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Mini Review

Obesity in Patients with Chronic Obstructive Pulmonary Disease as a Separate Clinical Phenotype

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Abstract

Chronic obstructive pulmonary disease (COPD) is a heterogeneous, progressive disease characterized not only by pathological changes in the lungs but also by significant extrapulmonary manifestations and serious concomitant diseases. The current problem for the study is the features of the relationship between COPD and adipose tissue since there are contradictory data in the literature. This review presents studies that claim that obesity aggravates the course of COPD, as well as the results of studies that describe the "obesity paradox" in patients with COPD. Due to the lack of unambiguous data, it is necessary to continue studying this problem to optimize the tactics of managing this group of patients and draw up clear recommendations for patients with COPD.

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous, progressive, and treatable disease characterized by persistent respiratory symptoms and airflow limitation [1]. COPD is characterized not only by chronic airflow limitation and various pathological changes in the lungs but also by significant extrapulmonary manifestations and serious comorbidities that can aggravate the course of COPD in individual patients and worsen the prognosis [2]. Despite a number of published studies devoted to the relationship between obesity and the risk of development, course, and prognosis of COPD, this problem remains insufficiently studied and relevant at present.

Adipose tissue and chronic obstructive pulmonary disease

Adipose tissue is not only a lipid depot. It is a complex hormonally active organ and is capable of synthesizing a large number of biologically active substances that participate in the regulation of a wide variety of body functions. Among them are leptin, adiponectin, resistin, visfatin, tumor necrosis factor-α, interleukin-6, interleukin-8, etc. [3]. Obesity causes dysregulation of adipokines, which induces and maintains subclinical systemic inflammation [4]. Obesity-induced systemic inflammation may play a role in the pathogenesis of decreased lung function. C-Reactive Protein (CRP) is a sensitive marker of mild systemic inflammation and a generally accepted indicator in clinical practice. An inverse relationship has been found between plasma CRP levels and Forced Expiratory Volume in 1 second (FEV1) and Forced Vital Capacity (FVC) [5]. Leptin and adiponectin receptors are expressed in peripheral tissues, including the lungs. In patients with COPD, increased leptin expression in the bronchial mucosa is associated with inflammation and airway obstruction [6]. A long-term inflammatory process in the lung tissue promotes the release of proinflammatory cytokines and chemokines into the blood, which leads to excessive formation of leukocytes, CRP, fibrinogen, interleukin-6, interleukin-8, tumor necrosis factor-α [2,7,8]. In patients with COPD and obesity, there is a more pronounced increase in the content of systemic inflammation markers [6]. However, the ECLIPSE study showed that out of 1755 patients with COPD, about 30% did not have systemic inflammation, and only a minority (16%) had persistent inflammation during 1 year of observation [9]. This study also showed that high body mass index (BMI) is one of the independent risk factors for systemic inflammation both at the beginning of the study and after 1 year of observation. This association was not found for the fat-free mass index, which suggests an important role of adipose tissue in systemic inflammation [10]. J. Garcia-Aymerich et al. also identified a "systemic" COPD subtype characterized by a higher proportion of obesity in 342 COPD patients with significant systemic inflammation.

This condition persisted over a 4-year follow-up period. Overweight and obese patients demonstrated higher levels of tumor necrosis factor-α, interleukin-1β, interleukin-6 and interleukin-8 mRNA, interferon-γ, and inducible NO synthase [10,11]. A study conducted in China reported that abdominal obesity indices (waist circumference, waist-to-hip ratio, and waist-to-height ratio) were negatively associated with FEV1 and FVC and significantly positively associated with plasma CRP concentrations. However, no significant association was found between BMI and lung function [12].

There are two types of obesity: abdominal and peripheral. Abdominal obesity is characterized by predominant fat deposition in the abdominal area and is usually associated with metabolic disorders. Peripheral obesity is characterized by the deposition of adipose tissue in the buttocks and thighs, most common in women [13]. Abdominal obesity is associated with both obstructive and restrictive changes in lung function, regardless of BMI [14,15]. Obesity reduces the elasticity of the chest, and its excursion decreases. With a high diaphragm in patients with visceral obesity, the respiratory volume of the lungs decreases, and congestion in the pulmonary circulation causes ventilation-perfusion mismatch [16]. There is evidence that obesity is common among people with COPD and is associated with worse outcomes: from quality of life and dyspnea to severe exacerbation of COPD. The more severe the obesity, the stronger these associations were. In addition, an increase in the degree of obesity is associated with an increase in the number of comorbidities and is independently associated with deterioration in lung function and quality of life, increased dyspnea, and a higher likelihood of severe exacerbation of COPD. Moreover, the association between obesity and worse outcomes was independent of the presence of comorbidities [17].

However, there are conflicting data in the literature. The fat mass index has not been established as a predictor of prognosis in patients with moderate to severe COPD [18]. Notably, the relative risk of mortality is reduced in overweight and obese patients with GOLD stage 3–4 COPD. This possible association between obesity and improved outcomes in COPD is inconsistent with epidemiological data for the general population, where obesity is associated with a significant reduction in life expectancy regardless of smoking status. This phenomenon has been called the “obesity paradox”. In obese men with COPD, the annual decline in FEV1 was significantly smaller than in men with normal BMI values, while this effect was not observed in women. These facts suggest the presence of gender differences and some protective role of obesity in the progression of chronic airflow limitation in the lungs [18]. Obese patients with COPD had more comorbidities, but despite this, obese patients still had lower mortality [19]. In Spain, a large retrospective study of 313233 patients with COPD hospitalized for exacerbation found a lower risk of in-hospital mortality and early readmission in obesity [20]. The risk of readmission was 13% lower in obese patients and 29% higher in malnourished patients. However, it was noted that this “protective effect of obesity” disappeared at BMI > 32 kg/m^2 [21]. The authors believe that this difference in data may be influenced by the lack of measurements of the amount of adipose tissue, fluid, and muscle tissue, and the nature of the distribution of adipose tissue. To improve the quality of research, it is necessary to determine the composition of the body and the hormonal activity of adipose tissue.

Conclusion

The data from the studies reviewed indicate a relationship between COPD and adipose tissue. However, the mechanisms of the relationship between the pathogenesis of COPD and the dysfunction of adipose tissue have not been sufficiently studied, and the role of adipose tissue and body composition in the course of the disease and its prognosis has not been studied. Despite the inconsistency of these data, recent studies confirm that in severe stages of COPD, excess adipose tissue performs a protective function. A promising direction is to study the distribution of adipose tissue in the body and its hormonal activity, as well as determine body composition to clarify the relationship between obesity and COPD. Thus, further study of this problem is necessary to improve patient management and define clear goals to achieve optimal nutritional status, which is individual for each COPD patient.

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