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Review Article

EFFECT OF PATIENTS' DEPRESSION AND ANXIETY ON QUALITY OF LIFE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): LITERATURE REVIEW

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ABSTRACT

The World Health Organisation (WHO) was estimated that 65 million people have moderate or severe chronic obstructive pulmonary disease (COPD). WHO was stated that more than 3 million people died of COPD in 2005 that corresponds to 5% of all deaths globally. COPD is characterised by airflow obstruction. The airflow obstruction is usually progressive, not fully reversible and does not change markedly over several months. Airflow obstruction is defined as a reduced FEV₁ (forced expiratory volume in 1 second) and a reduced FEV₁/FVC ratio (where FVC is forced vital capacity), such that FEV₁ is less than 80% predicted and FEV₁/FVC is less than 0.7; the airflow obstruction is due to a combination of airway and parenchymal damage. COPD has been defined as an umbrella term covering a range of conditions including chronic bronchitis and emphysema. The literature review indicated that both depression and anxiety were significantly related to negative quality of life; surprisingly high prevalence of anxiety and depression in COPD patients.

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INTRODUCTION

The World Health Organisation (WHO) was estimated that 65 million people have moderate or severe chronic obstructive pulmonary disease (COPD). WHO was stated that more than 3 million people died of COPD in 2005 that corresponds to 5% of all deaths globally (WHO 2016). Most of the information available on COPD prevalence, morbidity and mortality comes from high-income countries. Even in those countries, accurate epidemiologic data on COPD are difficult and costly to gather (WHO 2016). It is known that about 90% of COPD death occurs in low and middle - income countries (WHO 2016). It was estimated that the prevalence of depression in COPD to be 40% and suggested that anxiety symptoms may have a prevalence of 36% (Yohannes *et al* 2000). It has also been predicted that COPD will be the world's fifth ranking cause of disability by 2020 (Murray and Lopez 1997).

COPD is characterised by airflow obstruction. The airflow obstruction is usually progressive, not fully reversible and does not change markedly over several months (NICE 2004). Airflow obstruction is defined as a reduced FEV₁ (forced expiratory volume in 1 second) and a reduced FEV₁/FVC ratio (where FVC is forced vital capacity), such that FEV₁ is less than 80% predicted and FEV₁/FVC is less than 0.7; the airflow obstruction is due to a combination of airway and parenchymal damage (NICE 2004). Parenchyma is 'the predominant function tissue of the organ. Parenchymal cells can occur in masses, cords, strands or tubules, depending on the organ' (Montague

et al 2005 p 6). National Service Framework (NSF) defined COPD as an umbrella term covering a range of conditions including chronic bronchitis and emphysema (NSF 2009).

Tobacco smoking is the major cause of COPD (NICE 2004). Nearly 10% to 20% of smokers show an accelerated rate of decrease in FEV₁. Smokers have 10 times the risk of non-smokers of dying of COPD (Habermann and Ghosh 2007; Weinberger *et al* 2008). Smoking also increases the risk of developing COPD in people who have alpha-1- antitrypsin deficiency (Habermann and Ghosh 2007; Weinberger *et al* 2008). Air pollution caused by oxidants, oxides of nitrogen, hydrocarbons, and sulphur dioxide has an important role in exacerbating COPD (Habermann and Ghosh 2007). Other factors, particularly occupational exposure, may also contribute to the development of COPD (NICE 2004; Habermann and Ghosh 2007).

There is well documented association between COPD and anxiety and depression (Dowson *et al* 2001; Mikkelsen *et al* 2004; Kunik *et al* 2005). It has been found that the prevalence of depression and anxiety in patient with COPD is greater than that in the general population (Putman-Casdroph and McCrone 2009). Whilst the exact causes of these symptoms have not been well defined, several variables, such as long-term oxygen therapy, poor quality of life, living alone, current smoking and low social class status have been implicated (Maurer *et al* 2008). Prevalence estimates vary widely, due in part to the use of varied measurement tools and to the different degrees of

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disease severity across studies (Maurer *et al* 2008). In stable COPD, the prevalence of clinical depression ranges between 10% and 42%, while that in anxiety ranges between 10% and 19% (Karajgi *et al* 1990; Kunik *et al* 2005)

RESEARCH LITERATURE REVIEW

Cully *et al* (2006) found that both depression and anxiety were significantly related to negative quality of life outcomes. They examined 179 veterans with COPD to determine the relative contribution of clinical depression and/or anxiety to their quality of life. This is a US study was conducted with a subsample of 179 patients from a randomized controlled trial of the use of cognitive-behavioural therapy in persons with COPD and comorbid anxiety and/or depression. All research subjects participated in informed consent procedures approved by the Baylor College of Medicine Institutional Review Board. All individuals who received care at the Michael E. DeBakey Veterans Affairs Medical Centre in the previous year (2002-2003) and had an International Classification of Diseases, 9th Revision (ICD-9) diagnosis of chronic breathing disorder were targeted for recruitment. 21-item Beck Depression Inventory, 2nd Edition (BDI) (Beck *et al* 1996) was used to assess severity of depression. The BDI is a highly reliable and valid tool for medical patients, with excellent internal consistency and factorial and convergent validity (Arnau *et al* 2001). 21-item Beck Anxiety Inventory (BAI) was used to assess the severity of anxiety symptoms (Beck *et al* 1988). The BAI possess strong psychometric properties related to internal consistency, test-retest reliability, and validity (Beck *et al* 1990). The chronic Respiratory Questionnaire (CRQ) (Guyatt *et al* 1987) and the Medical Outcomes Survey Short Form (SF-36) (Ware *et al* 1994) were used to assess the quality of life. CRQ is a reliable quality of life tool developed specifically for use with COPD patients; the tool provides incremental validity on changes in quality of life, as compared with less specific measures (Guyatt *et al* 1987; Salek 1998). SF-36 has been for use in patients with COPD (Mahler and Mackowiak 1995; Harper *et al* 1997). The authors concluded that the impact of depression and anxiety on patients with COPD is of high importance. Although further studies are needed to clarify this relationship, early detection and treatment of psychological difficulties may play a critical role in improving quality of life for COPD patients with comorbid psychological symptoms.

Several limitations of the present investigation have been noted; because of the methodological design of the investigation, assumptions of causality between mental health distress and quality of life were not warranted. Data indicated that both anxiety and depression are significant factors associated with quality of life, however, further studies are needed to determine whether mental health distress is a cause of reduced quality of life or if such conditions are simply a product of reduced quality of life. The sample of patients consisted of veterans who were primarily male, limiting the generalisability of the results, with further studies are needed for non-veterans and women with COPD. The specific recruitment of patients with COPD and comorbid clinical depression and/or anxiety may also limit the generalisability of the results to similar patient populations. Specifically, the sample consisted of patients identified with COPD by chart diagnosis who subsequently tested positive for depression,

anxiety, or both, and results may not apply in the case of subclinical mental health symptoms (Cully *et al* 2006).

Kunik *et al* (2005) found that a surprisingly high prevalence of anxiety and depression using PRIME-MD (80%). 80% of those who screened positive by the PRIME-MD also met criteria for depression and/or anxiety with the Beck anxiety and depression inventories. They used a randomized controlled trial to test the use of cognitive behavioural therapy in persons with COPD and comorbid anxiety and/or depression. A large sample of 1334 individuals with chronic breathing disorder diagnoses were participated in this study, using the Primary Care Evaluation of Mental Disorders (PRIME-MD) screening questions. PRIME-MD was developed and validated for use in primary care settings (Spitzer *et al* 1994). All research was in accordance with recommendations found in the Helsinki Declaration of 1975, and all research participants participated in informed consent procedures approved by the Baylor College of Medicine Institutional Review Board. The authors concluded that a mere 31% of COPD patients with depression or anxiety are being treated, particularly given their high prevalence in this population. They also concluded that practical screening instruments may help increase the recognition of anxiety and depression in medical patients.

This study is limited in that it is an all-veteran, mostly male sample, lacks BAI/BDI data for individuals who screened negative on the PRIME-MD questions, has BAI/BDI data on only 52% of eligible participants, and has SCID diagnoses for only a screened sample of people with COPD. However, the study has unique strengths, including its large size, inclusion of Structured Clinical Interview for the Diagnostic (SCID) for a subsample, and use of non-clinic, non-inpatient sampling frame (Kunik *et al* 2005). The SCID assesses for the presence of such as anxiety disorders, psychotic disorders and mood disorders (Ramsay and Rostain 2007).

Ampon *et al* (2005) study showed that adults of working age with asthma have poorer health status and quality of life outcomes than those with no asthma. The information was obtained on self-reported current asthma status, arthritis and diabetes as well as measures of life satisfaction, self-assessed health status, psychological distress, and interference with usual activities for 14641 respondents aged 18-64 years in the 2001 national health survey of the general population in all states and territories in Australia. Log linear models were fitted separately for each of the dichotomised quality of life measures as dependent variables. The estimates of the adjusted rate ratio obtained from each model were used to compute the Population Attributable Fraction (PAF) of self-reported asthma, arthritis, and diabetes for each of the health status and quality of life measures. The authors concluded that asthma is an important contributor to the burden of ill health and impaired quality of life in the community. They also concluded that strategic approach is needed to develop and implement strategies to address the impact of asthma on quality of life. The findings were based on a survey conducted among a large nationally representative sample of the Australian population with a high participation rate and, therefore, can be regarded as a generalisable to people with asthma in the broader community.

Unlike this study, most previous studies have not attempted to quantify the relative impact of chronic disease in terms of population attributable risk, however, further research is needed to develop a framework of interventions that will help reduce the burden of the disease, therefore reducing its impact on individuals' quality of life (Ampon *et al* 2005).

Andenaes *et al* (2004) found that psychological distress had a statistically significant association with quality of life and accounted for 34% of the total 39% variance explained by the study model. They examined how disease factors and health status affect psychological distress and subjectively perceived quality of life in patients admitted for an acute exacerbation of chronic obstructive pulmonary disease. The study approved by the Regional National Committee for Research Ethics in Norway. Patients' competence to consent may be reduced in an acute illness phase. A convenience sample of 92 inpatients (mean age 69) was interviewed using the St George's Respiratory Questionnaire (SGRQ), Hopkins Symptoms Check List-25 (HSCL-25), and World Health Organization Quality of Life Assessment (WHOQOL-Bref). SGRQ-C (version 1.1 2008) is a standardised self-completed questionnaire for measuring impaired health and perceived well-being 'quality of life' in airways disease (Jones 2008). The WHOQOL-Bref provides a short form quality of life assessment. HSCL-25 is considered a screening tool, yielding information on the extent of unspecified distress and adjustment to somatic and psychiatric disease, including symptoms that may also secondary to the physical disease. Disease variables (disease duration and pulmonary function) and health status were entered in blockwise multivariate regression analyses to examine the relationships between disease variables, psychological distress, and a single item assessment of overall quality of life. The St George's Respiratory Questionnaire Total and Impact subscores showed statistically significant associations with psychological distress. Pulmonary function showed a moderately significant association with subjective perceived quality of life. Pulmonary function and disease duration explained a minor part of the variance in quality of life. The authors concluded that the influence of psychological distress on quality of life implies that bringing about change in psychological distress factors may have important consequences for quality of life.

There are some possible limitations should be noted, and may influence the generalisability of the findings; there may have been selection bias in the respondents included in the study. The criteria for inclusion were strict, and five more patients were excluded because of severe illness. Ten eligible patients declined to participate. The main reason for not participating was fear that the interviews would be too strenuous. This could indicate that the interviewed sample was biased toward the less severely affected but, as the sample as a whole was severely affected according to FEV1%, it has believed that the patients formed a representative sample of acutely admitted patients with COPD (Andenaes *et al* 2004). The WHOQOL-Bref questionnaire provides subscale scores for physical, psychological, social relationships and environmental domains; however, the overall global question about quality of life is not included in any subscale. Future research concerning quality of life needs to move beyond cross-sectional analyses and investigate changes over time. However, the results draw

attention to the negative effects of an exacerbation of COPD and provide new information about important factors influencing quality of life in COPD patients in an acute phase of the disease (Andenaes *et al* 2004).

Adams *et al* (2004) stated that people with asthma and psychological distress had significantly lower scores on the SF-12 PCS than those with either asthma or psychological distress alone. An introductory letter was sent to every selected household from the health department of every state. A household interview survey of adults (age>18) was carried out in Western Australia, the Northern Territory, and South Australia. Data obtained were weighted to the closest census data to provide population representative estimates. Positive answers to two questions: 'Have you ever been told by a doctor that you have asthma?' and 'Do you still have asthma?' determined current doctor-diagnosed asthma. Other items included the SF-12, the Kesler-10 index of psychological distress, questions on feeling of lack of control in different areas of life, and on mental health conditions. SF-12 is a 12-item subset of the SF-36 that measures the same eight domains of health; it is a brief, reliable measure of overall health status (John and Ware 2008). It is a valid measure of health status in Australia (McCallum 1995). SF-12 is also acceptable and valid as health status instruments in large community-based studies of older people, but is not acceptable and valid for people with dementia (Pettit *et al* 2001). The Kessler 10 Psychological Distress Scale (K10) is a brief 10-item questionnaire designed to measure the level of distress and severity associated with psychological symptoms in population surveys (Brooks *et al* 2006). It is being used widely, including in the World Health Organisation World Mental Health Survey, and as a clinical outcome measure, although little information is available about the structure of the measure (Brooks *et al* 2006). The factorial composition of the K10 was examined in a prospective community survey and cross-validated in a separate large community survey (Brooks *et al* 2006). In a representative population survey psychological distress was significantly more frequent in individuals with asthma and a higher proportion with asthma were at higher risk for anxiety or depression. Diagnosed mental health conditions were also significantly more common, as was the frequency of those who sometimes or always felt a lack of control over their health, finances, and life in general. People with asthma and psychological distress had significantly lower scores on the SF-12 PCS than those with either asthma or psychological distress alone. The authors concluded that these results, from a representative population sample, show that psychological distress and decreased feelings of control are common in asthma and are significantly associated with physical health status.

This study has several limitations; the cross sectional nature of this study prevented the researchers from determining a causal relation between asthma, psychological distress, perceived lack of control, and impaired quality of life. They were also unable to examine the relationship between differing levels of asthma severity and psychological factors as data on clinical variables were not collected (Adams *et al* 2004). This study was also limited by relying on self-reports of a doctor's diagnosis of asthma. People are more likely to report respiratory symptoms if they have an abnormal psychological condition such as

anxiety or depression (Rimington *et al* 2001). It is possible that in some cases, the doctor could also be misguided in the diagnosis of asthma because of the presence of anxiety or depression (Adams *et al* 2004).

McCathie *et al* (2002) found that physical status of COPD patients medically stabilised, but psychological factors need to be carefully assessed. 92 males agreed to participate in the study and completed questionnaires to determine their coping strategies, levels of self-efficacy of symptoms management and social support. Adjustment was measured in terms of depression, anxiety and quality of life. Symptoms severity, socioeconomic status, duration of disease and age, which have been demonstrated to be consequence in COPD, were used as control variables in hierarchical multiple regression analyses. The study found that higher levels of catastrophic withdrawal coping strategies and lower levels of self-efficacy of symptom management were associated with higher levels of depression, anxiety and a more impaired quality of life. Higher levels of positive support were linked to lower levels of anxiety and depression, while lower levels of negative support were linked to higher levels of depression and anxiety. The Beck BDI was used to measure depressive symptoms experienced over the past week. The state Trait Anxiety Inventory (STAI Form X-2) was used to measure the level of anxiety 'generally' felt, rather than the form X-1, STAI, which asks subject to indicate how they 'feel right now, that is, at this moment'. STAI has been validated for various situations and populations in several studies (Spielberger *et al* 1983; Okun *et al* 1996). SGRQ was used to measure quality of life. The authors concluded that psychological interventions should focus on the introduction of psychological techniques to decrease catastrophic withdrawal coping strategies, to raise levels of self-efficacy of symptom management and to cope with the inevitable negative interactions encountered, this, in turn, could increase the quality of life for this debilitated patient population.

The study has some limitations; as the sample was elderly, male, with the subjects predominantly from the middle to lower end of the socioeconomic scale, and patients of a metropolitan public hospital, the results may not generalise to other populations (McCathie *et al* 2002). As physical status is being medically stabilised, psychological factors need to be carefully assessed. The researchers stated that future research should apply the knowledge that has been gained from this research in a controlled and evaluated treatment programme (McCathie *et al* 2002).

Cleland *et al* (2007) found that depressive and anxious symptoms in COPD are related to age and high levels of symptoms. They examined the associations of depression and anxiety with demographic, health-related quality of life and clinical characteristics of COPD patients seen in UK primary care. Cross-sectional population-based postal survey of COPD patients comprising the EQ-5D visual analogue scale (EQ-5D(VAS)), the COPD symptom control questionnaire, the Hospital Anxiety and Depression Scale, the Medical Research Council dyspnea index, demographic and spirometric data were collected from general practice records. A total of 170 (57%) patients consented to take part. Data were reported on 110 of these patients for whom up to date Spirometry was available. Approximately one in five participants reported 'caseness' for

depression (20.8%) and one in three reported anxiety (32.7%). Age and high levels of symptoms were independent predictors of anxiety and depression, as was the EQ-5D (VAS) of depression. The authors concluded that these data suggest that in UK primary care, depressive and anxious symptoms in COPD are related to age and high levels of symptoms. Depression is also associated with lower patient-reported generic health status. The data suggest that assessment and treatment for depression and anxiety should be considered for all COPD patients, not just those with more severe clinical levels of disease. The potential of the EQ-5D (VAS) as a screening tool for anxiety and depression in primary care COPD patients also merits study.

The possible criticism of this study is that the researchers did not measure functional status in their population and therefore they were unable to examine the relationship between that and psychological health, health-related quality of life and symptoms (Cleland *et al* 2007).

Gudmundsson *et al* (2005) Multicentre study showed that anxiety and depression are common in patients with COPD, and, furthermore, that patients with psychological disorders have poor health status. Screening for depression and anxiety may help to identify patients with poor quality of life and an urgent need for intervention in order to improve their health status.

Gudmundsson *et al* (2005) carried out a prospective study of 416 patients in five university hospitals in each of the Nordic countries. All the participants were informed and gave their formal consent. Data included demographic information, lung function and co-morbidity. The Hospital Anxiety and Depression Scale and SGRQ were applied to all patients. Both anxiety and depression were common among these patients. Anxiety was more common in women than in men (47% vs. 34%, $P=0.009$ $P=0.009$) and current smokers had a higher prevalence of both anxiety (54% vs. 37%) and depression (43% vs. 23%) than non-smokers ($P<0.01$ $P<0.01$). In general, the studied COPD patients had poor health status, especially those with anxiety, depression or both. Psychological status was independently related to all dimensions of SGRQ. Higher GOLD stages were significantly associated with increasing impairment in health status. This multicentre study showed that anxiety and depression are common in patient with COPD, and, furthermore, the patients with psychological disorders have poor health status.

The strengths of this study are the large number of patients included. The study also included patients from five countries, a mixture of males and females.

Brenes (2003) also found that not surprisingly, anxiety has a significant and negative impact on quality of life of COPD patients. Brenes (2003) reviewed the prevalence of anxiety disorders in patients with COPD as well as the impact of comorbid anxiety on quality of life in patients with COPD. A PubMed search was conducted of the literature from 1966 through 2002 using the keywords anxiety, chronic obstructive pulmonary disease, respiratory diseases, obstructive lung diseases, and pulmonary rehabilitation. Any articles that discussed the prevalence of anxiety symptoms or anxiety disorders among patients with COPD, the impact of anxiety on

patients with COPD, or the treatment of anxiety in COPD patients were included in this review. It has been found that anxiety disorders, especially generalised anxiety disorder (GAD) and panic disorder occurs at a higher rate in patients with COPD compared with the general population. Brenes (2003) stated that a few studies have examined pharmacological, psychotherapeutic, or pulmonary rehabilitation treatments for anxiety disorders in the context of COPD. Brenes (2003) concluded that studies examining the treatment of anxiety disorders in patients with COPD are promising, yet their efficacy needs to be established. The long-term effects of treatment of anxiety disorders on quality of life of COPD patients have yet to be explored.

The possible criticism is that researchers need to examine the efficacy of the treatment among patients with comorbid anxiety disorder and COPD. The studies to date did not formally assess participants for clinical anxiety disorder. Rather, they focused on self-reported anxiety symptom severity. The long term effects of anxiety treatment on quality of life among COPD have not been determined.

Van Manen *et al* (2002) found that patients with severe COPD are at increased risk of developing depression. They carried out this study to investigate whether depression occurs more often in patients with COPD than in controls. The demographic and clinical variables associated with depression were also determined. Patients with a registered diagnosis of obstructive airway disease in general practice, aged >40 years, forced expiratory volume in 1 second (FEV1) <80% predicted, FEV1 reversibility <12%, FEV1/VC < predicted - 1.64 X SD, and a history of smoking were selected. A total of 1106 patients who were willing to participate were consented. A random sample of 676 subjects without a registered diagnosis of asthma or COPD aged 40 years or older acted as controls. Depression was assessed using the Centers for Epidemiologic Studies Depression (CES-D) scale. CES-D scale is a short self-report scale designed to measure depressive symptomatology in the general population (Radloff 1977). The scale validity was established by patterns of correlations with other self-report measures; the scale should be useful tool for epidemiologic studies of depression (Radloff 1977). In patients with severe COPD (FEV1 <50% predicted), the prevalence of depression was 25.0% compared with 17.5% in controls and 19.6% in patients with mild to moderate COPD. When the results were adjusted for demographic variables and comorbidity, the risk for depression was 2.5 times greater for patients with severe COPD than for controls (OR 2.5, 95% CI 1.2 to 5.4). Van Manen *et al* (2002) found that in patients with mild to moderate COPD this increased risk of depression was not seen. Living alone, reversibility of FEV1 % predicted, respiratory symptoms and physical impairment were significantly associated with the scores on the CES-D scale. The results of this study highlighted the importance of reducing symptoms and improving physical functioning in patients with COPD.

The strengths of this study are the large number of COPD patients included. The study also included patients with a broad range of severity of COPD and a large number of controls.

CONCLUSION

The literature review indicated that both depression and anxiety were significantly related to negative quality of life;

surprisingly high prevalence of anxiety and depression in COPD patients. Adults of working age with asthma have poorer health status and quality of life outcomes than those with no asthma. Psychological distress had a statistically significant association with quality of life. Psychological distress and decreased feelings of control are common in asthma and are significantly associated with physical health status. Psychological interventions should focus on the introduction of psychological techniques to decrease catastrophic withdrawal coping strategies, to raise levels of self-efficacy of symptom management and to cope with the inevitable negative interactions encountered, this, in turn, could increase the quality of life for the debilitated patient with COPD. Depressive symptoms are common in patients with COPD and those with severe COPD. Anxiety and depressive symptoms are common in patients affected by COPD, even when their disease is mild in terms of FEV1 and respiratory symptoms. In UK primary care, depressive and anxious symptoms in COPD are related to age and high levels of symptoms. Depression is associated with lower patient-reported generic health status. Anxiety and depression are common in patients with COPD, and, also, that patients with psychological disorders have poor health status. Screening for depression and anxiety may help to identify patients with poor quality of life; urgent need for intervention in order to improve their health status. Anxiety disorders, especially generalised anxiety disorder (GAD) and panic disorder occurs at a higher rate in patients with COPD compared with the general population. Patients with severe COPD are at increased risk of developing depression. However, there is a question remains unanswered that what is the level of anxiety and depression in patients with COPD and how does this affect their quality of life?

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