

Chronic Obstructive Pulmonary Disease: Epidemiology, Pathogenesis, Disease Course, and Prognosis

Dennis E. Doherty, MD, FCCP

*Professor of Medicine and Chief
Division of Pulmonary and Critical Care Medicine
University of Kentucky Medical Center
Lexington Veterans Administration Medical Center
Lexington, Kentucky
Chairman, National Lung Health Education Program (NLHEP)*

Dick D. Briggs, Jr., MD, MACP, Master FCCP

*Emeritus Professor and Eminent Scholar Chair
University of Alabama, Birmingham
Chief Medical Officer, Best Doctors™
Boston, Massachusetts*

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death in the United States and is increasing in incidence. COPD is easily identified in its early stages by spirometry, yet it is still underdiagnosed, largely because this simple test is not being done in patients at risk for the development of COPD. The most important risk factor by far is cigarette smoking—smoking cessation or even a decrease in smoking can substantially reduce the risk for the development and/or rate of progression of COPD. Increased public awareness, early diagnosis and intervention, and secondary prevention by primary care providers may help reverse the trend of escalating prevalence, mortality, and premature morbidity associated with COPD. (*Clinical Cornerstone*.[®] 2004;6[Suppl 2]:S5–S16) Copyright © 2004 Excerpta Medica, Inc.

Chronic obstructive pulmonary disease (COPD) is the most common chronic lung disease seen on a day-to-day basis in the offices of primary care clinicians, and is associated with significant morbidity and mortality. In the United States, COPD is the fourth leading cause of death behind coronary heart disease, cancer, and stroke, and accounts for more than \$30 billion in annual health care costs.¹ An estimated 16 million adults are affected by COPD,² and each year ~120,000 Americans die of the disease.³ In contrast to the mortality rates for coronary artery disease, stroke, and cancer, which have consistently declined since 1965, mortality related to COPD has increased dramatically in the last 40 years.³ These alarming

statistics have prompted the need for increased awareness of COPD among clinicians, patients, health care organizations, and the general public.

KEY POINT

COPD is the fourth leading cause of death in the United States behind coronary heart disease, cancer, and stroke.

DEFINITION OF COPD

The following description of COPD is a composite of the definitions proposed by the Global Initiative for Chronic Obstructive Lung Disease (GOLD),⁴ American Thoracic Society (ATS),^{5*} and British Thoracic Society⁶ (COPD, rather than chronic bronchitis or emphysema, is now the preferred term):

COPD is a chronic disease characterized by airway/alveolar/systemic inflammation, with measured airflow obstruction ($FEV_1/FVC^{\dagger} < 70\%$ and $FEV_1 < 80\%$ predicted) that is partially reversible (but usually not to normal) with bronchodilator therapy.

This definition of COPD reflects a new level of optimism; COPD is no longer considered an irreversible obstructive lung disease, but rather a disease in which airflow obstruction and other key characteristics may be partially reversed with the appropriate use of pharmacologic and nonpharmacologic therapies.^{4,6} This proposed definition also stresses the idea that COPD influences systemic inflammatory disease in addition to being an inflammatory disease of the airways and alveoli.⁷ The local and systemic release of inflammatory mediators by the lung cells leads to airways disease (chronic obstructive bronchitis) and, in

KEY POINT

COPD is partially reversible with the appropriate use of pharmacologic and nonpharmacologic therapies.

a minority of patients, to destruction of parenchymal tissue (emphysema), both of which can result in the airflow limitation that characterizes COPD. The release of these inflammatory mediators by the lung cells may also exacerbate inflammation in other organ systems, such as that observed in coronary, cerebrovascular, and peripheral vascular conditions.⁷ In fact, COPD in itself is a risk factor for the development of osteoporosis.⁸

*New ATS guidelines are available at www.thoracic.org.

[†] FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

As suggested by the above definition, COPD comprises a partially reversible component (chronic obstructive bronchitis) and, in some patients, an irreversible component (fibrosis and emphysema). Chronic obstructive bronchitis is most common in all stages of COPD, whereas <10% of COPD patients have clinically significant emphysema (Figure 1).⁹ Not all patients with chronic obstructive bronchitis progress to significant emphysema, but most patients with significant clinical emphysema have or have had chronic bronchitis.

EPIDEMIOLOGY

Risk Factors for COPD

The major risk factor for the development of COPD is the inhalation of toxic substances, such as tobacco smoke and some chemicals.⁴ Smoking (including cigarettes, pipes, and cigars) is the cause of ~85% to 90% of COPD cases.¹⁰ The commonly cited statistic that only 15% to 20% of smokers develop COPD is a gross underestimate, because many smokers with mild to moderate symptoms are not currently recognized to have or diagnosed with COPD. In fact, 70% to 90% of smokers develop COPD, and 20% of these patients develop the disease rapidly.¹¹ A small percentage of smokers do not appear to develop clinically significant COPD, suggesting that genetic factors may modify the risk of developing disease in a few fortunate individuals. Conversely, <1% of COPD patients have α_1 -antitrypsin deficiency, a known genetic defect that

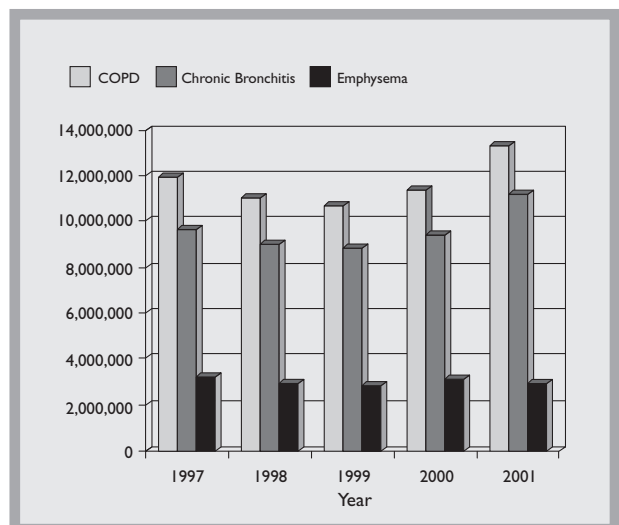


Figure 1. Number of chronic obstructive pulmonary disease (COPD) conditions in US adults, 1997–2001.⁹

makes smokers and nonsmokers more susceptible to a rapidly progressing form of COPD. Passive exposure to cigarette smoke (also known as environmental tobacco or secondhand/sidestream smoke) may contribute to respiratory symptoms and the development of COPD, as this exposure increases the lungs' total burden of inhaled particles and toxic tobacco gases.^{12,13}

Other risk factors for COPD include exposure to other types of smoke or "biomass fuels" (eg, chronic exposure to wood-burning fumes from ovens used for cooking and/or as a continuous source of heat). Chronic occupational exposure to organic and inorganic dusts, particulate matter, and fumes alone rarely leads to the development of COPD; rather the inhalation of these airborne particles may increase the risk of COPD in the presence of concurrent cigarette smoking.^{12,13} Air pollution adds to the overall burden of inhaled particles but a direct role in causing COPD has not been well defined.¹

Prevalence

Results of the 2001 National Health Interview Survey indicate that ~16 million adults aged ≥ 18 years (12.1 million adults aged ≥ 25 years) have received a COPD diagnosis from a physician.^{1,2} However, a recent report from the Centers for Disease Control and Prevention reported that the number of adults who *self-reported* that they had received a COPD diagnosis was 10 million, yet they estimated that >24 million individuals in the United States have COPD; based on all the questions contained in the survey.¹⁴ Millions of adults may be unaware that they have COPD because they only have mild to moderate symptoms which they often do not acknowledge. The Third National Health and Nutrition Examination Survey (NHANES III) found that $>70\%$ of 16,000 surveyed US adults who had abnormal lung function (measured by spirometry) characteristic of COPD had not been diagnosed with COPD.¹⁴ It is likely, therefore, that the prevalence of COPD is grossly underestimated and is closer to 40 to 50 million.¹

In 2001, of the 12.1 million COPD patients aged ≥ 25 years, 9.2 million had chronic bronchitis, 2.0 million had emphysema, and 0.9 million had both conditions.¹ The prevalence of chronic bronchitis was lowest among adults in the 25 to 44 age group.¹ In this age group as well as the elderly (≥ 65 years), the prevalence of chronic bronchitis was higher for

whites than blacks among women and men.¹ In the 45 to 64 age group, the prevalence of chronic bronchitis was higher among women, and highest among black women.¹ The prevalence of chronic bronchitis among the 45 to 64 and ≥ 65 age groups declined from 1997 to 1999 but increased in 2001.¹

As discussed, clinically significant emphysema is present in only a small percentage of COPD patients. From 1997 to 2001, the prevalence of emphysema was more than twice as high in the ≥ 65 age group than in the 45 to 64 age group, higher in men than in women, and higher in whites than in blacks.¹ The prevalence was lowest in black women.¹

Mortality

Of the top 5 leading causes of death in the United States, COPD is the only one with an increasing mortality rate in the past few decades. Since 1965, there has been a 59% decline in mortality due to coronary artery disease, a 64% decline in stroke-related deaths, and a 35% drop in deaths due to other cardiovascular diseases (**Figure 2**).³ In stark contrast, mortality from COPD has increased dramatically in the last 4 decades, by 163% from 1965 to 1998, and by 183% based on year 2000 data.³ Early detection and primary and secondary prevention widely applied to heart disease, stroke and cancer, need to be directed at COPD.

In 2000, nearly 120,000 adults ≥ 25 years died from COPD; for the first time more women (50.3% of deaths) than men died from COPD.¹ Mortality varies considerably when subcategorized by gender and/or race; death rates were consistently higher for men compared with women (82.6 vs 56.7 per 100,000) and for whites compared with blacks (70.1 vs 42.9 per 100,000) from 1995 to 2000.¹ Mortality also varies with geographic region, with the Mountain states having the highest mortality from COPD.¹

Smokers have a greater COPD mortality rate than nonsmokers; a smoker is 10 times more likely than a nonsmoker to die of COPD.¹⁰ The age at which an individual starts to smoke, total pack-years smoked, and current smoking status are all predictive of COPD mortality.

Populations at Risk

The significant epidemiologic changes in the United States reported previously, have not only identified which populations are at risk of developing

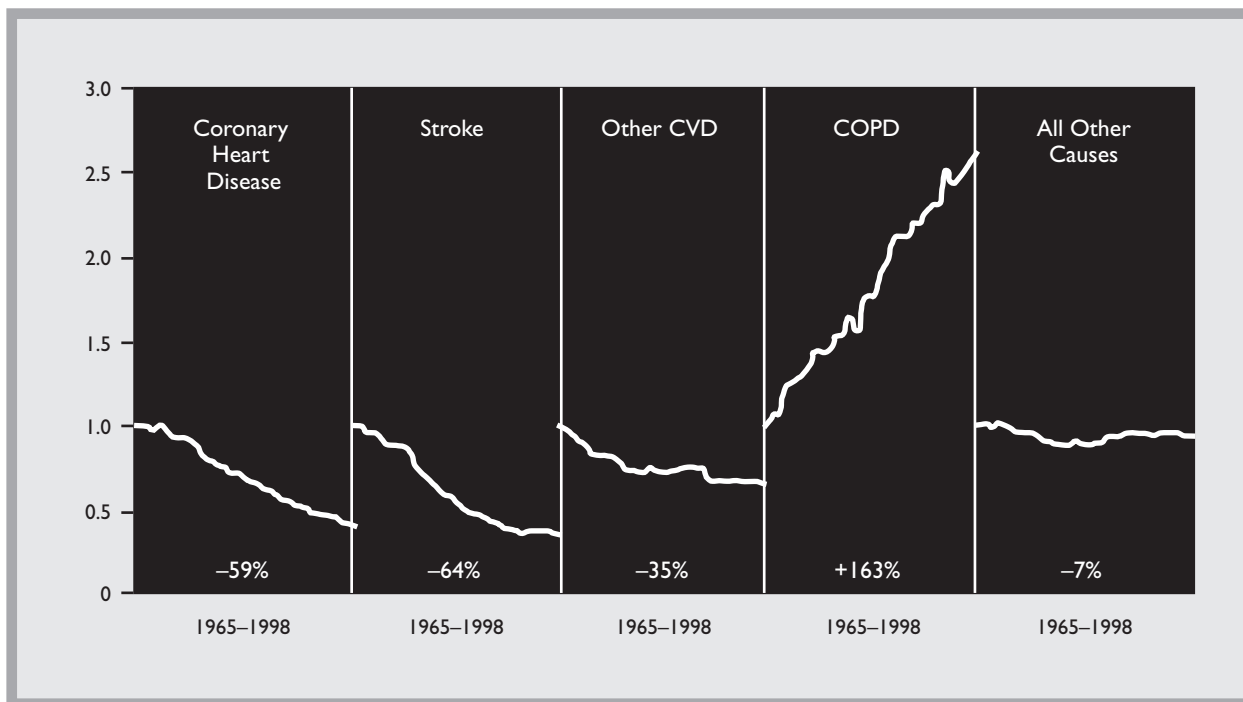


Figure 2. Percentage change in age-adjusted death rates in the United States, 1965–1998. CVD = cardiovascular disease; COPD = chronic obstructive pulmonary disease.

KEY POINT

The major risk factor for the development of COPD in the United States is the inhalation of tobacco smoke.

COPD, but also those which are dying at a higher rate from the disease. COPD is often thought of as a disease of the elderly. However, the lowering of the mean age at which the first cigarette is smoked (~10 years of age) has dramatically decreased the age at which individuals are at risk for COPD. A 20 pack-year history of smoking, often quoted as the average amount placing an individual at risk for COPD, could be reached by age 30. Therefore, even young adults who have a significant smoking history of 20 pack-years or more are at risk for COPD.

COPD is also often stereotyped as a disease of men. However, in 2000, the prevalence of self-reported COPD was higher among women than men, and in 2000, for the first time, the number of women dying from COPD exceeded the number of men dying from the disease.¹ The increase in mortality rate is also

skewed: from 1980 to 2000, the mortality rate from COPD among women increased 185%, compared with a 13% increase in men. Several hypotheses have been proposed to explain these gender differences in mortality rate. While the smoking rate among men has declined during the past 20 years, this has not been the case among women, who may be driven by peer pressure and the perception that weight gain or depression will occur with smoking cessation. It has also been hypothesized that women may be more susceptible than men to the adverse effects of tobacco smoke. Studies have shown that the effect of smoking (quantified in pack-years) on lung function parameters such as FEV₁ is significantly greater in women than in men.¹⁵ Women have been shown to have more bronchial hyperactivity to some inhaled agents; the US Lung Health Study has documented gender differences in airway hyperresponsivity to methacholine challenge (airway hyperresponsivity occurred in 85% of women smokers compared with 59% of men).¹⁶

The idea that COPD is primarily a disease of men has led to the underdiagnosis of COPD in women and the misdiagnosis of asthma in women who actually have COPD. In one study,¹⁷ primary care physicians presented with a hypothetical case—a COPD

patient with classic signs and symptoms of cough, dyspnea, a heavy smoking history, and airflow obstruction on spirometric testing—made the diagnosis of COPD 58% of the time when the patient was a man versus only 42% of the time when the patient was a woman. The women in the study were diagnosed as having asthma, which could have led to misdirected preventive and interventional therapies and delays in treatment of COPD. Delays in diagnosis and treatment of COPD may explain the dramatically increasing mortality rates for women with COPD. These trends suggest that women with a smoking history, regardless of age, should be tested for COPD with spirometry.¹⁸

Disease Burden

Results of epidemiologic surveys show that COPD does not occur predominantly in the elderly. In the NHANES III study, 70% of patients with COPD were <65 years of age; 52% of outpatient visits, 63% of emergency department visits, and 33% of hospital admissions for COPD occurred in patients <65 years of age.³ These individuals are part of the active workforce and therefore contribute to the overall economy of the United States. Accordingly, COPD in this patient population has a significant economic impact. In 2002, the cost of COPD to the health care system in the United States was estimated to be \$32.1 billion; of this, direct medical services accounted for \$18 billion and the indirect cost of morbidity and premature mortality accounted for the remainder.¹

PATHOGENESIS

The chronic inflammation, airway obstruction, and tissue damage that occur in COPD all result from chronic exposure to inhaled toxic substances, primarily cigarette smoke. Inhalation of tobacco smoke (from cigarettes, pipes, or cigars) causes inflammation of the lungs. Inflammation is the body's defensive response to any noxious substance. The inflammation can lead to tissue damage if the body's protective or repair mechanisms are uncontrolled or are overwhelmed. The inflammation in turn leads to mucous gland hypertrophy, narrowing and fibrosis of the airways, destruction of the parenchyma (the connective tissue/cells in the lungs), and changes in the blood vessels. These pathologic changes manifest themselves as mucus hypersecretion, limited airflow, hyperinfla-

tion, and gas exchange abnormalities: the major physiologic abnormalities that characterize COPD.

The Inflammatory Process in COPD

In response to the chemical insult of inhaled tobacco smoke, inflammatory cells (including macrophages, neutrophils, and T-lymphocytes, primarily CD8 lymphocytes) are activated in the small and large airways as well as in the lung parenchyma. These activated inflammatory cells release a host of cytokines and other mediators (including tumor necrosis factor- α , interleukin [IL]-8, and leukotriene B₄), which can influence damage to lung tissue.¹⁹ The release of these chemotactic cytokines attracts more inflammatory cells (neutrophils [polymorphonuclear leukocytes] and monocytes) into the lung perpetuating the process. Neutrophils can release several proteinases, including neutrophil elastase, cathepsin G, and proteinase-3, which regulate mucus hypersecretion and in some cases, the destruction of the lung parenchyma and alveolar walls.¹⁹

As previously noted, COPD is sometimes confused with asthma, particularly in women. Although asthma and COPD have airflow obstruction in common, their pathogenesis, natural history, and presentation are quite different. The cells, cytokines, and other mediators that are involved in the inflammatory process of asthma are distinctly different from those involved in the pathogenesis of COPD (**Figure 3**).²⁰ In asthma, CD4+ lymphocytes (CD4), activated eosinophils, and mast cells produce IL-4, IL-5, and IL-13, as well as a

COPD	Asthma
Macrophages	Eosinophils
PMNs	CD4 T-cells
CD8 T-cells	Activated mast cells
Proteases	Mediators
IL-8	IL-4
LT B ₄	IL-5
TNF- α	IL-13

Figure 3. Inflammatory cells and mediators involved in chronic obstructive pulmonary disease (COPD) and asthma. PMNs = polymorphonuclear leukocytes; IL = interleukin; LT = leukotriene; TNF- α = tumor necrosis factor- α .

host of other inflammatory and bronchoconstrictive mediators. All of these inflammatory cells, and thus the majority of the mediators they release, are responsive to treatment with systemic or inhaled corticosteroids, whereas the inflammatory cells and mediators in COPD are not.

The end result of the release of these cytokines and mediators may be the development of chronic inflammation of the airways, mucus gland hypertrophy and goblet-cell hyperplasia with increased mucus secretion, fibrosis around smaller airways, and in a few cases, centriacinar emphysema; ie, COPD. Abnormalities of the pulmonary vasculature can also occur; especially in those patients who have chronic hypoxemia. When vasoconstriction due to hypoxemia stimulates the proliferation of smooth muscle in the intimal layers of the pulmonary arterioles, the result can be arterial wall thickening and increased pulmonary vascular resistance that may eventually result in the development of sustained pulmonary hypertension, right heart failure, and other manifestations of cor pulmonale (peripheral edema and hepatic congestion).⁴

Narrowing of the lumen and fibrosis of the airways cause airflow obstruction. A loss in the integrity of the lung's connective tissue can lead to a decrease of elastic recoil and hyperinflation, making it even more difficult for COPD patients with airflow obstruction during exercise to exhale completely while breathing. That is, these pathophysiologic abnormalities are accentuated during exercise—as respiratory rate increases and the breath cycle time shortens, these patients do not have sufficient time for complete exhalation. Consequently, they have increased air trapping in the lung, which results in further hyperinflation (dynamic hyperinflation), and encroachment on inspiratory capacity with a decreased ability to take in air. This condition, termed dynamic hyperinflation, is a major cause of shortness of breath in patients with more severe COPD and is worsened with increased activity. Bronchodilators, especially anticholinergic agents, help to decrease hyperinflation, therefore increasing inspiratory capacity and relieving dyspnea and the work of breathing; even when no improvement occurs in FEV₁ on spirometry testing (postbronchodilator FEV₁).

The development of the chronic bronchitic component of COPD in airways is in part the consequence of

the chronic inflammation that begins in the small airways of the lung, airways that are less than a millimeter in diameter and proximal to the terminal bronchioles. COPD can also affect the alveoli, as shown by the fact that 1 in 10 patients have clinically significant emphysema. Emphysema is manifested as a destruction of alveolar attachments and a widening of the air spaces distal to the terminal bronchioles. This latter phenomenon is what leads to a progressive loss of elastic recoil and air trapping during exhalation in patients with more advanced COPD.⁴

CLINICAL CHARACTERISTICS

In its early stages, COPD may be perceived as “asymptomatic.” Some individuals may experience respiratory symptoms such as chronic cough, excess sputum production, wheezing, and shortness of breath on mild physical exertion, out of proportion to that expected for their age, although they may not acknowledge it. Tobacco smokers are more likely to experience these respiratory symptoms, but they may dismiss the symptoms as the normal consequences of smoking and fail to report them to their health care provider. These symptoms, however, can be early signs of COPD. As the disease progresses, dyspnea may become more prominent because of increased airflow obstruction and the effect of air trapping on inspiratory capacity, as well as due to the increased work of breathing needed for certain activities.

In advanced stages of disease, anorexia and weight loss, including a loss of lean body mass, may occur. The weight loss is due, in part, to increased levels of circulating tumor necrosis factor- α and dysregulation of leptin production, a hormone that regulates satiety.^{21,22} Decreased eating due to dyspnea, the effects of stomach distention on the diaphragm, and the weight loss that often occurs due to acute exacerbations can also contribute to the low body mass index (BMI) of pulmonary cachexia. This loss of lean body mass can result in decreased muscle strength and endurance, both of which negatively affect the ability to carry out activities of daily living. Low BMI adversely affects survival.^{4,20}

COPD patients also experience acute exacerbations that result in greater dyspnea, cough, sputum production, and purulent sputum than usual. Acute exacerbations have an enormous impact on the patient's quality of life and account for 70% of the

total health care dollars utilized annually to treat COPD. A median of 1.5 to 2.5 acute exacerbations occur yearly in COPD patients, if their incidence is tabulated across all stages of COPD. Acute exacerbations occur in all severity stages; however, acute exacerbations tend to occur more frequently in patients who continue to smoke and in those who have more severe airflow obstruction.²³ At least half of all acute exacerbations are precipitated by bacterial and/or viral respiratory infections. Prevention of acute exacerbations is accomplished by aggressive comprehensive care of COPD patients, that includes daily bronchodilators (especially anticholinergics), vaccinations for influenza and pneumococcus, pulmonary rehabilitation and control of comorbidities.

DIAGNOSIS

COPD can easily be diagnosed in its early stages by spirometry performed in the primary care clinician's office. During spirometry, patients inhale as deeply as possible, and exhale as hard and fast as they can, for as long as they can. The amount they exhale in the first second is termed FEV₁ and the entire amount they exhale is termed FVC. Some spirometric devices measure the volume of air exhaled from the lungs in 6 seconds (FEV₆), a surrogate for the FVC. Reference values have been validated for FEV₆²⁴ and FVC as well as FEV₁. Measurement of FEV₆ may be less demanding on patients. Measurement of FEV₁ and the FEV₁/FVC

or FEV₁/FEV₆ ratio is sufficient to identify the characteristic airway obstruction of COPD. This simple, inexpensive, and reproducible diagnostic test should now be performed in the primary care office setting using 1 of several reliable handheld portable spirometers available at low cost (\$600–\$800).¹⁸ When COPD is suspected, it is now mandatory that spirometry be performed to confirm the diagnosis, and that the results be documented in the medical record. COPD should be suspected in current or former smokers and in patients with respiratory symptoms.

Most guidelines define COPD as an FEV₁/FVC ratio <70% and an FEV₁<80% of predicted. The ATS staging system⁵ uses FEV₁ to stratify the severity of COPD. In this system, mild COPD is FEV₁<80% of predicted but ≥50% of predicted; moderate COPD is FEV₁≥35% but <50% of predicted; and severe COPD is FEV₁<35% of predicted. The GOLD initiative base their staging system on the severity of airflow obstruction measured by spirometry after bronchodilator therapy has been administered (**Table I**)²⁵; symptoms and comorbidities are also included in this staging system. With the introduction of Stage 0 disease by GOLD, wherein pulmonary function may actually still be normal but patients have risk factors or are symptomatic, GOLD emphasizes earlier recognition of the disease. Like the ATS system, the GOLD staging system stratifies COPD as mild, moderate, and severe disease (**Figure 4**). It also includes a Stage IV (very severe dis-

TABLE I. CLASSIFICATION OF SEVERITY OF COPD (GOLD).

Stage	Characteristics
0: At risk	Chronic symptoms (cough, sputum production) Normal spirometry
I: Mild COPD	FEV ₁ /FVC <70% Postbronchodilator FEV ₁ ≥80% of predicted +/- chronic symptoms (cough, sputum production)
II: Moderate COPD	FEV ₁ /FVC <70% 50% ≤ Postbronchodilator FEV ₁ <80% of predicted +/- chronic symptoms (cough, sputum production)
III: Severe COPD	FEV ₁ /FVC <70% 30% ≤ Postbronchodilator FEV ₁ <50% of predicted +/- chronic symptoms
IV: Very severe COPD	FEV ₁ /FVC <70% Postbronchodilator FEV ₁ <30% of predicted, or postbronchodilator FEV ₁ <50% of predicted with the presence of respiratory failure or right heart failure

COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity. Adapted from the GOLD Workshop Report.²⁵

ATS criteria based on simple prebronchodilator FEV ₁	% Predicted FEV ₁	New GOLD criteria based on postbronchodilator FEV ₁ with FEV ₁ /FVC <70%
	100	I Mild
I Mild	80	II Moderate
II Moderate	50 35	III Severe
III Severe	30	
	0	IV Very Severe

Figure 4. Staging of severity of chronic obstructive pulmonary disease by the American Thoracic Society (ATS)⁵ and the Global Initiative for Chronic Obstructive Lung Disease (GOLD).²⁵ FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity.

ease) category, which comprises COPD disease characterized by postbronchodilator FEV₁ <30% of predicted, or an FEV₁ <50% of predicted with the presence of respiratory failure or right heart failure.

Because the symptoms of COPD are often not acknowledged or reported to the clinician, all patients with a history of smoking and all patients with respiratory symptoms such as chronic cough, excess

mucus production, and/or dyspnea should undergo a spirometric evaluation. These patients often have air-flow obstruction on spirometry and meet the criteria for a diagnosis of COPD.

Differential Diagnosis

As discussed, COPD is often misdiagnosed as asthma. Although the 2 conditions have similar symptoms, such as coughing and wheezing, they are quite different with respect to the underlying inflammatory process. A careful patient history can help distinguish COPD from asthma (Table II). Asthma can occur at any age, but typically has an onset during infancy, childhood, or adolescence.²⁶ An initial onset of asthma after 40 years of age is rare. When a patient >40 years of age presents with symptoms consistent with an obstructive lung disease and has no history of asthma as a child or adolescent, the diagnosis is commonly COPD. This is especially true when the patient has a history of tobacco smoking. Mild COPD usually begins to develop in smokers and former smokers between the ages of 30 and 45 years, depending on the age that they started smoking and the amount that they have smoked. On average, COPD begins to develop after a 20 pack-year smoking history. Allergies and atopy are key indicators in asthma, but are relatively unimportant in COPD. Exacerbations of asthma are typically triggered by allergens, exercise, or cold air.¹⁰ However, COPD patients have exacerbations commonly caused by respiratory tract infections (bacterial or viral).²⁰ In addition, asthma symptoms are often reversible with

TABLE II. DIFFERENTIAL DIAGNOSIS OF COPD VERSUS ASTHMA.

	COPD	Asthma
Age of onset	Usually >30 years	Usually <30 years, but any age
Atopic history (family, personal)	Rarely	Usually present
Smoking history	Often >20 pack-years	Little smoking history
Symptoms	Chronic and persistent	Intermittent, usually symptom-free
Response to inhaled bronchodilators	Significant to little response; PFTs do not normalize	Rapid response; PFTs may greatly improve
Response to corticosteroids	Nonresponsive during stable disease (ie, when no exacerbation is present)	Responsive; improved PFTs

COPD = chronic obstructive pulmonary disease; PFTs = pulmonary function tests. Adapted with permission.¹⁸

treatment; patients may become symptom-free, with near-normal lung function between exacerbations.¹⁰ On the other hand, COPD symptoms tend to persist although they may decrease in intensity. The airflow obstruction in COPD may be only partially reversible with the use of a bronchodilator and/or smoking cessation.⁵ In-office spirometry can sometimes aid in the differential diagnosis of COPD versus asthma or other respiratory diseases, if airflow obstruction reverses 100% to normal, after bronchodilator administration as it may in some asthma patients. As discussed earlier, the inflammatory processes underlying asthma and COPD are distinct from each other. The inflammation in asthma is highly corticosteroid-responsive; hence, first-line therapy for asthma patients is generally an inhaled corticosteroid (ICS) with or without a leukotriene modifier, plus the addition of a bronchodilator as needed for symptom control.¹⁰ In stable COPD, the inflammatory process is not responsive to steroids; however, COPD symptoms, exacerbations, and lung function are responsive to therapy with bronchodilators, which in turn often leads to decreased dyspnea and an improved quality of life. Current guidelines for the pharmacologic management of stable COPD recommend initial treatment with a bronchodilator, ie, an anticholinergic agent as maintenance therapy, with the addition of a second bronchodilator, ie, a β_2 -agonist as needed to maximize bronchodilation and control symptoms. A trial of ICSs with β_2 -agonists, that may be added to ongoing maintenance therapy with an anticholinergic agent, is reserved for patients with severe COPD whose symptoms and exacerbation frequency are not controlled with maximized bronchodilator therapy (more than 1 bronchodilator in the maintenance regimen).⁴ If 6 to 12 weeks of ICS therapy does not decrease acute exacerbations, symptoms, or other measurable outcomes, the ICS trial should be stopped.

Patient Evaluation

An effective evaluation of the COPD patient does not end with spirometry. The severity of the patient's symptoms (eg, dyspnea, cough, sputum production) and his/her exercise capacity must be evaluated. These parameters often affect the patient's ability to carry out activities of daily living and therefore qual-

ity of life. Routine quantitation of these parameters, in conjunction with serial spirometry measurements, throughout the course of the disease can help clinicians assess the progression of COPD in their patients, as well as the impact/efficacy of the therapies that they prescribe.²⁷ Six-minute walk distances may be a helpful functional measurement. Details of the frequency and severity of a patient's exacerbations should also be a routine part of a COPD patient's evaluation. While acute exacerbations occur at all stages, patients with moderate to severe COPD can have as many as 2 or 3 acute exacerbations of their disease every year. Exacerbations contribute to the accelerated decline in FEV₁ and the progressive loss of exercise capacity and can have a great impact on the patient's quality of life.

Prognosis

According to its definition, COPD is a partially reversible process, especially with a reduction in or cessation of smoking and/or after the initiation of treatment with the appropriate bronchodilator regimen and other nonpharmacologic therapies. Although smoking cessation or decreasing the amount of smoking does not lead to recovery of lost lung function, it does cause the accelerated rate of decline in FEV₁ to revert toward that of a nonsmoking subject (**Figure 5**).²⁸ Smoking cessation or even decreasing the amount of smoking, will in itself decrease mortality, not just that caused by COPD, but also mortality from other tobacco-related diseases; mortality from coronary artery disease, stroke, and lung cancer; and all-cause mortality.²⁹

Early diagnosis and initiation of appropriate bronchodilation therapy can help improve pulmonary function, relieve symptoms, and improve exercise capacity and quality of life while also decreasing the frequency of acute exacerbations. Smoking cessation (or a decrease in smoking), optimal pharmacotherapy, vaccination, appropriate use of supplemental oxygen, and pulmonary rehabilitation, alone or ideally in combination, can all decrease morbidity and premature mortality in patients with COPD. Participation in a pulmonary rehabilitation program has been shown to reduce the number of hospital admissions, the duration of hospital stay, and the frequency of acute exacerbations.⁵

The cost of caring for patients with COPD at different stages of disease has been estimated in a

recently published study. Differences in the costs per patient per year are striking if separated based on the severity of illness: ~\$1700 for mild COPD, \$5000 for moderate COPD, and \$11,000 for severe COPD.³⁰ Two thirds of the cost of treating severe disease was attributed to the cost of treating acute exacerbations, hospitalization and medication costs, and providing supplemental oxygen.^{30,31} Data from a Scandinavian study showed remarkably similar results; the cost of treating moderate disease was 3 times that of treating mild disease and the cost of treating severe disease was ~10 times that of treating mild disease.³² The results from these 2 cost-analysis studies clearly support the premise that the early diagnosis and treatment of COPD is crucial not only for improving quality of life, but also to slow the progression of COPD and ultimately to curtail the spiraling increased cost of care for this disease. Early intervention designed to prevent acute exacerbations and progression to moderate or severe disease will also clearly yield economic dividends.

CONCLUSIONS

COPD is increasing in prevalence and its associated mortality rate continues to climb at an alarming rate, especially among women. COPD remains grossly underdiagnosed—~72% of all individuals with spirometric values of COPD in the United States have not

KEY POINT

A combination of smoking cessation, pharmacotherapy, vaccines, supplemental oxygen, and pulmonary rehabilitation can prevent premature mortality in patients with COPD.

received a diagnosis of COPD.³ The reasons for this are multifold. Spirometry is not being performed in all individuals at risk for developing COPD (any current or former smoker, or anyone with one or more of the cardinal signs/symptoms of COPD, such as chronic cough, increased mucus production, wheeze, or shortness of breath on minimal exertion out of proportion to that expected for age). It may be that patients are not being questioned carefully enough about a smoking history or are not being motivated to stop smoking.¹⁸ Smoking cessation should be discussed with every patient at every visit, and appropriate persuasive measures used to convince the patient to quit. If a patient cannot or will not quit, at least get them to decrease the number of cigarettes smoked daily. There is a deficit in patient knowledge about COPD, and there is a stigma that it is self-inflicted

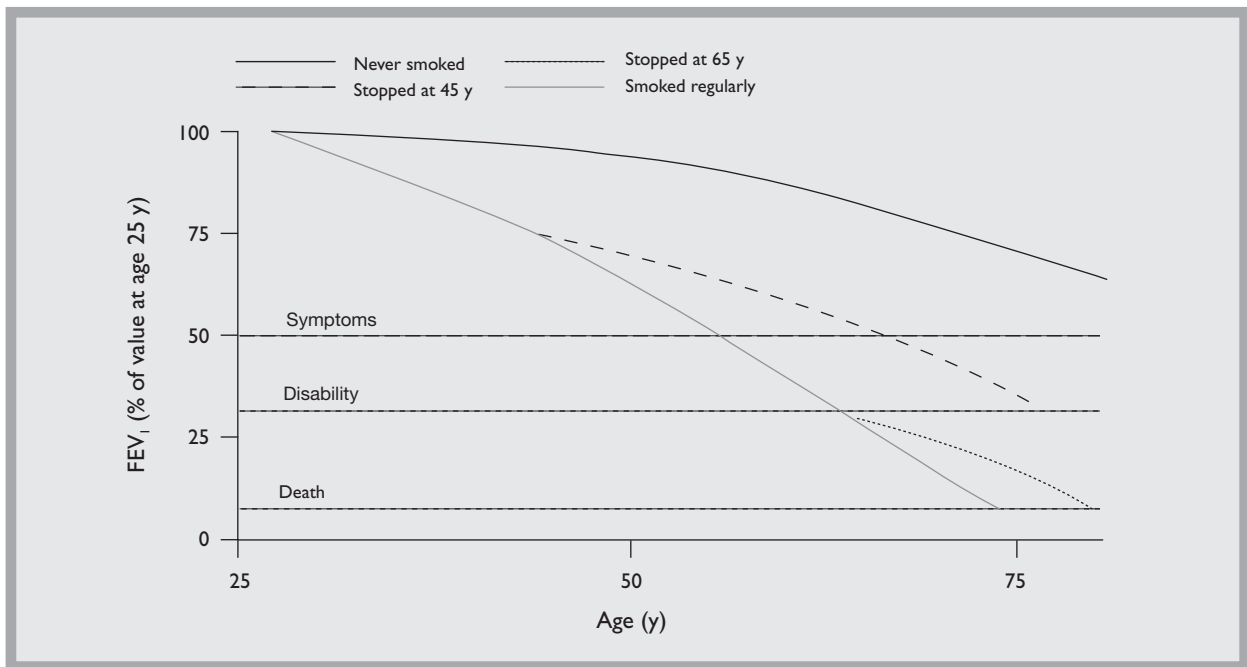


Figure 5. Changes in lung function after age 25 in smokers, nonsmokers, and ex-smokers, based on FEV₁ (forced expiratory volume in 1 second). Adapted with permission.²⁸

and untreatable. Spirometry, a valuable early detection tool, which motivates patients to stop smoking when they are presented with abnormal results, is not used as widely as it should be; widespread use of spirometry testing by family practitioners, internal medicine specialists, and Ob/Gyn physicians who provide primary care to female smokers, can help ensure that all populations at risk are tested for COPD.¹⁸

Early diagnosis by spirometry is essential since patients at risk may dismiss telltale symptoms as the normal consequences of smoking. Prompt initiation of smoking cessation therapy can help improve airflow, partially reverse impaired lung function, slow the accelerated annual decline of FEV₁ caused by tobacco smoke, and reduce the premature morbidity and mortality associated with COPD and other tobacco-related diseases. Initiation of appropriate interventions earlier rather than later, especially bronchodilator therapy, can improve symptoms, quality of life, and exercise capacity while decreasing the acute exacerbation rate and perhaps help to slow the progressive accelerated decline in lung function at minimal cost.

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