Prognostic assessment in COPD: Health related quality of life and the BODE index

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KEYWORDS
COPD; BODE index; Quality of life; Mortality

Summary
Rationale: COPD is a debilitating disease with increasing mortality worldwide. The BODE index evaluates disease severity and the St George’s Respiratory Questionnaire (SGRQ) measures health status.
Objective: To identify the relationship between BODE index and the SGRQ and to test the predictive value of both tools against survival.
Methods: Open cohort study of 1398 COPD patients (85% male) followed for up to 10 years.
Measurements and main results: At the time of the inclusion, clinical data, forced spirometry and 6 min walking distance were determined and BODE index and SGRQ were calculated. Vital status and cause of death were documented at the end of follow-up.
Results: The cohort’s mean of FEV1% predicted was 46 ± 18%, BODE index was 3.6 ± 2.5, and SGRQ% total score was 49 ± 20. The SGRQ scores increased progressively as severity of COPD increased by BODE quartiles. The correlation between SGRQ and BODE index was good (r = 0.58, p < 0.0001). Both tests correlated with COPD survival (BODE = −0.4 vs. SGRQ = −0.20, p < 0.0001). The area under the curve (AUC) for the BODE index was 0.77 vs. 0.66 for the SGRQ% total score (p < 0.001).

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h Deceased.
**Introduction**

Chronic obstructive pulmonary disease (COPD) is a progressive chronic respiratory illness, which is rapidly becoming a leading cause of mortality and disability worldwide. The disease is associated with both respiratory as well as multisystemic impairment that often impacts on the functional capacity of patients, and in their ability to perform normal activities of daily living affecting their quality of life. Health Related Quality of Life (HRQoL) is an important patient reported health outcome that is currently receiving increasing recognition. The impairment in HRQoL in COPD is seen even at levels of relatively modest airflow limitation. This weak association between HRQoL and the forced expiratory volume in 1 s (FEV1) has long been described and reflects the marked heterogeneity and complexity of this disease. The dissociation between FEV1 and patient centered outcomes such as HRQoL, and even survival has prompted an increasing interest in the multi-systemic evaluation of COPD. The BODE index is a multidimensional instrument that incorporates measurements of nutritional status, the Body Mass Index (BMI), airflow limitation (FEV1), dyspnea, Modified Medical Research Council (MMRC) and functional status as measured by the 6-min walk distance test (6MWD). BODE provides an integrated evaluation of the respiratory and non respiratory expressions of the disease that better reflects disease severity. BODE also includes domains that relate to the quality of life of patients with COPD. BODE has been shown to predict mortality, hospitalizations and to be sensitive to change with interventions like pulmonary rehabilitation and surgical procedures like lung volume reduction surgery (LVRS). The same interventions have also been associated with meaningful improvements in HRQoL. Conversely, it is well known that exacerbations cause worsening of HRQoL. We have recently shown that exacerbations significantly contribute to worsening disease severity of COPD as measured by the BODE index. So, it is quite possible that changes in the BODE index would translate in better or worse HRQoL for patients with COPD. The St. George’s Respiratory Questionnaire (SGRQ) is a disease specific quality of life instrument designed to assess the quality of life of patients with COPD. The SGRQ score has also been shown to have an association with increased health care resource utilization (HCRU) and with decreased survival. SGRQ is also responsive to pharmacological and non-pharmacological interventions. Some studies suggest a relationship between BODE index and SGRQ but the studies have included a limited number of patients with short follow up and none has explored the relative value of either test to predict survival.

The primary purpose of this study was to explore the possible correlation between disease severity as measured by the BODE index, and HRQoL as measured by the SGRQ in a large cohort of patients with COPD. In addition, we aimed to determine thresholds of critical value for both the BODE index and the SGRQ in relation to COPD mortality, and to compare the two instruments in their capacity to predict survival in this disease.

**Methods**

**Patients**

A total of 1398 patients with COPD as accepted by the American Thoracic Society (ATS) were sequentially recruited into an observational study, between January 1997 and September 2006, at several of the BODE study sites. Inclusion/exclusion criteria have been previously published. The protocol was approved by the institutional review board of each institution and all patients signed a consent form.

**Measurements**

Baseline data were collected in clinical stable conditions that are at least one month after COPD exacerbation. Pulmonary function test was obtained according to the ATS. The 6MWD was performed following ATS guidelines. Dyspnea was assessed using the Modified Medical Research Council Dyspnea Scale or MMRC scale. The BODE index was measured and staged in quartiles as previously published. To determine HRQoL we used the validated SGRQ questionnaire. For the purpose of this study, the SGRQ % total scores were divided into quartiles as follows: Q1 = 0–25, Q2 = 25–49, Q3 = 0.50–74 and Q4 ≥ 75. Co-morbidity was measured by the Charlson score.

**Follow-up and outcome**

The patients were followed at six month-intervals until August of 2007 or until death. Data for mortality was confirmed by reviewing the medical records and by contacting patient’s next of kin in every site.

**Statistical analysis**

Normally distributed variables are reported as mean ± standard deviation (SD). ANOVA was used to compare baseline characteristics for intra and inter-group. Pearson’s correlation coefficients were obtained between different variables and SGRQ. Kaplan Meier survival analysis was used to assess survival by BODE and SGRQ quartiles. Logistic regression analysis using survival and COPD survival as dependent variables was used to assess the contribution of variables showing significant correlations with these outcomes. We computed

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**Conclusions:** Health status as measured by SGRQ worsens with disease severity evaluated by the BODE index. Both tools predict mortality and provide complimentary information in the evaluation of patients with COPD. © 2011 Elsevier Ltd. All rights reserved.
the C-statistics to compare the power of the BODE and SGRQ values to predict mortality. In this analysis the area under the receiver operating curves (ROC) were quantified and compared to assess the performance of both indices. All analyses were run with STATA version 11.1.

## Results

### Baseline characteristics

A total of 1398 patients with COPD were included in the study. The patients were followed for 53 ± 28 months until death. Most patients had symptomatic COPD. 7% of patients were in stage I by GOLD classification, 31% in stage II, 41% in stage III, and 21% in stage IV. The mean SGRQ % total score was 49.6 ± 20. The baseline characteristics of patients divided according to disease severity by BODE quartiles are shown in Table 1.

### Relationship between BODE and SGRQ

The relationship between the components of the SGRQ and the BODE index are shown in Table 2. The SGRQ total correlated better with BODE index than with FEV1% (r = 0.58, vs r = -0.37, both p < 0.0001). The activity domain of the SGRQ correlated best with all of the components of BODE No SGRQ domains correlated with BMI. Overall, we found that the SGRQ scores worsened exponentially as disease severity increased by BODE quartiles. When the analysis was done separately for each country, the SGRQ-BODE relationships were similar; therefore, the data are presented together. The activity domain and the impact domain scores of the SGRQ, showed the most increase from quartile 1 to 4 (47.7% and 43% respectively), while symptom scores increased only 30%. On the other hand, the difference in SGRQ total score of patients from quartile 1 to 4 exceeded 50%.

### Mortality

There were 430 deaths during the study period (30.8%). The mean follow-up time from enrollment to death was 38 ± 24 months. Most deaths (n = 296, 68.8%) were due to respiratory causes: 49.5% were directly related to COPD, 15.8% to lung cancer, 2.6% to lower respiratory tract infection and 0.7% to pulmonary embolism. Cardiovascular diseases were the cause of 8.8% of deaths and 8.1% died to malignancies other than lung cancer, 4.7% to various medical or surgical illnesses and in 9.8% the cause of death could not be determined. We found both tests (the BODE index and SGRQ total) to correlate with all cause mortality (r = 0.34, p < 0.001 and r = 0.19, p < 0.01 respectively). BODE correlation with COPD mortality was r = 0.41, p < 0.0001, while SGRQ correlation with this outcome was: r = 0.21, p < 0.001. The correlations of BODE and SGRQ with non-COPD death were non-significant: 0.06 and 0.03 respectively.

When the cohort was stratified by BODE quartiles or by SGRQ quartiles, as expected median survival decreased as quartiles increased for both indexes but there were no differences in the median survival among BODE vs SGRQ quartiles (Table 3). We also used Kaplan Meier analysis and compared the survival of patients divided by SGRQ quartiles and by BODE quartiles (Fig. 1). Mortality of patients with SGRQ Q4 was 64% vs BODE Q4 which was 63%. Overall, SGRQ and BODE quartiles survival curves were different, but these differences appear better defined when the cohort was grouped in BODE quartiles. Logistic regression analysis with all cause mortality as dependent variables showed: age, BODE, and Charlson index as the only elements of the model (unadjusted r² = 0.34, p < 0.001). Changing the BODE index with the SGRQ total, the model included age, Charlson index, FEV1%, 6MWD and BMI as independent variables predicting total mortality (unadjusted r² = 0.33, p < 0.001) (Table 4). The C-statistics was 0.77 for BODE index and 0.66 for SGRQ total score, with a difference in of 0.11 (95% confidence interval, 0.08–0.05, p < 0.01).

### Table 1

Baseline characteristics of patients according to disease severity by BODE quartiles.

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>ALL, n = 1398</th>
<th>Q1, n = 483</th>
<th>Q2, n = 457</th>
<th>Q3, n = 270</th>
<th>Q4, n = 188</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up (months)</td>
<td>53 ± 28</td>
<td>53 ± 31</td>
<td>55 ± 28</td>
<td>53 ± 29</td>
<td>52 ± 31</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66 ± 9</td>
<td>65 ± 9</td>
<td>66 ± 9</td>
<td>67 ± 9</td>
<td>67 ± 9</td>
</tr>
<tr>
<td>Gender (male %)</td>
<td>85</td>
<td>83.8</td>
<td>84.6</td>
<td>83.7</td>
<td>94.6*</td>
</tr>
<tr>
<td>Post BD FEV1 (L)</td>
<td>1.35 ± 0.58</td>
<td>1.89 ± 0.58</td>
<td>1.32 ± 0.5</td>
<td>1.07 ± 0.4</td>
<td>0.86 ± 0.3*</td>
</tr>
<tr>
<td>Post BD FEV1 (%)</td>
<td>46 ± 18</td>
<td>62.5 ± 16</td>
<td>42.9 ± 12.5</td>
<td>36 ± 13</td>
<td>28 ± 10**</td>
</tr>
<tr>
<td>MMRC (Points)</td>
<td>2.12 ± 1.1</td>
<td>1.15 ± 0.7</td>
<td>2.08 ± 0.7</td>
<td>2.94 ± 0.6</td>
<td>3.64 ± 0.5**</td>
</tr>
<tr>
<td>6MWD (Meters)</td>
<td>387 ± 130</td>
<td>475 ± 80</td>
<td>414 ± 91</td>
<td>319 ± 95</td>
<td>179 ± 90**</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>26.8 ± 5.5</td>
<td>28 ± 5</td>
<td>27.2 ± 5.6</td>
<td>27 ± 6</td>
<td>25 ± 6**</td>
</tr>
<tr>
<td>BODE Index (Points)</td>
<td>3.63 ± 2.5</td>
<td>1.2 ± 0.8</td>
<td>3.5 ± 0.5</td>
<td>5.4 ± 0.5</td>
<td>7.9 ± 0.9**</td>
</tr>
<tr>
<td>Charlson (Points)</td>
<td>4.16 ± 2.4</td>
<td>3.45 ± 2.3</td>
<td>4.16 ± 2.4</td>
<td>4.44 ± 2.3</td>
<td>5.22 ± 2.4**</td>
</tr>
<tr>
<td>SGRQ Symptoms</td>
<td>54.2 ± 24</td>
<td>43.4 ± 24</td>
<td>56 ± 24</td>
<td>63 ± 23</td>
<td>70 ± 20**</td>
</tr>
<tr>
<td>SGRQ Impact</td>
<td>39.4 ± 22</td>
<td>27 ± 20</td>
<td>37 ± 19</td>
<td>46 ± 20</td>
<td>57 ± 18**</td>
</tr>
<tr>
<td>SGRQ Activity</td>
<td>65.3 ± 24.6</td>
<td>48 ± 23</td>
<td>64 ± 21</td>
<td>77 ± 18</td>
<td>87 ± 14**</td>
</tr>
<tr>
<td>SGRQ Total</td>
<td>49 ± 20.4</td>
<td>36 ± 18</td>
<td>48 ± 18</td>
<td>58 ± 17</td>
<td>68 ± 13**</td>
</tr>
</tbody>
</table>

ANOVA: **Intra and inter-group comparison, p < 0.05, * Only Q4 is different from others. SGRQ: Saint George’s Respiratory Questionnaire; BODE: Body mass index, Obstruction, Dyspnea, Exercise capacity; Post BD FEV1: Forced Expiratory Volume in 1 s 20 min after inhaled bronchodilator; MMRC: Modified Medical Research Council Dyspnea Scale; 6MWD: Six-Minute Walking Distance; BMI: Body Mass Index.
indicating a best performance of BODE score as predictor of all cause mortality (Fig. 2).

Discussion

To our knowledge this is the largest study of quality of life performed in a cohort of patients with well characterized COPD, followed over an extended period of time and not partaking on a pharmaceutical clinical trial. Our study has several novel findings. First, it shows that there is a better correlation between the BODE index and the SGRQ quality of life questionnaire, when compared to the gold standard FEV₁. Second, we have found that the SGRQ scores worsen as COPD severity increases by BODE index quartiles (Table 1). Third, the BODE index is more strongly associated with mortality in COPD than the SGRQ scores. Finally, we have confirmed prior observations about the impact of comorbidity in the HRQoL of patients with COPD, using the validated Charlson score.²⁵

Over the last few years it has become evident that patients with COPD may express important multi-systemic involvement, as evidenced by malnutrition, muscle wasting, anemia, osteoporosis and depression. In patients with clinical disease and a wide range of airflow obstruction, it has been shown that several of these factors are better predictors of survival than the simple degree of airflow limitation as measured by the FEV₁.¹⁸,²⁶–²⁸ That’s why recent reviews propose that the global assessment of an affected patient should include different aspects of the consequences of this disorder, beyond the “gold-standard” assessment of airflow limitation.²⁹

The BODE index was a better predictor of outcome than the FEV₁ in a large cohort of patients with COPD,⁶ and better than all of the individual components of the index in patients undergoing lung volume reduction surgery.⁷

In parallel with these observations, it has become evident that the clinical complexity of COPD can not solely be expressed in physiological terms but that the actual compromise of a patient may also be expressed by tools that reflect the quality of their life. The disease specific St. George’s Respiratory Questionnaire is perhaps the most widely used and better tested of those instruments available for patients with COPD. It has proven to be responsive to several interventions in COPD such as pharmacological agents,¹⁹,³⁰ pulmonary rehabilitation¹²,¹³ and lung volume reduction.¹¹ Secondary analyses of some of those studies have also suggested that the SGRQ can be useful in predicting survival, although one study using a different disease specific questionnaire, the CRQ, failed to observe an association between the scores obtained and mortality.³¹ Our results indicate that both instruments (the BODE index and the SGRQ) in a way reflect the severity of COPD as conventionally graded with the FEV₁ and show that the correlations of SGRQ and BODE were stronger than with airflow obstruction.

The BODE index and SGRQ have a significant but modest correlation between themselves indicating that they do not measure the exact same dimension (Table 2). Interestingly, the best correlations between BODE and SGRQ domains were seen with activity and impact and not with symptoms, in spite of the fact that there is a very good correlation between MMRC and SGRQ, indicating that functional capacity is likely a very important determinant of quality of life in COPD.

Both, the BODE index and the SGRQ scores are moderate predictors of survival. However, using all cause mortality as the outcome, the BODE index proved to be superior to the simultaneously obtained SGRQ (Fig. 2). The most likely explanation for this finding reflects the development and reasons for instrument development; whereas the St. George’s questionnaire was developed to evaluate and reflect patient’s physical, emotional and social well-being,¹⁶ the BODE index was specifically designed and validated to predict mortality in patients with COPD.⁶

Indeed, all four components of the index have been found to be independent predictors of outcome and in aggregate well express the multidimensional severity of an individual patient’s disease state. On the other hand, the perceptive compromise of well-being may be better reflected by the SGRQ than by the BODE as that questionnaire was specifically developed for that purpose.

This study was not meant to prove that one instrument is better than the other. Rather it was designed to evaluate similarities and differences. We believe the results show that one should not be used as a reflection of the other. We view the evaluation of health related quality of life as an outcome in of itself, of important value like health resource utilization or even mortality can be. Indeed, quality of life

### Table 2

<table>
<thead>
<tr>
<th>Domains</th>
<th>BODE</th>
<th>FEV₁%</th>
<th>MMRC</th>
<th>6MWD</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGRQ % Symptoms</td>
<td>0.4</td>
<td>-0.28</td>
<td>0.41</td>
<td>-0.34</td>
<td>-0.02</td>
</tr>
<tr>
<td>SGRQ % Activity</td>
<td>0.59</td>
<td>-0.39</td>
<td>0.63</td>
<td>-0.52</td>
<td>0.02</td>
</tr>
<tr>
<td>SGRQ % Impact</td>
<td>0.5</td>
<td>-0.32</td>
<td>0.53</td>
<td>-0.43</td>
<td>0.03</td>
</tr>
<tr>
<td>SGRQ % Total</td>
<td>0.58</td>
<td>-0.37</td>
<td>0.61</td>
<td>-0.5</td>
<td>0.02</td>
</tr>
</tbody>
</table>

SGRQ: Saint George’s Respiratory Questionnaire; BODE: Body mass index, Obstruction, Dyspea, Exercise capacity; FEV₁: Post-bronchodilator Forced Expiratory Volume in 1 s 20 min after inhaled bronchodilator; MMRC: Modified Medical Research Council Dyspnea Scale; 6MWD: Six-Minute Walking Distance; BMI: Body Mass Index.

### Table 3

<table>
<thead>
<tr>
<th>SGRQ Quartiles</th>
<th>Months (95%CI)</th>
<th>BODE Quartiles</th>
<th>Months (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (&lt;25)</td>
<td>60 (55–64)</td>
<td>Q1 (0–2)</td>
<td>62 (57–66)</td>
</tr>
<tr>
<td>Q2 (25–49)</td>
<td>56 (50–62)</td>
<td>Q2 (3, 4)</td>
<td>56 (51–61)</td>
</tr>
<tr>
<td>Q3 (50–74)</td>
<td>52 (47–60)</td>
<td>Q3 (5, 6)</td>
<td>52 (48–59)</td>
</tr>
<tr>
<td>Q4 (≥75)</td>
<td>50 (44–56)</td>
<td>Q4 (7–10)</td>
<td>49 (44–50)</td>
</tr>
</tbody>
</table>

P value for trend <0.001

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*Table 2* Pearson’s correlations coefficients (with p values) for SGRQ % total and the components of the BODE index.

*Table 3* Median and 95% Confidence Interval (95%CI) survival by BODE quartiles and Total SGRQ quartiles.
has become and should continue to be one of the outcomes evaluated when planning interventions as it better expresses the composite effect of the intervention on patient's well-being. On the other hand, the BODE index better reflects stages of COPD if mortality is considered the ultimate expression of disease severity. Further, BODE has proven sensitive to reflect exacerbation severity, the response to surgery and to pulmonary rehabilitation and as such, is beginning to emerge as a tool to assess disease modification and future disease outcome. Perhaps, new studies underway, can use the strength of both tools to express the complex nature of COPD better.

There were some limitations to this study. First, the majority of patients were men and perhaps the findings may not totally apply to women. We believe that gender related differences in COPD warrant further investigation. Second, we only evaluated the SGRQ and the results may not extend to other instruments of HRQoL. However, Hajiro et al., have shown that all of the questionnaires designed to evaluate health related quality of life are highly correlated. We would expect further studies to validate our findings.

In summary, this study shows that the BODE index and the Saint George’s questionnaire are instruments of value in the evaluation of patients with COPD. They provide different information. BODE is a slightly better predictor of mortality than the SGRQ, and therefore a better instrument to determine severity of COPD. The SGRQ on the other hand should be considered an outcome in of itself as it may better reflect the overall interpretation of the compromise of patients with this disease.

### Table 4

<table>
<thead>
<tr>
<th></th>
<th>Risk Ratio</th>
<th>Confidence Interval (95%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model without SGRQ, $r^2 = 0.34$</td>
<td>Risk Ratio</td>
<td>Confidence Interval (95%)</td>
<td>p value</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>1.04</td>
<td>1.02–1.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BODE Index (Points)</td>
<td>1.34</td>
<td>1.28–1.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson (Points)</td>
<td>1.09</td>
<td>1.02–1.99</td>
<td>0.003</td>
</tr>
<tr>
<td>Model without BODE, $r^2 = 0.33$</td>
<td>Risk Ratio</td>
<td>Confidence Interval (95%)</td>
<td>p value</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.04</td>
<td>1.02–1.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SGRQ total (Points)</td>
<td>1.00</td>
<td>0.98–1.03</td>
<td>0.53</td>
</tr>
<tr>
<td>Charlson (Points)</td>
<td>1.09</td>
<td>1.03–1.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6MWD, (meters)</td>
<td>0.98</td>
<td>0.98–0.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.97</td>
<td>0.93–0.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV₁ (% Predicted)</td>
<td>0.99</td>
<td>0.97–0.99</td>
<td>0.00</td>
</tr>
</tbody>
</table>

SGRQ: Saint George’s Respiratory Questionnaire; BODE: Body mass index, Obstruction, Dyspnea, Exercise capacity; Post BD FEV₁: Post-Bronchodilator Forced Expiratory Volume in 1 s 20 min after inhaled bronchodilator; 6MWD: Six-Minute Walking Distance; BMI: Body Mass Index.
References


