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Comprehensive Assessment of Cardiometabolic Risk in Patients with Chronic Obstructive Pulmonary Disease and Obesity

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Abstract

Background: Currently, comorbid patients with chronic obstructive pulmonary disease (COPD) and obesity are becoming increasingly common in clinical practice. The objective of this study was to conduct a comparative analysis of indicators of various types of body metabolism (carbohydrate, lipid, adipokine profile) in COPD patients with obesity and normal body weight.

Methods and Results: The study included 86 patients with COPD (GOLD 3-4, group D). The diagnosis of COPD was established in accordance with GOLD, revision 2021.The patients were divided into two groups. Group 1 consisted of 43 COPD patients with NBW [31(72.7%) men and 12(27.3%) women aged 43 to 75 years (mean age of 62.40 ± 8.83 years)] and Group 2 consisted of 43 COPD patients with obesity [32(77.27%) men and 11(22.73%) women aged 48 to 72 years (mean age of 62.94 ± 5.96 years)]. All patients underwent an analysis of the composition of the body by the bioelectrical impedance method. Blood levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were determined by the enzymatic colorimetric method. The glucose level was determined by the glucose oxidant method. The serum adipokine levels (leptin, adiponectin, resistin), as well as testosterone and immunoreactive insulin, were determined using ELISA. To assess insulin resistance, the HOMA-IR index was calculated. To determine cardiovascular risk, the visceral adiposity index (VAI) was calculated according to the formula, which considers body mass index, triglycerides, HDL-C, and waist circumference.

The level of HDL-C was significantly lower (P=0.0000)), and the levels of TC (P=0.0479), LDL-C (P=0.0020), glucose (P=0.0020), immunoreactive insulin (P=0.0000), and HOMA-IR index (P=0.0000), were significantly higher in Group 2 than in Group 1. As for the content of adipose tissue hormones, the leptin level was significantly higher in Group 2 (P=0.0000) than in Group 1, while there were no statistically significant differences between groups in the level of resistin (P=0.4996). The adiponectin level was significantly lower in Group 2 than in Group 1 (P<0.0001). The VAI level in Group 2 was significantly higher than in Group 1 (2.13±1.56 and 1.18±0.41, respectively, P=0.0002). In contrast, the testosterone level was significantly lower in Group 2 than in Group 1 (10.59±6.94 nmol/l and 20.02±12.25 nmol/l, respectively, P=0.0000).

Conclusion: The high metabolic activity of adipose tissue in patients with COPD and obesity is directly related to the progression of comorbid conditions.(**International Journal of Biomedicine. 2023;13(1):31-36.**)

Keywords: COPD • cardiometabolic risk • body mass index • leptin

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Abbreviations

BMI, body mass index; **COPD**, chronic obstructive pulmonary disease; **CHF**, chronic heart failure; **HC**, hip circumference; **HOMA-IR**, Homeostasis Model Assessment of Insulin Resistance; **HDL-C**, high-density lipoprotein cholesterol; **LDL-C**, low-density lipoprotein cholesterol; **NBW**, normal body weight; **TC**, total cholesterol; **TG**, triglycerides; **VAI**, visceral adiposity index; **WC**, waist circumference.

Introduction

Currently, comorbid patients with chronic obstructive pulmonary disease (COPD) and obesity are becoming increasingly common in clinical practice.[1,2] This combined pathology causes difficulties in managing such patients and in assessing the prognosis and outcomes of the disease.[1,3,4]

COPD is one of the leading global health problems, which significantly increases the number of deaths.[1,2] As is known, both endogenous factors and the impact of environmental factors play a role in the development of COPD.[5] About 2.75 million people die from COPD every year, which is 4.8% of all causes of death.[5] The main causes of death in patients with COPD are cardiovascular diseases (25%) and tumors of various localization (mainly lung cancer, 20%-33%); other causes account for up to 30% of cases.[5]

Obesity is a chronic disease caused by an excess of adipose tissue, which can significantly reduce health and alter the functionality of various organs, including the lungs.[6,7] Excessive deposition of fat in the abdomen can lead to malposition of the diaphragm and subsequent reduction in lung volume, leading to an increased need for ventilation and an increased susceptibility to respiratory diseases, including COPD.[6-8] The altered secretion profile of adipokines from dysfunctional adipose tissue in obesity contributes to low-grade systemic inflammation, impairing lung immune response and promoting airway hyperresponsiveness.[6-8]

But now there is also evidence of the "obesity paradox."[9] Twenty years ago, Gruberg and coworkers observed better outcomes in overweight and obese patients with coronary heart disease undergoing percutaneous coronary intervention compared with very lean patients (BMI<18.5 kg/m^2) and those with BMI within the normal range. This unexpected phenomenon was described as "an obesity paradox."[10] Following this, more research on the obesity paradox in various conditions has been conducted. It is known that overweight or obese patients initially have a greater resource of lean muscle mass, and therefore, better tolerate its loss than patients with COPD and normal body weight (NBW), resulting in their higher chances of survival.[11-13]

Excess body weight in combination with COPD leads to an increased risk of developing diseases, primarily of the cardiovascular system.[7] There is evidence that the combination of low muscle mass and abdominal obesity may adversely affect the cardiometabolic risk profile in COPD, even in NBW individuals.[7]

Objective: to conduct a comparative analysis of indicators of various types of body metabolism (carbohydrate, lipid, adipokine profile) in COPD patients with obesity and normal body weight.

Materials and Methods

The study included 86 patients with COPD (GOLD 3-4, group D). The diagnosis of COPD was established in accordance with GOLD, revision 2021.The patients were divided into two groups. Group 1 consisted of 43 COPD patients with NBW [31(72.7%) men and 12(27.3%) women aged 43 to 75 years (mean age of 62.40 ± 8.83 years)] and Group 2 consisted of 43 COPD patients with obesity [32(77.27%) men and 11(22.73%) women aged 48 to 72 years (mean age of 62.94 ± 5.96 years)]. Groups 1 and 2 were comparable in terms of gender ($\chi 2$=1.658; P=0.224) and age (P=0.628). The main criterion for diagnosing NBW or obesity was BMI (kg/m^2). According to WHO recommendations, a BMI of 18.5-24.99 kg/m^2 corresponds to NBW, ≥30 kg/m^2 corresponds to obesity.

The criteria for exclusion from the study were: 1) participation of the patient in any intervention study, 2) COPD in the acute stage, 3) concomitant diseases of the lungs, such as confirmed or suspected malignant lung disease or other disease of the respiratory system such as lung tumor, pulmonary fibrosis, interstitial pulmonary fibrosis, tuberculosis, sarcoidosis, bronchial asthma, bronchiolitis obliterans, bronchiectasis, 4) concomitant diseases of other organs and systems, such as acute cardiac pathology, CHF Stage IIA and higher., and chronic renal or hepatic insufficiency.

Basic therapy for COPD included a long-acting anticholinergic drug or a long-acting β2-agonist in combination with a long-acting anticholinergic drug, or a long-acting β2-agonist in combination with an inhaled glucocorticosteroid (GCS). Patients used short-acting β2-agonists as needed.[14]

Functional and biochemical tests

All patients in the study groups underwent an analysis of the composition of the body by the bioelectrical impedance method using a fat mass analyzer BC-555 (Tanita Corporation, Tokyo, Japan). The percentages of fat, water, MM, and bone mass were evaluated.

Blood levels of TC, TG, HDL-C, and LDL-C were determined in the venous blood by the enzymatic colorimetric method. The glucose level was determined by the glucose oxidant method. The serum adipokine levels (leptin, adiponectin, resistin), as well as testosterone and immunoreactive insulin, were determined using ELISA. To assess insulin resistance, the HOMA-IR index was calculated using the formula: HOMA-IR = fasting insulin (μU/ml) × fasting glucose (mmol/l)/22.5.[15] To determine cardiovascular risk, the VAI was calculated according to the formula, which considers BMI, TG, HDL-C, and WC. The value of VAI for men: VAI = (WC / 39.68 + (1.88 × BMI)) × (TG / 1.03) × (1.31/HDL-C). The value of VAI for women: VAI = (WC/36.58 + (1.89 × BMI)) × (TG/0.81) × (1.52/HDL-C).[16]

Statistical analysis was performed using STATGRAPHICS Plus 5.1. For descriptive analysis, results were presented as mean±standard deviation (SD). Inter-group comparisons were performed using One-Way ANOVA. Group comparisons with respect to categorical variables were performed using chi-square test. Pearson's correlation coefficient (r) was used to determine the strength of the relationship between the two continuous variables. A probability value of P<0.05 was considered statistically significant.

The study was conducted in accordance with ethical principles of the WMA Declaration of Helsinki (1964, ed. 2013) and approved by the Ethics Committee of Voronezh State Medical University named after N. N. Burdenko. Written informed consent was obtained from all participants.

Results

Groups 1 and 2 were comparable in relation to the use of long-acting anticholinergics (*P*=0.6494), long-acting β2-agonists (*P*=0.8801), inhaled corticosteroids (*P*=0.8784), and short-acting β2-agonists (*P*=0.1735).

The results of a comparative analysis of an anthropometric examination with the determination of BMI, HC, WC, as well as the body composition of COPD patients are presented in Table 1. In Group 2, a relationship between increased BMI and a high WC/HC ratio (r=5.34, *P*=0.004) and a high fat percentage (r=6.29, *P*=0.001) was determined, which may indirectly indicate metabolic disorders associated with excess fat tissues in the body. The results of assessing the percentage of water content in patients of both groups are interesting. Thus, in Group 1 patients, the water percentage in the body was significantly higher than in Group 2 patients (*P*=0.0000). At the same time, there were no significant differences between groups in the indicator of the percentage of muscle mass.

Table 1.

Comparative characteristics of body composition parameters in COPD patients in study groups.

Index	Group 1 (n=43)	Group 2 (n=43)	*P*-value
BMI, kg/m^2	23.02±1.93	35.28±5.94	0.0000
% fat	16.72±7.91	40.62±10.32	0.0000
% of muscle mass	44.72±9.58	48.26±22.36	0.3427
% of water	53.56±4.02	42.65±12.06	0.0000
% of bone mass	4.09±1.15	6.24±4.76	0.0051
WC, cm	85.92±12.79	124.90±12.74	0.0000
HC, cm	95.30±4.76	102.58±21.91	0.0362
WC/HC	0.90±0.12	1.30±0.58	0.0000

The prevalence of diabetes mellitus in Group 2, 14(31.8%), was significantly higher than in Group 1, 0(0%) (P=0.0000). Hypertension in Group 2 was also significantly more common than in Group 1 [36(81.81%) and 21(47.72%), respectively (*P*=0.0001). Groups 1 and 2 did not significantly differ in the frequency of occurrence of coronary heart disease and CHF (*P*>0.05 in both cases).

Changes in lipid profile, insulin sensitivity, and adipokine status were detected only in Group 2 (Tables 2 and 3). In particular, the level of HDL-C was significantly lower (*P*=0.0000), and the levels of TC (*P*=0.0479), LDL-C (*P*=0.0020), glucose (*P*=0.0020), immunoreactive insulin (*P*=0.0000), and HOMA-IR index (*P*=0.0000), were significantly higher in Group 2 than in Group 1. As for the content of adipose tissue hormones, the leptin level was significantly higher in Group 2 (*P*=0.0000) than in Group 1, while there were no statistically significant differences between groups in the level of resistin (*P*=0.4996). The adiponectin level was significantly lower in Group 2 than in Group 1 (*P*<0.0001). The VAI level in Group 2 was significantly higher than in Group 1 (2.13±1.56 and 1.18±0.41, respectively, *P*=0.0002). In contrast, the testosterone level was significantly lower in Group 2 than in Group 1(10.59±6.94 nmol/l and 20.02±12.25 nmol/l, respectively, *P*=0.0000).

Table 2.

Comparative characteristics of carbohydrate metabolism parameters and adipokine levels in COPD patients in study groups.

Index	Group 1 (n=43)	Group 2 (n=43)	*P*-value
Glucose, mmol/l	5.34±1.10	7.32±1.21	0.0000
Insulin, mcME/ml	11.34±4.24	28.46±3.54	0.0000
HOMA-IR	2.69±1.82	7.76±1.09	0.0000
Resistin, ng/ml	9.38±4.92	8.61±5.59	0.4996
Leptin, ng/ml	13.32±10.81	45.58±29.47	0.0000
Adiponectin, μg/ml	32.21±4.15	26.57±4.42	<0.0001

Table 3.

Comparative characteristics of lipid profile parameters in COPD patients in the study groups.

Index	Group 1 (n=43)	Group 2 (n=43)	*P*-value
TC, mmol/l	5.36±1.54	6.20±2.27	0.0479
LDL-C, mmol/l	3.48±1.84	4.87±2.18	0.0020
HDL-C, mmol/l	1.28±0.30	1.04±0.40	0.0023
TG, mmol/l	0.96±0.14	1.12±0.72	0.1563

Discussion

Consistent with the data obtained in our study, it is possible to describe obesity in COPD patients as a metabolically "active" state. This is confirmed as a direct indicator of metabolic disorders (the correlation of increased BMI with the percentage of body fat), and an indirect indicator (an increased WC/HC ratio). It can be concluded that the high metabolic activity of visceral fat becomes a key factor in the development of diseases associated with obesity and the development of complications.

In the course of body composition analysis, it was found that patients with COPD and obesity had a higher percentage of fat and a lower percentage of water content than the non-obese COPD group. Changes in muscle mass parameters were not statistically significant. It is worth mentioning that various studies have shown that sarcopenia, muscle wasting, and low muscle strength are associated with an increase in inflammatory biomarkers, a decrease in lung function, and, because of all the above, a drop in the quality of life and a worse prognosis.[17] However, at the same time, there are studies with a completely opposite result: some authors argue that a higher BMI has a positive relationship with FEV1, and the higher the BMI, the better the lung function.[18]

It must be remembered that COPD is a chronic disease, the development and progression of which are influenced by concomitant pathology. Thus, according to scientists, the combination of COPD with various diseases of the cardiovascular system is reflected in the deterioration of the prognosis, which ultimately increases mortality.[19] Special attention in this context should be given to hyperlipidemia, which is one of the risk factors for cardiovascular diseases.[20] Given the prevalence of hyperlipidemia in patients with COPD, it can be concluded that it may play some role in the pathophysiology of COPD,[20] which, however, requires further clarification. Our study found a significant decrease in HDL-C, and an increase in TC, LDL-C and TG in obese patients with COPD, compared with normal-weight COPD patients.

As is known, VAI is a more specific and sensitive examination tool than BMI. VAI is considered a reliable indicator of the increased risk of cardiometabolic diseases in patients.[21] According to the results of our study, this indicator was significantly higher in COPD patients with obesity, which indicates a higher functional activity of visceral adipose tissue in this group of subjects.

In recent years, there has been an active search for biomarkers that would allow diagnosing exacerbations of COPD at an earlier stage, which would allow for maintaining a higher lung function in a patient. However, the results of such studies are somewhat inconsistent and sometimes contradictory.[22] The role of adipokines involved in various metabolic processes, systemic inflammatory reactions, and atherogenesis is discussed. There is evidence that patients with COPD and bronchial asthma are characterized by a higher level of these markers.[22] Thus, the dysregulation of adipokines may have an impact on the course of patients with these diseases. According to the results of our study, the average values of leptin concentration are significantly higher in the group of patients with COPD and obesity, which probably causes a higher activity of systemic inflammation in this group.

It has been suggested that inflammation mediated by alveolar macrophages may be inhibited by adiponectin, which thus exerts a protective effect on the respiratory system. It is known that obesity, especially central obesity, is associated with an increase in inflammatory factors such as IL-6 and TNF-α,[23] which have a negative impact on lung function and, as a result, increase morbidity and mortality.[24] According to some researchers, genetically induced adiponectin deficiency in mice resulted in increased expression of TNF-α, defining an emphysema-like phenotype.[25] However, no full-fledged studies that determine the place of adiponectin as a prognostic factor in COPD have been conducted. Our study showed that obese COPD patients had lower mean adiponectin levels than normal-weight COPD patients.

In addition to the above, it is worth mentioning that metabolic syndrome is one of the factors that worsen the course and prognosis of COPD.[24,26] It is known that patients with COPD have an increased prevalence of metabolic syndrome, compared with the general population (21%-62%), with the highest prevalence of metabolic syndrome observed in the early stages of COPD.[27] Immediate manifestations of deterioration in the course of this combination of diseases: a more predictable decrease in FEV1 in percent, increased dyspnea, and increased use of inhaled steroids.[28] Data from some studies suggest that diabetes is more common in patients with respiratory diseases than emphysema on a CT scan.[29] It has been suggested that both the direct effect of hyperglycemia and the support of systemic inflammation in insulin resistance have a negative effect on lung function.[30] Our study found higher insulin levels in obese COPD patients than in normal-weight COPD patients. In addition, high HOMA-IR values were indicative of insulin resistance.

The role of systemic inflammation as an important cause of hypogonadism should also be noted. The following chain of events is observed: men with COPD often suffer from hypoxemia, have many comorbidities, and are exposed to long-term exposure to glucocorticoids,[31] which increases the risk of developing hypogonadism. It is known that testosterone deficiency exacerbates COPD symptoms in two ways: 1) by a direct effect on the respiratory muscles; 2) by reducing overall strength and physical performance.[32] All this leads to a decrease in FEV1 and FVC. Recent studies have shown that low circulating testosterone levels are associated with adverse respiratory outcomes.[32] Our data support lower serum testosterone levels in patients with COPD and obesity.

Conclusion

The high metabolic activity of adipose tissue in patients with COPD and obesity is directly related to the progression of comorbid conditions. Patients with COPD and obesity are more likely to have comorbidities like diabetes mellitus and hypertension, which further determines cardiac outcomes. It is necessary to evaluate VAI in patients with COPD and obesity, since early diagnosis and timely preventive measures can improve the prognosis in terms of comorbidity. The role of adipokines in the COPD pathogenesis needs additional study that may open novel therapeutic strategies for COPD. The management of patients with COPD and obesity should be carried out comprehensively,[33,34] with pulmonologists, cardiologists, and endocrinologists involved in the diagnostic and treatment process.

Competing Interests

The authors declare that they have no competing interests.

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