COPD adopting a healthier lifestyle that will eventually lead to long lasting weight loss [38].

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