The Association of the COPD Assessment Test (Cat) Score with Chronic Obstructive Lung Disease (GOLD) Grade among Chronic Obstructive Pulmonary Disease (COPD) Outpatients in the North East of Peninsular Malaysia

Nani Draman 1*, Hazleena Mohamed Hasnan 2, Wan Mohd Izani Wan Mohamed 2, Mat Zuki Mat Jaeb 3

1 Department of Family Medicine, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, 16150, Kelantan, Malaysia
2 Department of Internal Medicine, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, 16150, Kelantan, Malaysia
3 Department of Medicine, Hospital Raja Perempuan Zainab II, 15200 Kota Baharu, Kelantan, Malaysia

* Corresponding author: Dr. Nani Draman
Lecturer, Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia,
Tel: +609-767 6610 | Email: drnani@kb.usm.my

Abstract

Objective: To determine the association between the Malay version of COPD Assessment Test (CAT) with severity of airflow limitation based on The Global Initiative for Chronic Obstructive Lung Disease (GOLD) grade, cardiovascular co-morbidities and frequency of acute Chronic Obstructive Pulmonary Disease (COPD) exacerbation among stable COPD outpatients in the two main hospitals of Kota Bharu, Kelantan over a period of one year.

Methodology: This was a cross-sectional study which was conducted among 95 COPD Chronic Obstructive Pulmonary Disease) patients who attended the respiratory clinics at Hospital Universiti Sains Malaysia (HUSM) and Hospital Raja Perempuan Zainab II (HRPZ II). The Malay version of the COPD assessment test (CAT) and associated COPD data were used to obtain COPD severity. Spirometry was then performed on the subjects. Previous angiogram, echocardiogram (ECHO) and electrocardiogram (ECG) results were reviewed separately for patients who had a background history of cardiovascular disease.

Results: Of the 95 subjects, 89.5% were male and 94.7% were Malay with a mean age of 66.43±8.61 years. Most (48, 50.5%) had moderate CAT scores with 40 (42.1%) patients having severe airflow limitation ie GOLD grade III. There was a significant difference between the mean CAT score, between each GOLD grade. The association between CAT score with cardiovascular co-morbidities and frequency of acute exacerbation however were not statistically significant.
Conclusion: There was a significant difference in the CAT score between each GOLD grade, especially in GOLD grade 1 and 4. The CAT score was not found to have a statistically significant association with cardiovascular co-morbidities and frequency of acute exacerbation within the one-year period.

Key words: Chronic Obstructive Pulmonary disease (COPD), GOLD, Malaysia

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common illness associated with high morbidity and mortality throughout the world. Many people suffer from COPD for years and die prematurely from it or its complications. In 1990, COPD was ranked twelfth as the cause of loss of disability adjusted life years (DALYs). However, by 2020, it is expected to be ranked fifth. Meanwhile, in 1990, COPD was ranked sixth as the commonest cause of death worldwide but by 2020 it is expected to be the third leading cause of death. This alarming increased in trend is contributed by expanding epidemic of smoking especially in the developing countries, reducing mortality from other common causes of death and aging of the world population.

Cigarette smoking is the most important risk factor for COPD. About 25% of continuous smokers develop COPD. Tobacco smoke is the risk factor for as much as 90% of the cases of COPD and it is dose-related. The likelihood of developing COPD increases with age and cumulative smoke exposure. Cigarette smokers have a higher prevalence of respiratory symptoms, lung function abnormalities and mortality rate compared to non-smokers. Smoking cessation is the most important step in slowing down the COPD progression and it is most beneficial in the early stages of COPD.

In Malaysia, the prevalence of moderate to severe COPD is 4.7% of the population which translates to approximately 448,000 cases. COPD-related illness was higher in men, with rates of 32.6 to 334 per 10,000 verses 21.2 to 129 per 10,000 for women. A 2006 Malaysian survey showed that 77% of health-related economic burden was contributed by COPD; COPD also had the highest growth in projected health care cost. Therefore, without any doubt COPD represents an important public health challenge that is both preventable and treatable.

COPD is associated with the risk of cardiovascular events (CVEs), but its impact on overall mortality has not been well quantified. Therefore an assessments of COPD patients are important to determine the severity of the disease, the clinical impact of COPD on the patient’s overall health status and to estimate the risk of future exacerbation in order to guide treatment. Questionnaires such as the COPD Assessment Test (CAT) have thus been developed to help patients and their clinicians to assess and quantify symptoms as well as the impact of COPD on their health, therefore enabling better communication between patients and physicians regarding consequences of their disease. Study by Lee HM et al noted the addition of global CVE risk
scores to lung function data significantly improves risk stratification of patients with COPD for CVE and total mortality, thus adds to predicting long-term survival of these patients.

COPD has also been established as one of the risk factors for cardiovascular morbidity and mortality. In a study done by Sin and Man, it was noted that cardiovascular risk in COPD was related to the severity of the airflow limitation as measured by post-bronchodilator FEV1. With further decline in FEV1, there is more severe airflow limitation that is linked to a higher chance of having a cardiac event. In this study, we investigated the association of severity of clinical symptoms of COPD as measured by the CAT score with cardiovascular co-morbidities amongst stable COPD outpatients on our follow-up.

COPD Assessment Test (Cat) questionnaire was used in this study to see the clinical impact of COPD because it has the advantage of being easier and faster to complete.

Methods

A prospective cross sectional study was conducted from October till November 2012 at the Respiratory Clinics of Hospital Universiti Sains Malaysia (HUSM) and Hospital Raja Perempuan Zainab II (HRPZII) in the city of Kota Bharu, Kelantan. The inclusion criteria used were that subjects had to be more than 30 years of age, had a smoking history of ≥10 pack-years, diagnosed as having COPD for at least 6 months prior to recruitment and had no deterioration in COPD symptoms within 4 weeks before recruitment. COPD patients with acute exacerbation on the day of recruitment, patients with history of pneumonia ≤4 weeks before recruitment, patients with concomitant history of atopy (history of allergy or asthma or allergic rhinitis), being a passive smoker or having occupational COPD, was unable to perform spirometry, and being illiterate were excluded. A universal sampling method was used in this study due to a limited number of potential subjects. The study protocol was approved by the Research Ethics Committee, Universiti Sains Malaysia in 2012.

Research tools

The Malay version of the CAT questionnaire was validated before it was used in this study. It consists of 8 questions, each having the option of 6 answers. Each answer was assigned a score ranging from 0 to 5 with the total score ranging from 0 to 40 points. A CAT score of 1-10, 11-20, 21-30 and 31-40 represents a mild, moderate, severe and very severe clinical impact of COPD respectively. Those who fulfilled the inclusion criteria and did not have any of the exclusion criteria were invited to be involved in the study Patients were then given the CAT questionnaire and COPD data collection form to fill in. Following this spirometry was performed.

COPD outpatients were defined as patients who previously had been diagnosed to have COPD by a respiratory physician for a period of at least 6 months prior to entering the study as well as
attending the respiratory clinics of either HUSM or HRPZII. These were stable patients with no history of deterioration of COPD symptoms for the preceding 4 weeks.

COPD severity based on airflow limitation was measured by post-bronchodilator FEV1. Spirometry was performed pre- and post-400mcg of salbutamol inhalation where FEV1 was measured 10-15 minutes after bronchodilator administration.

<table>
<thead>
<tr>
<th>GOLD 1</th>
<th>Mild</th>
<th>FEV1 ≥ 80% predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 2</td>
<td>Moderate</td>
<td>50% ≤ FEV1 &lt; 80% predicted</td>
</tr>
<tr>
<td>GOLD 3</td>
<td>Severe</td>
<td>30% ≤ FEV1 &lt; 50% predicted</td>
</tr>
<tr>
<td>GOLD 4</td>
<td>Very Severe</td>
<td>FEV1 &lt; 30% predicted</td>
</tr>
</tbody>
</table>

COPD severity based on COPD group was a combined assessment of symptoms, airflow limitation by spirometry and frequency of acute exacerbation. COPD group was a combined severity classification and may be used to predict the risk of future exacerbations. COPD symptoms were assessed by using the CAT questionnaire whilst airflow limitation was measured by spirometry. There were several groups: Group A – low risk with less symptoms, group B - low risk with more symptoms, group C – high risk with less symptoms and group D – high risk with more symptoms. Low/high risk refers to the risk for these patients to have future acute exacerbations of COPD. On the other hand, less/more symptoms refer to cough and sputum production experienced by the patient.

The term cardiovascular co-morbidities in this study refers to: Ischaemic heart disease (IHD), Atrial fibrillation (AF), Heart failure (HF), and Hypertension (HPT).

Results

In total 130 stable COPD outpatients were screened to participate in this study. Out of that number, 110 patients fulfilled the inclusion criteria and consented to be involved in the study. From that number of patients, 5 patients were unable to complete the CAT questionnaire and were excluded from the study. Finally, only 95 patients were able to successfully perform spirometry and were thus eligible for inclusion into the final analysis. Therefore the response rate was approximately 86% for this study.

Table 1 describes the socio-demographic characteristics of the COPD patients in this study. The majority were male, Malays, ex-smokers with a mean duration of smoking of about 37 years, a mean duration of COPD of about 7 years with a patient mean age of 66.4 ± 8.6 years.

Figure 1 COPD severity based on CAT score.
Of our COPD patients, 19 (20%) had a CAT score ranging from 1-10, 48 (50.5%) had a CAT score ranging from 11-20, 26 (27.4%) had a CAT score of 21-30 and 2 (2.1%) had a CAT score within the 31-40 range.
Figure 2 COPD severity based on GOLD Grade
Seven (7.4%) of our patients were in GOLD grade I, 34 (35.8%) in GOLD grade II, 40 (42%) in GOLD grade III while 14 (14.7%) were in GOLD grade IV.

Figure 3 COPD severity based on COPD group
Five (5.3%) of our patients were in Group A, 23 (24.2%) in Group B, 14 (14.7%) in Group C while 53 (55.8%) were in Group D.

Table 2 shows the association between CAT score mean and GOLD grade. The mean CAT scores for GOLD grade I, II, III and IV were as follows: 10.43+/-3.91, 15.29+/-7.05, 16.50+/-6.91 and 20.71+/-7.28. One-way ANOVA test revealed that there was a statistically significant difference between the mean CAT score amongst each GOLD grade with F(3,91)=3.89, P-value=0.011.

Post-Hoc Analysis (Scheffe) – only the mean CAT score of GOLD grade I is significantly different from GOLD grade IV with a mean difference of -10.29 and a P-value of 0.019. (The mean difference is significant at the 0.05 level).

Table 3 shows the association between the CAT score mean and CV co-morbidities. The difference between mean CAT score in COPD patients with and without CV co-morbidities was not statistically significant (mean difference -1.585 (95% CI -4.55, 1.383); p = 0.292).

Table 4 shows the association between the CAT score mean and frequency of acute exacerbations within a one year period. The difference between CAT score mean in COPD patients with at least one acute exacerbation within a year versus two or more acute exacerbations within a year was not statistically significant (mean difference -2.415 (95%CI -5.459, 0.630); p = 0.119).

Discussion

Patients with COPD may experience a considerable restriction in numerous everyday activities and consequently have a poor quality of life. Importantly, international guidelines recommend assessing the impact of the severity of the disease on the patient's health status in order to guide therapy. As reported by Scichilone N and Chetta A, it was suggested that the administration of the CAT to COPD patients in outpatient clinics as a simple and unproblematic method of measuring outcome in clinical practice. A study done by Natya Raghavan et al, showed that the triad of smoking history, age at least 55 years and the presence of exertional breathlessness in the components of the COPD Assessment Test (CAT) were had reliable measurement properties and may help identify patients at risk for COPD for whom spirometry testing is recommended.

Based on the results of the CAT score from this study, the largest number of participants (51%) had a moderate clinical severity of COPD (CAT score 11-20). On the other hand, according to severity of airflow limitation the vast majority of enrolled patients (42%) had severe COPD ie GOLD grade III. The correct determination of COPD severity is therefore important to guide
appropriate therapy for these patients. An inability to do so will lead to further deterioration in patient health status and also a subsequent decline in lung function due to an increased number of acute exacerbation and hospitalisation episodes.

Our results showed that there was a statistically significant difference in the mean CAT score between each GOLD grade. The higher the mean CAT score, the higher the GOLD grade. However, only the difference of the mean CAT score between GOLD grades I and IV was statistically significant in the post-hoc analysis. Hence it was the one and only contributor to the significant difference in the mean CAT score in between each GOLD group. Our finding in this study was consistent with a previous study done by Jones et al in six European countries and the USA, focusing on the Caucasian population. However, in contrast with our study they noted the CAT score mean differences between GOLD grades II-III and III-IV were statistically significant.

Previous studies revealed COPD as a risk factor for cardiovascular morbidity and mortality. In the Tuscan Epidemiologic Study of Airways Obstructive Disease done by Camilli et al, they noted that even among those with severe COPD (defined as FEV1 less than 50% of predicted), less than a quarter died due to COPD but in nearly 50% the primary cause of death was due to cardiovascular causes. Sin and Man reported the association between severity of airflow limitation which was measured by FEV1 with cardiovascular events. For every 10% decline in FEV1, cardiovascular mortality was increased by approximately 28% and nonfatal coronary events increased by approximately 20% in those with mild to moderate CAT scores.

In our study, we investigated the association of COPD symptom severity as assessed by CAT score with the presence of cardiovascular co-morbidities. More than half of our study patients (58.9%) had cardiovascular co-morbidities versus 41.1% who did not have any cardiovascular disease. The mean CAT score was slightly greater in those with cardiovascular co-morbidities (16.89 ± 7.59 verses 15.31 ± 6.51). Nonetheless, there was no statistically significant association between the CAT score mean and the occurrence of cardiovascular co-morbidities. Therefore, a higher CAT score may not be used to predict the likelihood of COPD patients in having cardiovascular illnesses. The most likely explanation for this result was that the CAT score is more of a tool for the assessment of symptoms in COPD.

Mackay et al reported COPD patients with frequent episode of exacerbations had significantly higher baseline CAT scores than those with infrequent exacerbations (19.5 ± 6.6 versus 16.8 ± 8.0, p = 0.025). We expected to observe a higher CAT score with an increased frequency of acute exacerbations. We however found that the association between the CAT score mean and frequency of acute exacerbation within a one year period was not statistically significant, even though the mean CAT score for those with at least one exacerbation versus two or more exacerbations within a year was 15.40 ± 7.34 and 17.82 ± 6.65 respectively. Thus, in our study a higher CAT score did not mean the patients had more episodes of acute exacerbations within the one year. One possibility that could explain our result was that the majority of our participants were ex-smokers (82.1%) as compared to 17.9% of active smokers.

Therefore, in our study we can conclude that our COPD outpatients in GOLD grade I have less symptoms as compared to those in Grade IV. Amongst GOLD grade I-II, II-III and III-IV
however, COPD symptoms can be slightly different or almost equal. The main difference in the study results occurred most likely due to a different sampling frame. We only included stable COPD outpatients who were free from acute exacerbations within four weeks prior to recruitment, whereas in their study 237 patients were experiencing an exacerbation.

**Conclusion**

Most COPD patients in this study had a moderate CAT score (score 11-20) with a severe GOLD grade (GOLD grade III). There was a statistically significant difference between the CAT score mean in between each GOLD grade, especially in GOLD grade I and IV. The higher the mean CAT score, the higher the GOLD grade. However, there were no statistically significant associations between the CAT score mean with cardiovascular co-morbidities as well as the frequency of acute exacerbation within one year. Therefore for future study we suggest the definition of acute exacerbation of COPD should be revamped to include those COPD patients who had variation of symptoms beyond normal day-to-day, required multiple nebulisation at home but did not come for medical attention. This will help to surmount underestimation of COPD patients with acute exacerbation. We also recommend this study to be conducted in other respiratory clinics in other part of Malaysia to observe the consistency of the Malay version of CAT questionnaire across the races and states in Malaysia.

**Limitations**

In this study, we were unable to do systematic randomized sampling because the number of patients attended to our clinics was not sufficient, in addition to this, many COPD patients defaulted their follow-up visit during monsoon season due to the bad weather or limitation of public transportation. Therefore, the result of this study might not represent the true COPD population.

Apart from that, we might have underestimated the number of our COPD patients who had acute exacerbation of COPD. We only considered our COPD patients to have acute exacerbation of COPD if they had any episode of worsening of respiratory symptoms beyond normal day-to-day variations and led to a change in medication. This was consistent with our current GOLD guideline 2011. Nonetheless, there were a few numbers of our patients who had multiple episodes of COPD attacks at home that relieved by home nebulizer. These kinds of patients had deterioration of COPD symptoms from the daily basis but did not seek medical attention.

Last but not least, this study was done in Kelantan and nearly 95% of our patients were ethnic Malay who spoke in Kelantanese Malay dialect. Thus, the result of this study could not be extrapolated to ethnic Malay in other states as well as to the general population in Malaysia.

**Conflict of Interest:** None
Authors' contributions
Hazleena: Conception and design, Data collection and analysis, drafting article and final approval
Nani D: Conception and design of the study, interpretation and final approval
WMI Wan Mohamed: Conception and design of the study, interpretation, drafting and final approval
Mat Zuki MJ: Conception and design of the study, interpretation, drafting and final approval

Acknowledgements: We would like to acknowledge the Ethical committee of Universiti Sains Malaysia for allowing us to conduct this study and we also greatly acknowledge and appreciate the cooperation of all participants and clinic staff for their assistant in this study.

References
5. Regional Copd Working Group. COPD prevalence in 12 Asia-Pasific countries and regions: projections based on the COPD prevalence estimation model. Respirology. 2003; 8: 192-198
15. Scichilone N, Chetta A. It's time to let the CAT out ..patient!. Respiration. 2012;84:189-90.

Table 1: Demographic and clinical characteristic of COPD outpatients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N = 95</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>66.43 (8.61)a</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>85 (89.5)b</td>
</tr>
<tr>
<td>Female</td>
<td>10 (10.5)b</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>90 (94.7)b</td>
</tr>
<tr>
<td>Chinese</td>
<td>4 (4.2)b</td>
</tr>
<tr>
<td>Siamese</td>
<td>1 (1.1)b</td>
</tr>
<tr>
<td>Others</td>
<td>0 (0)b</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
</tr>
<tr>
<td>Active smoker</td>
<td>17 (17.9)b</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>78 (82.1)b</td>
</tr>
<tr>
<td>Duration of smoking (years)</td>
<td>37.64 (13.20)a</td>
</tr>
<tr>
<td>Pack-years</td>
<td>39.77 (32.23)a</td>
</tr>
<tr>
<td>Duration of having COPD (years)</td>
<td>7.76 (6.03)a</td>
</tr>
<tr>
<td>No of medication</td>
<td></td>
</tr>
<tr>
<td>One type</td>
<td>7 (7.4)b</td>
</tr>
<tr>
<td>Two types</td>
<td>37 (38.9)b</td>
</tr>
</tbody>
</table>
Three types 40 (42.1)\(^b\)
Four types 11 (11.6)\(^b\)

**Cardiovascular status**
With CV co-morbidities 56 (58.9)\(^b\)
Without CV co-morbidities 39 (41.1)\(^b\)

**No of exacerbation within a year**
0-1 62 (65.3)\(^b\)
More than 2 33 (34.7)\(^b\)

\(^a\) = mean (SD) \quad \(^b\) = n(%) \quad N = number of subjects

---

**Figure 1:** COPD severity based on CAT score

Percentage of COPD patients based on CAT score (n=95)

<table>
<thead>
<tr>
<th>CAT score</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 10</td>
<td>20.0%</td>
</tr>
<tr>
<td>11 to 20</td>
<td>50.5%</td>
</tr>
<tr>
<td>21 to 30</td>
<td>27.4%</td>
</tr>
<tr>
<td>31 to 40</td>
<td>2.1%</td>
</tr>
</tbody>
</table>

```csharp
Figure 1: COPD severity based on CAT score
```
Figure 2: COPD severity based on CAT score and GOLD grade

Figure 3: COPD severity based on CAT score and COPD group
Table 2: Result of one-way ANOVA test on the association between the CAT score mean and GOLD grade

<table>
<thead>
<tr>
<th>GOLD grade</th>
<th>CAT score</th>
<th>F-stat (df)</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>10.43 +/- 3.91</td>
<td>3.893(3,91)</td>
<td>0.011</td>
</tr>
<tr>
<td>II</td>
<td>15.29 +/- 7.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>16.50 +/- 6.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>20.71 +/- 7.28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> = one-way ANOVA

Post-Hoc Analysis (Scheffe) – only the mean CAT score in GOLD grade I is significantly different from GOLD grade IV with a mean difference of -10.29 and a P-value of 0.019. (The mean difference is significant at the 0.05 level)

Table 3: The association between the CAT score mean and CV co-morbidities

<table>
<thead>
<tr>
<th>Variables</th>
<th>With CV co-morbidity (n = 56)</th>
<th>Without CV co-morbidity (n=39)</th>
<th>Mean difference (96% CI)</th>
<th>t-stat(df)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAT score</td>
<td>15.31 (6.51)</td>
<td>16.89 (7.59)</td>
<td>-1.585(-4.55, 1.383)</td>
<td>-1.061(93)</td>
<td>0.292</td>
</tr>
</tbody>
</table>

CV= cardiovascular, CI = confident interval, SD = standard deviation, n = number of subjects

Table 4: The association between the CAT score mean and frequency of acute exacerbations within one year

<table>
<thead>
<tr>
<th>Variables</th>
<th>One exacerbation (n = 62)</th>
<th>≥2 exacerbations (n = 33)</th>
<th>Mean difference (95% CI)</th>
<th>t-sta(df)</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAT score</td>
<td>15.40(7.34)</td>
<td>17.82 (6.65)</td>
<td>-2.415 (-5.459, 0.630)</td>
<td>-1.575(93)</td>
<td>0.119</td>
</tr>
</tbody>
</table>

<sup>a</sup> = independent t-test, CI = confident interval, SD = standard deviation, n = number of subjects