

## The Significance of BODE (BMI, Obstruction, Dyspnea, Exercise) Index in Patients with Mustard Lung.

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### ARTICLE INFO

Article type:  
Original article

Article history:  
Received: 28 Nov 2013  
Revised: 28 Dec 2013  
Accepted: 22 Jan 2013

Keywords:  
BODE  
COPD  
Mustard lung  
Sulfur mustard

### ABSTRACT

**Introduction:** Chronic Obstructive Pulmonary Disease (COPD) secondary to sulfur mustard exposure, known as mustard lung, is an important late pulmonary complication. The BODE (Body mass index, Obstruction, Dyspnea, and Exercise) index has been established as a valuable tool for determining the adverse consequences of COPD. The aim of this study was to evaluate the role of the BODE index in patients with mustard lung.

**Materials and Methods:** Eighty-two consecutively stable patients with mustard lung with all levels of severity were entered this study. The following parameters were recorded in all patients: standard spirometry, pulse oximetry, health-related quality of life, the BODE index. Additionally, the severity of COPD was determined by GOLD (Global initiative for chronic Obstructive Lung Disease) staging. The correlation of the BODE index with pulmonary parameters was determined.

**Results:** The mean age of the patients was  $47.30 \pm 7.08$  SD years. The mean BODE index was  $3.16 \pm 2.25$  SD. There was a statistically significant inverse correlation between the BODE index and oxygen saturation ( $r = -0.30$ ,  $p = 0.007$ ). Also a statistically significant correlation was found between the BODE index and quality of life ( $r = 0.80$ ,  $p = 0.001$ ). The BODE index was not correlated with age of the patients and duration of disease.

**Conclusions:** The results of this study showed that the BODE index is correlated with important clinical parameters and can be used in clinical practice.

### Introduction

Chronic Obstructive Pulmonary Disease (COPD) is an important cause of morbidity and mortality and is assumed to be the fourth cause of death till 2020 (1, 2). During previous decades, spirometric findings, especially Forced Expiratory Volume in one second (FEV<sub>1</sub>), have been used for determining the severity of COPD and therapeutic guidelines were configured based on FEV<sub>1</sub> staging (3). Although the FEV<sub>1</sub> is an important factor in

determining the severity and including therapeutic options, it is not completely enough for detecting the total burden of COPD on patient (4-6). Celli and colleague proposed a multidimensional grading system that included the respiratory, systemic, and perceptive aspects of COPD (5). This system is known as the BODE index which is consisted of 4 variables: Body Mass Index (BMI), airflow Obstruction according to FEV<sub>1</sub>, Dyspnea severity according to Modified Medical Research Council (MMRC), and Exercise based on the 6 Minute Walk Distance (6MWD)

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test (5). With the progression of COPD severity, the total BODE scores would be increased. It is well accepted that the BODE index is a better predictor of all causes of death in patients with COPD (5).

Sulfur mustard (SM), a toxic alkylating gas, can cause serious early and late complications (7, 8). SM was used as a chemical warfare agent during Iran and Iraq conflict between 1983 and 1988 (7). Now more than 100000 have major late complications of SM exposure (9). Pulmonary complications are the most common sequels of SM exposure (10). Asthma, COPD, bronchiolitis obliterans, bronchiectasis, and pulmonary fibrosis are the main pulmonary complications (10-12). COPD due to SM exposure is a unique form of COPD known as "Mustard Lung" (13).

Since at the moment, COPD is considered as a systemic inflammatory condition (14), especial attention to systemic manifestations of disease seems to be necessary in the management of patients. Spirometric findings alone cannot reveal all aspects of COPD. Previous studies in patients with mustard lung have shown that inflammatory markers are increased in stable phase, although there are studies that show reversely (10, 15). While the possible existence of inflammation in patients with mustard lung, in this study we will calculate the BODE index in patients with mustard lung and find the correlation of the BODE index with important clinical factors.

## Materials and methods

Between March 2010 and April 2011, all chemical warfare patients with COPD who had validated documents of SM exposure were enrolled into this cross-sectional study. Patients were included if they had Forced Expiratory Volume in one second (FEV<sub>1</sub>) / Forced Vital Capacity (FVC) < 0.7 after 400 µg of inhaled albuterol which was according to the American Thoracic Society (ATS) definition (16). Patients were excluded if their FEV<sub>1</sub> increased more than 12% and 200 mL after bronchodilator, if they were current or ex-smoker, if they had hospitalization or exacerbation in recent 2 months, and if they had difficulty in walking.

Standard spirometry (Multi-Functional Spirometer HI-801; Chest MI Inc., Tokyo, Japan) was performed in all patients and FEV<sub>1</sub>, FVC, and FEV<sub>1</sub>/FVC were measured and expressed as percentage of the predicted values. The best of the three consecutive recordings of spirometry was used. The severity of airway obstruction was determined according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline (3) including: stage 1 (mild) FEV<sub>1</sub>/FVC < 70%, FEV<sub>1</sub> ≥ 80%; stage 2 (moderate) FEV<sub>1</sub>/FVC < 70%, 50% ≤ FEV<sub>1</sub> < 80%; stage 3 (severe) FEV<sub>1</sub>/FVC < 70%, 30% ≤ FEV<sub>1</sub> < 50%, and stage 4 (very severe) FEV<sub>1</sub>/FVC < 70%, FEV<sub>1</sub> < 30%. All patients performed 6MWD test in a 30 meter flat indoor corridor according to the ATS guideline (17). The percent of oxygen saturation (SpO<sub>2</sub>) was recorded with pulse oximeter (PC60C, Devon Medical,

USA) before and after 6MWD test. The severity of dyspnea was determined according to the MMRC scale which was graded between 0 and 4 based on the patient's response (5). Weight (with clothes on) and height (without shoes) were recorded. BMI was calculated as weight (kg) divided by height (m) squared. By considering the BMI, FEV<sub>1</sub>, MMRC scale, and 6MWD, the BODE (body mass index, obstruction, dyspnea, and exercise capacity) index was calculated in all patients with total possible values in the range of 0 to 10 (5).

The health-related quality of life was determined by validated Farsi versions of the St. Georges Respiratory Questionnaire (SGRQ) and COPD Assessment Test (CAT) (18-19). SGRQ consists 3 parts including: symptoms, activity, and impact. Finally total SGRQ was also recorded. The scores of SGRQ were calculated by an Excel-based scoring calculator (20). CAT consists of 8 questions about cough, phlegm, chest tightness, breathlessness during activities, activity limitations at home, and confidence in leaving home, sleep, and energy (21). The scoring range of each item is from 0 to 5 with the maximal score of 40 (21).

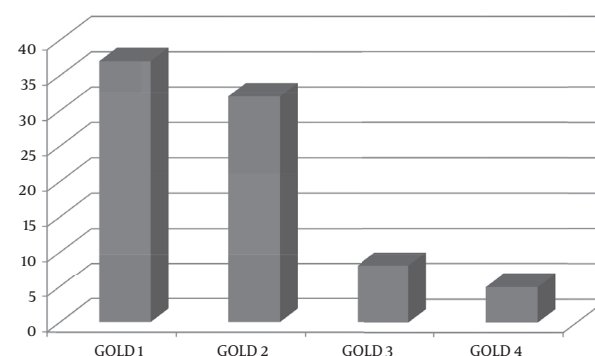
## Statistical analysis

The variables are presented as percentages and means ± SDs. Descriptive statistics were used to summarize the demographic characteristics of the patients. The normality of continuous variables was checked using the one sample Kolmogorov-Smirnov test. Pearson and Spearman correlation coefficients were calculated. P Values less than 0.05 were considered as significant. The data was analyzed using statistical package for social sciences (SPSS, version 11.5).

## Results

Eighty-two chemical warfare male patients were included in this study. The mean age of the patients was 47.30 ± 7.08 (SD) years. The demographic characteristics of the patients are shown in Table 1. The frequency of different stages of GOLD in our patients is shown in Fig 1.

**Figure 1.** The Frequency of Different GOLD Stages in Patients With Mustard Lung.



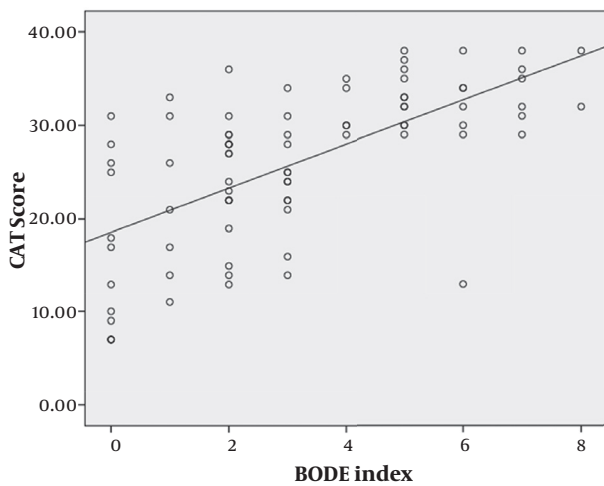
**Table 1.** The Demographic and Paraclinical Data of Patients With Mustard Lung.

Data	Value
Age ( years)	47.30±7.08*
BMI( kg/m2 )	27.44±4.62*
Duration of disease ( years)	23.12±5.17*
FEV1(%pred.)	72.04±26.72*
6MWD(m)	295±164*
CAT score	26.03±8.2*
Total SGRQ score	57.91±19.92*
SpO2 (%)	94.79±3.53*
BODE index	3.16±2.25*

\*The data are presented as mean ±SD.

BMI: Body Mass Index, CAT: COPD Assessment Test, FEV1: Forced Expiratory Volume in one second, GOLD: Global initiative for Chronic Obstructive Lung Disease, 6MWT:6 minute walk test, SGRQ: St.George Respiratory Questionnaire.

**Figure 2.** The Correlation of the BODE Index and CAT Scores in Patients With Mustard Lung (r= 0.8, p=0.001)

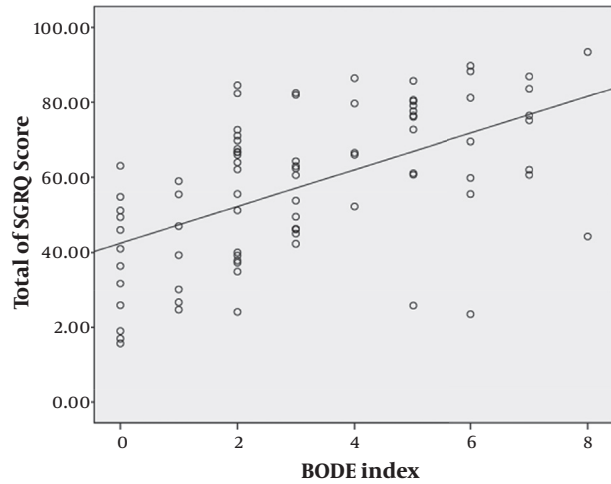


There was a statistically significant correlation between the BODE index and CAT scores ( $r= 0.80, p=0.001$ ) as shown in Fig. 2. Additionally, the correlation of the BODE index with total SGRQ scores and all compartments were statistically significant (Figs.3-6).

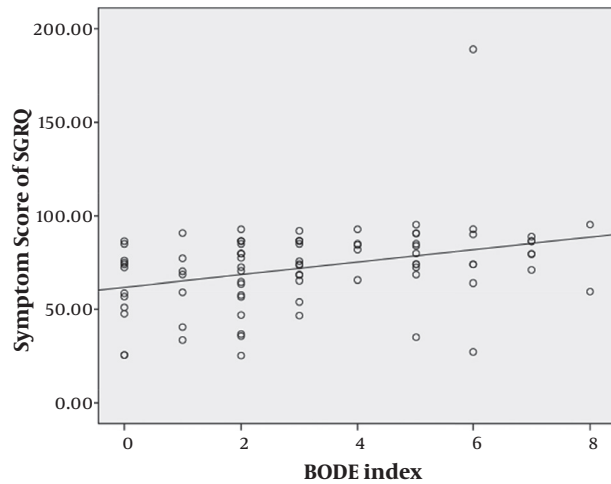
We did not find any statistically significant correlation between the BODE index and age of the patients and also duration of disease ( $r=0.20$  and  $p=0.09, r=0.06$  and  $p=0.60$ ; respectively).

Finally, there was an inverse correlation between the BODE index and SpO2 ( $r=-0.3, p=0.007$ ).

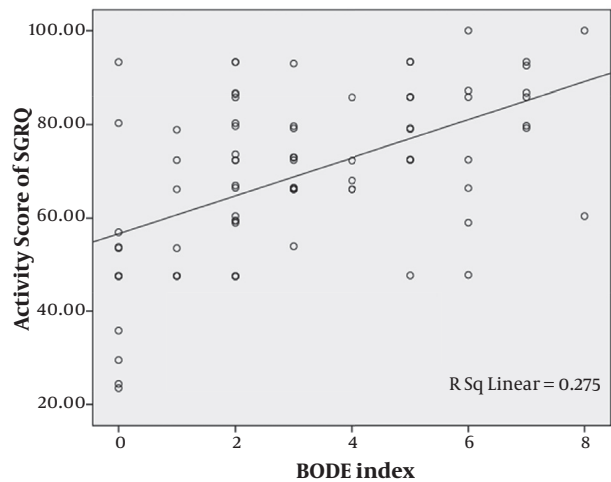
**Figure 3.** The Correlation of the BODE Index and Total SGRQ Scores ( $r=0.6, p=0.001$ ).



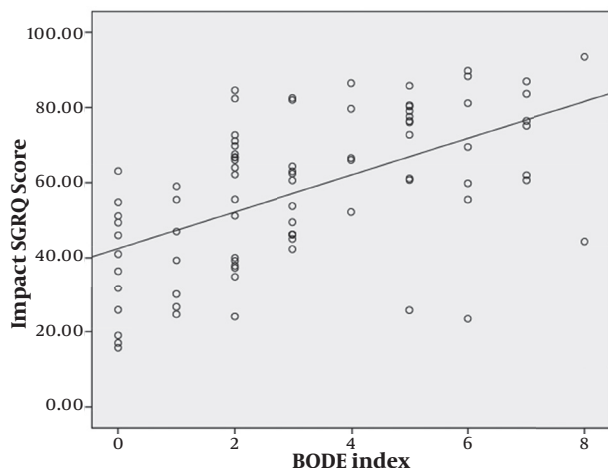
**Figure 4.** The Correlation of the BODE Index and Symptom Score of SGRQ (r= 0.4, p=0.002).



**Figure 5.** The Correlation of the BODE Index and Activity Score of SGRQ (r= 0.5, p=0.001).



**Figure 6.** The Correlation of the BODE Index and Impact SGRQ Score ( $r=0.6$ ,  $p=0.001$ ).



## Discussion

Mustard lung, a unique form of COPD, is one of the main late pulmonary complications of sulfur mustard exposure. In this study, we found statistically significant correlations between the BODE index and SGRQ, CAT, and SpO<sub>2</sub>. These results emphasize the role of the BODE index in the management of patients with mustard lung.

As we mentioned earlier, COPD is now considered as a systemic inflammatory syndrome with significant extrapulmonary complications (2). Therefore, evaluation of systemic presentations of COPD beside the lungs is necessary and spirometry alone, could not demonstrate the total impact of disease. The BODE index includes 4 major variables, which can predict the severity and more importantly the mortality rate of COPD (5). Despite the presence of several studies signifying the role of systemic inflammation in patients with mustard lung (8, 10), it is still a matter of debate. Therefore, evaluation of probable underlying systemic inflammatory condition in this group of patients seems to be necessary.

In the overall approach in COPD treatment, improvement of health-related quality of life is one of the important aspects (21, 22). Health-related quality of life is a combination of physical, social, and psychological fields of health (23). There are different types of questionnaires for evaluating quality of life in patients with COPD, which CAT and SGRQ are the more studied ones in patients with mustard lung (8, 10). We found significant correlations between the BODE index and important quality of life questionnaires, CAT and SGRQ. Additionally, the correlations of the BODE index with 3 compartments of SGRQ were significant. The results showed that with the progression of disease severity based on the BODE index, quality of life was significantly worsened.

Typically with the progression of airway obstruction in COPD, hypoxemia is an inevitable event and can be used as a severity marker beside the other evaluations. This event is also encountered in patients with mustard lung (8). We found an inverse correlation between the BODE index and SpO<sub>2</sub>. As we expected, with the increments in the BODE scores, the severity of hypoxemia was increased.

Our study has some limitations. First, we included only stable patients with mustard lung. It is better that patients with mustard lung be also studied in the exacerbation phase. Secondly, we did not evaluate the serum inflammatory markers in our patients for finding the possible correlation with the BODE index. Thirdly, our study was a cross-sectional one. Therefore we could not determine the significance role of the BODE index in predicting the mortality rate of patients with mustard lung.

## Conclusion

Mustard lung, a major late pulmonary complication of sulfur mustard exposure, is now an important problem in survivors. Monitoring the disease severity and overall treatment approach is highly recommended. The BODE index, which is a multidimensional grading system, has a considerable role in patients with COPD. In this study, we found a significant correlation between the BODE index and CAT, SGRQ, and SpO<sub>2</sub>. It is recommended that the BODE index be applied in clinical practice for evaluation of patients with mustard lung.

## Acknowledgements

This study was financially supported by the research council of Mashhad University of Medical, Mashhad, Iran. The authors wish to thank M.Aalami and H Sadraei for their valuable assistance in data collection.

## Conflict of interest

None of the authors have a conflict of interest to declare in relation to this work.

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