ORIGINAL RESEARCH

BODE index correlated with Charlson comorbidity index and medical burden in COPD

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 doi:10.20944/preprints201909.0296.v1

Keyword: Chronic Obstructive Pulmonary Disease; BODE index; Charlson comorbidity index; medical burden

Abstract

COPD is currently the fourth leading cause of death in the world. Globally, due to continued exposure to COPD risk factors and an aging population, the burden of COPD is expected to increase in the coming decades. The BODE (body mass index, airflow obstruction, dyspnea, and exercise capacity) index is a practical and multidimensional predictor for prognosis of COPD, and better than FEV1.We used the database of Kaohsiung Chang Gung Memorial Hospital medical center, Taiwan to analyze the correlation between BODE index, healthcare resource utilization, and Charlson comorbidity index (CCI). This retrospective study to collect COPD patients with complete BODE index data who had undergone a 6-minute walk examination in our hospital from January 2015 to December 2016. The medical cost and comorbidities database were analyzed from January 1, 2015, to August 31, 2017. Of 396 patients, 382 (96.5%) were male, with an average age of 71.3 ± 8.4 years. There was a significant association between the BODE index and the CCI of COPD patients ($p < 0.001$). Healthcare resource utilization was positively correlated with the BODE index during the 32 months of retrospective clinical outcomes: positively correlated with the number of hospitalizations ($p<0.001$), hospitalization days ($p<0.001$), hospitalization expenses ($p=0.005$), and total medical expenses ($p=0.024$), respectively. Our findings provide the crucial information for clinician to predict medical burden and comorbidities in patients with COPD by using BODE index.

 doi:10.20944/preprints201909.0296.v1

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common chronic respiratory disease characterized by progressive and irreversible airflow limitation. Symptoms of COPD may include: dyspnea, chronic cough, productive cough, weight loss, decreased exercise and daily activity tolerance. Hypoxia occurs when blood oxygen levels drop during the rest, sleep, or activity. And develop into respiratory failure after recurrent exacerbations. COPD often coexists with other diseases; comorbidities are common among COPD patients at any stage of the disease[1,2].

The Charlson comorbidity index(CCI) was first developed by Charlson et al. in 1987 as an assessment of disease severity and mortality prediction. It is criterion of 15 chronic diseases, including myocardial infarction, chronic heart failure, COPD, peripheral vascular disease, cerebrovascular disease, dementia, diabetes mellitus, systemic hypertension, liver disease, renal disease, cancer, connective tissue diseases, HIV, skin ulcers, peptic ulcer disease, depression and anticoagulants use[3]. CCI scores comorbidity on a 0–33 scale. A higher CCI indicates a greater number and severity of comorbidity with higher medical needs which lead to a higher medical burden[4-7] . Multiple comorbidities are common among COPD patients; as a consequence, there is a correlation between CCI and the mortality rate[8] and hospitalization days[9] of COPD patients.

At present, many tools are used to assess the severity and prognosis of COPD patients. The study by Celli et al. introduced the BODE index, which has been clinically proven to be a significant prediction of disease severity and mortality[10]. The BODE index is a multidimensional index of disease severity in COPD that incorporates four independent predictors: the body mass index (BMI), the degree of airflow obstruction assessed by the Forced Expiratory Volume in one second(FEV_1),

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the modified Medical Research Council (mMRC) dyspnea scale, and the exercise capacity assessed by the 6-minute walking distance(6MWD) test. Among patients with COPD, the BODE index is a better predictor of disease severity, the number of acute exacerbation and mortality than the FEV_1[11]. Saint George's Respiratory Questionnaire (SGRQ) is also an instrument evaluating COPD patients and provides information on health status (quality of life). Studies have shown that the BODE index is better than SGRQ at predicting mortality[5].

The score of the BODE index was divided into four quartiles[10]. The highest quartile indicates the most serious disease. Increasing BODE quartiles were associated with a higher risk of death[12,13]. Except for the survival prediction, BODE quartiles are a good predictor of both the number and severity of exacerbations in patients with COPD[11]. Acute exacerbation of COPD is the main cause of increasing hospitalization[13] and medical needs, which accounts for most of the economic burden of the disease. The purpose of this study was to analyze the correlation between the BODE index, healthcare resource utilization and CCI in COPD.

2. Methods and Material

2.1. Data Source

A retrospective study on clinical outcomes was conducted in this study. The data was from the electronic database of the Kaohsiung Chang Gung Medical Center (KCGH) and was reviewed and approved by the Institutional Review Board Committee (IRB: 201701293B0) of Chang Gung Medical Center. Patients who had undergone a 6-minute walking test (6MWT) in the respiratory therapy department (n=1063) between 2015 and 2016 were collected for data collection and analysis. The patient’s retrospective report of those who undergo 6-minutes waking test was from

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January 31, 2015, to August 31, 2017(a total of 32 months). The electronic data of the medical records and healthcare resource utilization was from KCGH. The inclusion criteria of patients with COPD in KCGH were as follows: 1) diagnostic code ICD-9-CM: 490-496, ICD-10-CM: J41-J44 (n = 507); 2) at least a complete clinical record of 6MWT; 3) diagnosed as COPD by a post-bronchodilator FEV1/FVC < 70% with persistent expiratory flow obstruction according to COPD GOLD guideline[14,15]; 4) excluded those who were less than 40 years old. We collected medical information, the number of outpatient visits, the number and days of hospitalization, and medical expenses of the selected patients (n=396). The selection process was shown below (Figure 1).

2.2. Study Population

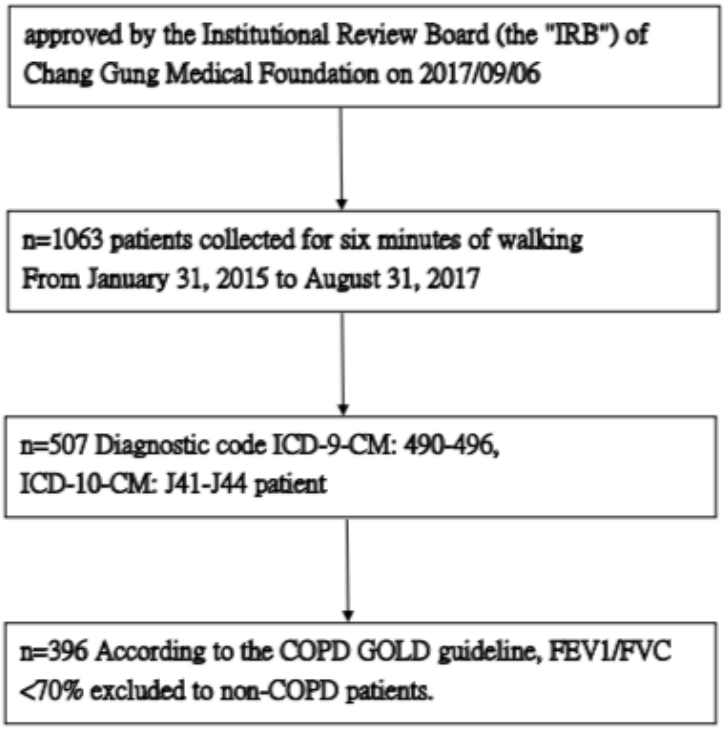

Figure 1. Flow chart of selected participants in this study

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According to Celli et al., the BODE index was categorized into 4 quartiles: quartile 1 is a score of 0–2; quartile 2 is a score of 3–4; quartile 3 is a score of 5–6; and quartile 4 is a score of 7–10[10,13]. The CCI data were obtained from those specific diagnostic codes that appear during 32 months of the patient's retrospective report. The data of healthcare resource utilization were a total medical expense including outpatient clinic visits, hospitalization days, examination fees, and drug costs during 32 months of the patient's retrospective report. Then analyzed the correlation between the BODE index, CCI and medical expenses in patients with COPD.

2.3. Statistical Analysis

Data distribution was presented by mean and standard deviation (mean ± SD), median (Interquartile range, IQR) or N (%). Using the Chi-square test, Fisher's exact test and one -way analysis of variance (one -way ANOVA) to compare the differences of variables between quartiles then conduct a posteriori comparison by Scheffe test. Lastly, use one -way ANOVA and linear contrast to check if there was a linear trend. Analysis of data was performed using the Statistical Package for the Social Sciences (SPSS) version22.

3.Results

Of the 396 patients with COPD who met the inclusion criteria, 382 were male, which was 96.5% of the total, with an average age of 71.3 ± 8.4 years, and their average length of smoking was 31.7 ± 18.5 years. The BMI was 23.5 ± 4.1. According to the definition of severity by COPD GOLD guideline, the rate of patients with moderate to severe severity were 82.6% and was the highest of this study. Among them, 187 patients with moderate severity were 47.2% of the total and 140 patients with severe severity were 35.4% of the total. The score of CCI was 3.3 ± 2.8,

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mMRC was 1.72 ± 0.9, the BODE index was 3.3 ± 2.1(quartile 1: 47.5 % (n=188); quartile 2: 27.5%(n=109); quartile 3: 17.9%(n=71); quartile 4: 7.1%(n=28). The mean distance of 6MWT was 351.9 ± 11.6 meters (Table 1).

Table 1. Baseline characteristics of COPD patients included in the study (n=396)

Factors	Mean±SD or N(%)
Age (yr)	73.1 ± 9.5
Male (%)	382 (96.5)
Smoking history (pack-yr)	31.7±18.5
Body-mass index (BMI)	23.5 ± 4.1
FVC (% of predicted value)	79.7±16.7
FEV1/FVC (%)	52.7 ± 10.6
FEV1 (% of predicted value)	55.2 ± 18.2
DLCO (%)	68.5 ± 21.0
GOLD stage (%)	
GOLD I	46 (11.6)
GOLD II	187 (47.2)
GOLD III	140 (35.4)
GOLD IV	23 (5.8)
MIP	72.2 ± 30.5
MEP	98.3 ± 46.8
CCI	3.3 ± 2.8
BODE INDEX	3.0 ± 2.1
BODE quartile: Q1, Q2, Q3, Q4 (%)*	
quartile 1	188 (47.5)
quartile 2	109 (27.5)

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quartile 3 quartile 4	71 (17.9) 28 (7.1)
mMRC	1.72 ± 0.9
mMRC dyspnea scale‡ Scale 0/1/2/3/4	 25 / 133 / 173 / 56 / 9
6MWD (m)	351.9 ± 111.6

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; 6MWD, 6-minutes walking distance; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; MRC score, Medical Research Council dyspnea scale; BODE index, composite index of Body mass index, airflow maximum expiratory pressure Obstruction, Dyspnea, and Exercise; MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure.

*Quartile 1 was defined by a score of 0 to 2, quartile 2 by a score of 3 to 4, quartile 3 by a score of 5 to 6, and quartile 4 by a score of 7 to 10.

The severity of COPD was correlated with the Charlson comorbidity index (CCI). The higher the BODE quartile score, the higher the CCI score was. There was a positive correlation between them (Figure 2).

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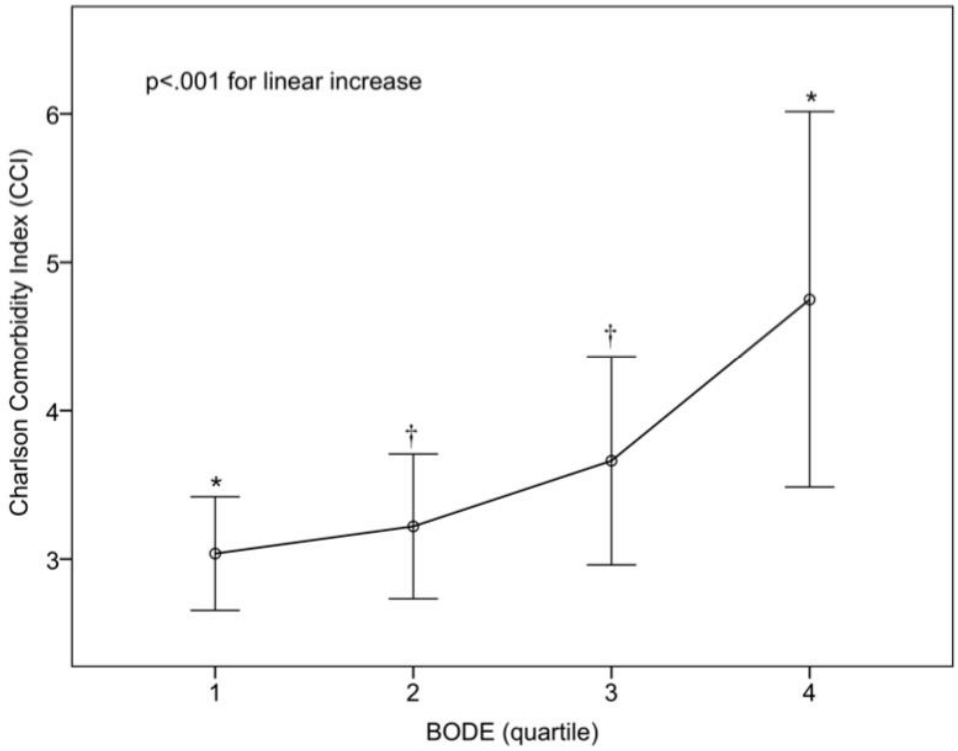

Figure 2. This shows the line of positive correlation between BODE quartile and Charlson comorbidity index

*Post hoc comparison with Scheffe method BODE Q1 Q4 p<0.024 † BODE Q2 Q3 no significant difference

And to health care utilization, the median (IQR) of visiting the outpatient clinics was 16(10-23), the outpatient medical expense was NT$45,393 (29,259-67,440), the number of hospitalizations was 0 (0-1), the hospitalization days were 0 (0-12), hospitalization expense was NT$0 (0-20,367), the total medical expenses were NT$54,668 (32,715-105,324). COPD patients with higher BODE quartile, need more medical service as increasing the hospitalization and hospital stay ($p < 0.001$) (Figure 3B) (Figure 3C). The hospitalizations of BODE quartile 3 was 1.17 times more than quartile 1 ($p < 0.001$). The hospitalization days of BODE quartile 3 was 14.78 days

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more than quartile 1 ($p < 0.001$) and quartile 4 was 13.79 days more than quartile 3($p=0.042$), which indicate a statistically significant difference.

For the need of the outpatient medical service, BODE quartile 2 was the highest (Figure 3A). At the part of health care utilization, BODE quartile, hospitalization expense ($p = 0.005$) (Figure 4B), and total medical expenses were positively correlated, and were statistically significant differences.

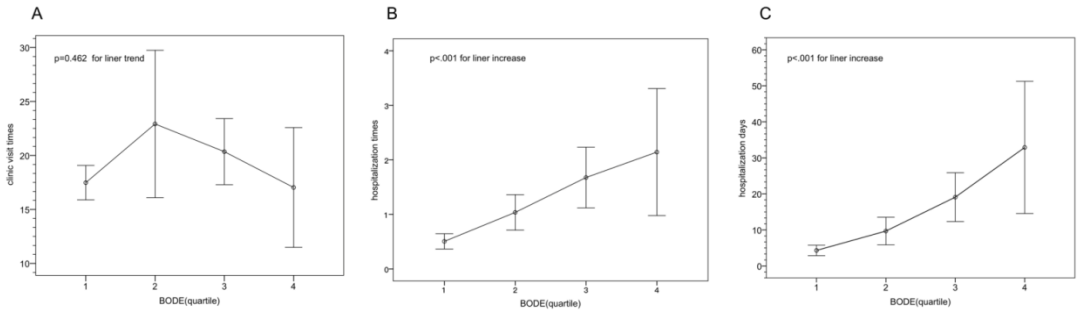

Figure 3. The relation among BODE quartile, number of outpatient visit and length of hospital stay. (A)number of outpatient visit(B)number of hospitalization(C)length of hospital stay

* Figure 3A. BODE quartiles no significant; Figure 3B BODE Q1=Q2 <Q3<Q4; Figure 3C BODE Q1=Q2 <Q3<Q4.

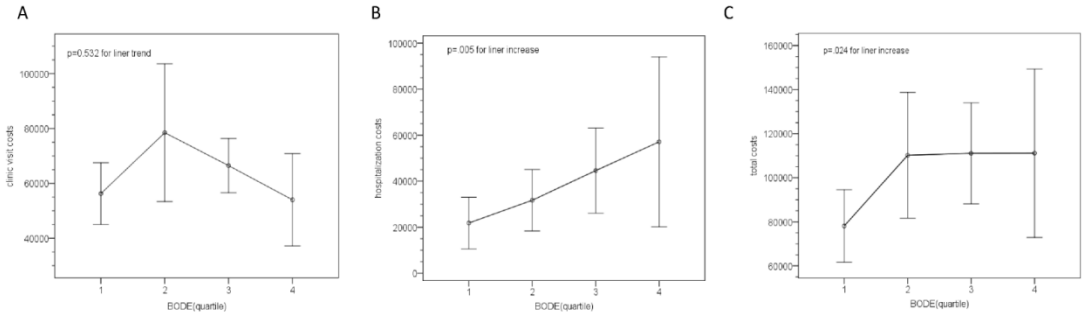

Figure 4. The relation between BODE Quartile and the fees: (A) Outpatient expenses (B) Hospitalization expenses (C) Total medical expenses

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* Figure 4A BODE Quartiles no significant; Figure 4B Overall p value is marginal significant(p=0.047) after multiple comparisons there are significant between Quartiles ; Figure 4C BODE Quartiles no significant.

4.Discussion

Our study confirmed that there was a positive correlation between BODE quartile and CCI in patients with COPD. Higher BODE quartiles were associated with higher needs for medical services as the increase in hospitalizations and hospital stays.

COPD has frequently triggered a series of systemic reactions with respiratory diseases or systemic inflammation and come out with other comorbidities[16,17]. The incidence of COPD was increased by comorbidities, leading to an increase in hospitalization, mortality, and medical costs. Among them, hospitalization costs most of the medical expenses of COPD[18,19]. Cavaillès et al[20]indicate that comorbidities increase the incidence of COPD which increases hospitalization and medical costs. CCI was also associated with increased mortality. In the study which conducted a multivariate study of COPD patients, analyzed variables after adjusting FEV_1. It showed that the mortality of patients with a CCI score of 3 or more (equivalent to two chronic diseases or one serious disease, except COPD) may increase two times more than those with lower CCI score[8]. Among the 2900 hospitals study by Buhr RG et al[19], 243,113 patients were diagnosed with COPD.

The CCI score of patients with COPD was found to be related to the overall readmission rate. The CCI score for readmission (average 2.8±1.5) was significantly higher than non-readmission (average 2.2 ± 1.8). The overall readmission rate was 14%. The Swedish National study[21] found that among the 88,548 patients with COPD, CCI of female patients was (mean 2.5 ± 1.9), and of male patients was (mean

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2.9 ± 2.1) ($p < 0.001$). The overall mean (SD) CCI score was 2.7 ± 2.0. In this study, the mean (SD) CCI score was 3.3 ± 2.8.

COPD is characterized by irreversible airflow limitation. FVC and FEV_1% are typically used to determine the severity of COPD[14,22]. Using the BODE index as a multidimensional index, it is a better predictor of disease severity, hospitalization needs and risk of death than FEV_1 alone[10,13,23]. BODE quartile is a good predictor of predicting the frequency and severity of acute exacerbations of COPD and hospitalization needs[11,13]. Acute exacerbations are the main cause of hospital admissions in patients with COPD, which leads to an increased hospitalization cost[24].

This study confirmed that with the increase in the severity of COPD, health care utilization increased among those with higher BODE quartile. The BODE index was positively correlated with hospitalizations ($p<0.001$), hospitalization days ($p<0.001$) (Figure 3B.C), hospitalization expense ($p = 0.005$), and total medical expenses ($p = 0.024$) (Figure 4B.C). Quartile 2 had the highest need for outpatient care. The reason why the less frequent outpatient clinics visit of quartile 3 and quartile 4 is that these patients with higher disease severity need someone to accompany to outpatient clinics due to dyspnea or mobility problems. It doesn't mean a reduction in outpatient requirements, which is consistent with the study of Cote and Celli[12]. Hospitalizations and the length of hospital stay would increase according to the BODE index prediction of severe exacerbation of COPD[25]. In other studies, COPD patients with high BODE index scores have higher medical resource utilization rates[24,26]. These studies are consistent with our study. For now, the correlation between BODE and CCI can't be found in document verification. In our study, BODE had a positive correlation with CCI, which further confirms that BODE was related to medical expenses.

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5.Conclusion

The BODE index is the most convenient and effective clinical assessment tool. In addition to a predictor of disease severity and survival analysis, it was also a good predictor of the number of acute exacerbations of COPD. This study also add that the BODE index provide the crucial information for clinician to predict medical burden and comorbidities in patients with COPD.

6.Limitation

There were some limitations of our study. First of all, retrospective study on clinical outcome was not a continuously prospective study. Second, the source of the case was from a single medical center, which could not become more objective and could not represent all groups of COPD. Third, the study had a lack of indirect cost data related to COPD and comorbidities. These costs (including the loss of productivity for businesses, loss of productivity due to early retirement, the payment for disability pensions and care) are much higher than COPD's direct medical costs.

Author Contributions

These authors' individual contributions were as follows. Conception/design: C-L.L., S-F.L.; provision of study material and patients: C-L.L.,Y-H.T.; collection and assembly of data: C-L.L., M-H.L.; data analysis and interpretation: C-L.L., S-F.L.; manuscript writing: C-L.L., S-F.L.,P-S.C.; final approval of manuscript: C-L.L., S-F.L.

Funding

This research received no external funding.

Acknowledgments

 doi:10.20944/preprints201909.0296.v1

We appreciated the Biostatistics Center, Kaohsiung Chang Gung Memorial Hospital for statistics work.

Conflicts of Interest

The authors declare no conflict of interest.

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