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Chronic Obstructive Pulmonary Disease in the Older Patient

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Chronic obstructive pulmonary disease (COPD) is one of the most common chronic diseases in the world. It is a major cause of morbidity, mortality, and health care use, particularly in older adults. Although the definition of COPD has changed with time, an all-encompassing consensus definition is still lacking [1]. COPD includes a heterogeneous group of conditions characterized by expiratory airflow limitation. A key distinction from asthma is that the airflow limitation is not fully reversible, although COPD and asthma may frequently coexist [2].

The burden of COPD has been increasing for the last two decades, and it is projected to continue to increase for the next few [3,4]. In the year 2000, COPD became the fourth leading cause of death and is projected to be the fourth leading cause for disability worldwide by 2020 [5]. Worldwide it is the only leading cause of death with an increasing prevalence [6]. COPD is a leading cause of hospitalization in the United States and accounts for 19.9% of the total hospitalizations for patients aged 65 to 75 years and 18.2% of the total hospitalizations for patients aged 75 years and older [7].

The annual per-patient costs of COPD parallel those of other diseases, such as diabetes, arthritis, and cardiovascular disease [8]. The mean inpatient, outpatient, and pharmacy costs of patients aged 65 years or older who have COPD are more than twice those of age- and gender-matched control subjects who do not have COPD [9]. As the median age of the United States population increases, treatment of chronic conditions in older adults will have a significant impact on overall health care costs [10].

In the following sections, the authors review the diagnosis and management of COPD with a focus on special issues in older adults.

Risk factors

The major risk factor for the development of COPD is tobacco smoking, which accounts for 80% to 90% of the risk in the United States [11,12]. A highly significant quantitative relationship exists between pack-years of smoking and functional impairment [13]. In 2004 an estimated 20.9% (44.5 million) of United States adults were current smokers; of these, 81.3% (36.1 million) smoked every day and 18.7% (8.3 million) smoked some days [14]. Persons aged older than 65 years have the lowest prevalence (8.8%) of current cigarette smoking among all adults [14]. Data from all 50 states in the United States for 1996 through 2001 indicated that the median proportion of some-day smokers among current smokers decreased with age except in those aged 65 years and older, who had a rate of 20.3%, suggesting that older adults may smoke less heavily and less frequently [15].

Other risk factors for COPD include alpha-1 antitrypsin deficiency [16,17], occupational [18], environmental [19], and domestic air pollution, particularly in developing countries [20,21],

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mucous hypersecretion [22], and possibly airway hyper-responsiveness and asthma [23,24]. The prevalence of COPD is higher in men, but with the changing patterns in smoking habits, women may be at increased risk [25–27].

Diagnosis

The diagnosis is confirmed by the presence of mostly irreversible expiratory airflow limitation, also known as an obstructive defect, on spirometry. An obstructive defect is defined as a reduced post-bronchodilator forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) ratio. Most older subjects (approximately 80%) can perform reliable spirometry according to established standards [28–30]. Just what constitutes a reduced FEV_1/FVC ratio, however, has been the subject of some debate. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) scientific committee has recommended assigning an FEV_1/FVC ratio of 0.7 as the lower limit of normal, or the cutoff value, in all subjects [2,31]. Other authorities recommend setting this cutoff at the fifth percentile of the normal distribution range of FEV_1/FVC ratios, rather than at a fixed value of 0.7 [32–36].

The criteria chosen to define airflow limitation on spirometry, and therefore to diagnose COPD, are especially important in older patients. The FEV_1/FVC ratio decreases with age, and this relative degree of airflow limitation is attributed to increased airway collapsibility in the normal aging lung [37,38]. Using a fixed FEV_1/FVC ratio to separate normal from "obstruction" creates a risk for over-diagnosis of COPD in older subjects [39–41]. Up to one fifth of current smokers and one seventh of never-smokers beyond the sixth decade may be misidentified as abnormal when a fixed cut-off is used [42]. Approximately one half of people greater than 80 years old would be misclassified as having COPD [40]. The debate is further complicated by data from the Cardiovascular Health Study, which showed that subjects aged 65 years or older who are identified as normal using the normal distribution cut-offs but who have an FEV_1/FVC ratio less than or equal to 0.7 are more likely to die and have COPD-related hospitalizations [43]. A clear consensus definition of pathologic airflow limitation and related diagnostic criteria for COPD in older patients is thus urgently needed.

On the other hand, under-diagnosis may also occur when the disease is mild. A population study applying the GOLD criteria found that only 5% of patients who had mild COPD were correctly diagnosed [44]. Older patients may be underdiagnosed because they are less likely to report mild symptoms [45,46]. Older subjects who have asthma may be misdiagnosed as having COPD, although the two conditions frequently coexist [47,48].

Prevalence

The estimation of the prevalence of COPD has been influenced by various factors, such as by the differences in the rates of disease occurrence, the definition used, and whether spirometry was used to confirm the diagnosis. Most well-designed studies have found a measured prevalence of between 4% and 10% of adults in Europe and North America [49]. Data from the Third National Health and Nutrition Examination Survey (NHANES III) estimated a prevalence of 6.8% across all age groups in the United States [50]. The prevalence of all classes of COPD increases with increasing age [45]. A Finnish population-based study found a prevalence of 12.5% in men and 3% in women of age greater than 80 years, and this increased among active smokers to 35% in men and 13% in women [51]. Using the GOLD criteria, 25% of the United States population aged 75 years or older have moderate COPD [7].

Management of stable chronic obstructive pulmonary disease

Smoking cessation

The most important intervention in the care of patients who have COPD is smoking cessation. Smoking cessation slows the smoking-induced accelerated rate of decline in lung function [52,53]. Older COPD patients are no exception; smoking cessation in older patients improves health and reduces mortality regardless of the severity of the pulmonary impairment [54,55]. Male smokers who quit at age 65 years stand to gain 2.0 years of life expectancy and female smokers who quit at age 65 years stand to gain 3.7 years [56].

Interventions to quit smoking, though not uniformly successful, significantly decrease mortality [57]. Useful interventions include physician counseling, behavioral therapy, and pharmacologic adjuncts. Effective first-line pharmacologic agents include nicotine replacement, bupropion, and varenicline. Nicotine [58], bupropion [59],

and varenicline [60,61] seem to be effective, safe, and well-tolerated in the subgroups of subjects aged 65 to 75 years included in clinical trials. Unfortunately physicians are less likely to advise smoking cessation to older patients [62].

Pharmacologic management

After smoking cessation, pharmacologic treatment is focused on improving symptoms, exercise tolerance, and rates and severity of exacerbations. To date, none of the existing medications for COPD have been proven to modify the long-term decline in lung function.

Bronchodilators

Bronchodilators have long been the mainstay of symptom management in patients who have COPD, although they have not been shown to affect the rate of decline in lung function or survival [63,64]. The three main categories of bronchodilators are the β-agonists, the anticholinergics, and the methylxanthines. Current bronchodilator treatment emphasizes inhaled β-agonists, anticholinergics, or combinations of both. Short-acting bronchodilators increase exercise tolerance acutely and decrease dynamic hyperinflation, thereby decreasing the sensation of dyspnea [65,66]. Combination therapy with short-acting β-agonists and anticholinergics (ipratropium) may be better than monotherapy for improving spirometry and reducing the need for systemic steroids [67–69]. Long-acting β-agonists (LABA) improve lung function, health status, and frequency of exacerbations compared with placebo [70,71]. LABA improve lung function and possibly health status when compared with short-acting ipratropium [72], and combination therapy with these agents improves lung function and quality of life (QOL) more than either agent alone [73]. LABA and theophylline in combination may be more effective than either agent alone [74].

The long-acting anticholinergic agent tiotropium has shown to improve lung function, dyspnea, QOL, and frequency of exacerbations compared with placebo and with ipratropium [75,76]. Although no significant differences were found when tiotropium was compared with LABA in frequency of exacerbations or hospitalizations [77], tiotropium was shown to be superior in improving lung function [78,79].

Inhaled corticosteroids

Although anti-inflammatory inhaled corticosteroids (ICS) have a clear-cut role in the treatment of asthma, proof of benefit in patients who have COPD has been much harder to demonstrate or quantify. Use of ICS has been associated with some improvement in lung function, airway reactivity, frequency of exacerbations, and respiratory symptoms, but ICS do not affect the progressive decline in FEV_1 [80–83]. Higher rates of exacerbations were noted when ICS were withdrawn [84,85]. More data are needed on the incidence of adverse effects of ICS, particularly when used in a high-dose, prolonged maintenance approach that has been the objective of recent clinical trials. Although budesonide and fluticasone have not been shown to increase the risk for fractures or to decrease bone mineral density (BMD), BMD was significantly lower in those treated with triamcinolone for 3 years [80,82,86]. The long-term effects of ICS on BMD beyond 5 years are unknown. Recently the probability of having pneumonia has also been reported to be higher in those who were treated with ICS [87].

Combination therapy of inhaled corticosteroids and bronchodilators

Combination therapy with ICS and LABA has been associated with better lung function and symptom control, decreased frequency of exacerbations, and improved health status than either component alone, with greater benefit seen in those with more severe disease ($FEV_1 < 50\%$ predicted) [87–91]. Thus far no survival benefit has been shown [87]. A recent trial showed that a combination of tiotropium plus fluticasone–salmeterol improved lung function and disease-specific QOL and reduced the number of hospitalizations for COPD exacerbation and all-cause hospitalizations compared with tiotropium plus placebo, without affecting the rates of COPD exacerbation [92]. The same study also showed that tiotropium plus salmeterol did not statistically improve lung function or hospitalization rates compared with tiotropium plus placebo, suggesting that these agents may work best in the presence of an ICS [92].

Aerosol formulations and delivery devices

Inhaled bronchodilators and corticosteroids can be delivered by way of metered dose inhaler (MDI), dry powder inhaler (DPI), or compressor nebulizer. The efficacy of inhaled medications depends on the amount of drug delivered to the airways. Drug deposition depends on several factors, including inhalation technique. In older patients, inhalation technique may be hindered by

cognitive impairment and physical problems with vision, arthritis, and manual dexterity [93–96].

Although the MDI is most commonly prescribed, only 60% of older people have been reported to have adequate MDI technique subjectively, and the number decreases to 36% when objective criteria are used [97]. Most older patients are able to use MDI correctly when it is connected to large-volume spacer devices [98]. Up to 85% of older patients, however, do not use the spacer when prescribed [94].

As an alternative to the MDI, the breath-activated DPI requires less coordination, but a certain minimum negative peak inspiratory flow (PIF) is needed during inhalation for adequate drug delivery [99]. Older patients may not be able to generate sufficient PIF, because there is a significant negative correlation between age and the PIF, regardless of the severity of the underlying COPD [94].

For sicker, less capable patients, nebulizers are an option, but the benefits and limitations have not been adequately studied. Whichever device is prescribed, proper patient education on its use is critical, and assessment of inhalation technique should be part of subsequent visits to the physician [100].

Nonpharmacologic interventions

Long-term oxygen therapy

Two well-designed trials showed that, in COPD patients who have a resting Pa_{O_2} of less than or equal to 55 mm Hg on room air, long-term oxygen therapy (LTOT) for at least 15 hours daily improves survival, exercise tolerance, sleep, and cognitive function [101,102]. Continuous long-term home oxygen therapy is therefore recommended for patients in this category. Although comparable benefits have not been demonstrated in patients who have mild to moderate hypoxemia (Pa_{O_2} 56–65 mm Hg) or nocturnal desaturation, some questions remain about the potential benefits of LTOT in these and other subgroups of patients [103,104]. The National Heart, Lung and Blood Institute (NHLBI) has targeted several unanswered questions about LTOT for future research [105].

Pulmonary rehabilitation

Patients who have advanced COPD complain of significant dyspnea and exercise intolerance. These symptoms have been attributed to ventilatory and gas exchange limitations, skeletal and respiratory muscle weakness, cardiac dysfunction, and deconditioning [106,107]. Pulmonary rehabilitation improves dyspnea, exercise tolerance, and QOL, and these gains are maintained over an extended period of time [107–109]. It has also shown to improve anxiety and depression independent of the changes in dyspnea and QOL [110]. Although pulmonary rehabilitation does not have any significant effect on hospitalization rate or mortality, it has been shown to be cost-effective and benefits all stages of COPD [108,109,111]. Pulmonary rehabilitation can also be successfully undertaken from home [112]. Pulmonary rehabilitation is as successful in increasing effort tolerance in older patients as it is in younger patients [113]. Hence, age itself is not a limiting factor, and pulmonary rehabilitation should be offered to all patients who have COPD.

Immunizations

Older persons who have COPD are at high risk for complications from influenza. Immunization against influenza in this group is associated with a 52% reduction in hospitalizations for all episodes of influenza and pneumonia, a 70% reduction in deaths from all causes, and significant cost savings [114,115]. The role of pneumococcal vaccine in COPD is less clear. Although pneumococcal vaccine has shown to reduce mortality and hospitalization in the general older population, data for its effectiveness in patients who have COPD are sparse [116,117]. A recent Cochrane review found no evidence that pneumococcal vaccination in patients who have COPD had any significant impact on mortality or morbidity [118]. Large-scale randomized trials would be needed to address this issue.

Nutrition

A low body mass index (BMI) is widely prevalent in older patients, particularly in hospital or institutional settings, and is a key determinant of morbidity and mortality [119–124]. Malnutrition is a long-recognized complication of COPD; 20% to 30% of patients who have advanced COPD have a BMI of less than 20 [125–127]. A low BMI has been shown to be an independent predictor of mortality, regardless of the pulmonary status, even in those on long-term oxygen therapy [126–130]. Intervention to stop weight loss and to also reverse weight loss has been shown to be feasible in older patients [131]. Small studies have shown that nutritional supplementation in patients who have COPD improves respiratory muscle strength and endurance but not

necessarily lung function [132–134]. In a prospective study, weight gain of greater than 2 kg over 8 weeks with either nutritional therapy alone or in combination with anabolic steroids was a significant predictor of survival [129]. A low fat-free mass (FFM) has been shown to be an independent predictor of mortality in patients who have COPD, even in patients who have a normal BMI [135–137]. This may explain why even a normal BMI in patients who have COPD has been shown to be associated with increased mortality [130]. A decline in FFM has also been shown to be associated with the frequency of COPD exacerbations and the use of corticosteroids [138]. The use of anabolic steroids in patients who have COPD has been shown to improve muscle strength, mass, and endurance, and the weight gained with their use is associated with increased survival [129,139,140]. Caution, however, has to be exercised, particularly in light of the adverse events associated with another anabolic hormone, growth hormone, noted in older patients [141]. Increased attention to nutrition in this vulnerable population may improve survival.

Role of comorbidities

Most patients who have COPD, particularly older adults, have additional clinically significant illnesses, or comorbidities, which are projected to have an increasing impact on QOL, health care costs, mortality risk, and actual cause of death [142–145]. Common comorbidities include cardiovascular diseases, lung cancer, and osteoporosis. In a cohort study of 270 patients discharged after a COPD exacerbation, the most common comorbidities were hypertension (28%), diabetes mellitus (14%), and ischemic heart disease (10%) [146]. In a small study of 27 older patients who had a mean age of 76 years, there was a significant correlation between increasing comorbidity and declining QOL and activities of daily living scores [147].

Among patients hospitalized with COPD exacerbation, individuals who have more comorbidities are more than five times more likely to die in hospital compared with patients who have COPD without comorbidities even after adjustment for a wide range of confounders, including age and sex [148]. Comorbidities are also predictive factors for all-cause and respiratory mortality in patients who have COPD treated with LTOT [130]. In evaluating the causes of death in patients who had chronic respiratory failure, Zielinski and colleagues [149] reported that acute-on-chronic respiratory failure caused death in only 38% of patients, whereas heart failure, pulmonary infection, pulmonary embolism, cardiac arrhythmia, lung cancer, and other malignancies were responsible for the remaining deaths. Furthermore, in the much larger Lung Health Study, deaths caused by respiratory causes other than lung cancer accounted for only 7.8% of the deaths, whereas lung cancer, cardiovascular disease, and non-lung organ cancers accounted for 33%, 22%, and 21%, respectively, highlighting the importance of comorbidities [57].

Cardiac dysfunction and cardiovascular diseases are emerging as major causes of death in patients who have COPD [145,146]. Pulmonary embolism nearly doubled the risk for dying within 1 year [150]. As the role of these other illnesses is further elucidated, future study design and patient management are likely to focus more on all-cause mortality and the role of adjunctive therapies for comorbid conditions.

Depression and anxiety

Depression and anxiety affect the functional status of older patients who have COPD [151]. Up to 42% of patients who have COPD across all age groups may be depressed [152,153]. Among older patients who have COPD, 42% to 46% have been reported to be depressed, and new onset of depression in these patients is a risk factor for the development of cognitive decline [154–156]. The rates of depression in community-dwelling patients who have COPD are comparable to the rates of depression in hospitalized older patients [157,158]. QOL measures correlate more with depression than spirometry or exercise tolerance [153,154,159]. Patients who report poor QOL caused by their COPD are more likely to be depressed and poorly adherent to treatment, and depressed patients are more likely to smoke [152,155].

Anxiety in patients who have COPD may be less prevalent, with reported prevalence ranging from 2% to 37% [152,153,155,160]. In older patients, anxiety is associated with the level of physical functioning and disability and is a major predictor for the frequency of hospital admission for the exacerbation of COPD [155,161].

Early detection and treatment of depression and anxiety may play a critical role in improving QOL for patients who have COPD. Smaller trials including patients from all age groups have attempted to address this issue using pharmacotherapy [162,163]. In one study from the United

Kingdom, use of the antidepressant paroxetine for at least 3 months was associated with significant improvement in depression and exercise tolerance as measured by the 6-minute walking test [164]. A small feasibility study, however, looking at the usefulness of antidepressants in older patients who had COPD and depression showed a high rate of refusal to take therapy (72%) [165]. Adding patient education to traditional pharmacotherapy for depression may improve adherence to depression and COPD treatments in older adults [166].

Quality of life

Factors that contribute to QOL in patients who have COPD are poorly understood. Studies looking at the relationship between FEV_1 and QOL have shown variable results. When studies used non–disease-specific measures of QOL, no relationship was noted between the percentage predicted of the FEV_1 and the QOL measures [167,168]. Others have shown that physiologic variables such as air flow limitation and diffusing capacity may have a correlation with QOL measures [169,170]. A disease-specific instrument is believed to give a more reasonable estimate of the QOL in a specific subpopulation [171]. In a larger study looking at 321 patients staged based on the American Thoracic Society criteria [33], patient scores on the St. George's Respiratory Questionnaire [172] were moderately to strongly associated with disease staging, and comorbid conditions influenced the deterioration of QOL across all stages [142].

Anxiety and depression in older adults seem to influence not only respiratory symptoms but also QOL [161,169,173]. QOL after a hospital discharge following a COPD exacerbation was poor, and in one study the frequency of exacerbations and the severity of dyspnea had the most significant effect on QOL [174].

Prognosis

Determining prognosis or remaining life expectancy in individual patients who have COPD is fraught with uncertainty. Across all age groups, age, smoking status, poor pulmonary function, and low BMI are important predictors of mortality [128,175–178]. Predictors of mortality in older outpatients who have COPD include FEV_1, the severity of physical disability, advancing age, and the use of long-term oxygen therapy, whereas smoking status, depression and QOL scores, presence and number of comorbid diseases, and the frequency of hospitalization did not predict mortality [179]. Of note, in the same study, mortality was much higher in those on LTOT, which may define a subgroup of older patients who have a poor prognosis [179].

The frequency of COPD exacerbations, particularly those that result in hospitalization, correlates with increasing mortality and is an independent predictor of poor outcome [180]. In patients aged 65 years or older, mortality following an intensive care unit admission for COPD exacerbation may be as high as 30% at hospital discharge and 59% at 1 year [181]. The same study also showed that the hospital and longer-term mortality strongly correlated with the development of nonrespiratory organ system dysfunction and the severity of the lung disease, but not with the need for mechanical ventilation [181]. Following a hospital admission for COPD exacerbation, comorbidities, depression, marital status, and QOL have been shown to be strong predictors of mortality in older patients who have COPD [182].

Palliative care, end of life, and care-giver issues

Even with various mortality predictions, it can be difficult to identify when a patient who has COPD might be entering the terminal phase. In addition, much of the usual COPD treatment is symptom-related and of low toxicity. These factors limit the usefulness of sharp distinctions between active and palliative treatment in many patients during periods of relative stability. Usual care should address symptoms of pain, dyspnea, anxiety, and depression at all stages of disease. Approximately 20% to 25% of patients who have COPD experience severe pain, however, and many experience depression, anxiety, and breathlessness toward the end of their life [183–185]. Older patients who have severe COPD have worse QOL and emotional well-being than patients who have unresectable non-small cell lung cancer [186]. There is a definite role for symptom management by palliative care specialists, but management guidelines may not provide this emphasis [187,188].

In contrast to typical outpatient management, acute severe illness may offer major end-of-life choices, such as whether to forego intubation and mechanical ventilation or to limit its duration, whether to accept less invasive modes of treatment, or whether to forego hospitalization itself. Although patients who have advanced COPD are

just as unwilling to remain on mechanical ventilation as patients who have lung cancer, they are provided with fewer palliative options than those who have cancer [183]. Patients need opportunities to discuss the benefits and burdens of these interventions versus a less invasive, comfort-based approach and they need adequate palliative care services to support the latter approach if preferred.

Older patients who have COPD should identify specific surrogate decision-makers, who should, along with other appropriate family members, be included in end-of-life discussions whenever possible. Patients and families are frequently unaware of the extent to which interventions such as mechanical ventilation may reduce the patient's own decision-making capacity and require a family member or other surrogate to act on the patient's behalf.

Caregivers suffer from excess strain in caring for these patients [189], and spouses may have levels of psychologic problems comparable to the patients themselves [190]. Attention to these issues over the entire course of the disease improves the lives of patients who have COPD.

Summary

The incidence and burden of COPD is high and continues to increase. With the aging of the general population, COPD will be an increasingly common problem in older adults. Most older patients can perform spirometry, which is needed for an accurate diagnosis. Consensus criteria are needed to define normal spirometry versus airflow limitation in older subjects. Older patients who have COPD benefit from all effective therapies available to treat COPD, including smoking cessation, immunization, home oxygen, and inhaled medications. The forms of inhaled medications prescribed for older patients must take into account their individual limitations with technique and the need for instruction. Older patients have more comorbidities that influence QOL, prognosis, and medical management. Many older patients who have COPD need guidance and support for end-of-life decisions and discussions, and adequate support services for a more palliative approach should be available if desired.

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