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Chronic Obstructive Lung Disease

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Maanasi Samant and Thomas M. Ciesielski

GENERAL PRINCIPLES

- Chronic obstructive pulmonary disease (COPD) is commonly encountered in the general inpatient setting. A systematic approach is particularly useful in evaluating those suffering from this condition. COPD is a preventable and treatable disease.[1]
- COPD is the fourth leading cause of death in the United States, behind heart disease, cancer, and cerebrovascular accidents. The burden and prevalence of COPD is expected to increase.[2]
- The economic burden of COPD is also concerning; in the United States, the estimated direct costs of the disease are $29.5 billion. COPD exacerbations account for the majority of this figure.[1]

Definition

The pulmonary component of COPD is characterized by **airflow limitation that is not fully reversible**. Significant extrapulmonary effects may be present.

Classification

- Historically, COPD has been classified as **chronic bronchitis** and/or **emphysema**.[1]
- Chronic bronchitis and emphysema are descriptive terms and may not reflect the severity of airflow limitation.[1]
- Chronic bronchitis is defined as cough productive of at least two tablespoons of sputum on most days of 3 consecutive months in 2 consecutive years.[1]

- Emphysema is defined pathologically as nonuniform enlargement of the distal airspaces with destruction of the acini, loss of lung elasticity, and absence of any fibrotic changes.[3]
- The forced expiratory volume in 1 second (FEV_1) is more reflective of the degree of airflow limitation and is used in conjunction with the patient's symptoms and physical findings to gauge the severity of disease (Table 10-1).[3]

TABLE 10-1 CLASSIFICATION OF COPD BASED ON POSTBRONCHODILATOR FEV_1

Severity	FEV_1/FVC	FEV_1 (% Predicted)	Symptoms
Stage I: Mild	<70	≥80	Chronic cough and sputum production may be present, but not always.
Stage II: Moderate	<70	79–50	Dyspnea on exertion, cough, and sputum production sometimes present
Stage III: Severe	<70	30–49	Increasing dyspnea, reduced exercise capacity, fatigue, and repeated exacerbations
Stage IV: Very severe	<70	<30 or <50 plus chronic respiratory failure	Respiratory failure defined as PaO_2 <60 mm Hg with or without $PaCO_2$ >50 mm Hg; respiratory failure may lead to cor pulmonale; quality of life very impaired; and exacerbations may be life threatening.

COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second.

Adapted from Rabe KF, Hurd S, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007;176:532–55.

Etiology

The airflow limitation is usually progressive and associated with an abnormal inflammatory response to noxious particles or gases. The disease is polygenic

with deficiency of α_1-antitrypsin being a well-documented genetic risk factor.[4]

Pathophysiology

- Inflammation leading to repeated injury and repair leads to many structural changes throughout the lung parenchyma and airways. Airway remodeling and loss of alveolar attachments result in decreased elastic recoil.[3] These changes lead to the following:
  - Airflow limitation
  - Hypersecretion of mucus
  - Air trapping
  - Abnormal gas exchange
  - Cor pulmonale (right heart failure)[1]
- **Acute exacerbations** of COPD may be related to multiple factors including the following:
  - Viral infections (more common)
  - Bacterial infections (less common)
  - Poor air quality (fine particulates, NO_2, SO_2, ozone)
  - Nonadherence to medical therapy[3]

Risk Factors

- **Cigarette smoking** is the most common risk factor for the development of COPD.[4]
- Only a minority of smokers (about 15%) develop clinically significant COPD.[1]
- Other risk factors include hereditary deficiency of α_1-antitrypsin, inhalation exposure to occupational dusts and chemicals, as well as exposure to indoor pollution from the burning of biomass fuels in confined spaces.[3]

DIAGNOSIS

Clinical Presentation

History

COPD should be considered in those with known exposure to risk factors. There is considerable variability in the clinical course of individual patients with COPD. In most patients, the course is usually progressive, especially if exposure to noxious insults has not ceased. Hallmark clinical symptoms consist of the following:

- Chronic cough: Cough is usually the initial symptom, occurring in the fifth decade of life.
- Dyspnea that is gradually progressive over time. Dyspnea on exertion (DOE) generally presents in the sixth to seventh decades of life.
- Sputum production[3]
- When COPD becomes severe, weight loss may occur, though malignancy needs to be excluded.
- Obstructive lung disease in the absence of a significant smoking history should bring other pathologies into consideration.
- An **acute exacerbation of COPD** may be indicated by increased dyspnea, increased cough, and increased sputum production and/or sputum purulence.[2] The severest exacerbations are characterized by the presence of all three and mild exacerbations by only one.

Physical Examination

- Acute exacerbation
  - Vitals signs are essential. Admit to an intensive care unit (ICU) those with unstable vital signs and those who require assisted ventilation.
  - Altered mental status may be a result of hypercarbia or hypoxemia.
  - Fever may be suggestive of an infection.
  - Inspection of the respiratory status (pursed-lip breathing, prolonged expiration, accessory muscle use, nasal flaring, paradoxical abdominal movements, cyanosis) is helpful in identifying those in distress.
  - Pulmonary auscultation may reveal prolonged expiration, expiratory wheezes, rales, or bronchial breath sounds. In severe exacerbations, breath sounds may be barely audible.
- Chronic findings of COPD should be evaluated.

    - Signs of cor pulmonale may be present (right ventricular heave, jugular venous distention, and lower extremity edema).
    - Cachexia may be present, but malignancy and other causes of weight loss should be ruled out.[1]
    - Clubbing is generally not a feature of COPD; its presence should prompt an evaluation for etiologies such as lung cancer.

Differential Diagnosis

Other diagnoses should be considered in evaluating those suspected of suffering from COPD, as signs and symptoms may overlap significantly with other diseases, such as:

- Asthma
- Congestive heart failure (CHF)
- Bronchiectasis
- Obliterative bronchiolitis
- Diffuse panbronchiolitis
- Tuberculosis

Diagnostic Testing

The diagnosis of COPD should be supported by spirometry in those with the signs and symptoms suggestive of the disease. Spirometry is the “gold standard” for measuring airflow limitation.[1]

Laboratories

- Arterial blood gases (ABGs) must be checked in order to assess the PaO_2 and $PaCO_2$. Pulse oximetry provides no information about $PaCO_2$. Reliance solely on pulse oximetry during an acute exacerbation can result in life-threatening hypercarbia.[1]
- A complete blood count (CBC) may reveal polycythemia if chronic hypoxemia is present.[1]
- Blood chemistries may indicate an increased concentration of bicarbonate if chronic hypercapnea is present.
- An ECG may show signs of cor pulmonale, myocardial ischemia, or an

arrhythmia.[3]

Imaging

- CXR may show signs of hyperinflation/air trapping: flattened diaphragms; bullae; increased retrosternal clear space; long, narrow heart shadow; and hyperlucency. These findings have a limited sensitivity for a diagnosis of COPD.[1]
- Pulmonary edema, pneumonia, and pneumothorax can cause increased dyspnea and should be evaluated and treated appropriately if present.[1]

Diagnostic Procedures

- Spirometry is the primary method for diagnosing COPD, but its use is of limited value during acute exacerbations in patients with known COPD.[2]
- A postbronchodilator FEV_1/forced vital capacity (FVC) of <0.70 confirms the presence of airflow limitation. The FEV_1 defines the severity of expiratory airflow obstruction and is an important predictor of prognosis and mortality (Table 10-1).[3]
- Total lung capacity (TLC), residual volume (RV), and functional residual capacity (FRC) are typically elevated and are indicative of hyperinflation.[1]

TREATMENT

The global initiative for chronic obstructive lung disease (GOLD) was formed in 1998 to bring more attention to the prevention and management of COPD. The first consensus report in 2001 created a staging system of severity that has been used to assist in management of COPD.

Treatment of Stable COPD

- After diagnosis of COPD, treatment should aim to relieve symptoms and prevent exacerbations. The GOLD report suggests a treatment approach that is based on the GOLD stage classification of severity of COPD (Table 10-1)

along with exacerbations, hospitalizations, and other symptom scores, including the Modified British Medical Research Council (mMRC) Questionnaire, which primarily rates breathlessness and the COPD assessment test (CAT) and looks at health status impairment with COPD.[1] The following treatment approach takes into account these factors[1]:

- Low-risk patients with low symptom scores (GOLD stage I or II with few if any exacerbations or other limitations): PRN short-acting anticholinergic or short-acting β_2-adrenergic agonists (SABA)
- Low-risk patients with more symptoms (GOLD stage I or II with more exacerbations but not hospitalizations, some symptoms/limitations): long-acting anticholinergic and/or long-acting β_2-adrenergic agonists (LABA)
- High-risk patients with low symptom scores (GOLD stage III or IV, exacerbations with hospitalizations, symptoms/limitations): inhaled corticosteroid (ICS) + long-acting anticholinergic or LABA
- High-risk patients with more symptoms (GOLD stage III or IV, exacerbations with hospitalizations, significant symptoms/limitations): ICS + long-acting anticholinergic and/or LABA

- **Supplemental oxygen** therapy has been shown to decrease mortality and improve physical and mental functioning in hypoxemic patients with COPD. Long-term oxygen therapy should be prescribed for those who qualify and are willing to comply with its use. Oxygen therapy is indicated for the following:
  - Oxygen needs should be reassessed at least yearly and adjustments made as warranted.
  - Any patient with a $PaO_2 \leq 55$ mm Hg or $SaO_2 \leq 88\%$.[4]
  - Patients with evidence of pulmonary hypertension, polycythemia (hematocrit > 55%), or heart failure and $PaO_2 \leq 59$ mm Hg or $SaO_2 \leq 89\%$.
- **Smoking cessation** should be encouraged, with referral to a counselor if available. Discuss and prescribe smoking cessation aids (nicotine replacement therapy, bupropion, or varenicline) if needed.[1]
- **Phosphodiesterase 4 inhibitor (roflumilast)** can be offered to patients with severe COPD who are at risk for severe exacerbations despite treatment with ICS, LABA, and tiotropium.[5]
- **Azithromycin** can be considered in patients at increased risk of exacerbation (on continuous supplemental oxygen or with one exacerbation in the past year). However, baseline cardiovascular risk must be considered

before starting treatment.[6]

- **Pulmonary rehabilitation** improves quality of life and exercise tolerance and should be offered.[4]
- **Influenza and pneumococcal vaccines** should be kept current.[4]
- Adherence with therapies along with correct usage (particularly inhaled therapies) should be reviewed.[1]

Treatment of Acute Exacerbations of COPD

If patients are presenting with increased cough, sputum production, and worsening dyspnea and there is concern for acute exacerbation, the following therapies are available:

- **Supplemental oxygen** is frequently needed and should be provided in order to achieve a PaO_2 > 60 mm Hg or SaO_2 > 90%. Hypercarbia may result from overzealous oxygen administration; an ABG should be obtained if this is suspected, with subsequent adjustments in FiO_2 as indicated.[2]
- **Bronchodilators** administered via nebulizer or metered-dose inhalers are the mainstay of therapy. Inhaled β_2-adrenergic agonists and anticholinergics are the bronchodilators of choice. Both are similarly effective for acute exacerbations. Combined therapy may also be used.[2]
- **Systemic steroids** are indicated to shorten recovery time, improve lung function, and reduce the risk of relapse.[1]
  - The REDUCE trial demonstrated that a 5-day course of 40 mg of prednisone was noninferior with respect to re-exacerbations to a 14-day course of prednisone.[7] Thus, the GOLD committee recommends a 5-day course of 40 mg of prednisone.[1]
  - Inhaled corticosteroids do not have a role in treating exacerbations.
- **Antibiotics** are indicated in those patients who suffer from pneumonia, severe exacerbations (requiring assisted ventilation), or moderate exacerbations with increased sputum purulence as one of the presenting symptoms.
  - The course of mild exacerbations is unlikely to be altered by antibiotic therapy.[8]
  - Antibiotics should be chosen based on local resistance patterns.[1]
  - Pneumonia should be treated following the appropriate guidelines.[1]
  - The most common bacterial pathogens are *Streptococcus pneumoniae*,

Haemophilus influenzae, and *Moraxella catarrhalis*.[9] Patients with more severe exacerbation have a higher incidence of infection with gram-negative bacilli including *Pseudomonas aeruginosa*.[1]
    - For moderate to severe exacerbations, recommended antibiotics include a macrolide, amoxicillin/clavulanate, a second- or third-generation cephalosporin, or quinolones with enhanced activity against penicillin-resistant *S. pneumoniae*.[1]
    - Patients requiring mechanical ventilation should receive antibiotic therapy that also covers *P. aeruginosa*.[1]
    - Duration of antibiotics therapy is typically 5–10 days depending on the specific clinical scenario and the agent used.[1]
- **Noninvasive ventilation** (NIV) has been shown to decrease length of hospital stay, endotracheal intubation rates, and mortality.[10]
    - Indications for NIV include respirations > 25 breaths per minute, pH < 7.35, and/or $PaCO_2$ > 45 mm Hg and moderate to severe dyspnea with signs of distress.[1]
    - Contraindications to NIV include craniofacial trauma, cardiovascular instability, respiratory arrest, uncooperative patient, high aspiration risk, and extreme obesity.[2]
- **Mechanical ventilation** is indicated when there is a contraindication to NIV or failure to respond to NIV. Risks of mechanical ventilation include ventilator-associated pneumonia, barotrauma, and failure to wean.[1]
- **Smoking cessation** should be encouraged.[2]
- **Methylxanthines** (e.g., aminophylline and theophylline) are not indicated in acute exacerbations owing to the significant risk for side effects.[2]

OUTCOME/PROGNOSIS

- The BODE index may be useful in assessing the risk of death. The BODE index consists of the following[11]:
    - **B**ody-mass index (BMI)
    - airway **O**bstruction (FEV_1)
    - **D**yspnea (as measured by the Medical Research Council dyspnea score)
    - **E**xercise capacity (6-minute-walk distance)

- BODE index scores can range from 0 to 10. For each quartile increase in the BODE score, there was a statistically significant increase in the associated mortality rate. At the highest quartile (BODE score 7–10), there was a mortality rate of 80% at 52 months. For the lowest quartile (BODE score 0–2), the rate was ~ 20% at 52 months. While the study does have limitations, the BODE index appears to be a better predictor than the FEV_1 alone of the risk of death due to any cause and also respiratory causes.[11]

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