

Evaluation of Quality of Life with the Chronic Obstructive Pulmonary Disease Assessment Test in Chronic Obstructive Pulmonary Disease and the Effect of Dyspnea on Disease-Specific Quality of Life in These Patients

Oguzhan Okutan, Dilaver Tas, Ersin Demirer, and Zafer Kartaloglu

GATA Haydarpasa Training Hospital, Department of Pulmonary Diseases, Istanbul, Turkey.

Received: September 11, 2012

Revised: October 22, 2012

Accepted: October 29, 2012

Corresponding author: Dr. Dilaver Tas,
GATA Haydarpasa Training Hospital,
Department of Pulmonary Diseases,
34668 Istanbul, Turkey.

Tel: 902165422020, Fax: 902165422990

E-mail: dilavertas@gmail.com

The authors have no financial conflicts of interest.

Purpose: The chronic obstructive pulmonary disease (COPD) assessment test (CAT) was recently introduced for use in assessing disease-specific quality of life and follow-up of patients with COPD. The purpose of this study was to evaluate the effect of the dyspnea on disease-specific quality of life detected by CAT score in patients with COPD. **Materials and Methods:** In this study, 90 stable patients with COPD as defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria were included. The level of dyspnea was assessed with the Medical Research Council (MRC) dyspnea scale, and disease-specific quality of life was assessed with CAT score. **Results:** The mean±SD age was 68.5±10.9 (range 41-97) years. A significant relationship was established between CAT score, MRC dyspnea scale score and GOLD stage in patients with COPD. There was also a positive correlation between dyspnea scale scores and GOLD stage in the patients ($p<0.001$), as well as positive correlation between CAT score and dyspnea scale score ($p<0.001$). CAT score showed a significant correlation with hospitalization and exacerbations ($p<0.05$). **Conclusion:** Dyspnea is an important symptom that may impact quality of life in patients with COPD. CAT was shown to be a simple, fast and intelligible measurement of disease-specific quality of life, and was correlated with levels of dyspnea in patients with COPD.

Key Words: Chronic obstructive pulmonary disease, dyspnea, quality of life

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by progressive and partially reversible airflow limitations associated with an abnormal inflammatory response of the lungs to noxious particles or gases.¹ COPD restricts daily activities as a result of reduced pulmonary function, dyspnea, or limitations in exercise tolerance. Pulmonary function tests remain the standard method for grading COPD severity in international treatment guidelines. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommended that both pulmonary

© Copyright:

Yonsei University College of Medicine 2013

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

function and disease-specific quality of life be monitored regularly to guide any changes in treatment.¹

Dyspnea is one of the major symptoms of COPD and it impairs quality of life in such patients. Moreover, dyspnea is known to be correlated with objective and subjective measurements of COPD.² Several instruments are available to assess dyspnea: The Medical Research Council (MRC) dyspnea scale has been in use for many years to assess the effect of breathlessness on daily activities.³ Other dyspnea scales include the Visual Analogue Scale, Oxygen Cost Diagram, Borg dyspnea scale, and baseline or transitional dyspnea index for use in clinical practice. The MRC scale measures activity limitation or disability due to dyspnea rather than the severity of dyspnea itself, and thus, measures the chronic effect of disease.

Disease-specific quality of life is being recognized as an important outcome when evaluating patients with COPD.^{4,5} COPD-specific quality of life measurements, including the St. George's Respiratory Questionnaire (SGRQ)⁶ and Chronic Respiratory Questionnaire,⁷ have been validated and used extensively in clinical studies. However, these questionnaires are complex and time-consuming to complete and may require specialist software or licenses to use, which limits their applicability in routine practice.

The COPD assessment test (CAT) was recently developed as a short, simple instrument for qualifying the symptom burden of COPD in routine practice, and enables better communication between patients and healthcare professionals about the consequences of the disease. The CAT was derived from 21 candidate items identified through qualitative research of patients with COPD from COPD prospective international studies.⁸⁻¹¹

In the present study, dyspnea severity was evaluated by the MRC scale. Patient COPD-specific quality of life was assessed with CAT score as a disease specific measure. The purpose of this study was to evaluate the effect of the dyspnea on disease-specific quality of life detected by CAT score in patients with COPD.

MATERIALS AND METHODS

Subjects

Patients with stable COPD, as defined by GOLD, were recruited from our outpatient clinic from October 2010 to May 2011. All patients had undergone at least 6 months of outpatient management. The entry criteria for the study were

as follows: 1) a known post-bronchodilator forced expiratory volume in 1 s/forced vital capacity (FEV1/FVC) ratio of <70% and an FEV1 <80% (except GOLD I patients) of the predicted value for all measurements made over the prior six months; 2) a smoking history of >10 packet-years; 3) no history suggestive of bronchial asthma; 4) no exacerbations of the airflow limitation over the preceding six weeks; and 5) no changes in treatment regimen over the preceding four weeks. Exclusion criteria were any current pulmonary disorder other than COPD and serious, unstable cardiovascular or neurological disease.

All eligible patients finished the following examinations on the same day: pulmonary function tests, assessment of their dyspnea, and assessment of their disease-specific quality of life by CAT. All tests and questionnaires were administered by investigators in a face-to-face interview. The ethics committee of our institute approved the research protocol and written informed consent was obtained from all participants.

Demographic information, medical history, blood chemistry, previous and current COPD medications were recorded. The history of exacerbations in the previous one year was also recorded. An exacerbation was defined as a worsening of the symptoms that required oral corticosteroids and/or antibiotics and/or hospitalizations. All patients were treated according to GOLD guidelines.

Pulmonary function tests

The diagnostic classification was performed by pulmonary physicians according to GOLD guidelines. Post-bronchodilator FEV1 was assessed at 20 min after the inhalation of salbutamol 200 mcg plus ipratropium 40 mcg using a metered dose inhaler. Spirometry was performed using a FlowScreen Pro spirometer (JAEGGER Inc., Hoechberg, Germany) according to established guidelines.¹²

Assessment of dyspnea

Level of dyspnea was evaluated by the MRC dyspnea scale.³ The MRC dyspnea scale is a 5-point scale based on levels of dyspnea. Based on the patient's responses, the observer was able to grade the degree of dyspnea-related impairment.¹³

Assessment of the CAT

The disease-specific quality of life was assessed with the Turkish version of the CAT.¹⁴ The CAT comprised eight items assessing cough, phlegm, chest tightness, breathlessness going up hill/stairs, activity limitations at home, confidence leaving home, sleep and energy. Each item was scored

from 0 to 5 giving a total score from 0 to 40, corresponding to the best and worst health status in patients with COPD, respectively.⁹ Scores of 0-10, 11-20, 21-30 and 31-40 represented mild, moderate, severe or very severe clinical impact, respectively.¹⁵

Statistical analysis

Data were analyzed using SPSS-PC (Version 15.0, SPSS Inc., Chicago, IL, USA). All indices are expressed as mean±SD. The relationship between variables of patients was calculated by Pearson's correlation coefficient(*r*). Proportions of patients with different MRC grades across the GOLD stages and CAT scores were analyzed by chi-square test. Multiple group comparisons of quantitative variables were made using analysis variance. Inter-group comparisons were carried out using multivariate analysis and the Bonferroni's test to identify significantly different groups. *p*-values less than 0.05 were considered significantly.

RESULTS

Ninety patients with COPD were evaluated. The average age of the patients was 68.5±10.9 (range: 41-97) years; duration of COPD, 8.1±8.4 (range: 1-50) years; and duration of management, 6.1±7.1 (range: 1-40) years. Nineteen patients were GOLD stage I, 43 patients were GOLD II, 26

patients were GOLD III, and 2 patients were GOLD IV. Table 1 shows the demographic and clinical characteristics according to GOLD stage.

Table 2 shows the inter-correlations among the CAT score and clinical characteristics of the patients. The CAT scores were correlated with duration of COPD, duration of management, hospitalization days, and exacerbation.

With respect to the CAT scores, 24 patients were CAT I (mild), 33 patients were CAT II (moderate), 27 patients were CAT III (severe), and 6 patients were CAT IV (very severe). Table 3 shows the study variables according to CAT score. The dyspnea scale, exacerbation, and disease duration were significantly different among the CAT score groups.

Table 4 shows the differences in CAT scores between classes of other COPD impairment measurements. There were significant differences between GOLD I and GOLD II stages (*p*=0.001), as well as between MRC scales 1 and MRC scales 2 and 3 (*p*=0.021, *p*=0.001, respectively). Other measurements were not significant.

DISCUSSION

In our study, CAT scores were shown to be associated with disease features, including duration of COPD, duration of management and exacerbation, while GOLD stages were not. While stage of the disease was evaluated with a spirom-

Table 1. Demographic and Clinical Characteristics According to GOLD Stage

	GOLD I (n=19)	GOLD II (n=43)	GOLD III (n=26)	GOLD IV (n=2)
Age*	63.7 (11.2)	69.1 (10.3)	71.3 (10.3)	66.5 (23.3)
Smoking pack-yrs*	38.8 (32.8)	38.9 (24.5)	36.5 (21.2)	40.0 (56.6)
Duration COPD yrs*	4.3 (4.1)	8.7 (8.9)	10.2 (9.3)	1.5 (0.7)
Duration management yrs [†]	2.2 (2.0)	6.7 (7.5)	8.2 (8.1)	1.5 (0.7)
Exacerbation*	0.3 (0.4)	0.8 (1.6)	1.1 (1.2)	0.0 (0.0)
Hospitalization days*	3.1 (6.1)	6.5 (11.5)	12.0 (14.4)	0.0 (0.0)
CAT score [‡]	9.5 (6.2)	18.2 (8.1) [§]	20.9 (8.2)	22.5 (0.7)
MRC dyspnea scale [‡]				
1	5 (45.5)	5 (45.5)	1 (9.0)	0 (0)
2	13 (27.7)	22 (46.8)	10 (21.3)	2 (4.2)
3	1 (8.3)	10 (83.3)	1 (8.3)	0 (0)
4	0 (0)	4 (36.4)	7 (63.6)	0 (0)
5	0 (0)	2 (22.2)	7 (77.8)	0 (0)

GOLD, Global Initiative for Chronic Obstructive Lung Disease; COPD, chronic obstructive pulmonary disease; CAT, COPD assessment test; MRC, Medical Research Council; ANOVA, analysis variance; SD, standard deviation.

All data represent mean (SD) except MRC dyspnea scale that show frequency (row percentage). ANOVA results (column 1).

*Not significant (*p*>0.05).

[†]*p*<0.05.

[‡]*p*<0.001.

Post-hoc Bonferroni's test: vs. column 3: [§]*p*<0.001.

Table 2. Correlation Coefficient(r) of the Study Variables

	CAT score	BMI	Duration COPD yrs	Duration management yrs	Exacerbation	Hospitalization days	Smoking pack-yrs
CAT score	1						
BMI	0.007	1					
Duration COPD yrs	0.325 [†]	-0.163	1				
Duration management yrs	0.346 [†]	-0.169	0.871 [†]	1			
Exacerbation	0.445 [†]	-0.310 [†]	0.299 [†]	0.369 [†]	1		
Hospitalization days	0.518 [†]	-0.173	0.326 [†]	0.442 [†]	0.763 [†]	1	
Smoking pack-yrs	0.034	-0.036	-0.251*	-0.174	0.007	-0.034	1

COPD, chronic obstructive pulmonary disease; CAT, COPD assessment test; BMI, body mass index.

* $p < 0.05$.

[†] $p < 0.01$.

Table 3. The Study Variables According to CAT Score

	CAT I (n=24)	CAT II (n=33)	CAT III (n=27)	CAT IV (n=6)
Age ^{ns}	68.1 (11.4)	67.3 (9.6)	69.2 (12.5)	74.5 (7.8)
BMI ^{ns}	26.2 (3.4)	27.2 (4.8)	25.9 (5.9)	28.6 (4.4)
Smoking pack-yrs ^{ns}	41.0 (28.7)	33.6 (18.8)	38.5 (27.6)	50.8 (38.8)
Duration COPD yrs*	4.8 (4.3)	7.9 (7.6)	9.7 (10.2)	15.0 (12.3) ^{††}
Duration management yrs [†]	3.1 (3.2)	6.3 (5.8)	6.4 (8.3)	15.5 (12.3) ^{§§}
Exacerbation [†]	0.2 (0.4)	0.4 (0.7) [¶]	1.5 (2.0) ^{**}	1.3 (1.4)
Hospitalization days [§]	1.7 (3.1)	4.7 (9.3)	12.0 (12.9) ^{††}	20.8 (22.3) ^{§§}
MRC dyspnea scale [§]				
1	11 (100)	0 (0)	0 (0)	0 (0)
2	12 (25.5)	26 (55.3)	9 (19.2)	0 (0)
3	0 (0)	5 (41.7)	6 (50.0)	1 (8.3)
4	0 (0)	0 (0)	10 (90.9)	1 (9.1)
5	1 (11.1)	2 (22.2)	2 (22.2)	4 (44.4)

CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; MRC, Medical Research Council; ANOVA, analysis variance; BMI, body mass index; SD, standard deviation; ns, not significant.

CAT I: mild; CAT II: moderate; CAT III: severe; CAT IV: very severe. All data represent mean (SD) except MRC dyspnea scale that show frequency (row percentage). ANOVA results (column 1).

* $p = 0.03$.

[†] $p = 0.003$.

^{††} $p = 0.001$.

[§] $p < 0.001$.

Post-hoc Bonferroni test: vs. column 2; ^{||} $p < 0.001$, vs. column 3; [¶] $p = 0.003$, vs. column 4; ^{**} $p = 0.007$, ^{††} $p = 0.005$, vs. column 5; ^{§§} $p = 0.001$.

etry test according to GOLD guidelines, CAT score measures clinical, symptomatic state and quality of life. This may be the reason for the close relationship between characteristics of the disease and CAT score.

Dyspnea is a major symptom in patients with COPD. Several studies have investigated the relationship between dyspnea severity and spirometric measurements of FEV1 or FVC to determine the relationship between dyspnea scales and pulmonary function. Some authors found that pulmonary function was significantly correlated with dyspnea scales.¹⁶⁻¹⁸ In contrast, other authors found that it was not correlated with dyspnea scales.^{19,20} Ozalevli and Ucan¹³ observed that dys-

pnea score obtained from MRC was correlated with spirometric measurement (FEV1). The MRC scale is the most commonly used scale because of its simplicity, easy of administration and established validation as a useful marker in COPD.²¹ Additionally, MRC scale was shown to predict the likelihood of survival in patients with COPD.²²

The relationship between dyspnea and quality of life in COPD has previously been indicated in a few studies.^{23,24} Perceived dyspnea was shown to have a greater impact on health-related quality of life than spirometric or functional measurements in these patients.²⁵ In an international study, the most frequently reported symptom was dyspnea (78%)

Table 4. Difference in CAT Scores and between Classes of Other COPD Impairment Measures

	CAT score	Difference between classes*	<i>p</i> value
GOLD stage			
I	9.5 (6.2)		
II	18.2 (8.1)	-8.7 (I vs. II)	0.001
III	20.9 (8.2)	-2.7 (II vs. III)	Ns
IV	22.5 (0.79)	-1.6 (III vs. IV)	Ns
MRC dyspnea scale			
1	7.7 (2.2)		
2	13.9 (6.1)	-6.2 (1 vs. 2)	0.021
3	21.7 (5.9)	-7.7 (2 vs. 3)	0.001
4	27.5 (2.2)	-5.8 (3 vs. 4)	Ns
5	27.3 (9.7)	0.2 (4 vs. 5)	Ns

Ns, not significant; GOLD, Global Initiative Chronic Obstructive Lung Disease; MRC, Medical Research Council; COPD, chronic obstructive pulmonary disease; CAT, COPD assessment test; SD, standard deviation.

All data presented as mean (SD).

*Differences among below scores.

and the most frequent complaint reported by patients with COPD was daily activity limitation.²⁶ Hajiro, et al.²⁴ showed that dyspnea is one of the main determinations of disease-specific health related quality of life, and has moderate-to-strong correlations with impairments in the health related quality of life in patients with COPD. On the other hand, quality of life measurements did not correlate well with the severity of airflow limitation.²⁷ Furthermore, factors such as dyspnea, depression, anxiety and exercise tolerance were found to be more correlated with health status than the widely used spirometric values.²⁸

The CAT was developed as a short validated COPD-specific questionnaire for assessing the impact of COPD on health status. It provides a reliable measure of overall COPD severity from the patient's perspective, independent of language.⁹ The CAT has been translated to 58 different languages, available on their web site.¹⁴ It is not a diagnostic tool; its role is to supplement information obtained from lung function measurement and assessment of exacerbation risk.^{8,9} The relative frequency of severe exacerbations within these patients was shown to be higher in patients with higher CAT scores. We observed that the increase of exacerbation frequency was parallel to the increase of CAT scores. Additionally, CAT scores were the same in males and females, and were not influenced by age.⁹ In our study, it was observed that the CAT scores were not influenced by sex, age or body mass index.

It has been suggested that CAT is likely to offer relevant alternatives to complex tools such as the SGRQ. Jones, et al.⁸ reported an extremely strong correlation between CAT and SGRQ. They observed that small differences in health

status impairment between patients in GOLD stage I and II can be seen with the CAT. In present study, we discerned that no difference in health status impairment among GOLD II, III and IV stage patients can be seen with the CAT. In contrast, there was significant difference between patients of GOLD stages I and II according to CAT. Also, Jones, et al. reported a significant difference in all grades of MRC dyspnea scales according to CAT scores. We, however, observed a difference only in MRC 1, 2, and 3 grades.

In our study, CAT scores was classified as mild, moderate, severe and very severe. There was a significant relationship among these classifications of CAT and COPD patient features and dyspnea scale. We suggest that CAT classification is compatible with COPD severity levels.

As the CAT score was shown to be correlated with clinical characteristics and quality of life, it can also be expected to be associated with the prognosis of the disease. However, as this study is a cross-sectional study and has limitations to showing the prognostic value of CAT score, a follow-up study of patients may demonstrate relationships between CAT and prognosis.

We should mention some of the limitations of the present study. First, since we recruited only stable patients from an outpatient clinic, the study sample may not to be representative of patients with exacerbation. Additionally, the study sample was small, and the study was not a multicentre or an international study. Second, CAT and dyspnea scale are self-administered questionnaires, but we used an observer to complete the questionnaires.

In conclusion, dyspnea greatly impacts the health related quality of life of patients with COPD. We concluded that

the CAT, a novel COPD-specific measurement, was associated with dyspnea scale, duration of COPD and exacerbation, but not co-morbidities. The CAT may be a simple short questionnaire for assessing disease severity levels in patients with COPD. At the moment, more studies from other countries around the world are needed to ascertain the value of the CAT.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline: Global Strategy for the Diagnosis, management and Prevention of Chronic Obstructive Pulmonary Disease [Internet]. 2011 Dec [accessed on 2012 Feb 22]. Available at: <http://www.goldcopd.com>.
2. Oga T, Nishimura K, Tsukino M, Hajiro T, Mishima M. Dyspnoea with activities of daily living versus peak dyspnoea during exercise in male patients with COPD. *Respir Med* 2006;100:965-71.
3. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999;54:581-6.
4. Curtis JR, Deyo RA, Hudson LD. Pulmonary rehabilitation in chronic respiratory insufficiency. 7. Health-related quality of life among patients with chronic obstructive pulmonary disease. *Thorax* 1994;49:162-70.
5. Curtis JR, Martin DP, Martin TR. Patient-assessed health outcomes in chronic lung disease: what are they, how do they help us, and where do we go from here? *Am J Respir Crit Care Med* 1997;156(4 Pt 1):1032-9.
6. Meguro M, Barley EA, Spencer S, Jones PW. Development and Validation of an Improved, COPD-Specific Version of the St. George Respiratory Questionnaire. *Chest* 2007;132:456-63.
7. Wijkstra PJ, TenVergert EM, Van Altena R, Otten V, Postma DS, Kraan J, et al. Reliability and validity of the chronic respiratory questionnaire (CRQ). *Thorax* 1994;49:465-7.
8. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. *Eur Respir J* 2009;34:648-54.
9. Jones PW, Brusselle G, Dal Negro RW, Ferrer M, Kardos P, Levy ML, et al. Properties of the COPD assessment test in a cross-sectional European study. *Eur Respir J* 2011;38:29-35.
10. Dodd JW, Hogg L, Nolan J, Jefford H, Grant A, Lord VM, et al. The COPD assessment test (CAT): response to pulmonary rehabilitation. A multicentre, prospective study. *Thorax* 2011;66:425-9.
11. Al-Moamary MS, Al-Hajjaj MS, Tamim HM, Al-Ghobain MO, Al-Qahtani HA, Al-Kassimi FA. The reliability of an Arabic translation of the chronic obstructive pulmonary disease assessment test. *Saudi Med J* 2011;32:1028-33.
12. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. *Eur Respir J* 2005;26:319-38.
13. Ozalevli S, Ucan ES. The comparison of different dyspnoea scales in patients with COPD. *J Eval Clin Pract* 2006;12:532-8.
14. CAT Turkish version [Internet]. Nov 23, 2011 [accessed on 2012 Feb 22]. Available at: http://www.catestonline.org/english/index_Turkey.htm.
15. CAT Development Steering Group. COPD assessment test-health-care professional user guide [Internet]. Sep 1, 2009 [accessed on 2012 Feb 22]. Available at: <http://www.catestonline.org/images/UserGuides/CATHCPUser%20guideEn.pdf>.
16. Hajiro T, Nishimura K, Tsukino M, Ikeda A, Koyama H, Izumi T. Analysis of clinical methods used to evaluate dyspnea in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;158:1185-9.
17. Sahebajami H, Sathianpitayakul E. Influence of body weight on the severity of dyspnea in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;161(3 Pt 1):886-90.
18. Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea. Contents, interobserver agreement, and physiologic correlates of two new clinical indexes. *Chest* 1984;85:751-8.
19. Taube C, Lehnigk B, Paasch K, Kirsten DK, Jörres RA, Magnusson H. Factor analysis of changes in dyspnea and lung function parameters after bronchodilation in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;162:216-20.
20. Mahler DA, Harver A. A factor analysis of dyspnea ratings, respiratory muscle strength, and lung function in patients with chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1992;145(2 Pt 1):467-70.
21. Chhabra SK, Gupta AK, Khuma MZ. Evaluation of three scales of dyspnea in chronic obstructive pulmonary disease. *Ann Thorac Med* 2009;4:128-32.
22. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. *Chest* 2002;121:1434-40.
23. Hu J, Meek P. Health-related quality of life in individuals with chronic obstructive pulmonary disease. *Heart Lung* 2005;34:415-22.
24. Hajiro T, Nishimura K, Tsukino M, Ikeda A, Oga T, Izumi T. A comparison of the level of dyspnea vs disease severity in indicating the health-related quality of life of patients with COPD. *Chest* 1999;116:1632-7.
25. von Leupoldt A, Hahn E, Taube K, Schubert-Heukeshoven S, Magnussen H, Dahme B. Effects of 3-week outpatient pulmonary rehabilitation on exercise capacity, dyspnea, and quality of life in COPD. *Lung* 2008;186:387-91.
26. Miravittles M, Anzueto A, Legnani D, Forstmeier L, Fargel M. Patient's perception of exacerbations of COPD--the PERCEIVE study. *Respir Med* 2007;101:453-60.
27. Mahler DA, Mackowiak JI. Evaluation of the short-form 36-item questionnaire to measure health-related quality of life in patients with COPD. *Chest* 1995;107:1585-9.
28. Tsiligianni I, Kocks J, Tzanakis N, Siafakas N, van der Molen T. Factors that influence disease-specific quality of life or health status in patients with COPD: a review and meta-analysis of Pearson correlations. *Prim Care Respir J* 2011;20:257-68.