

Relationship between BODE index, quality of life and inflammatory cytokines in COPD patients

Correlazione tra indice BODE, qualità di vita e citochine infiammatorie nei pazienti con BPCO

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ABSTRACT

Background and aims: Recently a multidimensional grading system based on the body mass index (B), degree of airflow obstruction (O), dyspnea (D) and exercise capacity (E) - the BODE index - has begun to be used increasingly for the evaluation of chronic obstructive pulmonary disease (COPD) patients. The aim of our study was to investigate the relationship between the BODE index and disease duration, annual exacerbation and hospitalization rates, health related quality of life and systemic inflammatory markers like C-reactive protein (CRP), tumor necrosis factor (TNF)- α and interleukin (IL)-8.

Materials and methods: In 88 stable COPD patients we evaluated the body-mass index, pulmonary function tests, Modified Medical Research Council dyspnea scale and six-minute walk test (6MWT). BODE scores were determined. Disease duration, number of exacerbations and hospitalization in the previous year were recorded. We also performed arterial blood gases analysis, administered the St. George's Respiratory Questionnaire (SGRQ) and measured serum levels of CRP, TNF- α , IL-8.

Results: According to BODE score 52% of patients were BODE 1, 21% BODE 2, 15% BODE 3 and 12% were BODE 4. There was a significant relationship between BODE index and COPD stage as classified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) ($p < 0.001$). Correlations between BODE score and disease duration ($p = 0.011$), number of exacerbations ($p < 0.001$) and hospitalizations ($p < 0.001$) in the last year were also observed. SGRQ symptom, activity, emotion scores and total scores were found to be significantly correlated to BODE ($p < 0.001$). Serum CRP levels and BODE were also correlated ($p = 0.014$);

however, no correlation was found between serum levels of TNF- α and IL-8 and BODE.

Conclusions: As the BODE index shows a strong correlation with various prognostic and follow up parameters of COPD and systemic inflammation, its use should be considered for the evaluation of COPD patients.

Keywords: Biomarkers, BODE index, COPD, quality of life.

RIASSUNTO

Razionale e scopi: Nella valutazione dei pazienti con broncopneumopatia cronica ostruttiva (BPCO) è recentemente invalso l'uso in modo crescente di un sistema multidimensionale di misura basato su indice di massa corporea (B), entità dell'ostruzione funzionale respiratoria (O), dispnea (D) e capacità di esercizio fisico (E): l'indice BODE. Scopo del nostro studio era valutare la correlazione tra l'indice BODE e la storia di malattia, il numero di riacutizzazioni annue e il tasso di ospedalizzazioni, la qualità della vita legata alla salute e marker infiammatori sistemici come la proteina C reattiva (PCR), il fattore di necrosi tumorale (TNF)- α e l'interleuchina (IL)-8.

Materiali e metodi: Abbiamo valutato in 88 pazienti con BPCO stabile l'indice di massa corporea, le prove di funzionalità respiratoria, la scala Modified Medical Research Council della dispnea ed il test del cammino di 6 minuti (6MWT). Sono stati calcolati i punteggi BODE. Sono state registrate la durata della malattia, il numero di riacutizzazioni e di ospedalizzazioni nell'anno precedente. Inoltre sono state effettuate l'emogasanalisi, il St. George's Respiratory Questionnaire (SGRQ) e determinati i livelli serici di PCR, TNF- α e IL-8.

Risultati: Secondo il punteggio BODE 52% dei pazienti erano

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BODE 1, 21% BODE 2, 15% BODE 3 e 12% erano BODE 4. La correlazione era significativa ($p < 0,001$) tra indice BODE e stadio della BPCO determinato secondo la stadiazione del Global Initiative for Chronic Obstructive Lung Disease (GOLD). Erano significative anche le correlazioni tra punteggio BODE e durata di malattia ($p = 0,011$), numero di riacutizzazioni ($p < 0,001$) e ospedalizzazioni ($p < 0,001$) nell'ultimo anno. Il punteggio totale del SGRQ e dei campi sintomi, attività e emozioni era significativamente correlato al BODE ($p < 0,001$). Anche i livelli serici di PCR e il BODE erano correlati ($p = 0,014$), mentre non si è rilevata alcuna correlazione tra TNF- α e IL-8 con il BODE.

Conclusioni: Dal momento che l'indice BODE mostra una forte correlazione con vari indici di prognosi, di follow up ed infiammatori nella BPCO, una sua applicazione sistematica dovrebbe essere presa in considerazione nella valutazione dei pazienti con BPCO.

Parole chiave: Biomarker, BPCO, indice BODE, qualità di vita.

INTRODUCTION

Currently, chronic obstructive pulmonary disease (COPD) is regarded as a systemic disease causing structural and functional changes in many organs as well as in the lung. Malnutrition, weight loss, and peripheral muscle weakness are some of the systemic manifestations of COPD that seriously affect the health related quality of life and exercise capacity of patients [1,2]. Advances in understanding the systemic nature of COPD have given rise to the development of a combined index of multiple mortality predictors for this disease known as the "BODE index". The components of the index are: body mass index (BMI), airway obstruction (O), dyspnea (D) and exercise capacity (E). The BODE index includes both symptoms and physiological measurements and it has been reported as a better mortality predictor than forced expiratory volume in 1 second (FEV₁) [3]. It predicts mortality from any cause as well as respiratory causes and gives more comprehensive information than the FEV₁-based staging system described in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [3-5]. In view of the systemic nature of COPD, other tools such as quality of life questionnaires (QoLQ) have been developed to establish the systemic impacts of the disease. It has been recommended to administer QoLQs to determine disease severity and treatment responses in collaboration with physiological measurements [6]. St. George's Respiratory Diseases Questionnaire (SGRQ) was designed specifically for COPD patients and demonstrates the impact of the disease on daily life [6,7].

Since systemic inflammation has been recognized as an indisputable component of COPD, the role of inflammatory cytokines has also been widely investigated in the natural history of COPD [8]. It has been shown that C-reactive protein (CRP) levels are elevated in the serum of COPD patients even in stable disease [9]. In a follow up study of 8 years, basal CRP levels significantly predicted overall mortality, cardiovascular disease-related mortality and cancer-related mortality in patients with mild and moderate COPD. FEV₁ loss was shown to be correlated

to CRP levels [1] and CRP was found to be a specific marker of COPD exacerbations [10]. Increased levels of tumor necrosis factor (TNF)- α have been found in serum, induced sputum and bronchial biopsies of COPD patients, especially those in whom COPD was associated with weight loss [11-13]. Also, interleukin (IL)-8, a strong selective neutrophil chemo-attractant, showed increased levels in serum of COPD patients with respect to healthy controls [8].

Currently, clinical outcomes and biomarkers are two parameters being used to determine the pulmonary function and systemic effects of COPD. We think that evaluating COPD, a multicomponent disease, functionally and systemically will improve understanding of this disease. In our study we hypothesized that a composite index of clinical outcomes, the BODE index, was a better predictor of health status and systemic inflammation in COPD than FEV₁ alone and aimed to investigate the relationship of the components of BODE and the BODE index itself with systemic inflammatory biomarkers and quality of life as well as with prognostic factors like disease duration and annual exacerbation and hospitalization rates.

MATERIALS AND METHODS

Eighty-eight stable COPD patients diagnosed according to GOLD guidelines in our pulmonary diseases outpatient clinic were included in the study consecutively between November 2006 and May 2007. The study was approved by the human-research Ethical Review board and all patients provided written informed consent. Inclusion criteria were: COPD patients in stable conditions (no exacerbations due to any reason in the last 6 weeks). COPD was defined as a history of smoking of more than 20 pack-years and a FEV₁/forced vital capacity (FVC) ratio of less than 70% after 20 minutes after salbutamol administration [14]. Exclusion criteria were: patients with other inflammatory diseases (inflammatory bowel disease, rheumatologic diseases, vasculitis), interstitial lung diseases, active pulmonary tuberculosis, presence of atopy, history of myocardial infarction in the last 6 months, decompensated cardiovascular disease and walking disability.

Demographic features and medical history of the patients were recorded. Emergency service visits due to acute exacerbations and hospitalization to general ward or intensive care unit in the last year were investigated. Weight, height, dyspnea severity were measured and the six-minute walking test (6MWT), pulmonary function tests (PFT) were performed. SGRQ, arterial blood gases (ABG) analysis and measurement of serum levels of inflammatory cytokines (CRP, TNF- α , IL-8) were also performed. **Pulmonary Function Tests:** PFT were performed with the Jaeger Master Screen Pneumo device. The best test from three consecutive tests was accepted. FEV₁, FVC, FEV₁/FVC were measured according to ATS criteria. COPD staging was done according to

GOLD 2006 [14].

Body Mass Index: BMI was calculated according to the formula weight (kg) / height (m)² [15].

Dyspnea Severity: The Modified Medical Research Council (MMRC) scale was used for the evaluation of dyspnea [16].

Six-minute walking test: 6MWT was performed in a 35 m long corridor. Patients were motivated to walk at the fastest speed they could. Oxygen saturation was measured before and after the test and the distance walked was recorded [17].

BODE index: The overall index was calculated according to BMI, FEV₁, 6MWT, MMRC by summing the points as shown in Table I. Further subgroupings like BODE 0, 1, 2, 3 were made, as defined in the formula [3].

Quality of Life Questionnaire: The Turkish translation of the St. George's Respiratory Diseases Questionnaire (SGRQ) was used to determine the quality of life [18].

Arterial Blood Gases Analysis: ABG samples were obtained from the radial artery with heparinized injectors and studied with a Roche Diagnostics GmbH OMNI C, Mannheim (Germany) device with original reactive analyzers.

Measurement of CRP, TNF- α , IL-8 levels: Venous blood samples were centrifuged and serums were separated and preserved at -20° C to be analyzed together. Serum CRP levels were studied with original reactive analyzers (Beckman Coulter Inc. Unicel DxC 800 Synchron Clinical Systems Galway, Ireland). Serum TNF- α and IL-8 levels were studied according to the manufacturer's recommendations (BioSource Europe S.A Nivelles, Belgium) with the Enzyme Linked-Immuno-Sorbent Assay (ELISA) method.

Intra-assay variation coefficient (%CV) values for IL-8 kit were 3.9% for 74.9 pg/ml, 2.6% for 186.2 pg/ml, 5.3% for 991.8 pg/ml while the inter-assay variation coefficients were 5% for 89.8 pg/ml, 5.5% for 223.1 pg/ml, 7.8% for 981.2 pg/ml. Lowest measurement level for IL-8 kit was < 5.0 pg/ml. Intra-assay variation coefficient values for TNF- α kit were 5.2% for 8 pg/ml, 4.1% for 167 pg/ml, 3.9% for 459 pg/ml, while the inter-assay variation coefficients were 8.5% for 47 pg/ml, 8.2% for 170 pg/ml, 5.9% for 438 pg/ml. Lowest measurement level for TNF- α kit was 1.7 pg/ml. IL-8 and TNF- α levels were measured in only 65 of the patients, and CRP levels in 86 patients according to a table of random numbers, due to an inadequate number of kits.

Statistical analysis

Data were analyzed by the SPSS 15.0 package programme. Spearman's rank correlations and Pearson correlations were used to analyze comparisons.

RESULTS

Demographic characteristics of the 88 patients are shown in Table II. Duration of the disease ranged widely, from 6 months to 40 years, in the study population. Sixteen of the patients (18%) were non

smokers but had a history of passive exposure while 72 (82%) were current smokers. Most patients (53%) had comorbid diseases like hypertension, congestive heart failure and diabetes mellitus. Fifty-one (58%) patients had had no exacerbation and 65 (74%) had not been hospitalized in the previous 12 months. Functional parameters and serum cytokine levels of the study population are shown in Table III. Of the 88 patients, 16% were stage I, 42% were stage II, 27% were stage III, and 15% were stage IV according to GOLD guidelines. When patients were classified with respect to BODE score, 52% were BODE 1, 21% were BODE 2, 15% were BODE 3 and 12% were BODE 4. BODE scores and disease stages of the patients according to GOLD were significantly correlated, as expected ($p < 0.001$) (Figure 1).

Each single BODE component and the BODE index itself were compared with disease duration, number of exacerbations and number of hospitalizations in the last year, separately. BMI was not found to be correlated with any of these parameters. A significant relationship was found between MMRC and disease duration ($p = 0.003$), number of exacerbations ($p = 0.008$) and number of hospitalizations ($p = 0.001$). 6MWT was found to be correlated with disease duration ($p = 0.041$) and number of hospitalizations ($p = 0.002$). As for FEV₁, a significant correlation was observed for disease duration ($p = 0.001$) and number of exacerbations ($p < 0.001$). The BODE index itself was found to be correlated with all these parameters, showing the strongest correlation for number of exacerbations and number of hospitalizations in the last year ($p < 0.001$ for both). Among the single components of the BODE index, BMI was the one that showed the least correlation ($p = 0.020$) with BODE ($p < 0.001$).

Components of BODE index including BMI, MMRC dyspnea scale, 6MWT and pulmonary function parameters (FEV₁, FVC and FEV₁/FVC) were also compared. There was a significant relationship between BMI and FEV₁/FVC ($p = 0.011$). MMRC and 6MWT were also significantly correlated with FEV₁ ($p < 0.001$ for both), FVC ($p < 0.001$ for both) and FEV₁/FVC ($p = 0.016$, $p = 0.006$ respectively).

All components of BODE index and the BODE index itself were found to be significantly correlated with arterial PO₂ ($p < 0,05$). The correlation was determined negative for BODE and PaO₂, while it was positive for BODE and PaCO₂ ($p < 0.001$).

A significant correlation was observed between MMRC, 6MWT, FEV₁ and SGRQ total score ($p < 0.001$ respectively). Also, BODE index and SGRQ symptom, emotion, activity and total scores were found to be significantly correlated ($p < 0.001$, respectively) (Figure 2).

When inflammatory markers were compared with BODE index, CRP levels were shown to have a weak but statistically significant correlation ($r = 0.2$, $p = 0.014$) (Figure 3) while TNF- α and IL-8 did not show a correlation. CRP was not found to be correlated with FEV₁, FVC and FEV₁/FVC. However, a significant relationship was found between CRP

TABLE I: SCORING FOR THE COMPONENTS OF THE BODE INDEX: BODY-MASS INDEX, DEGREE OF AIRFLOW OBSTRUCTION, DYSPNEA, AND EXERCISE CAPACITY

Parameter	Points on BODE Index			
	0	1	2	3
Body mass index (kg/m ²)	> 21	≤ 21	-	-
FEV ₁ (% predicted)	≥ 65	50-64	36-49	≤ 35
6 minute walking distance (m)	≥ 350	250-349	150-249	≤ 149
MMRC dyspnea scale (score)	0-1	2	3	4

Definition of abbreviation: FEV₁, forced expiratory volume in 1st second; MMRC, Modified Medical Research Council. BODE groups are classified as: 1-2 points: BODE 0; 2-4 points: BODE 1; 4-7 points: BODE 2; 7-10 points: BODE 3.

and SGRQ total score (p = 0.015).

When the patients were divided into two groups according to the presence of comorbid diseases, there was no statistically significant difference with respect to dyspnea severity, 6MWT and CRP levels between the two groups.

DISCUSSION

The most recently discussed topic in COPD in the last few years is its inflammatory and systemic nature. Several clinical tests and biomarkers have been developed for the evaluation of systemic effects of the disease [1]. A weak correlation has been defined between pulmonary function tests, especially FEV₁ and clinical outcomes including the severity of dyspnea and other symptoms, mortality, health status, quality of life and frequency of exacerbations [18,19]. The BODE index has been suggested as a new follow up tool for the evaluation of COPD patients [3]. CRP is another systemic biomarker that has been widely used for inflammatory diseases like COPD [8].

In our study, among the 88 COPD patients we found a correlation between BODE index and COPD stages according to GOLD; this was surely due to the impact of FEV₁ in both GOLD staging and BODE index.

Ong et al. found the BODE index and number of emergency visits related in their study of 16 months follow up, and also showed a significant but lower grade relationship between number of emergency visits and FEV₁ [20]. In another study, the BODE index was shown to be more significant for determining the severity of COPD exacerbations with respect to FEV₁ [21]. In our study, we similarly found the BODE index to be related to annual rate of hospitalizations (p < 0.001), but this relationship was not observed for FEV₁. However, both BODE and FEV₁ had the same significant relationship for number of exacerbations (p < 0.001 for both). In the light of these results, we consider that FEV₁ is an important marker in determining exacerbations within the other components of BODE, while for hospitalizations other components of BODE than FEV₁ are more important.

Weight loss is one of the common systemic effects of COPD. In a retrospective study of 400 patients Schols et al. reported increased mortality in severe COPD patients with chronic hypoxemia and a BMI < 25 kg/m² [22]. Another study showed a significant correlation between fat free mass index (FFMI) and MRC, FEV₁, FEV₁/FVC. BMI and FFMI were found to be related to 6MWT, but there was no correlation between BMI and disease severity. It was suggested that FFMI showed a better correlation with disease

TABLE II: DEMOGRAPHIC CHARACTERISTICS OF STUDY POPULATION (N = 88)

Age (mean ± SD)	63.6 ± 10.5
Sex (female/male)	12/76
Disease duration, median (25 th to 75 th percentile)	5 (2-10) years
Smoking history, median (25 th to 75 th percentile)	40 (20-60) pack/year
Number of exacerbations, median (25 th to 75 th percentile)	0 (0-1) /last year
Number of hospitalizations, median (25 th to 75 th percentile)	0 (0-1) /last year
Comorbid diseases (present/absent)	47/41
Oxygen therapy (present/absent)	8/80
Maintenance therapy with inhaled steroid (present/absent)	49/39

TABLE III: SUMMARY OF FUNCTIONAL PARAMETERS AND SERUM CYTOKINE LEVELS FOR THE STUDY POPULATION

	Number (n)	Mean ± SD	Minimum	Maximum
BMI (kg/m ²)	88	25.7 ± 4.9	16.5	37.9
FEV ₁ (L)	88	1.51 ± 0.6	0.3	2.8
FEV ₁ % predicted	88	53.3 ± 17.4	21	103
FEV ₁ /FVC	88	55.9 ± 10.2	28	70
MMRC	88	1.9 ± 1.1	0	4
6MWT (m)	88	375.2 ± 137.0	65	640
BODE index	88	3.1 ± 2.6	0	10

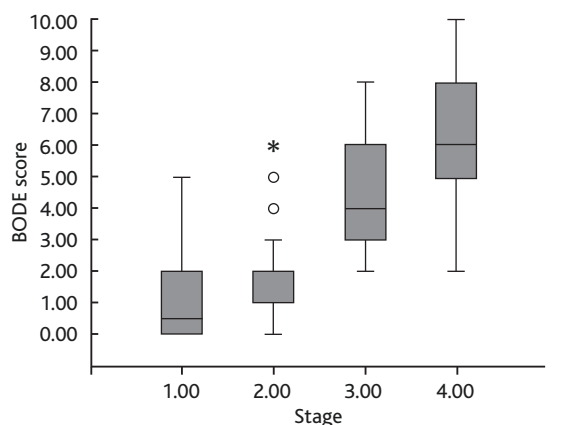
	Number (n)	Median ± IQR (25 th - 75 th)	Minimum	Maximum
SGRQ total score	88	43 (31-62)	7.4	95.8
CRP (pg/ml)	88	0.6 (0.25-1.20)	0.05	14.4
TNF-α (pg/ml)	65	19 (15-21)	12.4	57.7
IL-8 (pg/ml)	65	14 (8-23)	2.5	391.1

Definition of abbreviations: BMI, body mass index; CRP, C-reactive protein; FEV₁ (L), forced expiratory volume in 1 second, liter; FVC, forced vital capacity; MMRC, Modified Medical Research Council; 6MWT, 6-minute walking test; SGRQ, St. George's Respiratory Disease Questionnaire; TNF-α, tumor necrosis factor-α; IL-8, interleukin 8.

severity than BMI [23]. In our study, mean BMI of the patients was 25.7 kg/m² and a significant positive correlation was found only with FEV₁/FVC. No correlation was determined between BMI and disease severity according to GOLD. Also, the relationship between BMI and BODE index was the least with respect to the other components. This result leads us to consider that BMI has little contribution in determining disease severity. Dyspnea, one of the major symptoms of COPD, is a subjective symptom with perception differences depending on age or individual characteristics. Many dyspnea measurement scales have been developed and MMRC is one of the most widely accepted. Pulmonary function and dyspnea severity have been reported to be correlated in some studies;

however in other studies dyspnea has been found uncorrelated with obstruction degree [24-27]. In our study, MMRC and FEV₁, FVC, FEV₁/FVC were found to be related. In addition, a difference of our study with respect to other studies was the relationship between MMRC and disease duration, annual exacerbation and hospitalization rates and disease severity as well as arterial blood gas parameters (PaO₂, PaCO₂). 6MWT utilization has recently been increased in the evaluation of functional status and exercise performance of COPT patients. In our study, similarly to Marin's findings [28], 6MWT was found correlated with MMRC, COPD stage according to GOLD and PFT parameters. There was also a significant re-

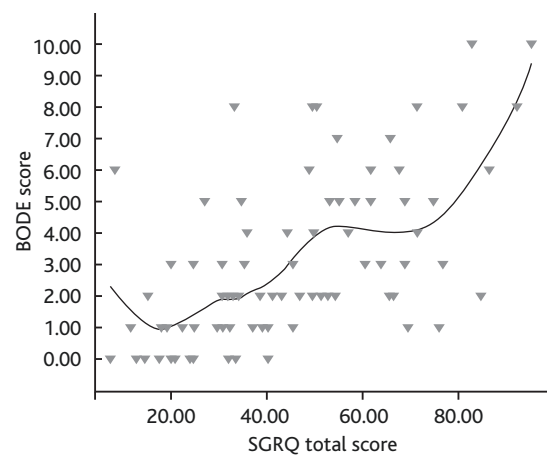
FIGURE 1: RELATIONSHIP BETWEEN BODE INDEX AND COPD STAGE ACCORDING TO GOLD



Box and plot showing median, 25th and 75th percentiles.

Definition of abbreviations: COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

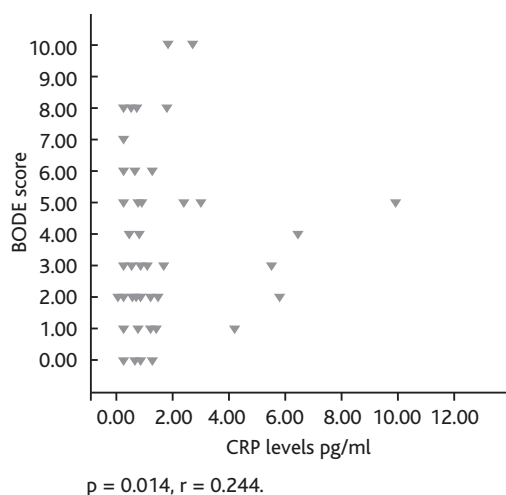
FIGURE 2: RELATIONSHIP BETWEEN BODE INDEX AND SGRQ TOTAL SCORES



p < 0.001; r = 0.570.

Definition of abbreviation: SGRQ, St. George's Respiratory Diseases Questionnaire.

FIGURE 3: RELATIONSHIP BETWEEN BODE INDEX AND SERUM CRP (PG/ML) LEVELS



Definition of abbreviation: CRP, C-reactive protein.

relationship between 6MWT and age, disease duration, and annual hospitalization rates. A distinctive finding of our study was the correlation between 6MWT and arterial blood gas parameters. In addition, 6MWT and SGRQ symptom, emotion, activity and total scores were found to be significantly related. In view of these data, 6MWT is suggested as a first step test for demonstrating the unfavorable effects of COPD on quality of life and reflecting daily activities of the patients.

Recent studies have reported that functional parameters like FEV₁ are insufficient to determine the health status in COPD, and quality of life measurements have gradually become more important for COPD [29]. In a study of COPD patients in which the relationship between BODE index and SGRQ was investigated, the BODE index was found to increase as SGRQ scores increased. There was a moderate and high relationship between BODE index and SGRQ; however COPD stage according to GOLD had a mild correlation with SGRQ [30]. In another study, a relationship between SGRQ total score and BODE severity scores was demonstrated; however this relationship was not observed between SGRQ total score and disease severity by GOLD stages [31]. In our study, we also found significant correlations between symptom, emotion, activity and total scores of SGRQ and BODE, and a weak correlation between all the SGRQ scores and COPD stage. These results suggest that the BODE index reflects the effects of disease on quality of life better than the GOLD stages do.

Several serum biomarkers have been defined in COPD. Among them, CRP, fibrinogen, interleukins (IL-6, IL-8), TNF- α and leucocytes are the ones most studied. Even in stable conditions, all these biomarkers have been shown to be elevated in COPD patients [8]. In our study, CRP, IL-8 and TNF- α levels were investigated. In a study by Wu et al., spu-

tum/serum CRP levels and pulmonary function tests of 30 COPD patients were compared and an inverse relationship was observed between sputum/serum CRP levels and FEV₁, and FEV₁/FVC levels [32]. Broekhuizen et al. found lower post bronchodilator FEV₁ levels in patients with high CRP levels in a group of 102 stable stage II and IV COPD patients. SGRQ scores were high and exercise capacity evaluated by 6MWT was low in this group of patients also [33]. Garrod et al. demonstrated that COPD patients with high CRP levels had lower quality of life and exercise capacity and a greater decline in lung functions [34]. In our study, unlike other studies in similar case series, CRP and pulmonary function tests were not found to be correlated. However, SGRQ and CRP were found to be inversely correlated, while there was a positive relationship between BODE index, COPD stage and CRP.

Nearly half of the patients in our study population had comorbid diseases like hypertension, congestive heart failure and diabetes mellitus related to systemic inflammation and this might have interfered with CRP levels, although these comorbidities had to be under control as an inclusion criterion. In an observational cohort study, in which moderate to severe COPD patients and two control groups without COPD (smokers and non-smokers) were tested using a high sensitivity CRP (hs-CRP) test, CRP levels were found to be elevated in patients with COPD independent of clinically significant ischemic heart disease and cigarette smoking [35]. Emerging laboratory and epidemiologic data have demonstrated that hs-CRP levels are associated with impaired insulin sensitivity and the development of type 2 diabetes [36]. Hence, diabetes mellitus might not be the cause of the high CRP levels in our study. However, we analyzed the CRP levels according to the presence or not of comorbidities and no statistically significant difference was observed between the two groups.

Many studies have shown a relationship between high TNF- α levels and weight loss in COPD [37,38]. In our study, we did not find a correlation between TNF- α levels and body mass index nor with the BODE index. IL-8 is another important biomarker in COPD and some studies have shown high levels of IL-8 in COPD patients [39], but also here we were not able to show any correlation between BODE index and IL-8.

In conclusion, in this study all components of BODE and the BODE index itself were compared with most of the clinical outcomes and biomarkers used in the evaluation of COPD. The most powerful correlation was observed between 6MWT, MMRC dyspnea scale and FEV₁. The BODE index is a comprehensive, feasible and simple clinical scoring system in the evaluation of COPD. It also reflects the quality of life and is correlated with CRP, one of the biological markers of systemic inflammation, while there is not a similar relationship with TNF- α and IL-8. Therefore, BODE is a clinical test which evaluates the pulmonary and extrapulmonary effects of

the disease all together. In this study, we showed the feasibility of BODE and the efficacy of CRP. In the future, we suggest that BODE could replace FEV₁ and could become the standard for the classifica-

tion and clinical evaluation of COPD.

CONFLICT OF INTEREST STATEMENT: None of the authors has any conflict of interest to declare in relation to the subject matter of this manuscript.

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