Factors Affecting Quality-of-Life in Patients with Chronic Obstructive Pulmonary Disease

Pooja Akhtar[1], Sujata Yardi[2], B.O. Tayade[3] and Murtaza Akhtar[4]

College of Physiotherapy[1]; School of Physiotherapy[2], D.Y. Patil University, Navi Mumbai; and Departments of Pulmonary Medicine[3] and Surgery[4], NKPSIMS and VSPM's Lata Mangeshkar Hospital, Nagpur, (Maharashtra), India

Abstract

Objectives. Multiple factors affect quality-of-life (QoL) in patients with chronic obstructive pulmonary disease (COPD). The study was done to explore possible factors which influence disease specific QoL in patients with COPD.

Methods. A cross-sectional study was carried out at our tertiary care hospital. Patients above 40 years of age, Global Initiative for Chronic Obstructive Lung Diseases (GOLD) category I-IV, irrespective of tobacco smoking status with disease duration of five years or more were included. Patients with other chronic respiratory diseases, co-morbid conditions and functional limitations, psychiatric or cognitive problems were excluded. Demographic factors, lifestyle and disease severity parameters; physical, physiological and mental factors were recorded. St. George's Respiratory Questionnaire-C (SGRQ-C) scores were used to assess the QoL. Correlation coefficient, bivariate analysis and multiple linear regression analysis were done.

Results. A total of 78 patients with a mean age of 61.6 years and male preponderance were enrolled. The mean six-minute walk distance (6MWD) test was 235.5 meters. Seventy-three patients were suffering from depression, 67 patients had anxiety and 71 had sleep disturbances. The mean SGRQ-C score was 45.4±14.7. On bivariate analysis, 6MWD, modified Medical Research Council (mMRC) dyspnoea score, depression, anxiety, and sleep disturbances were significantly correlated with the QoL scores (P<0.01). Linear regression analysis showed that 6MWD and sleep disturbance significantly correlated with QoL scores.

Conclusion. Results of the present study showed that functional capacity as measured by 6MWD and sleep disturbances were the two strongly correlated factors associated with QoL in patients with COPD.
[Indian J Chest Dis Allied Sci 2020;62:133-138]

Key words: COPD, QoL, Health status, St George's Respiratory Questionnaire-C, 6-minute walk distance

Introduction

Chronic obstructive pulmonary disease (COPD) is a commonly prevalent disease with considerable burden of patients in the society. According to a crude estimate there are 30 million COPD patients in India.[1] It is highly incapacitating health problem that affects physical functioning, leisure and professional activities, emotional and sexual relationship.[2] Dyspnoea and fatigue causes restriction on patients exercise tolerance leading to reduction in quality-of-life (QoL). The interventions in COPD are primarily aimed at improving patient's QoL.[3] The assessment of QoL is usually done using a battery of questionnaires, both generic and disease specific.

There are multiple factors which are associated with QoL in patients with COPD.[4,5] These are demographic factors, i.e., age, gender, body mass index (BMI); life style parameters, i.e., smoking status; disease severity indices, i.e. duration of disease, Global Initiative for Chronic Obstructive Lung Diseases (GOLD) staging, body-mass index, airflow obstruction, dyspnoea and exercise (BODE) index and modified Medical Research Council (mMRC) scale and physical factors, such as exercise capacity as evaluated by six-minute walk distance (6MWD) and psychological factors, i.e., depression, anxiety and sleep disturbances evaluated using Patient Health Questionnaire (PHQ-9), Generalised Anxiety Disorder (GAD-7) and Pittsburg Sleep Quality Index (PSQI), respectively.

During literature search, majority of the studies evaluated association of individual factor and literature was sparse where multiple factors were evaluated in a single homogeneous population. The present study was planned to assess the association of above-mentioned factors with QoL scores in patients with COPD.

Material and Methods

A cross-sectional study was carried out at a tertiary care academic hospital. Ethical clearance was obtained from Institutional Ethics Committee. The study aimed to evaluate the association of demographic, life-style, disease severity, physical, physiological and mental factors with QoL as assessed by the disease specific SGRQ-C questionnaire in patients with COPD. A total of 78 patients, above the age of 40 years, spirometry-confirmed COPD of GOLD category I-IV, with forced expiratory volume in the first second (FEV_1) (% predicted) <80, smokers, ex-smokers or non-smokers with disease duration of at least five years or more were included. Patients with acute or a recent (within 3 weeks) history of exacerbations, with co-existence of other chronic respiratory diseases (bronchial asthma, tuberculosis) with impaired pulmonary function, diagnosed cancer, uncontrolled hypertension, diabetes mellitus, cardiovascular, neurological and/or osteoarticular diseases with functional limitations, precluding safe testing, receiving home oxygen therapy, patients with known psychiatric illness, cognitive limitations and lack of motivation and patients not willing to participate, were excluded.

The sample size of 78 patients was calculated based on weighted Pearson's correlation coefficient of–0.53 from mMRC dyspnoea obtained in a pilot study[6] with α = 0.05 and β = 0.1. The factors studied were demographic and anthropometric factors, such as, age, gender, BMI, life-style parameters like smoking status, disease severity indices and symptoms [duration of disease in years, GOLD staging using GOLD guidelines[6], dyspnoea as measured by mMRC scale[7] and degree of airway obstruction, level of functional dyspnoea and exercise capacity index (BODE index)[8], exercise physical performance as measured by 6MWD test[9], mental factors that were studied included anxiety using GAD-7[10] scale, depression using PHQ-9[10] scale and sleep disturbances using PSQI[11] scale. The QoL scores were recorded using COPD specific SGRQ-C[12]. All the questionnaires were administered in validated translated local dialect, *i.e.*, either Hindi or Marathi.

Statiscal Analysis

The data were analysed using STATA (version 10.1, 2011). The descriptive data for the continuous variables are presented as mean ± standard deviation (SD) and for the categorical variables as percentages. Pearson's correlation coefficient (r) was used to assess the relationship between continuous variables. Bivariate linear regression analysis was performed to determine the relationship between each domain of SGRQ-C with study factors. The analysis of total SGRQ-C scores along with its sub-domains was done across various stages of GOLD, mMRC grades and BODE index using one-way analysis of variance (ANOVA) with appropriate post-hoc test. Statistically significant variables on bivariate analysis were included in multiple linear regression models to evaluate the relationship with QoL scores. This would determine the strongest associating factors with QoL score.

Results

Seventy-eight patients fulfilling the inclusion criteria were enrolled. The mean age of the patients was 61.6 ± 8.0 years. Majority of the patients (62.8%) were aged over 60 years. Of 78 patients, 70 (89.7%) were males. Forty-two patients had normal BMI (18.5-24.9 kg/m^2), 27 (34.6%) were underweight (BMI <18.5 kg/m^2); and nine patients were overweight (BMI ≥25 kg/m^2). The mean BMI of the study population was 20.4±4.4. Fifty-nine patients (79%) were smokers, *i.e.*, presently smoking with a mean duration of smoking as 23.0±14.3 years. Five (6.4%) were ex-smokers, *i.e.*, who smoked for an average duration of 35 years but left smoking, nine (11.5%) patients were not smoking cigarettes/*bidis* but were exposed to other forms of smoke, such as, biogas, *dhoop* and essence sticks and rest five patients were non-smokers. The mean duration of the disease was 7.8±4.8 years.

The stratification of patients according to GOLD staging showed that the maximum number of patients (71.8%) in the present study was in GOLD stage II and III. According to mMRC grading, maximum number of patients, *i.e.*, 57 (73.1%) were in grade 2 and grade 3. Almost three-fourths of the patients in the present study were in BODE index points 0-6 with a four-year survival chance ranging from 57% to 80%. The mean 6MWD recorded was 235.5±81.0 meters. On assessing the depression using PHQ-9 questionnaire, a majority of 73 (93.6%) patients were suffering from mild to severe depression. Of them, 18 patients (23%) had moderately severe to severe depression, 33 patients (42.3%) had moderate depression, and 22 patients (28.2%) had mild depression. The results suggest the presence of depression in majority of the COPD patients. A majority of 67 patients (85.9%) had varying degrees of anxiety and 11 patients (14.1%) had scores <5 were labelled as no anxiety cases. The mean PSQI score for the sleep disorders was 10.1±3.4. A majority of 71 patients (91%) had score >5, suggesting some sleep disturbances. Quality-of-life was the main outcome factor and the mean total SGRQ-C score was 45.4±14.7. Under sub-domain scores, the mean symptom score was 59.2±18.3, the mean activity score was 48.1±13.7 and the mean impact score was 38.5±14.2.

The 6MWD (P<0.01), mMRC dyspnoea score (P<0.01), PHQ-9 (P=0.02), GAD-7 (P=0.027) and PSQI (P<0.01) were found to be significantly correlated with the total and sub domain QoL scores (Table 1).

These five statistically significant correlating factors were subjected to ANOVA and of them, mMRC dyspnoea score was not fitting into the regression model while the other four were found to be statistically significant (Table 2). On multiple-linear regression, only 6MWD and PSQI scores were correlated significantly with SGRQ-C QoL scores, suggesting a strong correlation between physical activity and sleep disorder with QoL in patients with COPD (Table 3).

Discussion

The QoL measurements is a way of quantifying in a standardised and objective manner the impact of COPD on patient's daily life.[13] Present research communities regard changes in the symptoms, functional status and health status more important than change in lung function.[5] The QoL in patients with COPD is influenced by various factors which were evaluated in the present study.

Age was not a statistically significant factor correlating with total SGRQ-C scores and its sub-domains. Literature search showed no significant correlation between age and health status[14,15] while others reported it as a negatively predicting factor for health status.[5,13,16] BMI also had no statistical significant correlation with total and sub-domain QoL scores of SGRQ-C. Literature shows some correlation between health status and underweight[5]/overweight patients.[17] The results of present study are quite consistent

Table 1. Correlation of factors with sub-domains and total SGRQ-C

Parameter	Observations	Symptom SGRQ-C Score	Activity SGRQ-C Score	Impact SGRQ-C Score	Total SGRQ-C Score
6MWD	r value	−0.3434	−0.378	−0.414	−0.4196
	P value	0.0021	0.0006	0.0002	0.0001
mMRC	r value	0.2955	0.3578	0.3751	0.3916
	P value	0.0086	0.0013	0.0007	0.0004
PHQ-9	r value	0.3644	0.130	0.3435	0.2617
	P value	0.0010	0.2559(NS)	0.0021	0.0207
GAD-7	r value	0.3282	0.1299	0.3158	0.2503
	P value	0.0034	0.2570(NS)	0.0049	0.0271
PSQI	r value	0.3714	0.2335	0.4069	0.3464
	P value	0.0008	0.396(NS)	0.0002	0.0019
Age	r value	0.0125	0.0634	0.0021	0.0286
	P value	0.9137	0.5815(NS)	0.9855	0.0839
Duration of smoking (Pack-years)	r value	−0.0133	0.0451	0.0449	−0.0120
	P value	0.9083	0.6953	0.6964	0.9171
	r value	0.0136	−0.1306	−0.1920	−0.1566
	P value	0.9062	0.2543	0.0922	0.1710
Duration of disease	r value	0.0222	0.1060	0.1459	0.1372
	P value	0.8467	0.3558	0.2025	0.2311
FEV$_1$% predicted	r value	0.1187	0.1387	0.1458	0.1311
	P value	0.3007	0.2260	0.2027	0.2524
BMI	r value	0.1811	0.2194	0.1816	0.2026
	P value	0.1126	0.0536	0.1116	0.0752
BODE index	r value	0.0598	0.1402	0.0974	0.1299
	P value	0.6030	0.2209	0.3964	0.2569

Definition of abbreviations: SGRQ-C=St George's Respiratory Questionnaire-C, 6MWD=Six minute walk distance, mMRC=modified Medical Research Council, PHQ-9=Patient Health Questionnaire-9, GAD-7=Generalised Anxiety Disorder-7, PSQI=Pittsburg Sleep Quality Index, FEV$_1$=Forced expiratory volume in the first second, BMI=Body mass index, BODE=Body-mass index, airflow obstruction, dyspnoea and exercise

Table 2. Showing ANOVA model of total SGRQ-C scores with PHQ-9, GAD-7, PSQI and 6MWD

Source	Partial SS	dF	MS	F	Prob>F
Model	46951.7534	76	617.786229	950.73	0.0258
PHQ-9	12362.5828	22	561.935582	864.78	0.02
GAD-7	3964.7674	16	247.172963	380.38	0.04
PSQI	2462.35238	12	205.196032	315.78	0.04
6MWD	12962.3856	26	498.553292	767.24	0.02

Number of observations=78, R-squared= 1.0000, Root MSE=0.806101, Adjusted R-squared=0.9989

Definition of abbreviations: ANOVA=One-way analysis of variance, SGRQ-C=St George's Respiratory Questionnaire-C, PHQ-9=Patient Health Questionnaire-9, GAD-7=Generalised Anxiety Disorder-7, PSQI=Pittsburg Sleep Quality Index, 6MWD=Six minute walk distance

Table 3. Showing regression analysis of total SGRQ-C with PHQ-9, GAD-7, PSQI and 6MWD

Total SGRQ-C	Coefficient	SE	t value	P>|t|	95% Confidence Intervals	
PHQ-9	0.2497429	0.6172188	0.40	0.687	−0.9803724	1.479858
GAD-7	0.4002961	0.7366681	0.54	0.589	−1.067881	1.868474
PSQI	1.73145	0.9236043	1.87	0.045	−0.1092903	3.572191
6MWD	−0.1164246	0.0310449	−3.75	0.000	−0.178297	−0.0545523
Constant	48.66451	11.83424	4.11	0.000	25.07891	72.25012

Number of observations=78, F (4, 73)=6.78, Prob>F=0.0001, R-squared=0.2735, Adjusted R-squared=0.2337, Root MSE=21.617

Definition of abbreviations: SE=Standard error, SGRQ-C=St George's Respiratory Questionnaire-C, PHQ-9=Patient Health Questionnaire-9, GAD-7=Generalised Anxiety Disorder-7, PSQI=Pittsburg Sleep Quality Index, 6MWD=Six minute walk distance

with that of other studies[14,18], wherein they found no correlation between BMI and QoL.

Smoking status, duration of years of smoking and pack-years showed no correlation with QoL scores. Our results are in line with other studies[17,19] and meta-analysis[20]. Disease severity parameters were evaluated by GOLD staging, mMRC dyspnoea grades and BODE index. Only mMRC dyspnoea grades showed statistical significant correlation with total SGRQ-C. Majority of the published studies suggest that severity of the disease as measured by GOLD staging is related to QoL, which was not found in the present study. Our results are consistent with another study.[21] Although spirometry is traditionally seen as the most important determinant of the diagnosis and severity of COPD, meta-analysis[20] showed that weak correlation exists between health status and all spirometric values.

BODE index is reported to be good at predicting the worsening of health-related QoL in patients with COPD as measured by the SGRQ-C.[22] However, there was no correlation between BODE index and QoL in the present study. Two of the four components of BODE index, such as BMI and $FEV_1\%$ predicted independently did not show any statistically significant correlation with SGRQ-C scores. This could be the reason that the

results got diluted when the index was considered for correlation as a whole with QoL scores.

Dyspnoea is a key symptom in COPD that was measured using mMRC dyspnoea scale and it showed statistically significant moderate correlation with QoL scores. Dyspnoea leads to limited daily activities and impaired QoL in patients with COPD. The mMRC scores are found to be responsible for the SGRQ-C score variance in different studies which showed that dyspnoea perception could explain 25% to 54% of the QoL score variance in COPD patients[23] with a strong relationship between SGRQ-C assessed QoL and dyspnoea perception. Our results are quite consistent with other studies reported in the literature those found a strong associations between dyspnoea and health status.[5, 16, 17, 24]

The total duration of the disease showed no correlation with QoL scores. Various authors have proposed that the severity of the disease and limitation of the exercise capacity and impaired QoL are not essentially due to severe airway obstruction or pulmonary hyperinflation *per se*. Impairment of the lung function due to prolonged disease illness is a weak predictor of dyspnoea and exercise capacity, and hence, could have a less impact on QoL in severe COPD patients.[25]

The literature suggests that there exists a correlation between 6MWD and QoL scores and that exercise intolerance could negatively influence the QoL in patients with COPD.[26] Determination of walking distance in a standardised manner appears to be a simple method to assess limitation of exercise capacity in patients with COPD. Walking test seems to be realistic for describing patient's limitations in day-to-day activity.[27] The 6MWD, a measure of functional capacity showed a moderately significant correlation with QoL scores in the present study, which is quite consistent with many studies reported in the literature.[15, 28, 29]

Mental conditions, such as depression and anxiety, were observed in majority of our patients. The specific impact of these disorders on QoL remains poorly understood. The current COPD management focuses on symptom minimisation, maintenance of functional capacity and improvement in health related QoL. Little attention has been given to specific role of mental health conditions on QoL of COPD patients.[30] On evaluating the psychological factors, depression and anxiety showed weak to modest correlation with SGRQ-C score. Our results are quite consistent with the studies reported in the literature with depression and anxiety among the highest correlations with QoL in patients with COPD.[15,31,32] Anxiety significantly influences the health status of the patients with COPD and it is strongly dependent on patient's dyspnoea.[31, 32]

Sleep impairment not only worsens the QoL but also aggravates symptoms of underlying medical disorder.[32] Sleep scores in the present study showed significantly moderate correlation with QoL scores. Research work has been done on anxiety and depression but limited efforts were made to study the role of sleep on QoL. It could be hypothesised that sleep could be affected by persistent dyspnoea, nocturnal cough and sputum retention which could ultimately affect the QoL of these patients.

Conclusions

The present study was a cross-sectional and only correlation could be established and not aetiological evidence could be provided. The study is single centre survey, hence results could not be generalised to all Indian population, for which there is a need to carry out multi-centric surveys based on similar lines to gather strong Indian data which could vary due to vast geographical spread and cultural differences.

Quality-of-life in patients with COPD is determined by five significant factors, such as, namely dyspnoea, exercise tolerance, anxiety, depression and sleep disturbance from which the strongest are exercise tolerance and sleep factors. There is a need to carry out more QoL based research in Indian population.

References

1. Koul PA. Chronic obstructive pulmonary disease: Indian guidelines and the road ahead. *Lung India* 2013;30:175–7.

2. de Godoy DV, de Godoy RF. A randomized controlled trial of the effect of psychotherapy on anxiety and depression in chronic obstructive pulmonary disease. *Arch Phys Med Rehab* 2003;84:1154–7.

3. Jones PW. Health status: what does it mean for payers and patients? *Proceedings of the American Thoracic Society* 2006;3:222–6.

4. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, 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. Hesselink AE, Van Der Windt DA, Penninx BW, Wijnhoven HA, Twisk JW, Bouter LM, *et al.* What predicts change in pulmonary function and quality of life in asthma or COPD? *J Asthma* 2006;43:513–9.

6. Global Initiative for Chronic Obstructive Lung Diseases. Pocket guide to COPD Diagnosis, Management and Prevention. A guide for Health Care Professionals 2018 Report. *Available at URL:* www.golcopd.org. Accessed on

7. Mahler DA, Wells CK. Evaluation of clinical methods for rating dyspnea. *Chest* 1988;93:580–6.

8. Cote CG, Celli BR. Pulmonary rehabilitation and the BODE index in COPD. *Eur Respir J* 2005;26:630–6.

9. Enright PL. The six-minute walk test. *Respir Care* 2003;48:783–5.

10. PHQ and GAD-7 *Instructions. International Manual Instructions for Patient Health Questionnaire-9 and Generalized Anxiety Disorder-7 Measures. Available at URL:* https://www.ons.org/sites/default/files/PHQand GAD7_ InstructionManual.pdf. Accessed on

11. Dignani L, Toccaceli A, Lucertini C, Petrucci C, Lancia L. Sleep and quality of life in people with COPD: a descriptive-correlational study. *Clin Nursing Res* 2016;25:432–47.

12. Jones P W, Forde Y. *St George's Respiratory Questionnaire for COPD Patients (SGRQ-C) Manual*. London: (UK) University of London. Version No.1.2. April 2012.

13. Ferrer M, Villasante C, Alonso J, Sobradillo V, Gabriel R, Vilagut G, *et al.* Interpretation of quality of life scores from the St George's Respiratory Questionnaire. *Eur Respir J* 2002;19:405–13.

14. de Miguel Díez J, Izquierdo Alonso JL, Rodríguez Gonzaˈlez-Moro JM, de Lucas Ramos P, Bellón Cano JM, Molina París J. Quality of life with chronic obstructive pulmonary disease: the influence of level of patient care. *Arch Bronconeumol* 2004;40:431–7.

15. Engström CP, Persson LO, Larsson S, Sullivan M. Health-related quality of life in COPD: why both disease-specific and generic measures should be used. *Eur Respir J* 2001;18:69–76.

16. Maille AR, Koning CJ, Zwinderman AH, Willems LN, Dijkman JH, Kaptein AA. The development of the 'Quality-of-life for Respiratory Illness Questionnaire (QOL-RIQ)': a disease-specific quality-of-life questionnaire for patients with mild to moderate chronic non-specific lung disease. *Respir Med* 1997;91:297–309.

17. Shoup R, Dalsky G, Warner S, Davies M, Connors M, Khan M, *et al.* Body composition and health-related quality of life in patients with obstructive airways disease. *Eur Respir J* 1997;10:1576–80.

18. Tsukino M, Nishimura K, Ikeda A, Koyama H, Mishima M, Izumi T. Physiological factors that determine the health-related quality of life in patients with COPD. *Chest* 1996;110:896–903.

19. Ståhl E, Lindberg A, Jansson SA, Rönmark E, Svensson K, Andersson F, *et al.* Health-related quality of life is related to COPD disease severity. *Health Qual Life Outcomes* 2005;3:56.

20. Ioanna Tsiligiannia, Janwillem Kocksa, Nikolaos Tzanakisb, Nikolaos Siafakasb, Thys van der Molena. Factors that influence disease-specific quality of life or health status in patients with COPD: a systematic review and meta-analysis of Pearson correlations. *Prim Care Respir J* 2011;20:257–68.

21. Yeo J, Karimova G, Bansal S. Co-morbidity in older patients with COPD: its impact on health service utilisation and quality of life, a community study. *Age and Ageing* 2006;35:33–7.

22. Medinas-Amorós M, Alorda C, Renom F, Rubí M, Centeno J, Ferrer V *et al.* Quality of life in patients with chronic obstructive pulmonary disease: the predictive validity of the BODE index. *Chronic Respir Dis* 2008;5:7–11.

23. Katsura H, Yamada K, Kida K. Both generic and disease specific health-related quality of life are deteriorated in patients with underweight COPD. *Respir Med* 2005;99:624–30.

24. Hale K, Sibel E, Alev A, Mehdi Z, Sanem N, Berrin D. Effect of dyspnea and clinical variables on the quality of life and functional capacity in patients with chronic obstructive pulmonary disease and congestive heart failure. *Chinese Med J* 2008;121:592–6.

25. McGavin CR, Artvinli M, Naoe H, McHardy GJ. Dyspnoea, disability, and distance walked: comparison of estimates of exercise performance in respiratory disease. *Br Med J* 1978;2(6132):241–3.

26. González E, Herrejón A, Inchaurraga I, Blanquer R. Determinants of health-related quality of life in patients with pulmonary emphysema. *Respir Med* 2005;99:638–44.

27. Butland RJ, Pang JA, Gross ER, Woodcock AA, Geddes DM. Two-, six-, and 12-minute walking tests in respiratory disease. *Br Med J* 1982;284(6329):1607.

28. Ketelaars CA, Schlösser MA, Mostert R, Abu-Saad HH, Halfens RJ, Wouters EF. Determinants of health-related quality of life in patients with chronic obstructive pulmonary disease. *Thorax* 1996;51:39–43.

29. Jones PW, Baveystock CM, Littlejohns P. Relationships between general health measured with the sickness impact profile and respiratory symptoms, physiological measures, and mood in patients with chronic airflow limitation. *Am Rev Respir Dis* 1989;140:1538–43.

30. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med* 2001;163:1256–76.

31. Francés ME, Tordera MP, Fuster AB, Moragón EM, Torrero LC. Impact of baseline and induced dyspnea on the quality of life of patients with COPD. *Archivos de Bronconeumología* ((English Edition)) 2008;44:127–34.

32. Hynninen MJ, Pallesen S, Nordhus IH. Factors affecting health status in COPD patients with co-morbid anxiety or depression. *Int J Chronic Obstructive Pulmon Dis* 2007;2:323.