Chronic Obstructive Pulmonary Disease: Clinical Integrative Physiology

Denis E. O'Donnell, MD, FRCP(I), FRCP(C)[a,*],
Pierantonio Laveneziana, MD, PhD[b], Katherine Webb, MSc[a],
J. Alberto Neder, MD, DSc[a]

KEYWORDS

• Chronic obstructive pulmonary disease • Small airways • Lung mechanics • Dyspnea • Exercise • Cardiac output

KEY POINTS

- COPD is characterized by heterogeneous physiologic abnormalities that are not adequately represented by simple spirometry.
- Extensive peripheral airway dysfunction is often present in smokers with mild spirometric abnormalities and may have negative clinical consequences.
- Activity-related dyspnea and exercise intolerance in patients with mild airway obstruction are linked to increased ventilatory inefficiency and dynamic gas trapping during exercise.
- Progressive increases in dyspnea and activity restriction are explained, in many instances, by the consequences of progressive erosion of resting inspiratory capacity.
- Although restrictive mechanics and increasing neuromechanical uncoupling of the respiratory system contribute to exercise intolerance across the spectrum of COPD severity, coexistent cardiocirculatory impairment is also potentially important.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by inflammatory injury to the intrathoracic airways, lung parenchyma, and pulmonary vasculature in highly variable combinations. It follows that the measured physiologic abnormalities are equally heterogeneous and these, in turn, likely underscore the common clinical manifestations of this complex disease. Expiratory flow limitation (EFL) is a defining physiologic characteristic of COPD and represents the final expression of diverse derangements of respiratory mechanics. Spirometric measurement of reduced maximal expiratory flow rate is required for diagnosis of COPD and can be used to follow the course of the disease. However, such measurements as forced expiratory volume in 1 second (FEV_1) are not useful in predicting the cardinal symptoms of the disease, dyspnea and exercise intolerance. This article reviews the respiratory mechanical and cardiocirculatory abnormalities across the spectrum of mild to severe COPD, at rest and during the stress of exercise.

MILD COPD

Clinical Relevance

It is well established that those with mild-to-moderate disease severity represent most patients

[a] Division of Respiratory and Critical Care Medicine, Department of Medicine, Queen's University, 102 Stuart Street, Kingston, Ontario K7L 2V6, Canada; [b] Service d'Explorations Fonctionnelles de la Respiration, de l'Exercice et de la Dyspnée Hôpital Universitaire Pitié-Salpêtrière (AP-HP), Laboratoire de Physio-Pathologie Respiratoire, Faculty of Medicine, Pierre et Marie Curie University (Paris VI), 47-83 Boulevard de l'Hôpital,75013 Paris, France
* Corresponding author. Division of Respiratory and Critical Care Medicine, Department of Medicine, Kingston General Hospital, Queen's University, Richardson House, 102 Stuart Street, Kingston, Ontario K7L 2V6, Canada.
E-mail address: odonnell@queensu.ca

Clin Chest Med 35 (2014) 51–69
http://dx.doi.org/10.1016/j.ccm.2013.09.008
0272-5231/14/$ – see front matter

with COPD, yet this subpopulation is understudied.[1,2] For the purpose of this review, mild COPD refers to spirometrically defined mild airway obstruction (ie, FEV_1 80%–100 % predicted), which need not be synonymous with early COPD. There is evidence from several population studies that, compared with nonsmoking healthy populations, smokers with mild COPD show increased mortality (including cardiovascular mortality),[3,4] increased hospitalizations, decreased health-related quality of life,[5–10] increased activity-related dyspnea, and reduced daily physical activity levels.[11–15] The underlying pathophysiologic linkages between mild COPD, dyspnea, and activity restriction have only recently become the subject of systematic study.[16–18]

Resting Physiologic Abnormalities in Mild COPD

A recent cross-sectional study of patients with COPD attests to the vast physiologic heterogeneity that exists even in those with mild airflow obstruction (**Fig. 1**).[19] Thus, in patients with a largely preserved FEV_1 there is wide variability in airways resistance (and conductance); pulmonary gas trapping; resting lung hyperinflation; and the integrity of the alveolar-capillary gas exchanging interface. Quantitative computed tomography (CT) scans also confirm a broad range of structural abnormalities in mild COPD, which include emphysema, pulmonary gas trapping, airway wall thickening, and even vascular abnormalities.[20–22]

Small airways dysfunction

The small airways are believed to be the initial locus of inflammation in COPD, and refer to the membranous (<2 mm diameter) and respiratory bronchioles.[23] Previous studies have shown evidence of active inflammation and obliteration of peripheral airways in mild COPD.[23–25] McDonough and colleagues[25] have proposed that such loss of small airways precedes the development of centrilobular emphysema. Mucus hypersecretion as a result of chronic bronchitis can also result in extensive peripheral airway dysfunction.[24,25]

Hogg and colleagues[24] were the first to report that peripheral airway resistance, measured by retrograde catheters, was increased by up to four-fold in the excised lungs of smokers with mild emphysema compared with those of healthy control subjects. This increase occurred despite normal values of total airways resistance. With the progression of emphysema, the increasing

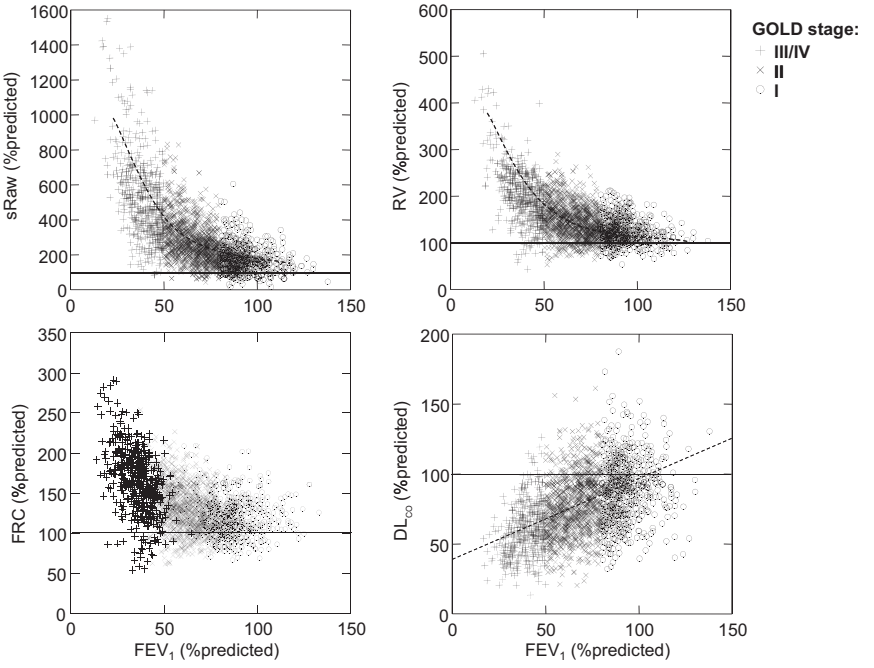

Fig. 1. Relationships between specific airway resistance (sRaw), residual volume (RV), functional residual capacity (FRC), and diffusing capacity of the lung (DL_{CO}) are shown against FEV_1 (all measurements expressed as % of predicted normal values). sRaw, RV, and FRC increased exponentially as FEV_1 decreased, and DL_{CO} decreased linearly as FEV_1 decreased. GOLD, Global Initiative on Obstructive Lung Disease. (*Modified from* Deesomchok A, Webb KA, Forkert L, et al. Lung hyperinflation and its reversibility in patients with airway obstruction of varying severity. COPD 2010;7(6):431; with permission.)