Prediction of mortality in Chronic obstructive pulmonary disease patient

Essay

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Contents

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is broadly defined and encompasses several clinical and pathologic entities, primarily emphysema and chronic bronchitis. Evidence of airflow obstruction that is chronic, progressive, and for the most part fixed, characterizes COPD. Notwithstanding the presence of irreversible airflow obstruction in COPD, most patients with the disease (60%-70%) demonstrate a reversible component of airflow obstruction when tested repeatedly (**Stevenson et al .,2005).**

Emphysema is specifically defined in pathologic terms as alveolar wall destruction with irreversible enlargement of the air spaces distal to the terminal bronchioles and without evidence of fibrosis. Chronic bronchitis is defined as productive cough that is present for a period of 3 months in each of 2 consecutive years in the absence of another identifiable cause of excessive sputum production.

The American Thoracic Society (ATS), British Thoracic Society (BTS), and European Respiratory Society (ERS) definitions of COPD emphasize chronic bronchitis and emphysema, but the Global Initiative for Chronic Obstructive Lung Disease (GOLD) proposes a definition of COPD that focuses on the progressive nature of airflow limitation and its association with abnormal inflammatory response of the lungs to various noxious particles or gases **(Celli and MacNee , 2004).**

According to the GOLD document, COPD is defined as a disease

state characterized 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 ***(Celli and MacNee, 2004)***.

Chronic obstructive pulmonary disease is associated with significant morbidity and mortality. It is estimated to affect 10–15% of the population over the age of 40 years and accounts for 3 million deaths worldwide annually. Although it is the fourth most common cause of death in the world, it is predictced to rise to the third position by the year 2020. Early identification of predictors of ulterior COPD mortality could be of benefit to many patients with this disease and could possibly facilitate the development of therapies and strategies that would improve outcomes ***(Sethi et al., 2006).***

The most tested and accepted clinical variable to help predictmortality in COPD patients is the severity of airflow obstruction as measured by the forced expiratory volume 1 (FEV_1). The same is true for decreased exercise capacity by the use of the 6-minute walk distance. Other clinically relevant variables include arterial hypercapnia, degree of breathlessness and high body mass index(BMI). From this it is clear that some of the predictive variables are not related to lung function itself and the concept evolved that the ability to predict outcome could be improved if the different variables were combined into a multidimensional index that captured the complexity of COPD One such tool is the BMI, obstruction, dyspnea and exercise

capacity (BODE) index, which includes assessments of BMI, FEV_1, dyspnea and 6-min walk distance. Other multidimensional tools that predict mortality better than the single FEV_1 have been developed, including The DOSE score, which combines dyspnea intensity, FEV_1, smoking status and frequency of exacerbations, have proven to be useful in predicting exacerbation. The DECAF score is a simple yet effective predictor of mortality in patients hospitalized with an exacerbation of COPD and has the potential to help clinicians more accurately predict prognosis, and triage place and level of care to improve outcome in this common condition **(Steer et al., 2012).**

The most recent predictors are systemic inflammatory biomarkers as C-reactive protein ratio have been observed to be independently associated with increased risk of death. When added to known clinical variables such as the BMI, obstruction, dyspnea and exercise capacity index, only IL-6 has been shown to further contribute to mortality prediction (**Kelly et al., 2013).**

List of tables:

Pathophysiology of Chronic Obstructive Pulmonary Disease

I. Definitions

Chronic obstructive pulmonary disease is a common respiratory condition involving the airways and characterized by airflow limitation. It affects more than 5 percent of the population and is associated with high morbidity and mortality. As a consequence of its high prevalence and chronicity, COPD causes high resource utilization with frequent clinician office visits, frequent hospitalizations due to acute exacerbations, and the need for chronic therapy. The definition of COPD and its subtypes (emphysema, chronic bronchitis, and chronic obstructive asthma) and the interrelationships between the closely related disorders that cause airflow limitation provide a foundation for understanding the spectrum of patient presentations ***(Lamprecht et al., 2011).***

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) – a project initiated by the National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO) defines COPD as a common preventable and treatable disease, characterized by airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients ***(Gershon et al., 2011).***

Chronic bronchitis is defined as a chronic productive cough for three months in each of two successive years in a patient in whom other causes of chronic cough (eg, bronchiectasis) have been excluded. It may precede or follow development of airflow limitation. This definition has been used in many studies, despite the arbitrarily selected symptom duration ***(Gershon et al., 2011).***

Emphysema is defined as abnormal and permanent enlargement of the airspaces distal to the terminal bronchioles that is accompanied by destruction of the airspace walls, without obvious fibrosis (ie, there is no fibrosis visible to the naked eye). Exclusion of obvious fibrosis was intended to distinguish the alveolar destruction due to emphysema from that due to the interstitial pneumonias. However, many studies have found increased collagen in the lungs of patients with mild COPD, indicating that fibrosis can be a component of emphysema. While emphysema can exist in individuals who do not have airflow obstruction, it is more common among patients who have moderate or severe airflow obstruction ***(Gershon et al., 2011).***

Exacerbation of COPD

An exacerbation is defined as increased shortness of breath, increased sputum production, a change in the color of the sputum from clear to green or yellow, or an increase in cough in someone with COPD. This may present with signs of increased work of breathing such as tachypnea and tachycardia , sweating, active use of muscles in

the neck, cynosis and confusion if in a severe exacerbation ***(Holland et al ., 2012).***

II. Causes of COPD

The primary cause of COPD is tobacco smoke; with occupational exposures and pollution from indoor fires being a significant cause in some countries. Typically these exposures must occur over several decades before symptoms develop. Genetics also affect the probability ***(Vestbo and Jorgen, 2013).***

1- Smoking

The primary risk factor for COPD globally is tobacco smoking. Other types of smoke are also a risk including: marijuana, cigar, second hand and water pipe smoke. Exposure to cigarette smoke is measured in pack /years, the average number of packages of cigarettes smoked daily multiplied by the number of years of smoking. The likelihood of developing COPD increases with age and cumulative smoke exposure, and almost all lifelong smokers will develop COPD, provided that smoking-related, extrapulmonary diseases (cardiovascular, diabetes, cancer) do not claim their lives beforehand***(Decramer et al ., 2012).***

2- Air pollution

People who live in large cities have a higher rate of COPD compared to people who live in rural areas. While urban air pollution may be a contributing factor to exacerbations, its likely overall role in causing COPD is believed to be small ***(Vestbo and Jorgen,2013).***

3- Occupational exposures

Intense and prolonged exposure to workplace dusts found in coal mining, gold mining, and the cotton textile industry and chemicals such as cadmium, isocyanates, and fumes from welding have been implicated in the development of airflow obstruction, even in nonsmokers. Workers who smoke and who are exposed to these particles and gases are even more likely to develop COPD. Intense silica dust exposure causes silicosis, a restrictive lung disease distinct from COPD; however, less intense silica dust exposures have been linked to a COPD-like condition. The effect of occupational pollutants on the lungs appears substantially less important than the effect of cigarette smoking ***(Carlucci A et al ., 2012).***

4- Genetics

Genetics play a role in the development of COPD. It is more common among relatives of those with COPD who smoke than unrelated smokers. An inherited genetic condition, alpha 1-antitrypsin deficiency is responsible for about 2% of cases ***(Vestbo and Jorgen, 2013).***

Alpha 1-antitrypsin deficiency (A1AD) is a genetic disorder that causes defective production of alpha 1-antitrypsin (A1AT), leading to decreased A1AT activity in the blood and lungs, and deposition of excessive abnormal A1AT protein in liver cells. Severe A1AT deficiency causes emphysema or COPD in adult life in many people with the condition (especially if they are exposed to cigarette smoke), as well as various liver diseases in a minority of children and adults, It is treated by avoidance of damaging inhalants, by intravenous infusions of the A1AT protein, by transplantation of the liver or lungs, ***(Strange et al ., 2012).***

5- Others

A number of other factors are less well linked to COPD. The risk is greater in those who are poor however it is not clear if this is due to poverty itself or other factors associated with poverty such as air pollution and nutrition. There is evidence that those with asthma and airway hyper reactivity are at increased risk. Birth factors such as low birth weight may also play a role as do a number of infectious diseases including HIV/AIDS and tuberculosis ***(Vestbo and Jorgen, 2013).***

III. Pathophysiology of COPD

Oxidative metabolism is over-activated in COPD. The major external source of oxidants is cigarette smoke. Bronchial inflammation involving phagocytes, such as neutrophils and macrophages, adds an internal production of oxidants. Antioxidants such as the glutathione system and the hemoxygenase (HO)-1 pathway may counteract oxidative stress. This complex antioxidant system may be insufficiently

efficient, since a reduced HO-1 expression has been described in macrophages from lung tissue and bronchoalveolar lavage (BAL) of smokers with COPD ***(Barnes, 2008)*** .

(A)-Mucus hypersecretion & Ciliary dysfunction

Chronic obstructive pulmonary disease is characterized by persistent and usually progressive airflow limitation. In genetically susceptible individuals, inhaled noxious particles and gases induce an enhanced inflammatory response in the airways and result in structural changes (a process often referred to as " remodeling ") in airways and in lung parenchyma. Although COPD is associated with exacerbations and comorbidities that contribute to the overall severity in selected patients, small conducting airways appear to be the site of airflow limitation in COPD, and the increase in expiratory resistance to airflow implies a reduction in the total cross-sectional area of the small airways. Theoretically, the reduction in cross-sectional area of the small airways may be related to a decrease in the number of small airways and/or a reduction in the cross-sectional area of a large number of individual small airways ***(Vestbo et al ., 2012).***

Airway inflammation and remodeling occur in the lungs of patients with COPD, and it is likely that inflammation contributes to the structural abnormalities. However, evidence linking these processes remains scarce. Loss of alveolar attachment in small conducting airways is correlated with leukocyte recruitment, suggesting a role for proteases secreted by leukocytes in this process. CD8+ T cells and

neutrophils have been correlated with goblet cell hyperplasia in small conducting airway epithelium, suggesting that these cells contribute to hypersecretion of mucus. CD8+ T cells were also found in the alveoli, where they were suggested to contribute to alveolar destruction via release of proteolytic enzymes (eg, granzymes and perforins). Increased numbers of mast cells have been found in the alveoli in centrilobular emphysema, but not in panlobular emphysema, suggesting a distinct role in the pathogenesis of centrilobular emphysema. These findings suggest that therapies targeting inflammatory cell recruitment and/or activation may result in improvement in structural abnormalities, but this concept will require confirmation when appropriate drugs become available for clinical trials***(McDonough et al.,2011).***

(B)-Airflow limitation & hyperinflation

Patients with COPD often have some degree of hyperinflation of the lungs. Hyper inflated lungs can produce significant detrimental effects on breathing, as highlighted by improvements in patient symptoms after lung volume reduction surgery. Measures of lung volumes correlate better with impairment of patient functional capabilities than do measures of airflow. Understanding the mechanisms by which hyperinflation occurs in COPD provides better insight into how treatments can improve patients' health. Both static and dynamic processes can contribute to lung hyperinflation in COPD. Static hyperinflation is caused by a decrease in elasticity of the lung

due to emphysema. The lungs exert less recoil pressure to counter the recoil pressure of the chest wall, resulting in an equilibrium of recoil forces at a higher resting volume than normal. Dynamic hyperinflation is more common and can occur independent of, or in addition to static hyperinflation. It results from air being trapped within the lungs after each breath due to a disequilibrium between the volumes inhaled and exhaled. The ability to fully exhale depends on the degree of airflow limitation and the time available for exhalation. These can both vary, causing greater hyperinflation during exacerbations or increased respiratory demand, such as during exercise. Reversibility of dynamic hyperinflation offers the possibility for intervention. Use of bronchodilators with prolonged durations of action, such as Tiotropium, can sustain significant reductions in lung inflation similar in effect to lung volume reduction surgery. How efficacy of bronchodilators is assessed may, therefore, need to be reevaluated **(Gary and Ferguson, 2006).**

(C)-Gas exchange abnormalities

In the healthy lung, the exchange of oxygen and carbon dioxide is balanced; In COPD, it is not. Repeated exposure to noxious stimuli destroys the alveoli, impairing the process of gas exchange. This often leads to hypoxemia and hypercapnia, both very common in COPD. As the disease progresses, the impairment of gas exchange generally worsens, leading to worsening symptoms, disability and severe illness ***(Deborah Leader, 2013).***