Don't overlook the impact of these comorbidities COPD and mood disorders, part 1: Anxiety and depression

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abstract: Depression and anxiety are common comorbidities in patients with chronic obstructive pulmonary disease (COPD), and like COPD, they are often underrecognized. Both of these comorbidities can adversely affect the course of COPD. Anxiety, for example, is associated with more severe dyspnea, greater disability, and impaired functional status; it also is a significant predictor of hospitalizations for acute exacerbations of COPD. When evaluating depressive symptoms, it is important to rule out cognitive impairment, particularly in patients with severe COPD and hypoxemia. Treatment options include antidepressants and cognitive behavioral therapy. Participation in a pulmonary rehabilitation program also can help reduce anxiety and depressive symptoms in patients with COPD. (J Respir Dis. 2007;28(3):94-103)

Chronic obstructive pulmonary disease (COPD) is a health problem worldwide, and the impact is expected to increase in the next several decades. In the United States, COPD has been diagnosed in more than 10 million persons, and an additional 14 million show signs of the disease, although they have not yet received the diagnosis. The COPD death rate for women has more than doubled in the past 20 years--from 20.1 to 56.7 per 100,000--and the financial burden of COPD is significant: an estimated $14.7 billion annually for direct medical costs and an estimated $15.7 billion annually for indirect costs (such as loss of productivity and premature mortality). Despite the fact that COPD is the fourth leading cause of death in the United States, behind heart disease, cancer, and stroke, it is underrecognized and undertreated. Primary care physicians have a central role in managing the care of persons with COPD at all stages. First is their effort to support and facilitate the patient's and family's smoking cessation, which many of them do in the office setting. However, the lack of office spirometry equipment, concerns about appropriate timing of home oxygen therapy, and the high frequency of other major morbidities in patients with COPD may encourage the family physician or general internist to send such patients to pulmonary or cardiology specialists.

While specialists are helpful in recommending certain types of therapy, generalists may be better able to provide help for mood disorders--a group of chronic conditions that often negatively affect the course of COPD. Research shows that deterioration in patient-reported outcomes only weakly correlated with declines in physiological indices, such as forced expiratory volume in 1 second, but more strongly correlated with the presence and severity of mood disorders and the ability to sleep.

Fatigue is one of the most common complaints of persons with COPD. Fatigue makes the activities of daily living difficult if not impossible and greatly decreases pleasure in any activity. Health care professionals often become so focused on the dyspnea and decline in lung function associated with COPD that they neglect the functional symptoms that are most important to the patient and his or her family. Kapella and colleagues have developed a model that focuses on fatigue in persons with COPD and places dyspnea in the context of the many other concomitant causes of fatigue. In this 2-part article, we review the 3 major nonpulmonary components of fatigue and COPD: depression, anxiety, and sleep disorders. The objective is to provide primary care physicians with effective tools to address the poor quality of life experienced by many of their patients with COPD.

DEPRESSION AND COPD

Few physicians are surprised by or unaware of the connection between COPD and depression. In fact, we may believe that depression is a normal part of the grief reaction to the diagnosis of COPD and fail to formally diagnose and treat this serious comorbidity. Depression is diagnosable and treatable even in patients with chronic life-threatening conditions.
The diagnosis of COPD is usually made only after patients present with significant symptoms associated with a change in lifestyle and a reduction in quality of life.\textsuperscript{21} Such lifestyle changes often result in isolation from productive endeavors and from family and friends, which might be expected to be depressing. However, recent work suggests that the association between depression and COPD goes beyond a reaction to required life changes.

In a study of older adults with a variety of chronic conditions, including diabetes with complications, cancer, and COPD, the overall medical burden was most powerfully associated with depression, and this was largely independent of functional status. This suggests that in general primary care populations, the relationship of illness to depression may be multimodal or may involve shared pathobiological or psychosocial mechanisms.\textsuperscript{15} Inflammation may be one such shared mechanism. Inflammation is a central factor in the pathophysiology of COPD, and recent research suggests that depression may also be linked to inflammation and inflammatory mediators in the brain.\textsuperscript{22,23} At present, this is only a fascinating possible association between pulmonary and brain inflammation, but in the future, it may prove to be of value when selecting treatments for both COPD and depression.

### Epidemiology

The exact percentage of persons with COPD and depression is unknown, primarily because COPD is often unrecognized. However, in those with diagnosed COPD, the rate of depression ranges from 20\% to 50\%\textsuperscript{16,24} and has varied little over the past 20 years. The rates of depression associated with COPD do not appear to vary by sex but do vary by the person’s use of coping skills.\textsuperscript{25} Depression is often associated with anxiety, and the combination of the two can amplify the adverse effects of COPD. For example, persons with COPD and depression walk shorter distances in 12 minutes than those with comparable lung impairment without depression.\textsuperscript{26} Felker and associates\textsuperscript{27} suggest that 11\% to 18\% of the variance in physical functioning in COPD can be attributed to depressive symptoms. In patients who require home oxygen therapy, rates of anxiety and depression are as high as 62\%,\textsuperscript{28} and fewer than two thirds of these patients receive therapy for depression.\textsuperscript{29}

Poorer quality of life and decreased rates of compliance with treatment are also more common in COPD patients who are depressed than in those who are not depressed.\textsuperscript{26} In fact, depression often affects the patient's desire for any treatment for COPD.\textsuperscript{30} The depressed patient is also more likely to perceive a lack of support from family, friends, and the medical community.\textsuperscript{26} Recognition of depression

There are many screening tools for depression in adults. One of the newest--the Patient Health Questionnaire (PHQ)-9--has become one of the most commonly used in primary care practices. The PHQ-9 can serve as a screening and follow-up tool. It translates directly to the established DSM-IV criteria for depression, and the results have been shown to improve as a person’s depression improves. A score of greater than 5 indicates the need for further evaluation, and a drop of 4 to 5 points is considered evidence of successful therapy with an anticipated return to near-normal status over several months.\textsuperscript{31-33}

No screening test should be considered diagnostic. The person with a high score still requires at least a short diagnostic interview to identify other potential causes, seek a history of previous depression, and assess suicidal thoughts. The diagnostic evaluation can be done by a generalist physician familiar with the diagnostic criteria for depression (Table 1).

No depression screening program should be started without first establishing a system of follow-up. To identify an illness without having a system to treat, monitor, or assess the impact of treatment is irresponsible. This is one of the reasons why general internists’ and family physicians’ offices can be excellent sites for screening for and diagnosing depression in patients with COPD as well as for treating or referring and monitoring these patients.\textsuperscript{13,18} Patients who have more complex problems, are at high risk for suicide, or have substance abuse problems should be referred for specialty mental health care.\textsuperscript{34}

Cognitive impairment must be ruled out when evaluating depressive symptoms in patients with severe COPD, especially those with hypoxemia. In a small study, the incidence of depression was not higher in patients with severe COPD than in age-matched controls, but more than three quarters of the patients had subjective and objective evidence of cognitive disturbance and were classified as having possible mild dementia.\textsuperscript{35} The patients with COPD had significant symptoms and functional impairments that were not attributable to depression.\textsuperscript{35} Treatment of depression

In patients with COPD, the first-line treatment of depression remains antidepressants and cognitive behavioral therapy (CBT).\textsuperscript{36} Pulmonary rehabilitation is an important adjuvant treatment. COPD patients who have completed pulmonary rehabilitation have shown improvements in self-concept and decreased depressive symptoms.\textsuperscript{37} Withers and associates\textsuperscript{38} demonstrated that the gain in
exercise capacity was greater for those who were more anxious at the outset of pulmonary rehabilitation and that depression scores were improved.\textsuperscript{39} There is no evidence for or against the use of a simple graded exercise program when formal pulmonary rehabilitation is not available. The very limited risk and the potential benefit suggest that such a program may be worth trying.

All types of antidepressants, including the older tricyclic antidepressants (TCAs) as well as the newer selective serotonin reuptake inhibitors and the serotonin-norepinephrine reuptake inhibitors, can improve depression in persons with COPD (Table 2).\textsuperscript{36} TCAs have been shown to be safe even in those with severe COPD.\textsuperscript{40} Most antidepressants have adverse effects that can be minimized by a few simple strategies (Table 3). All medications must be used very cautiously in patients who have marked hypoxia and end-stage COPD.

Adherence is a major problem with the use of antidepressants.\textsuperscript{41} Many persons stop taking their medication because of adverse effects in the first few days or weeks and before they begin to improve. Beginning the medications slowly and providing regular follow-up through visits and telephone calls can improve adherence in depression management and can improve patient outcomes.\textsuperscript{12} Brief CBT can effectively treat depression and may decrease the sensation of dyspnea as well as anxiety. A single session of CBT--as short as 2 hours--can make a difference.\textsuperscript{42} Follow-up visits are recommended at 2 weeks and at 4 to 6 weeks, then at least every 2 to 3 months to monitor the course of the depression. These visits can serve to manage both the COPD and the depression.

In summary, depression is a common comorbid condition in patients with COPD. Treatment with pulmonary rehabilitation, antidepressant medications, and CBT is effective. However, currently we are not doing well treating depression in these patients. Even when depression is recognized and treatment initiated, patients with COPD are about one third less likely to have adequate treatment in the first 3 months after the diagnosis of depression, compared with patients with other chronic conditions, including coronary heart disease, diabetes mellitus, and osteoarthritis (odds ratio, 0.67; 95% confidence interval, 0.47 to 0.96).\textsuperscript{43} ANXIETY AND COPD

Although anxiety and depression often coexist, anxiety alone is also common. The prevalence of clinical anxiety in patients with COPD is significantly higher than in the general population. Estimates for specific anxiety disorders range from a 3- to 10-fold increase in COPD; the highest rates are for panic disorder, which may occur in as many as one third of COPD patients.\textsuperscript{43-45} The diagnostic criteria for anxiety disorders for patients with COPD are the same as for those without COPD, but special care must be taken to avoid misdiagnosis. The DSM-IV criteria for panic disorder require the presence of one or more noncued panic attacks—that is, panic attacks that do not occur in the presence of an identifiable trigger. For example, a patient who has panic attacks only in the context of an exacerbation of COPD would not meet criteria for panic disorder.

Anxiety symptoms are very common in COPD patients,\textsuperscript{26,38,46-49} exceeding those of patients with other chronic medical conditions, such as heart failure and cancer.\textsuperscript{50} Anxiety has a significant effect on the course and impact of COPD. It is associated with decreased quality of life, more severe dyspnea, greater disability, and impaired functional status,\textsuperscript{14,27} even after controlling for lung function, baseline levels of dyspnea, and the presence of other chronic diseases.\textsuperscript{26,51} Anxiety is also a significant predictor of the frequency of hospitalizations for acute exacerbations of COPD.\textsuperscript{52} Many primary care physicians are less familiar and comfortable with the tools for the screening and diagnosis of anxiety than they are with those for depression. Compared with depression, the screening for anxiety disorders in medical clinics has received relatively little attention. Means-Christensen and coworkers\textsuperscript{53} were not exaggerating when they stated recently, "... there is little controversy surrounding the issue of screening for anxiety [in primary care] because guidelines, or even suggestions, for screening for anxiety are almost nonexistent." Nonetheless, there are some data, as well as expert consensus, that can be used to guide efforts to screen for and treat anxiety disorders in medical settings.

A number of different instruments have been used for screening for anxiety and depression. Effective screening tools need not be time-consuming. The Anxiety and Depression Detector is a 5-item screening instrument with good sensitivity and specificity in screening for anxiety and depressive disorder in primary care settings.\textsuperscript{53} Another 5-item instrument taken from the larger PHQ also has demonstrated effectiveness in screening for anxiety and depression in COPD patients.\textsuperscript{54} To our knowledge, there are no published randomized controlled studies of treatments for anxiety disorders in patients with COPD. However, a number of studies report decreased anxiety symptoms in COPD patients after they received pharmacological therapy, CBT, and exercise therapies (including pulmonary rehabilitation). In 2 small randomized controlled studies, nortriptyline\textsuperscript{49} and
buspirone were shown to significantly reduce anxiety symptoms in COPD patients who were not assessed for the presence of anxiety disorders. In 2 series of case studies, sertraline was also shown to significantly reduce anxiety symptoms in patients with COPD. In one study, 3 of 6 COPD patients had a diagnosed panic disorder; all reported improvement in anxiety when they were treated with sertraline. CBT has been shown to reduce anxiety and disability in many, but not all, published trials. For example, Kunik and colleagues reported significant reductions in anxiety following a single 2-hour session that included education about anxiety, relaxation training, cognitive modification strategies, information on exposure, and home practice materials. Two other small studies found no significant impact of CBT interventions on anxiety in COPD patients. However, in both studies, the choice of anxiety outcome measures and small sample sizes may have limited the ability to detect real treatment effects. Participation in comprehensive pulmonary rehabilitation programs has been shown to reduce anxiety symptoms in patients who have COPD. In a series of studies, Emery and colleagues reported improvement in anxiety in those who participated in programs that included exercise, education, and stress management components. Others have found similar benefits following pulmonary rehabilitation. Finally, de Godoy and de Godoy found that adding psychotherapy to a standard pulmonary rehabilitation program further reduced anxiety and depressive symptoms compared with pulmonary rehabilitation alone.

References:

REFERENCES


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