THE INFLUENCE OF BODY MASS INDEX ON THE PROGNOSIS OF PATIENTS WITH COPD: THE EFFECT OF METABOLIC SYNDROME AND THE VALIDITY OF THE OBESITY PARADOX

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BODY MASS INDEX- MORE THAN JUST A NUMBER IN THE PROGNOSIS OF PATIENTS WITH COPD AND METABOLIC SYNDROME (Abstract): Chronic obstructive pulmonary disease (COPD) is increasingly recognized as a complex systemic disease rather than a condition limited to the lungs. Malnutrition, cachexia, and obesity contribute to decreased exercise capacity, higher rates of exacerbations and increased mortality. The **aim** of the study was to investigate the influence of the body mass index (BMI) on the prognosis of patients diagnosed with COPD, in the presence or absence of MetS. **Materials and methods**: A total of 100 patients with a confirmed diagnosis of COPD were enrolled in the study, of whom 65 patients met the diagnostic criteria for MetS. Patients were evaluated based on clinical, anthropometric, and laboratory parameters. BMI was calculated for each patient, and its association with disease prognosis was subsequently analyses, considering the presence or absence of MetS. **Results:** The patients were divided into two groups based on the presence or absence of metabolic syndrome. Both BMI and waist circumference showed statistically significant differences between groups ($p<0.001$). Plasma glucose levels were significantly higher in COPD patients with MetS and BMI$\geq$ 25 kg/m^2 compared to those without MetS ($p= 0.020$). Plasma triglyceride levels were also significantly higher in the same group ($p= 0.034$). No statistically significant differences were observed for systolic and diastolic blood pressure across the groups ($p> 0.05$). **Conclusions:** Continuous monitoring of BMI and the prevention of cachexia are essential strategies for reducing mortality rates, whereas the prevention of obesity contributes to the reduction of cardiovascular complications. **Keywords**: COPD, METABOLIC SYNDROME, BMI, PROGNOSIS.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major global health problem, characterized not only by persistent respiratory symptoms and airflow limitation, but also by significant systemic effects (1, 2).

Among these systemic manifestations, nutritional disturbances such as malnutrition, sarcopenia, and obesity have been increasingly recognized as important factors influencing disease progression and prognosis (3-5).

In particular, body composition abnormalities and the presence of metabolic syndrome (MetS) are highly prevalent among COPD patients and are associated with increases morbidity and mortality (6, 7). Therefore, assessing and addressing nutritional status represents a crucial component of comprehensive COPD management (8). Moreover, the coexistence of MetS adds a substantial burden of cardiovascular morbidity. As pulmonary function worsens, COPD patients often reduce their physical activity levels, creating conditions that facilitate weight gain (9, 10). In COPD patients, there exists a paradox where individuals with higher body mass index (BMI) tend to have better survival rates than those with normal or low BMI, especially among those with advanced disease (11). One possible reason is that the severity of COPD may be overestimated in obese patients due to the physiological reduction in lung volumes (12).

However, when factors such as carbon dioxide levels, muscle mass, and exercise capacity are accounted for, this "obesity paradox" often disappears (13). Both physical inactivity and co-existing conditions negatively affect survival outcomes. Additionally, the presence of heart failure, diabetes, and hypertension in COPD patients is linked to heightened systemic inflammation, suggesting metabolic abnormalities may contribute to disease mechanisms (14-16).

Patients with COPD who have an elevated BMI are more likely to develop MetS, a cluster of conditions that includes abdominal obesity, insulin resistance, dyslipidemia, and hypertension (17). These metabolic disturbances contribute to a heightened risk of cardiovascular disease, which is already a major cause of morbidity and mortality in COPD populations (18). The presence of excess adipose tissue, particularly visceral fat, may exacerbate systemic inflammation and oxidative stress, further promoting insulin resistance and abnormal lipid profiles (19, 20). Consequently, the combination of COPD and MetS poses a significant challenge in clinical management and underscores the need for early screening and targeted interventions to reduce cardiovascular risk in this subgroup of patients (21, 22).

MATERIALS AND METHODS

This prospective study was conducted at the Clinical Rehabilitation Hospital in Iași and included 100 patients diagnosed with COPD. The study was carried out between January 2022 and June 2023. The diagnosis of COPD was established by spirometry, based on a post-bronchodilator forced expiratory volume in one second (FEV1)/ forced vital capacity (FVC) < 0.70. Patients aged over 35 years who provided written informed consent were enrolled. Exclusion criteria included advanced renal or hepatic failure, neurological or psychiatric disorders, malignancies, and refusal to sign the informed consent form. All participants underwent comprehensive clinical and laboratory evaluations, with particular emphasis on analyzing the impact of BMI on pulmonary function. This study aimed to assess the relationship between BMI, MetS, and clinical outcomes in patients with COPD, emphasizing the importance of early nutritional monitoring as part of comprehensive disease management. Demographic data, anthropometric measure-

ments, cardiovascular risk indicators, and lung function were assessed at the baseline and again after 6 months.

Statistical Analysis. Descriptive statistics were performed using *SPSS software (version 27.0, SPSS Inc., Chicago, IL, USA)* for Windows. Data were reported as mean ± standard deviation (SD) for continuous variables or as percentages for categorical ones. The Kolmogorov-Smirnov test was applied to verify the normality of data distribution. For comparisons of continuous variables, a parametric t-test was used, while categorical variables were analyzed using Fisher`s exact test. To evaluate the strength and reliability of correlations, Pearson`s and Spearman`s (r) coefficients were employed.

Ethics. This study received ethical approval from the Research Ethics Committee of the "Grigore T. Popa" University of Medicine and Pharmacy of Iasi, Romania (Approval No. 122, dated 11th of November 2021), as well as from the Ethics Committee of the Iasi Clinical Rehabilitation Hospital on 10th of December 2021.

RESULTS

The study included 100 patients, of whom 68% were male (fig. 1). We focused on investigating BMI within the study group, highlighting an average BMI of 30.63 ± 6.842 kg/m^2 (mean ± standard deviation), with a higher value observed in subjects with COPD and MetS (32.57 ± 6.635 kg/m^2 vs. 26.68 ± 5.488 kg/m^2, p< 0.001). Moreover, 79% of the subjects had a BMI≥ 25 kg/m^2, with the majority of them being diagnosed with MetS (92.5% vs. 51.5%, p< 0.001). We also investigated abdominal circumference, and statistically significant differences were recorded between the two study groups (110.93± 13.120 vs. 99.52± 14.871, p< 0.001).

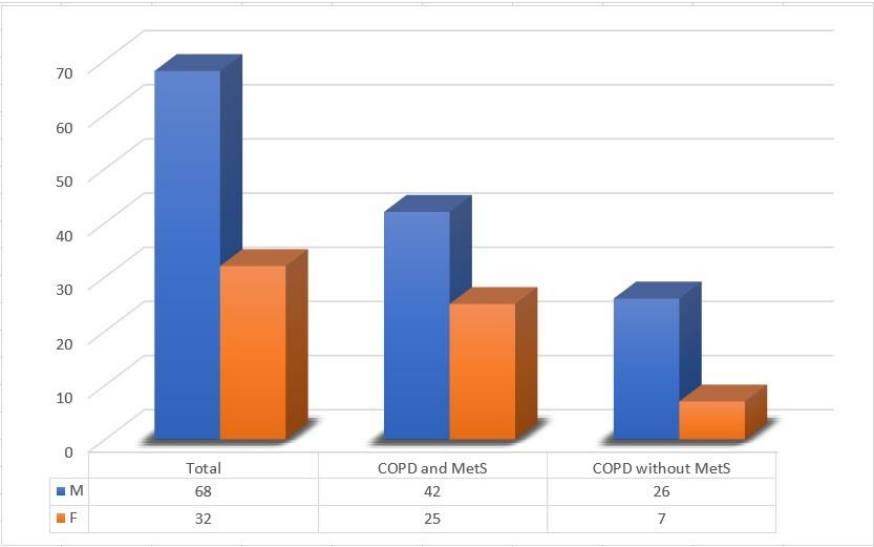

Fig. 1. Gender based distribution of COPD with and without MetS

The diagnostic criteria for MetS were analyzed by further subdividing the patients into two additional groups: those with a BMI< 25kg/m^2 and those with a

BMI≥ 25kg/m^2. The mean plasma glucose level was significantly elevated in patients with a BMI≥ 25kg/m^2 (p= 0.020). Moreover, statistically significant values were observed in the mean triglyceride levels among subjects with a BMI≥ 25kg/m^2 (p= 0.034). No statistically significant results were obtained regarding BMI, abdominal circumference, or systolic and diastolic blood pressure values (tab. I).

The patients underwent spirometric reevaluation at 6 months. At both baseline and 6- month follow-up, BMI showed a statistically significant positive correlation with FEV1 (%) and the FEV1/ FVC ratio in the total study population. These associations remained significant in the subgroup of patients with MetS, particularly for the FEV1/ FVC ratio, which demonstrated the strongest correlation (r= 0.379 at baseline and r= 0.349 at follow-up; p< 0.001). No statistically significant correlations were observed in the subgroup without MetS. Additionally, a weaker but significant correlation between BMI and FVC (%) was found at follow-up in the overall group (r= 0.223; p= 0.026) (tab. II).

The graphs illustrate the changes in BMI (fig. 2) and abdominal circumference by gender (fig. 3), between baseline and 6-month follow-up. At the initial evaluation, patients were educated on the importance of pulmonary rehabilitation programs. These programs were initiated during hospitalization and continued at home following discharge. Upon reevaluation at 6 months, both BMI and abdominal circumference showed a slight decrease in both male and female patients, reflecting a positive trend likely associated with adherence to the rehabilitation protocol.

TABLE I.

Criteria of MetS of the study population by BMI

	BMI < 25kg/m^2		**BMI ≥ 25kg/m^2**	
	COPD with MetS (n = 5)	COPD without MetS (n = 16)	COPD with MetS (n = 62)	COPD without MetS (n = 17)
BMI (kg/m^2)	21.76 ± 2.964	22.39 ± 1.815	33.44 ± 6.057	30.73 ± 4.619
	p = 0.905		p = 0.120	
Abdominal circumference (cm)	92.00 ± 11.225	90.44 ± 7.737	112.45 ± 12.093	108.06 ± 15.039
	p = 0.842		p = 0.397	
Plasma glucose level (mg/dL)	101.40 ± 7.807	100.29 ± 13.226	116.47 ± 29.446	106.31 ± 30.828
	p = 0.660		p = 0.020*	
Plasma TG level (mg/dL)	90.38 ± 12.912	98.90 ± 49.892	148.83 ± 67.618	114.71 ± 38.749
	p = 0.780		p = 0.034*	
SBP (mmHg)	136.00 ± 20.433	134.50 ± 19.135	137.10 ± 19.133	134.47 ± 12.319
	p = 0.603		p = 0.729	
DBP (mmHg)	82.00 ± 4.472	79.81 ± 11.173	81.81 ± 10.884	81.53 ± 5.970
	p = 0.548		p = 0.872	

Data are presented as mean±standard deviation (SD). Mann-Whitney test p<0.05* statistically significant
Abbreviations: BMI (body mass index), TG (triglyceride), SBP (systolic blood pressure), DBP (diastolic blood pressure)

TABLE II.

Correlations between BMI and spirometry results

Spirometry parameters	Total				COPD with MetS				COPD without MetS			
			95% C.I.				95% C.I.				95% C.I.	
	r	p	Lower bound	Upper bound	r	p	Lower bound	Upper bound	r	p	Lower bound	Upper bound
Baseline												
FEV1 (%)	0.342	<0.001*	0.157	0.505	0.389	0.001**	0.164	0.575	0.198	0.270	0.156	0.507
FVC (%)	0.171	0.089	0.026	0.355	0.071	0.570	0.173	0.306	0.114	0.526	0.238	0.440
FEV1/ FVC ratio	0.379	<0.001 *	0.198	0.536	0.508	<0.00 **	0.305	0.667	0.149	0.408	0.205	0.468
Follow-up												
FEV1 (%)	0.333	<0.001	0.146	0.497	0.361	0.003	0.132	0.553	0.149	0.409	0.205	0.468
FVC (%)	0.223	0.0260	0.028	0.402	0.127	0.304	0.116	0.357	0.202	0.259	0.151	0.510
FEV1/ FVC ratio	0.349	<0.001	0.164	0.510	0.484	<0.001	0.276	0.649	0.062	0.734	0.288	0.396

Abbreviations: FEV1, forced expiratory volume in the first second; FVC, forced vital capacity

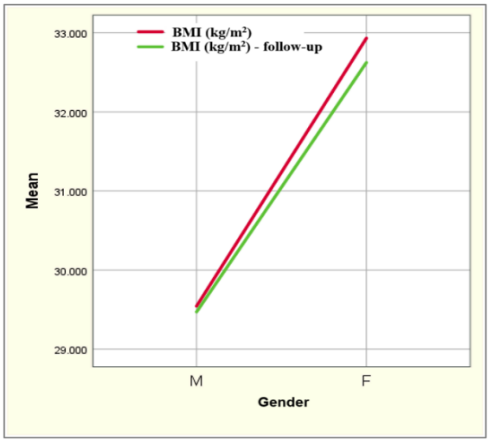

Fig. 2. Comparison of mean BMI (kg/m^2) at baseline and follow-up by gender

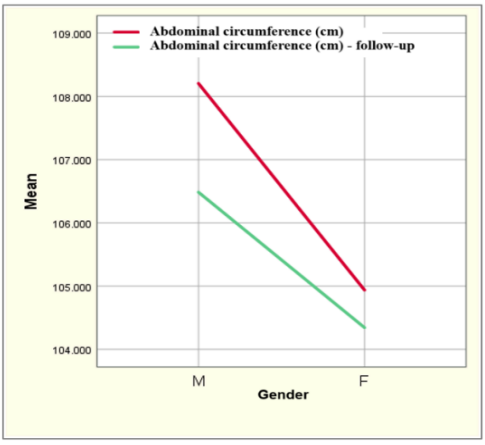

Fig. 3. Comparison of mean abdominal circumference (cm) at baseline and follow-up by gender

DISCUSSION

Earlier research has suggested a link between low BMI and decreased survival in individuals with COPD (23). However, more recent data indicate that specific adverse shifts in body composition may serve as more accurate predictors of mortality than BMI alone. In people with COPD, these changes are associated with reduced exercise capacity, poorer quality of life, and a higher risk of death (4). While some studies have explored the link between body composition and disease severity, few have investigated the role of sarcopenia in relation to COPD prognosis or addressed the importance of considering sarcopenia when evaluating BMI in overweight patients to prevent diagnostic errors (24, 25).

A retrospective cohort study involving 116,463 patients with COPD showed that individuals with both low and high BMI experienced a greater number of exacerbations over the course of one year. Moreover, a low BMI was associated with the presence of pulmonary comorbidities such as interstitial lung diseases, tuberculosis, and metabolic disorders (23, 26).

A decrease in BMI has been linked to an increased risk of overall mortality, even among overweight or obese individuals with COPD (27). Epidemiological studies in cancer patients have also found that being slightly overweight or in the early stages of obesity may lead to better survival outcomes. This trend has been consistently noted in COPD populations (28). One meta-analysis of five randomized clinical trials demonstrated that a higher BMI may help preserve lung function, with the slowest decline observed in those with a BMI of 30 kg/m² or higher (29). Another meta-analysis involving over 21,000 COPD patients found that individuals who were overweight or obese had lower mortality rates than those with a normal BMI (30). These findings support the concept of the "obesity paradox," where excess weight appears to be associated with reduced risk of death (23).

Our study highlights that in COPD patients with a BMI $\geq$ 25kg/m^2, the presence of MetS is associated with significantly higher plasma glucose and triglyceride levels, compared to those without MetS. These findings suggest that elevated BMI may exacerbate metabolic disturbances in patients with COPD, reinforcing the role of excess body weight as a contributing factor to the development and progression of MetS in this population. Consequently, they emphasize the importance of routine metabolic screening and individualized therapeutic strategies in COPD patients with increased BMI. Early detection and appropriate management of MetS may improve long-term clinical outcomes, reduce cardiovascular risk, and mitigate systemic complications in this vulnerable group.

Additionally, patients with lower BMI tended to have reduced spirometric values (FEV1 and FEV1/ FVC), both at baseline and follow-up, particularly in those without MetS. This pattern may reflect the detrimental impact of low body mass in respiratory muscle strength, nutritional status, and systemic inflammation. As supported by previous literature, a lower BMI in COPD patients is often associated with a poorer prognosis, increased risk of exacerbations, hospitalization, and overall mortality. These findings underscore the importance of early nutritional assessment and interventions aimed at preventing weight loss and muscle wasting in underweight or cachectic COPD patients.

In our patients, a positive correlation was observed between BMI and spirometric parameters (FEV1, FEV1/ FVC), both at baseline and at the 6-month follow-up, particularly in those with MetS. This suggests that a higher BMI is associated with better pulmonary function in this subgroup, supporting the concept of the "obesity paradox" in COPD.

Although the obesity paradox in COPD suggests that a higher BMI may be associated with lower mortality, this phenomenon should be interpreted with caution. Factors such as body composition, the presence of malnutrition or sarcopenia, and coexisting comorbidities must be considered. Consequently, weight management in COPD patients should be individualized, avoiding

both excessive weight gain and significant weight loss in order to optimize prognosis and enhance quality of life (31-33).

Recent studies have highlighted that the protective effect of obesity in COPD may be partially attributed to the greater nutritional reserves and muscle mass that overweight patients possess, which could contribute to better tolerance of disease exacerbations and improved survival (34). Moreover, adipose tissue may exert anti-inflammatory effects through the secretion of specific adipokines, potentially modulating the chronic systemic inflammation characteristic of COPD. However, this apparent advantage should not lead to the underestimation of obesity-related risks, such as cardiovascular disease, obstructive sleep apnea, and reduced physical performance. A nuanced understanding of the obesity paradox is necessary to tailor clinical interventions and to balance metabolic and respiratory risks in COPD management (30, 32).

CONCLUSIONS

BMI plays a significant role in the clinical profile of COPD patients, being associated with altered spirometric parameters and increased metabolic risk. Higher BMI values, particularly in patients with MetS, were significantly correlated with impaired pulmonary function, as demonstrated by reduced FEV1 and FEV1/ FVC ratios. Monitoring and managing BMI in COPD patients is essential, as excess weight contributes to increased systemic inflammation, cardiovascular risk, and reduced respiratory efficiency. Incorporating weight control strategies and structured pulmonary rehabilitation programs may improve both respiratory function and metabolic outcomes in COPD patients with elevated BMI.

CONFLICT OF INTERESTS AND FUNDING

The authors declare that they have no conflict of interest.

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