RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Depression in Japanese Patients with Chronic Obstructive Pulmonary Disease. A Cross-Sectional Study

[1]Nobuyuki Horita MD; Yokohama, Japan; nobuyuki_horita@yahoo.co.jp

[2]Takeshi Kaneko MD PhD; Yokohama, Japan; takeshi@med.yokohama-cu.ac.jp

[2]Masaharu Shinkai MD PhD; Yokohama, Japan; shinkai@yokohama-cu.ac.jp

[3]MakikoYomota MD; Tokyo, Japan; myomota@gmail.com

[4]Satoshi Morita MD PhD; Yokohama, Japan; smorita@urahp.yokohama-cu.ac.jp

[5]Bruce K. Rubin MD PhD; Richmond, Virginia; BRubin@MCVH-VCU.EDU

[1]Yoshiaki Ishigatsubo MD PhD; Yokohama, Japan; ishigats@med.yokohama-cu.ac.jp

[1]Department of Internal Medicine and Clinical Immunology, Yokohama City University Graduate School of Medicine;

[2]Respiratory Disease Center, Yokohama City University Medical Center;

[3]Department of Allergy and Respiratory Medicine, The Fraternity Memorial Hospital;

[4]Department of Biostatistics and Epidemiology, Yokohama City University Medical Center;

[5]Department of Pediatrics, Virginia Commonwealth University.

Correspondence to:

Takeshi Kaneko, M.D., Ph.D.

Respiratory Disease Center, Yokohama City University Medical Center

4−57, Urafune, Minami−ku, Yokohama City, 232−0024, Japan

Tel.: +80−45−261−5656; Fax: +80−45−241−2812

Email: takeshi@med.yokohama-cu.ac.jp

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

The study was performed in:

Department of Allergy and Respiratory Medicine, The Fraternity Memorial Hospital,

2-1-11, Yokoami, Sumida, Tokyo 130-8587, JAPAN; and

Department of Internal Medicine and Clinical Immunology, Yokohama City University Graduate School of Medicine; 3-9 Fukuura, Kanazawa-ku, Yokohama, 236-0004, Japan

Financial support

Financial support in any form was not offered for this study

Conflict-of-interest statement

Authors have no conflict-of-interest

Keywords:

Spirometry

Dyspnea

Exercise tolerance

Questionnaire

Review

Asian

Depression

COPD

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Abstract

Background: Some investigation revealed the association between depression and physical measurements of chronic obstructive pulmonary disease (COPD) patients in North America and Europe but limited studies in Asia were performed.

Methods: In this cross−sectional study, consecutive 84 stable outpatients with COPD (Age: 72.0 ± 9.0. Forced expiratory volume in one second (%predicted) 46 ± 15%. Fifteen females (17.9%)) in a Japanese community based hospital were recruited. "Probable depression" was defined as short form of the geriatric depression scale (SF−GDS) ≥ 6. Relationships among commonly used physical measurements, SF−GDS raw score, and probable depression were evaluated with Spearman's rank correlation test, multiple linear regression analysis, logistic regression analysis, and receiver operating characteristic curve.

Results: Thirty two (38.1%) had probable depression. Body mass index, obstruction, dyspnea, exercise capacity index; forced expiratory volume in one second (%predicted); modified medical research council dyspnea scale; six−minute walk distance; saturation of oxygen on artery by pulse oximetry had followings: (i) simple correlations (|r|:0.42-0.60 , $P < .001$ for all) for SF-GDS raw score, (ii) partial correlations (|r|:0.25-0.51 , $P < .05$ for all) for SF-GDS raw score after adjusting demographic and social factors, (iii) association for probable depression in logistic regression analysis after adjusting demographic and social factors ($P < .05$ for all), and (iv) area under the receiver operating characteristic curves for probable depression (area under the curves: 0.719−0.841, $P < .001$ for any),

Conclusions: Physical parameters were associated with depression in our Japanese COPD outpatients.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Abbreviations

AUC: the Area(s) under the curve

BODE index: Body mass index, obstruction, dyspnea, exercise capacity index

COPD: Chronic obstructive pulmonary disease

FEV1: Forced expiratory volume in 1 second

GOLD: Global initiative for obstructive lung disease

LTOT: Long–term oxygen therapy

MMRC: Modified medical research council dyspnea scale

QOL: Quality of life

ROC: Receiver operating characteristic

SF–GDS: Short form of the geriatric depression scale

SpO2: Saturation of oxygen on artery by pulse oximetry

6MWD: Six–minute walk distance

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Introduction

Chronic obstructive pulmonary disease (COPD), defined as not fully reversible airflow obstruction[1], is now the fourth leading cause of death in the world[2]. Among the many aspects of COPD, depression is a serious concern, because it is generally associated with longer hospitalization, poor survival rate, and impaired physical and social functioning[3]. Patients with depression also characteristically make fewer attempts to improve their health [4-6]. Therefore, examining symptoms of depression is an important part of comprehensive COPD treatment.

The prevalence and incidence of depression among COPD patients are high, but the depression is often underdiagnosed and undertreated in these patients[7-11]. Inadequate treatment for depression leads to insufficient care, poor quality of life (QOL) and premature death[12]. Several risk factors are well known risk factors to predict depression in COPD patients: female[7,13], current smoking[7,12,14], poor QOL[9,12-14], long−term oxygen therapy (LTOT)[15], living alone[16], and low social status[7]. Studies in North America and Europe have evaluated the association between depression and physical factors such as forced expiratory volume in 1 second (FEV1) (%predicted), six−minute walk distance (6MWD), and modified medical research council dyspnea scale (MMRC) score[3,13,14,16-30], but few studies have focused on the association between depression and COPD in Asians. Compared to Caucasians, Asians generally exhibited elevated levels of depression[31,32]. A recently published study in Japan reported that the prevalence of depression among COPD elderly inpatients (mean age of 72.7 years) was as high as 48.6%[33].

Thus, investigations of depression in Asian outpatients with COPD are warranted. If the link between depression and commonly used physical measurements becomes clear, physicians could respond by screening such patients for depression. This would increase the rate of diagnosis and adequate treatment of depression.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

This cross−sectional study to mainly evaluated following in a Japanese community based hospital: (i) the association between depression and physical measurements such as FEV1(%predicted), MMRC score, and 6MWD in Japanese COPD outpatients. (ii) the prevalence of depression in Japanese COPD outpatients

.

Methods

Procedure

All patients who visited the Fraternity Memorial Hospital from November 2010 to February 2011 for treatment of COPD were considered as possible study subjects. First, the investigators screened patients by reviewing their charts. Then investigators met all of the candidates and evaluated them for the inclusion criteria. Patients who satisfied the criteria and agreed for participation were then surveyed.

Study population

Inclusion criteria were followings: (i) COPD diagnosis as defined by the global initiative for chronic obstructive lung disease (GOLD) [1]; spirometry was newly performed at this time; (ii) stable medical condition without exacerbation or infection in the preceding two weeks; (iii) no orthopedic problem interfering with the six−minute walk test; (iv) saturation of oxygen on artery by pulse oximetry (SpO2) ≥ 0.90 on ambient air, and ability to safely complete the six−minute walk test; (v) not currently taking an antidepressant (the degree of depression may be affected by antidepressant; depressed patients not taking antidepressants were not excluded); and (vi) absence of severe disease such as active malignancy or human immunodeficiency virus that may influence the degree of depression. The 191 patients were

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

approached by investigator for recruitment. Of these 191 patients, 107 were excluded for the following reasons: 25 refused to participate, 23 missed appointments, 32 did not meet COPD diagnostic criteria (FEV1/FEV > 7 0% [n=15]; reversibility after inhaling salbutamol nebulizer > 12% [n = 15]; CT image not compatible [n = 2]), 3 had had recent exacerbations, 6 had orthopedic problems, 4 had SpO2 < 90 on ambient air, 1 was taking an antidepressant, and 3 had HIV or malignancy. Some patients had two or more reasons for exclusion. Finally, 84 COPD patients were included in the study. We obtained written informed consent from all patients. No patients were on respiratory rehabilitation, as our facility does not provide that for outpatients. This study was approved by the institutional review boards at Yokohama City University Hospital and the Fraternity Memorial Hospital.

Short form of the geriatric depression scale (SF–GDS)

Short form of the geriatric depression scale (SF–GDS), consisting of 15 yes-or-no questions, was originally designed as a depression screening tool. A total score ≥ 6 indicates probable depression [22 34]. While the SF–GDS was primarily used as a screening tool, Giordano showed that SF–GDS score correlates with the Beck depression inventory score, one of the most widely used instruments for measuring the severity of depression ($r = 0.777$, $p < 0.001$)[35]. This scale was originally developed for geriatrics but was later validated for younger adults as well[34].

Measurement of other clinical parameters

We selected the following clinical measurements: (i) physical measurements of COPD: GOLD stage[1], "body mass index, obstruction, dyspnea, exercise capacity (BODE) index"[36], its components, SpO2; (ii) known demographic and social risk factors for depression among COPD patients: age (depression is more prevalent in younger patients), sex (depression is

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

more prevalent in females), smoking history (in pack years), current smoking, low economic status, use of LTOT, living alone, and marital status (widowed or divorced) [37].

GOLD stage[1] is basically based on FEV1(%predicted) and ranges from I (mild) to IV (very severe). BODE index[36] is a comprehensive prognostic index with four components, whose total score ranges from 0 to 10. The score of 10 indicates the poorest prognosis. MMRC dyspnea scale score ranges from 0 to 4, with 4 indicating the severest dyspnea. Trained medical technicians performed spirometry (Autospiro AS−407, MINATO, Osaka, Japan). 6MWD was obtained by standardized method[38] on a 108 meter rounded track without oxygen supplementation. The subject inhaled 1.5 mg of salbutamol via nebulizer for 20 minutes and then FEV1 (%predicted) was measured. SpO2 was recorded with a portable pulse oximeter, (PULSOX−M, MINOLTA, Osaka, Japan) after a five-minutes resting period in a sitting position. Predicted spirogram values were based on a formula designed for Japanese subjects[39]. Low economic status was defined as receiving supplemental security income from the Japanese government. This supplemental income is offered to almost 1.5% of Japanese families.

Statistical analysis

Data were analyzed using unpaired Student's *t* test, Fisher's exact test, multiple linear regression analysis, logistic regression analysis, receiver operating characteristic curve, and Cochran-Armitage test. Rank correlation was evaluated with Spearman's rank correlation test, where by $|r| < 0.2$ indicated meaningless correlation, $0.2 \leq |r| < 0.4$ indicated weak correlation, $0.4 \leq |r| < 0.6$ indicated moderate correlation, $0.6 \leq |r| < 0.8$ indicated strong correlation, and $0.8 \leq |r|$ indicated very strong correlation. The sign "±" always indicates standard deviation, not standard error. P values less than 0.05 were considered statistically significant. Statistical analyses were performed with Excel Toukei (SSRI, Japan) and

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

GraphPad Prism ver. 5.

Results

Eighty four subjects met the criteria for this study; 69 were males and 15 were females. The average age was 72.0 ± 9.0 years. FEV1 (%predicted) was 45.9 ± 14.7%. Results from the SF–GDS indicated that 32 (38.1%) patients had probable depression while 52 (61.9%) did not. Demographic, social, and physical measurements among (i) all patients, (ii) patients with probable depression (SF–GDS ≥ 6) and (iii) patients without probable depression (SF–GDS < 6) were summarized in Table 1. Patients with and without probable depression had statistically significant ($P < 0.05$) difference in economic status, LTOT use, GOLD stage, BODE index, FEV1 (%predicted), MMRC score, 6MWD, and SpO2.

GOLD stage, BODE index, FEV1 (%predicted), MMRC score, 6MWD, and SpO2 each had a significant rank correlation of $|r| > 0.4$ with raw SF-GDS score. Scatter plots for SF–GDS, and six physical measurements are shown in Figure 1. These six physical measurements except for GOLD stage, which is not continuous variable, had significant associations with raw SF-GDS score even after adjusting for eight demographic and social factors such as use of LTOT (Table 2).

Probable depression significantly ($P < 0.05$) increased as BODE index, FEV1(%predicted), MMRC score, 6MWD, and SpO2 deteriorated in models adjusting for eight demographic and social factors such as use of LTOT (Table 3).

Receiver operating characteristic (ROC) curves to predict probable depression by each physical factor are shown in Figure 2. Area under the curve (AUC) was 0.719 – 0.841 for the six parameters ($P < 0.001$ for all). ROC curves were allocated near the Y-axis especially when sensitivity was < 0.3 meaning each parameter had good specificity rather than

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

sensitivity. The three factors with the highest AUC were BODE index, MMRC score, and 6MWD.

Positive predictive values for probable depression were 0.73 for MMRC = 2.5, and 0.86 for 6MWD = 250 m.

Discussion

In the current study, severity and prevalence of depression were associated with COPD severity measured by GOLD stage, BODE index, FEV1(%predicted), MMRC score, 6MWD, and SpO2.

Previous studies evaluating association between physical factors and depression are summarized in Table 4. The first was conducted by Light in 1985[17]. Until 2007, most studies denied an association between depression and physical measurements of COPD. On contrast, most studies since 2008 affirm a positive association between depression and physical measurements of COPD. Lack of concordance might be owing to the wide variation in nationality, measurement tools, study design and diagnostic criteria[40]. Homogenous severity of COPD especially makes it difficult to detect a relationship. For example, most studies found a significant relationship between dyspnea and depression; however, some studies conducted with patients who had relatively mild obstruction did not revealed an association [21 25]. Similarly, a study conducted with patients who had relatively severe disease could not show any association between depression and physical parameters [17].

Even though MMRC score and 6MWD are simple parameters of COPD, their links with depression are strong. Positive predictive values in this study were 0.73 for MMRC score = 2.5, and 0.86 for 6MWD = 250 m. If patients have worse dyspnea or limited exercise

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

capacity, they should be screened for depression.

Associations between depression and some physical parameters are indisputable, but the interpretation is difficult. The simplest explanation is that depression is caused by COPD symptoms or limited QOL. Another explanation is that depression makes physical signs and symptoms worse. The following evidence supports this hypothesis: subjective sensation of dyspnea increased with depression, even with normal lung function[41]; and 6MWD depends on both physical and psychological factors[42,43]. The other explanation is that systemic inflammation lowers both physical and mental status. There is a recent accumulation of evidence that somatic factors such as inflammation cytokines are also related to depression in COPD patients[44,45]. Further research is expected to clarify the interaction between physical factors and depression.

Some possible demographic and social risk factors did not prove to be related to depression in this study. This may be because this study was not designed to investigate such relationships. Our cohort did not include enough patients with these risk factors to research the association.

MMRC score and 6MWD had stronger associations with depression than FEV1(%predicted) in our study. The severity of COPD has traditionally been assessed by a spirometric parameter, FEV1(%predicted)[1]. However, whether the current FEV1 (%predicted) grading scale is an ideal single parameter for severity of COPD has long been discussed. The importance of dyspnea and exercise tolerance has recently been emphasized, because FEV1 (%predicted) underestimates the importance of the extra−pulmonary manifestations of COPD[36,46,47]. Our study confirmed the superiority of MMRC score and 6MWD over FEV1 (%predicted).

We also measured the prevalence of depression in our Japanese outpatient cohort (38.1%). Iguchi's recent study of Japanese COPD inpatients reported a prevalence of 49%. It

is difficult to compare prevalence in studies that vary with respect to patient background, COPD severity, depression scales, and cutoff values for depression. The prevalence of depression in Japanese patients, both our cohort and that studied by Iguchi, was greater than in patients in most other countries (Table 4). In 1996, Mishima reported that the prevalence of depression was as low as 19%; however, the cutoff value (10 point in Hospital Anxiety and Depression scale) is higher than usually used cutoff of 8 [20] Among European countries, the prevalence of depression is especially high in the UK (Table4).

Limitations: This study had some limitations. First, the cohort size is not large enough to warrant solid conclusion. Second, our study design had possible selection bias due to following reasons. (i) More than 90% of COPD patients in Japan have emphysema. In Western countries, emphysema type is less common. (ii) In recruiting process, 25 refused to participate and 23 were excluded because they missed their appointment in recruitment process. This may also have caused selection bias, because depressed patients are usually less motivated to participate in this kind of study. (iii) One (0.5%) patient was excluded because of antidepressant use. (iv) Majority of patients were male. (v) There exist several confounders such as socio-economic status.

In conclusion, COPD parameters including GOLD stage, BODE index, FEV1(%predicted9, MMRC score, 6MWD and SpO2 were generally associated with depression in our Japanese cohort. Dyspnea and exercise tolerance were especially important factors estimating depression.

Acknowledgments:

We would appreciate Mr. and Mrs. Narisada for their advice on statistics and Mrs. Yoriko Inoue for her editorial assistance.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

References

1. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med2007;176(6):532-555.

2. Mannino DM, Ford ES, Redd SC. Obstructive and restrictive lung disease and markers of inflammation: data from the Third National Health and Nutrition Examination. Am J Med2003;114(9):758-762.

3. Ng TP, Niti M, Tan WC, Cao Z, Ong KC, Eng P. Depressive symptoms and chronic obstructive pulmonary disease: effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. Arch Intern Med2007;167(1):60-67.

4. Dowson CA, Town GI, Frampton C, Mulder RT. Psychopathology and illness beliefs

influence COPD self-management. J Psychosom Res2004;56(3):333-340.

5. Norwood R, Balkissoon R. Current perspectives on management of co-morbid depression in

COPD. COPD2005;2(1):185-193.

6. Wilson I. Depression in the patient with COPD. Int J Chron Obstruct Pulmon

Dis2006;1(1):61-64.

7. Kunik ME, Roundy K, Veazey C, Souchek J, Richardson P, Wray NP, et al. Surprisingly

high prevalence of anxiety and depression in chronic breathing disorders.

Chest2005;127(4):1205-1211.

8. Kessler R, Stahl E, Vogelmeier C, Haughney J, Trudeau E, Lofdahl CG, et al. Patient understanding, detection, and experience of COPD exacerbations: an observational, interview-based study. Chest2006;130(1):133-142.

9. Cully JA, Graham DP, Stanley MA, Ferguson CJ, Sharafkhaneh A, Souchek J, et al. Quality of life in patients with chronic obstructive pulmonary disease and comorbid anxiety or depression. Psychosomatics2006;47(4):312-319.

10. Davidson JR, Meltzer-Brody SE. The underrecognition and undertreatment of depression: what is the breadth and depth of the problem? J Clin Psychiatry1999;60 Suppl 7:4-9; discussion 10-1.

11. Hirschfeld RM, Keller MB, Panico S, Arons BS, Barlow D, Davidoff F, et al. The National Depressive and Manic-Depressive Association consensus statement on the undertreatment of depression. JAMA1997;277(4):333-340.

12. Gudmundsson G, Gislason T, Janson C, Lindberg E, Suppli Ulrik C, Brondum E, et al. Depression, anxiety and health status after hospitalisation for COPD: a multicentre study in the Nordic countries. Respir Med2006;100(1):87-93.

13. Di Marco F, Verga M, Reggente M, Maria Casanova F, Santus P, Blasi F, et al. Anxiety and depression in COPD patients: The roles of gender and disease severity. Respir Med2006;100(10):1767-1774.

14. Hanania NA, Mullerova H, Locantore NW, Vestbo J, Watkins ML, Wouters EF, et al. Determinants of depression in the ECLIPSE chronic obstructive pulmonary disease cohort. Am J Respir Crit Care Med2011;183(5):604-611.

15. Lacasse Y, Rousseau L, Maltais F. Prevalence of depressive symptoms and depression in patients with severe oxygen-dependent chronic obstructive pulmonary disease. J Cardiopulm Rehabil2001;21(2):80-86.

16. van Manen JG, Bindels PJ, Dekker FW, IJzermans CJ, van der Zee JS, Schade E. Risk of depression in patients with chronic obstructive pulmonary disease and its determinants. Thorax2002;57(5):412-416.

17. Light RW, Merrill EJ, Despars JA, Gordon GH, Mutalipassi LR. Prevalence of depression and anxiety in patients with COPD. Relationship to functional capacity. Chest1985;87(1):35-38.

18. Yohannes AM, Roomi J, Waters K, Connolly MJ. Quality of life in elderly patients with COPD: measurement and predictive factors. Respir Med1998;92(10):1231-1236.

19. Wagena EJ, Arrindell WA, Wouters EF, van Schayck CP. Are patients with COPD psychologically distressed? Eur Respir J2005;26(2):242-248.

20. Funk GC, Kirchheiner K, Burghuber OC, Hartl S. BODE index versus GOLD classification for explaining anxious and depressive symptoms in patients with COPD - a cross-sectional study. Respir Res2009;10:1.

21. Ng TP, Niti M, Fones C, Yap KB, Tan WC. Co-morbid association of depression and COPD: a population-based study. Respir Med2009;103(6):895-901.

22. Omachi TA, Katz PP, Yelin EH, Gregorich SE, Iribarren C, Blanc PD, et al. Depression and health-related quality of life in chronic obstructive pulmonary disease. Am J Med2009;122(8):778.e9-778.15.

23. Mishima M, Oku Y, Muro S, Hirai T, Chin K, Ohi M, et al. Relationship between dyspnea in daily life and psycho-physiologic state in patients with chronic obstructive pulmonary disease during long-term domiciliary oxygen therapy. Intern Med1996;35(6):453-458.

24. Borak J, Chodosowska E, Matuszewski A, Zielinski J. Emotional status does not alter exercise tolerance in patients with chronic obstructive pulmonary disease. Eur Respir J1998;12(2):370-373.

25. Chavannes NH, Huibers MJ, Schermer TR, Hendriks A, van Weel C, Wouters EF, et al. Associations of depressive symptoms with gender, body mass index and dyspnea in primary care COPD patients. Fam Pract2005;22(6):604-607.

26. Quint JK, Baghai-Ravary R, Donaldson GC, Wedzicha JA. Relationship between depression and exacerbations in COPD. Eur Respir J2008;32(1):53-60.

27. Bentsen SB, Henriksen AH, Wentzel-Larsen T, Hanestad BR, Wahl AK. What determines subjective health status in patients with chronic obstructive pulmonary disease: importance of symptoms in subjective health status of COPD patients. Health Qual Life Outcomes2008;6:115.

28. Al-shair K, Dockry R, Mallia-Milanes B, Kolsum U, Singh D, Vestbo J. Depression and its relationship with poor exercise capacity, BODE index and muscle wasting in COPD. Respir Med2009;103(10):1572-1579.

29. Borge CR, Wahl AK, Moum T. Association of breathlessness with multiple symptoms in chronic obstructive pulmonary disease. J Adv Nurs2010;66(12):2688-2700.

30. Hynninen MJ, Pallesen S, Nordhus IH. Factors affecting health status in COPD patients with co-morbid anxiety or depression. Int J Chron Obstruct Pulmon Dis2007;2(3):323-328.

31. Young CB, Fang DZ, Zisook S. Depression in Asian-American and Caucasian undergraduate students. J Affect Disord2010;125(1-3):379-382.

32. Jamil H, Grzybowski M, Hakim-Larson J, Fakhouri M, Sahutoglu J, Khoury R, et al. Factors associated with self-reported depression in Arab, Chaldean, and African Americans. Ethn Dis2008;18(4):464-470.

33. Iguchi A, Senjyu H, Hayashi Y, Kanada R, Iwai S, Honda S, et al. Relationship Between Depression in Patients With Chronic Obstructive Pulmonary Disease and the Percent Predicted FEV(1), BODE Index, and Health-Related QOL. Respir Care2012.

34. Ferraro FR, Chelminski I. Preliminary normative data on the Geriatric Depression Scale-Short Form (GDS-SF) in a young adult sample. J Clin Psychol1996;52(4):443-447.

35. Giordano M, Tirelli P, Ciarambino T, Gambardella A, Ferrara N, Signoriello G, et al. Screening of depressive symptoms in young-old hemodialysis patients: relationship between Beck Depression Inventory and 15-item Geriatric Depression Scale. Nephron Clin Pract2007;106(4):c187-92.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

36. 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 Med2004;350(10):1005-1012.

37. Maurer J, Rebbapragada V, Borson S, Goldstein R, Kunik ME, Yohannes AM, et al. Anxiety and depression in COPD: current understanding, unanswered questions, and research needs. Chest2008;134(4 Suppl):43S-56S.

38. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med2002;166(1):111-117.

39. Japanese Respiratory Society, Committee of Respiratory Physiology. Reference values of spirogram and arterial blood gas analysis for Japanese. Tokyo, Japan: Japanese Respiratory Society; 2001. .

40. van Ede L, Yzermans CJ, Brouwer HJ. Prevalence of depression in patients with chronic obstructive pulmonary disease: a systematic review. Thorax1999;54(8):688-692.

41. Calikoglu M, Sahin G, Yazici AE, Yazici K, Ozisik S. Pulmonary muscle strength, pulmonary function tests, and dyspnea in women with major depression. J Womens Health (Larchmt)2004;13(1):93-98.

42. Spruit MA, Watkins ML, Edwards LD, Vestbo J, Calverley PM, Pinto-Plata V, et al. Determinants of poor 6-min walking distance in patients with COPD: the ECLIPSE cohort. Respir Med2010;104(6):849-857.

43. Lord SR, Menz HB. Physiologic, psychologic, and health predictors of 6-minute walk performance in older people. Arch Phys Med Rehabil2002;83(7):907-911.

44. Al-shair K, Kolsum U, Dockry R, Morris J, Singh D, Vestbo J. Biomarkers of systemic inflammation and depression and fatigue in moderate clinically stable COPD. Respir Res2011;12:3.

45. Eagan TM, Ueland T, Wagner PD, Hardie JA, Mollnes TE, Damas JK, et al. Systemic inflammatory markers in COPD: results from the Bergen COPD Cohort Study. Eur Respir J2010;35(3):540-548.

46. van Schayck CP. Is lung function really a good parameter in evaluating the long-term effects of inhaled corticosteroids in COPD? Eur Respir J2000;15(2):238-239.

47. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. Chest2002;121(5):1434-1440.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

48. Redelmeier DA, Bayoumi AM, Goldstein RS, Guyatt GH. Interpreting small differences in functional status: the Six Minute Walk test in chronic lung disease patients. Am J Respir Crit Care Med1997;155(4):1278-1282.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Figure legends

Figure 1: Scatter plots of SF–GDS and physical parameter of COPD.

r: Spearman's rank correlation coefficient

Each dot represents one COPD patient.

Figure 2: Receiver operating characteristic curves by COPD severity scales for depression

AUC: The area under the receiver operating characteristic curves.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Table 1 Patient characteristics and correlation with SF–GDS.

	All patients	Depression(+)	Depression(–)	P
N	84	32	52	
SF–GDS	4.7 ± 3.5	8.4 ± 2.5	2.4 ± 1.5	<.001
Age	72.0 ± 9.0	74.1 ± 9.1	70.7 ± 8.7	.09
Sex (Feale)	15(17.9%)	9(18.1%)	6(11.5%)	.08
Smoking history (pack year)	52.6 ± 29.8	59.1 ± 48.5	34.7 ± 25.9	.11
Current smoker	13(15.5%)	5(15.6%)	8(15.4%)	.98
Low economic status	11(13.1%)	8(25.0%)	3(5.8%)	.02
LTOT	16(19.0%)	13(40.6%)	3(5.8%)	<.001
Living alone	11(13.1%)	7(21.9%)	4(7.7%)	.09
Widowed or divorced	6(7.1%)	4(12.5%)	2(3.8%)	.20
GOLD stage				<.001
Stage I	2 (2.4%)	0 (0.0%)	2 (3.8%)	
Stage II	27 (32.1%)	6 (18.8%)	21 (40.4%)	
Stage III	43 (51.2%)	15 (46.9%)	28(53.8%)	
Stage IV	12 (14.3%)	11 (34.4%)	1 (1.9%)	
BODE index	3.6 ± 2.5	5.5 ± 2.7	2.4 ± 1.5	<.001
Body mass index (kg/m^2)	21.0 ± 3.0	21.0 ± 3.6	21.1 ± 2.6	.94
FEV1 (% predicted)	46 ± 15	38 ± 14	51 ± 13	<.001
MMRC	1.4 ± 1.4	2.5 ± 1.3	0.8 ± 0.9	<.001
6MWD (m)	409 ± 160	232 ± 183	477 ± 96	<.001
SpO2 (%)	94.9 ± 2.1	93.5 ± 2.1	95.6 ± 1.8	<.001
Anticholinergics	67 (79.8%)	24 (75.0%)	43 (82.7%)	0.42

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Long-acting beta agonist	38 (45.2%)	15 (46.9%)	23 (44.2%)	0.83
Theophylline	26 (31.0%)	8 (25.0%)	18 (34.6%)	0.47
Inhaled corticosteroids	16 (19.0%)	6 (18.8%)	10 (19.2%)	1.00

Patients characteristics among all patients, patients with depression, and patients without depression were summarized in this table. For binary variable, number of patients with each background and proportion of patients with each background were mentioned (Divided by 84, 32 or 52). For continuous variable, mean ± standard deviation were mentioned. P: comparison between depression(+) patients and depression (–) patients. Fisher's exact test for bivariate, unpaired Student's t test for continuous variable, or Cochran-Armitage for trend test was adopted.

Minimum clinically significant difference of 6MWD is 54 m [48]

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Table 2: Multiple linear regression analysis for SF–GDS

	Partial correlation coefficient	P
BODE index	0.51	< .001
FEV1 (%predicted)	−0.30	.009
MMRC	0.42	< .001
6MWD	−0.34	.003
SpO2	−0.25	.03

Multiple linear regression analyses with (i)eight demographic and social factors; and (ii)one of physical parameter in the table were performed.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Table 3: Multiple logistic regression analysis for probable depression (SG–GDS ≥ 6)

	Odds ratio	P
BODE index	2.3	< .001
FEV1 (%predicted) (10%)	0.48	.008
MMRC	3.6	< .001
6MWD (100 m)	0.45	.003
SpO2(%)	0.72	.03

Multiple logistic regression analyses with (i)eight demographic and social factors; and (ii)one of physical parameter in the table were performed. For example, 100 m increase of 6MWD is equivalent to odds ratio of 0.45 for probable depression after adjusting for eight demographic and social factors.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Table 4: Summary of studies evaluating relationship between physical factors and depression

Author	Relationsihp with physical factors						Preval ence	Depression scale	FEV based COPD severity,
	BMI	FEV	Dysp nea	Exer cise	BODE index	O2			
Light[17], 1985 USA		○		○		○	42%	BDI>15	FEV1(%pred) 29±9%
Mishima[23],1996 Japan		○	●			○	19%	HAD>10	FEV1 0.77±0.45 (L)
Yohannes[18] 1998, UK	○	○	○	○			46%	BASDEC≥7	FEV1(%pred) 51±20%
Borak[24], 1998 Poland		○		○		●	18%	BDI≥15	FEV1(%pred) 32±14%
Manen[16], 2002 Netherlans		#					22%	CES-D ≥16	mod 63%, sev & very−sev 37%
Wagena[19], 2005 Netherlands		○					30%	BDI≥15	FEV1(%pred) 56±27%
Chavannes[25], 2005, Netherlands	●	○	#				27%	BDI>10	FEV1(%pred) 64±19%
Di Marco[13] 2006, Italy	○	○	●			○	19%	SDS>50	FEV1(%pred) 54±SE1%
Hynninen[30] 2007, Norway		○					35%	BDI2≥20	FEV1(%pred) 54±24%
Quint[26], 2008 UK			●				41%	CED-D≥16	FEV1(%pred)

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

									47±19%
Bentsen[27], 2008 Norway				●			NA	HAD	FEV1(%pred) 46±15%
Funk[20], 2009 Austria	○	#	●	●	●		52%	HAD≥8	FEV1(%pred) 45±19%
Ng[21], 2009, Singapore		●	#				23%	SF-GDS≥5	mild 56%, mod 34%, sev & very−sev 10%
Omachi[22] , 2009 USA		●		●	●	●	27%	SF-GDS≥6	FEV1(%pred) 62±23%
Al−shair[28], 2009 UK	○	○	#	●	●		24% 19%	CES-D≥16 BASDEC≥7	FEV1(%pred) 52±18%
Borge[29], 2010 Norway		○	●				NA	HAD	FEV1(%pred) 59±23%
Hanania[14], 2011 USA etc.	○	#	●	#	●	#	26%	CES-D≥16	FEV1(%pred) 48±16%
Iguchi,[33]2012, Japan		●					49%	CES-D≥16	FEV1(%pred) 37±18%
Horita, 2012 Japan	○	●	●	●	●	●	38%	SF-GDS≥6	FEV1(%pred) 46±15%

BMI: Body mass index.

FEV: FEV(ml), FEV(%predicted), or GOLD stage.

Exercise: Exercise capacity measured by 6 or 12 minute walking distance test, or incremental shuttle walk test.

O2: Saturation or pressure of oxygen on artery.

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

●:the relationship was significant.

#: the result was controversial in a study depend on measurement and/or analysis method. For example, significant in single variable analysis and not significant in multiple variant analysis.

○:the relationship was NOT significant.

BDI: Beck Depression Inventory

HAD: Hospital Anxiety and Depression scale

BASDEC: Brief Assessment Schedule Depression New Card

CES-D: Center for Epidemiologic Studies Depression Scale

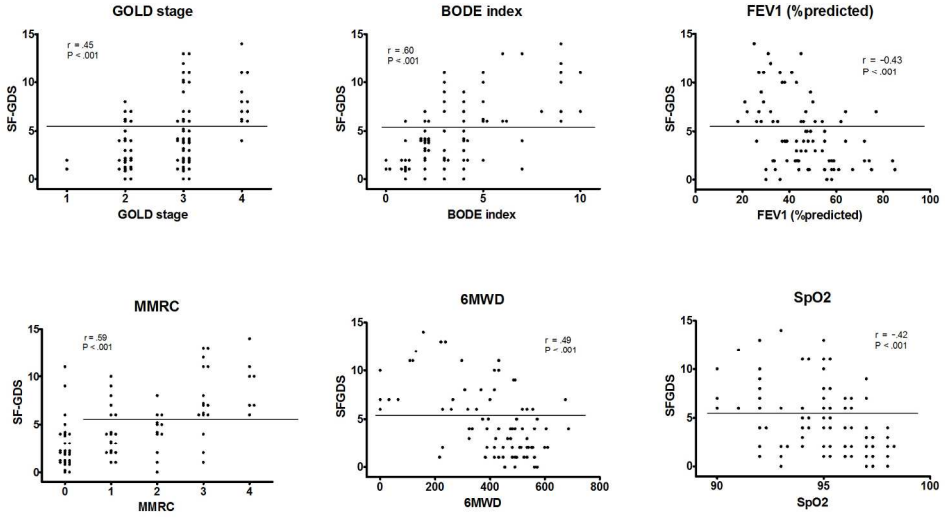
SDS: Self-Rating Depression Scale

BDI2: Beck Depression Inventory 2nd edition

SF-GDS: Short Form Geriatric Depression Scale

FEV based COPD severity: FEV1(%predicted) was preferably listed. If not available, substituted by FEV1(L) or GOLD stage. (mod: moderate, sev: severe, very−sev: very severe)

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065



189x106mm (300 x 300 DPI)

RESPIRATORY CARE Paper in Press. Published on December 4, 2012 as DOI: 10.4187/respcare.02065

Short-Form Geriatric Depression Scale

1.	Are you basically satisfied with your life?	yes	**no**
2.	Have you dropped many of your activities and interests?	**yes**	no
3.	Do you feel that your life is empty?	**yes**	no
4.	Do you often get bored?	**yes**	no
5.	Are you in good spirits most of the time?	yes	**no**
6.	Are you afraid that something bad is going to happen to you?	**yes**	no
7.	Do you feel happy most of the time?	yes	**no**
8.	Do you often feel helpless?	**yes**	no
9.	Do you prefer to stay at home, rather than going out and doing things?	**yes**	no
10.	Do you feel that you have more problems with memory than most?	**yes**	no
11.	Do you think it is wonderful to be alive now?	yes	**no**
12.	Do you feel worthless the way you are now?	**yes**	no
13.	Do you feel full of energy?	yes	**no**
14.	Do you feel that your situation is hopeless?	**yes**	no
15.	Do you think that most people are better off than you are?	**yes**	no

Total Score _____

Short-Form Geriatric Depression Scale
334x471mm (96 x 96 DPI)