Chronic Obstructive Pulmonary Disease: Knowing What We Mean, Meaning What We Say

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is defined in several different ways using different criteria based on symptoms, physiological impairment and pathological abnormalities. While some use COPD to mean smoking related chronic airway disease, others include all disorders causing chronic airway obstruction. When COPD is used as a broad descriptive term, specific disorders that cause chronic airway obstruction remain under-diagnosed and the prevalence estimates vary considerably. The lack of agreement over the precise terminology and classification of COPD has resulted in widespread confusion. Terminology includes definition, diagnostic criteria, and a system for staging severity. Recently, COPD is defined more clearly and diagnosed using precise criteria that include tobacco smoking greater than 10 pack years, symptoms and airway obstruction on spirometry. A multi-dimensional severity grading system, the BODE (body mass index, obstruction, dyspnoea, and exercise tolerance) index has been designed to assess the respiratory and systemic expressions of COPD.

This review proposes that the broad group of chronic disorders of the airways (with or without airway obstruction) be called chronic airway disease (CAD). The term COPD should be used exclusively for tobacco smoking related chronic airway disease. Chronic airway obstruction or obstructive lung disease may be used to define those conditions with airways obstruction caused by factors other than tobacco smoking. The aetiology may be appended to the label, for example, chronic airway obstruction/obstructive lung disease associated with bronchiectasis, chronic airway obstruction/obstructive lung disease associated with obliterative bronchiolitis or chronic airway obstruction/obstructive lung disease due to biomass fuel/occupational exposure. [Indian J Chest Dis Allied Sci 2008; 50: 89-95]

Key words: Chronic airways obstruction, Asthma, Bronchiectasis, Obliterative bronchiolitis, Lungs, Respiratory, Smoking, Sputum.

INTRODUCTION

Despite tremendous advances in diagnostic technology, the 21st century categorisation of diseases continues to be poor. Chronic obstructive pulmonary disease (COPD) is one such example and includes several different clinical labels (Table 1). Chronic obstructive pulmonary disease is defined differently by clinicians, pathologists, and epidemiologists, each using different criteria based on symptoms, physiological impairment, and pathological abnormalities. Whereas “lumpers” include all disorders causing chronic airway obstruction within COPD, “splitters” use the term to mean smoking related chronic airway disease. The diagnosis of COPD is usually made by the demonstration of irreversible airway obstruction on spirometry. However, several specific diseases, such as asthma, bronchiectasis and obliterative bronchiolitis also cause chronic irreversible airway obstruction. Several of these disorders remain under-diagnosed due to the uncritical use of the term “COPD”. These are distinct disorders and must not be “lumped” together only because they share the same physiological abnormality.

We need an exclusive term to describe the chronic progressive airway disorder that occurs in current or ex-smokers who develop symptoms of cough, dyspnoea and wheeze, physical signs of emphysema and airway obstruction on spirometry. Until recently, the British referred to the disease as “chronic bronchitis” while the Americans called it “emphysema”. In 1966, the differences in nomenclature were reconciled, and both were included under the term COPD. Since then the terminology of the disease has gone through a long and non-uniform development. Care givers now view it as an ambiguous name with an uncertain meaning. Hence, terms such as “tobaccosis” and “smoker’s lung”

Table 1. Various terms used for chronic obstructive pulmonary disease

| Chronic bronchitis/Emphysema |
| Chronic obstructive airways disease (COAD) |
| Chronic airflow limitation (CAL) |
| Chronic airways obstruction (CAO) |
| Chronic non-specific lung disease (CNSLD) |
| Non-reversible obstructive airways disease (NROAD) |

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have been suggested as alternatives.\textsuperscript{12} Another suggestion is to extend the term COPD by introducing the adjectives “guiltless” (for patient who never smoked) and emphysemal (for smokers).\textsuperscript{14} However, a change in terminology at this stage will only result in more confusion and will cancel out all public awareness efforts made with the “registered trademark”.\textsuperscript{12} The best option perhaps is to encourage the present term COPD and re-define its content, making it specific to indicate smoking related chronic airway disease. This review is an attempt to differentiate the common disorders that cause airway obstruction often included under the umbrella expression “COPD”, and suggest a more precise terminology and classification of COPD.

**DIFFERENTIATING ASTHMA FROM COPD**

The “Dutch hypothesis”\textsuperscript{15} proposed a unitary hypothesis for chronic airways disorders and suggested that all were due to endogeneous factors, airway hyperreactivity (AHR) and atopy. However, most workers considered COPD to be due to an exogeneous factor, \textit{i.e.} smoking; and the Dutch hypothesis was not universally accepted. While, AHR is a constitutional factor that indicates that the airways are hyperreactive to a variety of stimuli and is seen in several conditions including asthma, COPD, cystic fibrosis, and even allergic rhinitis without asthma,\textsuperscript{16} the role of atopy in asthma has now been demonstrated in most epidemiological studies.\textsuperscript{17} Even in advanced stages with irreversible airway obstruction (“fixed”) asthma can be diagnosed by history of atopy (allergic rhinitis, asthma, atopic dermatitis, urticaria or eczema in self or family), elevated total immunoglobulin (Ig) E levels and/or previously documented reversible airway obstruction on spirometry. Treatment with modern medication has tremendous impact on the quality of life of individuals with asthma and reduction in cost of hospitalisation. Hence, it is important of differentiate asthma, the leading cause of chronic airway obstruction\textsuperscript{18} from COPD and other airway disorders. Although the American Thoracic Society (ATS) 1995 guidelines\textsuperscript{19} included asthma with an irreversible component in COPD; most guidelines including the ATS 1987\textsuperscript{20} and the European Respiratory Society (ERS) 1995\textsuperscript{a} specifically excluded asthma from COPD. The recent ATS/ERS guidelines (2004),\textsuperscript{21} recommend that asthma is a different clinical entity from COPD and suggests that when the two diseases cannot be distinguished the patient should be treated for asthma.

**OBLITERATIVE BRONCHIOLITIS: UNDER DIAGNOSED DUE TO UNCRITICAL USE OF “COPD”**

Obliterative bronchiolitis or constrictive bronchiolitis is a specific cause for airway obstruction and is due to obliteration of the respiratory bronchioles or the small airways.\textsuperscript{30-32} Small airway obstruction is seen in COPD, asthma and bronchiectasis but may occur alone when it is called obliteratorive bronchiolitis. Obliterative bronchiolitis may be caused by several factors, such as infections, most commonly virus and mycoplasma infection, collagen vascular, drugs, graft \textit{versus} host reaction and rejection after transplantation. However when obliteratorive bronchiolitis occurs without any obvious aetiology, it is termed as cryptogenic obliteratorive bronchiolitis.\textsuperscript{33} Obliterative bronchiolitis may be misdiagnosed as COPD as the chest radiograph is often normal or shows hyperinflation, and physiological studies demonstrate irreversible airway obstruction and often no response to corticosteroid therapy.

**BRONCHIECTASIS: THE ‘OTHER’ OBSTRUCTIVE LUNG DISEASE\textsuperscript{22}**

Bronchiectasis is one of the chronic airway disorders defined by the presence of persistent or recurrent airway obstruction.\textsuperscript{22} Patients with bronchiectasis suffer from sputum over-production, recurrent exacerbation and progressive airway destruction Considered an “orphan disease” in the West\textsuperscript{23} due to the decreased prevalence as a result of vaccinations and extended-spectrum antibiotics, bronchiectasis is still common in the developing countries.\textsuperscript{23} Recent studies have shown evidence of airway obstruction in cases of bronchiectasis, which may be the dominant symptom even in patients with localised disease.\textsuperscript{24,25} Airway obstruction in bronchiectasis may be due to associated small airway disease, airways inflammation and increased bronchial hyperreactivity.\textsuperscript{24,26} The pattern of physiological dysfunction observed in bronchiectasis is quite similar to that occurring in chronic bronchitis.\textsuperscript{24} The severity is related to the duration of sputum production and is independent of the extent of bronchiectasis. High resolution computed tomography (HRCT) is indicated in cases of bronchiectasis for detecting extent and cause of disease and associated airway abnormality.\textsuperscript{27,28} A recent study reported bronchiectasis in 29% of “COPD” cases evaluated with HRCT after they were clinically stable following an acute exacerbation.\textsuperscript{29} Computed tomographic (CT) scanning may, therefore play an important role in defining the exact nature and subgroup of disorders causing chronic airway obstruction. Treatment of bronchiectasis includes postural drainage, preventive vaccinations, antibiotics bronchodilators and occasionally surgical resection. The prognosis of bronchiectasis depends on the predisposing conditions, which should be aggressively sought. Even though much less common than asthma and COPD,\textsuperscript{18,22} bronchiectasis is a specific cause for chronic airway obstruction.
Turton et al. have described clinical criteria for obliterative bronchiolitis. Diagnosis of obliterative bronchiolitis can be confirmed by the characteristic HRCT findings in the correct clinical context. The findings include heterogeneity of lung density, i.e., patchy areas of high and low attenuation of the lung parenchyma ("mosaic pattern/mosaic perfusion"), thought to be a consequence of reflex vasoconstriction in under-ventilated areas of the lung. This finding is exaggerated on expiratory HRCT scan due to air trapping. Other features include fibrosis, scarring and bronchial dilatation. Spirometry findings of small airway obstruction include reduced forced expiratory volume in one second (FEV₁), reduced forced vital capacity (FVC) and a normal or reduced forced expiratory ratio, i.e., FEV₁/FVC. A paradoxical fall in FEV₁/FVC may be seen in patients with small airways obstruction following effective treatment due to preferential opening of the small airways, resulting in reduction in air trapping and improvement in FVC. Patients who survive the initial episode stabilise for several years or progress to end-stage airway disease and cor-pulmonale due to recurrent infections causing increasing loss of pulmonary functions. Inhaled therapy may not be adequate in these cases and drugs delivered by the systematic route are more likely to reach the large surface area of the small airways. Obliterative bronchiolitis (particularly post infectious) may contribute significantly to the burden of chronic airway obstruction especially in the developing country, and unless HRCT scanning is incorporated in the diagnostic algorithm, obliterative bronchiolitis is likely to remain under-diagnosed.

OTHER OBSTRUCTIVE LUNG DISEASES: MISCELLANEOUS DISORDERS ASSOCIATED WITH AIRWAY OBSTRUCTION

In addition to the common disorders seen in practice a wide and heterogeneous spectrum of diseases, including connective tissue disorders and vasculitides like Sjogren syndrome, relapsing polychondritis, and some interstitial lung diseases, chest wall deformities such as kyphoscoliosis, congestive heart failure and even upper airway disorders may manifest evidence of airway obstruction. "Chronic obstructive pulmonary disease", therefore is not any pulmonary disorder which is chronic and in which obstruction of airflow is present.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): THE CONFUSING NOSOLOGY

Sound nosology (terminology and classification of diseases) is important to enhance communication among researchers and health care givers. Guidelines and standards for diagnosis of COPD have been published and analysed during the last years. Despite these and the recent global initiative on obstructive lung disease (GOLD), COPD continues to be undiagnosed and untreated, because care givers are confused by the multiplicity of terminologies. Terminology includes definition, diagnostic criteria, and a system for staging severity, of which diagnostic criteria are more important both for clinical practice and research.

Diagnostic Criteria for COPD: Stating the Criteria Clearly

The common criterion recommended for diagnosis of COPD is demonstration of “progressive irreversible airway obstruction” on spirometry. Unfortunately, spirometry is not readily available and spirometric test results are not routinely recorded or consistently interpreted. Further, only spirometries performed by experienced personnel are of acceptable quality, and the same is not true for primary care settings. To make matters worse, most spirometric criteria for diagnosis of COPD differ considerably. GOLD now recommends that post bronchodilator FEV₁/FVC ratio of less than 0.70 must be used for the diagnosis of COPD. Demonstration of “irreversible airway obstruction,” i.e. absence of bronchodilator reversibility is not required for diagnosis of COPD, as per the recent GOLD update. Although a reasonable consensus has been reached, spirometric criteria continue to have limitations.

The predicted FEV₁/FVC ratios decrease progressively with age in adults. Thus, a fixed FEV₁/FVC ratio over-estimates airway obstruction in the elderly and under-estimates it in young adults. Obstructive abnormality is most accurately diagnosed when a reduced FEV₁/FVC ratio is below lower limit of normal, i.e. the 5th percentile of the predicted value. However, the post-bronchodilator reference values that are required for accurate interpretation of spirometry have not yet been developed. The simplification of spirometry criteria by GOLD experts is perhaps to encourage spirometry for diagnosis of COPD in primary-care settings worldwide. However, widespread spirometric testing has been reported to result in a large number of individuals, many who do not report respiratory symptoms, labeled as COPD. On the other hand, false normalisation of the FEV₁/FVC ratio that occurs due to a greater reduction in FVC caused by air trapping in severe airway obstruction may result in more severe cases being missed. Therefore, spirometry-based diagnosis of COPD and the “one size fits all” spirometric criteria are inappropriate.

In resource limited settings, COPD is primarily diagnosed by its prototype chronic bronchitis. Chronic bronchitis is defined by symptom of persistent “smokers’ cough” or a productive cough for at least
tobacco smoking. However, only 15%-50% of exposed to the causative factor. More relevant way of diagnosing COPD in individuals combination of symptoms and spirometry may be a more relevant way of diagnosing COPD in individuals exposed to the causative factor.

The dominant, confirmed cause behind COPD is tobacco smoking. However, only 15%-50% of individuals who smoke develop COPD. Polymorphism for the genes controlling xenobiotic metabolism, hence oxidant-antioxidant balance may explain this susceptibility. Tobacco is commonly smoked in the form of cigarettes worldwide. In India and other South Asian Countries, bidi (sun dried tobacco hand rolled in a tendu leaf) smoking is common due to availability and low cost. Although a bidi contains about one-fourth the amount of tobacco, bidi smoking is comparable to cigarette smoking due to the greater puff frequency needed to keep the bidi alight. Cigarette (or bidi) smoking is measured in pack-years (cigarettes a day × years of smoking) or smoking index (cigarettes a day × years of smoking/20) or smoking index (cigarettes a day × years of smoking). Although some recommend more than 20 pack-years (smoking index = 400) for diagnosis of COPD, pulmonary symptoms increase in frequency once 10 pack-years (smoking index = 200) history is reached. Hence, individuals with a 10 pack-years history should be screened for COPD.

However, 10% to 15% of cases of "COPD" have been attributed to other risk factors, such as environmental tobacco smoke (ETS) and genetic factors like alpha-1 anti-trypsin deficiency. This makes allowance for the diagnosis of "COPD" in non-smokers, although alpha-1 anti-trypsin deficiency accounts for less than one per cent cases of emphysema. The magnitude of association between COPD and passive smoking is small. Studies indicate that inhalation of smoke from burning biomass fuels in unventilated indoor spaces accounts for increased risk of "COPD" in the developing world. Occupational exposures have also been reported to contribute to the burden of COPD. Unlike tobacco smoking, it is difficult to measure exposure to noxious particles and gases (including biomass fuel or occupational exposures) that can be linked causally to airway obstruction. Also, when tobacco addition is termed merely as a "risk factor" and confused with other environmental aggressions, it dilutes the emphasis on the role of tobacco smoking in COPD.

Recent criteria are more precise and recommend that the diagnosis of COPD be based on appropriate symptoms, evidence of airway obstruction and history of measured tobacco smoking. Similar criteria, i.e. spirometry with symptoms and a smoking history of more than 10 pack-years are used for diagnosis of COPD (Table 2) in drug trials. Only a few epidemiological studies on "COPD", however, use inclusive criteria based on spirometry, symptoms and smoking history, most either use spirometric criteria alone (spirometry-defined COPD) or symptom-based criteria, resulting in widespread confusion and variations in the prevalence estimates.

### Table 2. Diagnostic criteria for COPD

<table>
<thead>
<tr>
<th>Criteria</th>
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<tbody>
<tr>
<td>A history of tobacco smoking (usually) more than 10 pack-years or smoking index &gt; 200</td>
</tr>
<tr>
<td>History of chronic progressive symptoms, like cough and/or wheeze and/or breathlessness</td>
</tr>
<tr>
<td>Objective evidence of airway obstruction on spirometry (FEV₁/FVC &lt; 0.7 and FEV₁ % predicted &lt; 80)</td>
</tr>
</tbody>
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### Severity Assessment of COPD: Multi-dimensional Staging Systems

Chronic obstructive pulmonary disease severity was initially based on symptoms (Table 3). Global Initiative on Obstructive Lung Diseases recommends that the assessment of severity of COPD be based on physiological variables, FEV₁,% predicted (Table 4) as mild>80, moderate 50-80, severe 30-50 and very severe <30 ("rule of 30-50-80"). However, FEV₁ correlates poorly to all the things that matter to patients: symptoms, quality of life, exacerbation frequency, and exercise intolerance. Chronic obstructive pulmonary disease is now recognised to have systemic manifestations that are not reflected by the FEV₁. Hence, other environmental aggressions, dilutes the emphasis on the role of tobacco smoking in COPD.

### Table 3. Severity staging based on symptoms (dyspnea) [Modified from Medical Research Council (MRC Scale)]

<table>
<thead>
<tr>
<th>Severity</th>
<th>Description</th>
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<tbody>
<tr>
<td>Mild</td>
<td>Rapid walking on flat ground or a slight slope</td>
</tr>
<tr>
<td>Moderate</td>
<td>Walking slowly on flat ground, or must stop because of breathlessness when walking at a normal pace on flat ground</td>
</tr>
<tr>
<td>Severe</td>
<td>Walking 100 metres or a few minutes on flat ground</td>
</tr>
<tr>
<td>Very Severe</td>
<td>Getting dressed</td>
</tr>
</tbody>
</table>

### Table 4. Severity staging of COPD based on spirometry

<table>
<thead>
<tr>
<th>Severity</th>
<th>FEV₁/FVC</th>
<th>FEV₁ % predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (stage I)</td>
<td>FEV₁/FVC &lt; 0.7, FEV₁ &lt; 80% predicted, with or without symptoms</td>
<td></td>
</tr>
<tr>
<td>Moderate (stage II)</td>
<td>FEV₁/FVC &lt; 0.7, FEV₁ 50-80%</td>
<td></td>
</tr>
<tr>
<td>Severe (stage III)</td>
<td>FEV₁/FVC &lt; 0.7, FEV₁ 30-50%</td>
<td></td>
</tr>
<tr>
<td>Very Severe (stage IV)</td>
<td>FEV₁/FVC &lt; 0.7, FEV₁ &lt; 30% predicted; or FEV₁ &lt; 50% but signs of right heart failure</td>
<td></td>
</tr>
</tbody>
</table>

"The Rule of 30-50-80"
a simple multi-dimensional grading system the BODE (body mass index, obstruction, dyspnoea, and exercise tolerance) index has been used to assess the respiratory and systemic expressions of COPD. The BODE staging system also helps to better predict hospitalisation for COPD.

Chronic obstructive pulmonary disease patients have a disproportionate loss of fat free mass (FFM) which is not reflected in BMI referred to as pulmonary cachexia. Hence, it is suggested that FFM is a better measure of nutritional status in these cases. The FFM index (FFM corrected for height squared) has been shown to be significant predictors of mortality, independent of covariates such as sex, smoking, and lung function. Fat free mass may be measured using dual energy x-ray absorptiometry (DEXA), bioelectric impedance analysis (BIA) and skinfold anthropometry (SFA), choice of test depending on the availability and cost. Cor-pulmonale and depression that accompany advanced disease need to be measured additionally.

Definition of COPD: Knowing What We Mean

Clear definitions and description of disease do matter. The GOLD guidelines define COPD as “a disease state characterised by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. Snider recommends a revised definition as “COPD is a disease state characterised by incompletely reversible, progressive airflow obstruction that is associated with inflammation in the lungs due to prolonged exposure to tobacco smoke and other noxious particles and gases”. In order to define COPD unambiguously, Snider’s proposed definition should be modified as “COPD is a disease state characterised by incompletely reversible, progressive airflow obstruction that is associated with inflammation in the lungs due to prolonged exposure to tobacco smoke (deleting noxious particles and gases). Therefore, the description that sums up COPD best is as “COPD is a respiratory disorder (largely) caused by smoking, characterised by progressive, partially reversible airflow obstruction, systemic manifestations, and increasing frequency and severity of exacerbations.

The cardinal symptoms experienced by patients with COPD are shortness of breath and activity limitation. The symptoms are usually insidious in onset, progressive, and typified by frequent exacerbations. Although initially confined to the lungs, systemic manifestations of skeletal muscle dysfunction, right heart failure, secondary polycythemia, depression and altered nutrition accompany advanced disease. This description is the useful to understand that smoking cessation is most effective way to alter the progression of the disease and that therapeutic intervention should target both pulmonary and systemic manifestations of COPD.

Classification of Chronic Airway Disease: Meaning What We Say

This review proposes that the broad group of chronic disorders of the airways (with or without airway obstruction) be called chronic airway disease (CAD), restricting COPD to mean tobacco smoking related chronic airway disease. The term chronic airway obstruction (CAO), chronic airflow limitation (CAL) or obstructive lung diseases (OLD) may be used to define those conditions with airways obstruction caused by factors other than tobacco smoking. The term “airway obstruction” may be more appropriate to “airflow limitation” as expiratory airflow can be limited by severe restrictive disease or impaired muscle function, whereas airway obstruction means the expiratory flow of air is blocked. The term obstructive lung disease is also appropriate as OLD forms a part of GOLD, the international consensus guidelines. The specific aetiology may be appended to the label to denote the diagnosis, for example CAO/OLD associated with bronchiectasis, CAO/OLD associated with oblitative bronchiolitis (OB) or CAO/OLD due to biomass fuel/occupational exposure.

CONCLUSIONS

The importance of uniform usage of medical terminology is obvious. “COPD” when used as a broad descriptive term is an annoyance to those who want to maintain diagnostic clarity. Clinical discussions rely on a shared language so that we do not have to re-define everything in every discussion. The various disorders that cause chronic airway obstruction have a different natural history, response to treatment and prognosis. Therfore, it is important to recognise them as distinct entities not only for the purpose of discussion but also for clinical management and research. Chronic obstructive pulmonary disease (COPD) should, therefore, be defined exclusively as tobacco smoking related chronic progressive airway disease and must be diagnosed using the criteria that support this definition.

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