Central Asian Journal of Medical Sciences
CAJMS

Orginal Article

Cent Asian J Med Sci. 2019 Sep;5(3):163-169. https://doi.org/10.24079/CAJMS.2019.09.002

Identification of COPD Phenotypes and BODE Index of Mongolian Miners

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Submitted: April 5, 2019
Revised: May 18, 2019
Accepted: September 16, 2019

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Objective: We aimed to investigate the relationship between COPD phenotypes and the BODE index. **Methods:** A cross-sectional study was performed in 99 patients with COPD. COPD was classified using HRCT into the three morphological phenotypes. Lung function was analyzed by spirometry and the BODE index (Body-mass index, airflow Obstruction, Dyspnea, and Exercise) was calculated. **Results:** According to the survey, 53 (53.5%) patients had A phenotype, 31 (31.3%) had a M phenotype, and 15 (15.1%) had a E phenotype. Emphysema type has higher BODE index scores. BODE index scores increased significantly with increasing severity of COPD according to the GOLD classification (P<.001). **Conclusion:** BODE index scores were increased in associating with severity of COPD. Emphysema type COPD has a worse BODE scores than others.

Keywords: COPD, Phenotype, Pulmonary Emphysema, Tomography

Introduction

Chronic obstructive pulmonary disease (COPD) is a disorder characterized by progressive development of airflow limitation and an enhanced chronic inflammatory response in the airways[1]. COPD is predicted to become the third most frequent cause of death in the world by 2030[2]. The major manifestation of airflow obstruction in COPD is the reduction in forced expiratory volume in first second (FEV1) which forms the basis of the classification of COPD severity by the global initiative for chronic obstructive lung disease (GOLD)[3]. The BODE index (Body-mass index, airflow Obstruction, Dyspnea, and Exercise), is a simple multidimensional grading system and it gives more comprehensive information in predicting mortality from any cause as well as respiratory causes[4].

Diseases of respiratory thesystem were the 5th leading causes of population morbidity and the first leading causes of mortality in Mongolia[5]. It is interesting to note that the cause of work loss in 57.9-71.3% of people was due to respiratory disorders[6].

COPD is a heterogeneous condition with multiple clinical and functional profiles. There is as yet no clear criteria to characterize the many faces of COPD. High Resolution Computed Tomography (HRCT) of the chest helps to determine which structures are more involved, airways or lung parenchyma, and to quantify the damage[7]. It is interesting to correlate the predominant structural lesions with functional manifestations such as FEV1 and the 6-minute walking test (MWT). There are several studies that have investigated the relationship between COPD phenotypes and a multidimensional grading system, however, it is still not fully understood how COPD phenotypes could better represent the severity of airway disease in COPD.

We hypothesized that the diversity of morphological changes may be associated with the differences in BODE index, including clinical characteristics. If the morphological phenotype could be associated with the characteristic clinical features, we would be able to construct a strategy for management of COPD in accordance with each phenotype. Hence the aim of this study was to assess the relationship of a multidimensional grading system with COPD phenotypes, especially in Mongolian miners.

Materials and Methods

Study population

We performed a cross-sectional, prospective study on 99 miners with COPD. All participants were followed at the Medipas Hospital, Orkhon province, Mongolia, between January 2016 and May 2018 and were considered for participation in the study. Exclusion criteria were: inability to perform the spirometry and 6 MWT; patients with other pulmonary obstructive diseases like asthma, tuberculosis, lung cancer; patients with a history of acute myocardial infarction; unstable angina or congestive heart failure; and previous lung resection surgery.

Initially, we performed an evaluation of symptoms, a physical examination, and an assessment of the degree of dyspnea using the modified Medical Research Council (MMRC) scale. The MRC dyspnea scale is a questionnaire that consists of five statements about perceived breathlessness: grade 1, "I only get breathless with strenuous exercise"; grade 2, "I get short of breath when hurrying on the level or up a slight hill"; grade 3, "I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level"; grade 4, "I stop for breath after walking 100 yards or after a few minutes on the level"; grade 5, " I am too breathless to leave the house". Patients selected the grade that applied to them. A lung functional test was carried out before and 15 minutes after inhalation of 300 mg of salbutamol using a spirometer (CHESTGRAPH HI-105, Japan), and the values of force vital capacity (FVC), FEV_1 and FEV_1/FVC ratio were analyzed. The test was performed according to the ATS guidelines and reference values for the Caucasians were used. FVC and FEV_1 were expressed as percent of the predicted value. All patients performed the 6 MWT under supervision of the same technician. The distance was measured in meters.

Imaging and imaging analysis

The chest HRCT scans were performed by using a 128-channel multidetector CT scanner (Sceneria, Hitachi, Tokyo, Japan) with reconstructions 1 mm thick. The scans were performed in the supine position with the breath held at full inspiration, as well as in maximal expiration. The imaging parameters were 100-120 kV and 20-60 mAs (Low dose CT protocol). All low dose computer tomography (LDCT) images were independently reviewed by two radiologists and a pulmonologist. Their findings were individually recorded and then discussed, and the consensus findings were documented. COPD was classified morphologically using HRCT into the three morphological phenotypes in accordance with 1. absence of emphysema, bronchial wall thickening (A phenotype); 2. emphysema without bronchial wall thickening (E phenotype); and 3. emphysema with bronchial wall thickening phenotype (M phenotype). COPD staging was done according to GOLD 2017.

BODE index measurement

Measurements for modified BODE index used three situations:

1. Body mass index (BMI). BMI was obtained by dividing body weight in kilograms by height in square meters (kg/m2) as, BMI<21=score 0. If BMI>21=score 1.
2. FEV1% predicted post-bronchodilator: if >65%=score 0, if 50–64%=score 1, if 36–49=score 2, if <35=score 3.
3. Dyspnea: Baseline dyspnea was assessed using the modified Medical Research Council (MMRC) scale. Scale 0–1=score 0, Scale 2=score 1, Scale 3=score 2, Scale 4=score 3.4). and the 6-minute walking test measured in meters.

The participants were divided into four quartiles for the analysis according to their BODE index score, quartile I is a score

of 0–2 points, quartile II is 3–4 points, quartile III is 5–6 points, and quartile IV is a score of 7–10 points.

Statistical analysis

Data was analyzed by theStata 12 software program. Data was expressed as mean ± SD. When the data for the continuous variables showed a normal distribution, they were compared bytheone-way analysis of variance (ANOVA) method, with Bonferroni correction for multiple comparisons. Chi-square or Fisher exact test for independence was usedto determine whether there is a significant relationship between two categorical variables. P-value of less than 0.05 was considered significant for the results of all statistical analyses.

Ethical statements

All patients were in a stable clinical condition. The study was approved by the Research Ethics Committee of the board of MNUMS (Mongolian national university of medical science). All patients signed their informed consent forms before participating in the study.

Results

A total of 99 COPD miners (93 males and 6 females) with a mean age 59.9±8.4 years were randomly recruited in the study (Table 1). The BODE index mean score was found to be 4.6±2. BODE index scores also increased significantly with increasing disease severity of COPD according to the GOLD classification (P<.001) (Figure 1). BODE index scores were significantly higher in emphysema phenotype of COPD (P<.000) (Figure 2).

Table 1. General characteristics of miners

Variables	Miners with COPD (n = 99)
Gender[a]	
Male	93 (93.9)
Female	6 (6.1)
Age (years)	
Range	34-79
Mean ± SD	59.9 ± 8.5
Working duration (years)	
Range	5-28
Mean ± SD	17.3 ± 4.7
Smoking[a]	
Current smoker	65 (65.7)
Former smoker	6 (6.1)
Never	13 (13.1)
BMI	27.2±5.5

[a]Variable number, (%)

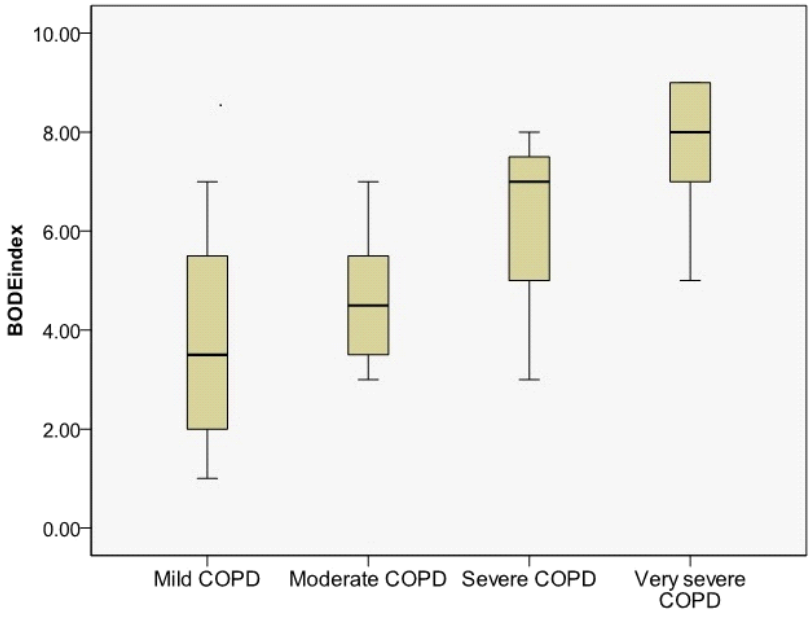

Figure 1. Relationship between BODE index score and GOLD stage in COPD patients.

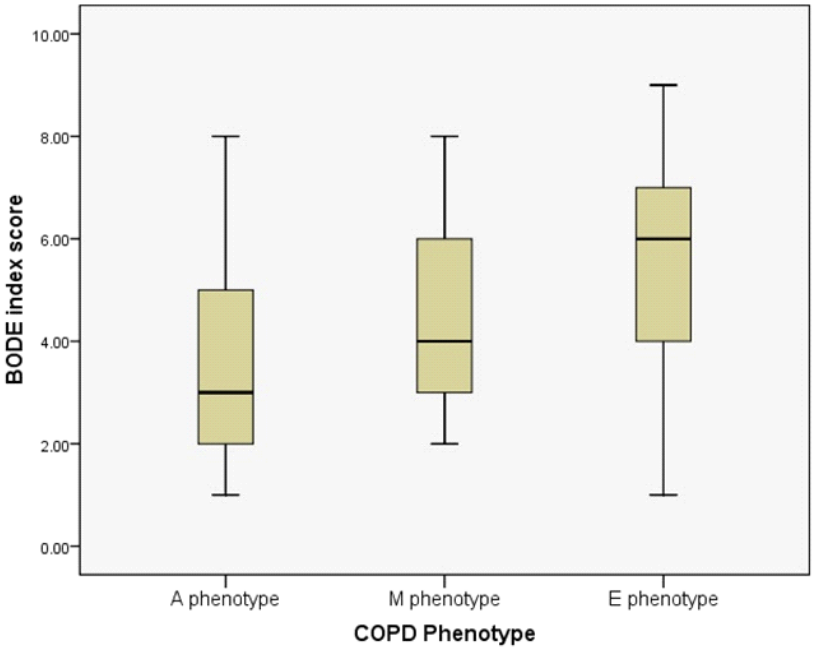

Figure 2. Relationship between BODE index score and COPD phenotypes

Emphysema type distribution was associated with a lower FVC, FEV1/FVC ratio and BMI ($p \leq .05$). However, a significant difference between years of dust exposure, smoking status, and the BODE index was not identified (Table 2).

According to post hoc Anova analysis, BMI is significantlydifferent between A phenotype, M phenotype, and A phenotype, E phenotype, also the Gensler index is significantly differentbetween A and E phenotype, and M and E phenotype of COPD (Table 3).

Discussion

Chronic obstructive pulmonary disease (COPD) is a growing global epidemic that is particularly important in developing countries. Celli and Khattab et al.reported that theBODE staging system helps to better predict hospitalization and mortality in patients with COPD[4,8]. The BODE index has been demonstrated in many studies to be a more accurate predictor of mortality among patients with COPD than lung function, FEV1 alone[9-13]. On the opposite position Faganello and Motegi et al. reported that unidimensional GOLD classification and multidimensional BODE index staging systems seem to have similar clinical utility in predicting exacerbation in ambulatory COPD patients[14,15]. This study aimed to investigate the relationship between the phenotypes of COPD and components of BODE index and also severity of COPD. In our study, among the 99 miners with COPD we found a significant relationship 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 and it is similar to the survey by Abdel-Aaty et al.[16]

This study illustrates clearly the functional heterogeneity of a group of miners with COPD, when were selected exclusively by spirometric parameters. HRCT phenotyping groups allow us to identify subsets of patients with distinct functional characteristics. Our study showed that CT measurements of emphysema or peripheral airways are significantly related to airflow obstruction in COPD patients. It is similar to the survey by XieX et al.[17]

Even though, according Silvia Maria Doria da Silvia et al., visual CT analysis for phenotyping COPD patients may help identify subsets of individuals with distinct functional profiles and spirometry, this findinghas proven insufficient as the only means to characterize COPD patients, especially for severe cases[18]. Using different tools that assess distinct dimensions of COPD, such as CT, 6MWT, and VC can help us understand the various COPDs and their consequences. In Mongolia the prevalence of COPD is progressively increasing due to air pollution, harsh climate, and smoking[19]. In our study64 (64.6%) miners involved in the study were smokers. The mean years of smoking was

Table 2. Baseline characteristics of COPD phenotypes

Variables	A Phenotype (n=53)	M Phenotype (n=31)	E Phenotype (n=15)	Total (n=99)	p-value [b]
Gender(n,%)					**.001****
Male	48 (48.5)	30 (30.3)	15 (15.2)	93 (93.9)	
Female	5 (9.4)	1 (3.2)	-	6 (6.1)	
Age(years)[A]	58.7±7.5	61.1±7.6	61.6±12.5	59.9±8.4	.321
Dust exposure (years) [a]	19.6±5.6	18.5±5.6	19.6±8.7	19.2±6.1	.712
Smoking (years)[a]	9.8±10.0	15.4±10.2	22.6±7.7	13.5±10.7	.000**
BMI(kg/m^2) [a]	29.4±5.4	25.3±4.5	23.2±3.3	27.2±5.5	.000**
Spirometry[a]					
FEV1 (%)	62.5±21.9	62.6±14.3	57±19.4	61.7±19.4	.591
FEV1/FVC (%)	66.1±3.8	65.8±5.1	57.0±11.5	64.6±6.7	.000**
FVC (%)	67.7±15.8	61.5±12.8	54.6±9.2	63.7±14.7	.005**
6 MWD(m)[a]	218.0±51.6	206.4±50.9	220.3±40.9	214.7±49.8	.531
mMRCscore[a]	1.3±1.3	1.5±1.2	2.0±1.0	1.5±1.2	.171
BODE index score [a]	4.4±2.1	4.4±1.9	5.8±2.0	4.6±2.0	.151
BODE index (n,%)					.165
Quartile 1	11 (20.8)	6 (19.4)	1 (6.7)	18 (18.2)	
Quartile 2	15 (28.3)	10 (32.3)	3 (20)	28 (28.3)	
Quartile 3	19 (35.8)	11 (35.5)	4 (26.7)	34 (34.3)	
Quartile 4	8 (15.1)	4 (12.9)	7 (46.7)	19 (19.2)	

**p < .001; [a]Values expressed as mean ± standard deviation; [b]p-values from one-way Anova test (for multiple variebles) or Chi-square test/Fisher exact test (for categorical variables)comparisons between the COPD phenotypes; Abbreviations: BMI, body mass index; BODE, Body mass index, airflow Obstruction as measured by the post-bronchodilator FEV1 (percentage of predicted value), Dyspnea assessed by the mMRC score, and Exercise tolerance measured by 6-minute walking distance; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; mMRC, modified Medical Research Council scale

13.5±10.7. That miners are smoking is also considered a risk factors to increase COPD.

Vázquez JH et al. showed that classification of COPD patients by phenotype makes it possible to identify subgroups with different prognoses[20]. In our study, comparing between the phenotypes of COPD, there was no difference in age, dust exposure, FEV1 (%), 6 MWD (m), BODE index score, and mMRC score. But there was significant a difference between smoking history, BMI and FVC%. However, patients in the E phenotype group had lower BMI (P=.000), higher degree of obstruction in spirometry (FVC, P=.003, and lower FEV_1/FVC ratio, P=.000). These factors resulted in a higher BODE index in the E phenotype group, but no statistical difference (p > .05).

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. In our study, dyspnea scores were different with severity of COPD (p = .000), but there was no significant differences between COPD phenotypes.

Several limitations in this study need discussion. First, the study was performed in a single center, thus limiting the generalizability of the results. Second, percentages of female COPD was very much less (6.1%) in our study. This might not represent the overall prevalence of female COPD patients in Mongolia. Lastly, some of the variables that might have influenced the results such as cumulative smoking, duration of COPD, and treatment of comorbidities were not available.

In terms of future directions of COPD, this study could improve the diagnostic usage of conventional spirometry as a good adjunctive diagnostic tool, andthus, impact on individual disease management. Ideally, with further advances in BODE

Table 3. Results of the Bonferroni post hoc analysis

Variable			p-value[a]	95% CI
Smoking (years)				
	A phenotype	M phenotype	.541	(7.0-2.0)
		E phenotype	.301	(9.8-1.8)
	M phenotype	A phenotype	.541	(2.0-7.0)
		E phenotype	1.000	(7.5-4.6)
	E phenotype	A phenotype	.301	(1.8-9.8)
		M phenotype	1.000	(4.6-7.5)
BMI (kg/m^2)				
	A phenotype	M phenotype	.001	(1.3-6.8)
		E phenotype	.000	(2.6-9.7)
	M phenotype	A phenotype	.001	(6.8-1.3)
		E phenotype	.569	(1.7-5.8)
	E phenotype	A phenotype	.000	(9.7-2.6)
		M phenotype	.569	(5.8-1.7)
FEV1/FVC (%)				
	A phenotype	M phenotype	1.000	(3.0-3.6)
		E phenotype	.000	(4.7-13.3)
	M phenotype	A phenotype	1.000	(3.6-3.0)
		E phenotype	.000	(4.1-13.3)
	E phenotype	A phenotype	.000	(13.3-4.7)
		M phenotype	.000	(13.3-4.1)

[a] p value with Bonferroni correction for multiple comparisons.
CI-Confidence interval

index, conventional spirometry, HRCT, and low-dose CT features of COPD phenotypes, automatic analysis could convertinto an estimate of riskfor quality of life.

Conclusion

BODE index scores increased significantly with increasing severity of COPD.

Miners with emphysema type have asignificantly higher BODE index than other COPD phenotypes.

Conflict of Interest

The authors report no conflicts of interest in this work.

References

1. Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, et al. Global strategy for the diagnosis, management and prevention of chronic obstructive lung disease 2017 report. Respirology 2017; 22: 575-601.
2. Lopez-Campos JL, Tan W, Soriano JB. Global burden of COPD. Respirology 2016; 21: 14-23.
3. Seemungal TA, Hurst JR, Wedzicha JA. Exacerbation rate, health status and mortality in COPDa review of potential interventions. Int J Chron Obstruct Pulmon Dis 2009; 4: 203.
4. Celli BR, Cote CG, Marin JM, Casanova C, de Oca MM, Mendez RA, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med 2004; 350: 1005-12.
5. Health Development Center, Ministry of Health, Health Indicators 2017. Ulaanbaatar; Mongolia. p 73-89.
6. Nandin-Erdene B, Chimedsuren O. Assessment of the fine particles dust exposure of coal mine workers. J Erin of Pub Health 2015; 4: 132-5.
7. Kitaguchi Y, Fujimoto K, Kubo K, Honda T. Characteristics

of COPD phenotypes classified according to the findings of HRCT. Respir Med 2006; 100: 1742-52.

8. Khattab AK, WagihK, Mohamed A. A multi dimensional grading system for assessment and follow up of COPD. Egypt J Bronchol 2009; 3: 24-33.
9. Roberts MH, Mapel DW, Bruse S, Petersen H, Nyunoya T. Development of a modified BODE index as a mortality risk measure among older adults with and without chronic obstructive pulmonary disease. Am J Epidemiol 2013; 178: 1150-60.
10. Oga T, Tsukino M, Hajiro T, Ikeda A, Nishimura K. Predictive properties of different multidimensional staging systems in patients with chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2011; 6: 521-6.
11. Georg-Christian F, Kathrin K, Chris BO, Sylvia H. BODE index versus GOLD classification for explaining anxious and depressive symptoms in patients with COPD a cross-sectional study. Respir Res 2009; 10: 1.
12. Pauwels RA, Buist AS, Ma P, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: National Heart, Lung, and Blood Institute and World Health Organization Global Initiative for Chronic Obstructive Lung Disease (GOLD): executive summary. Respir Care 2001; 46: 798–825.
13. Ong KC, Earnest A, Lu SJ. A multidimensional grading system (BODE index) as predictor of hospitalization for COPD. Chest 2005; 128: 3810–16.
14. Faganello MM, Tanni SE, Sanchez FF, Pelegrino NR, LuchetaPA, Godoy I. BODE index and GOLD staging as predictors of 1-year exacerbation risk in chronic obstructive pulmonary disease. Am J Med Sci 2010; 339: 10-4.
15. Motegi T, Jones RC, Ishii T, Hattori K, Kusunoki Y, Furutate R, et al. A comparison of three multidimensional indices of COPD severity as predictors of future exacerbations. Int J Chron Obstruct Pulmon Dis 2013; 8: 259-71.
16. Abdel-Aaty HES, Zamzam MA, Azab NY, El Wahsh RAER, El Beltagy SA. Comparison of GOLD classification and modified BODE index as staging systems of COPD. Egypt J Chest Dis Tuberc 2014; 63: 821-8.
17. Xie X, de Jong PA, Oudkerk M, Wang Y, Ten Hacken NH, Miao J, et al. Morphological measurements in computed tomography correlate with airflow obstruction in chronic obstructive pulmonary disease: systematic review and meta-analysis. Eur Radiol 2012; 22: 2085–93.
18. Silvia DSM, IlmaAP, Mello DCE, Marcos MM, Luciana CP, et al. COPD phenotypes on computed tomography and its correlation with selected lung function variables in severe patients. J Chron Obstruct Pulmon Dis 2016; 11: 503–13.
19. Jambaldorj J. Enviremental and genetic factors for COPD. Cent Asian J Med Sci 2018 4: 1-2.
20. Vázquez JH, García IA, Jiménez-García R, Meca AÁ, de Andrés AL. COPD phenotypes: differences in survival. Int J Chron Obstruct Pulmon Dis 2018; 13: 2245–51.