exacerbation of COPD

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The Global Initiative for Chronic Obstructive Lung Disease (GOLD), a report produced by the National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO), defines an exacerbation of chronic obstructive pulmonary disease (COPD) as :

"an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication"

This generally includes an acute change in one or more of the following cardinal symptoms:

- Cough increases in frequency and severity
- Sputum production increases in volume and/or changes character
- Dyspnea increases

EPIDEMIOLOGY

- Among patients with COPD, the frequency of exacerbation varies with the severity of disease, and some patients have more frequent exacerbations than others independent of other measures of disease severity
- Among almost 100,000 patients with COPD, approximately, 25 percent did not have an exacerbation; those with one baseline exacerbation were likely to have another; and those with ≥5 events were even more likely to have future events

- A study of Medicare beneficiaries found a 64 percent readmission rate after a discharge for a COPD exacerbation.

- In a survey that included over 4000 respondents with COPD, approximately 10 to 25 percent needed an emergency room evaluation for COPD and 5 to 10 percent required hospitalization

- In a separate survey of more than 1000 patients, 21 percent of those who reported a COPD exacerbation required hospitalization

Risk factors

- Advanced age
- Productive cough
- Longer duration of COPD
- History of antibiotic therapy
- COPD-related hospitalization within the previous year
- Chronic mucous hypersecretion
- Peripheral blood eosinophil count >0.3 x 10 cells/L (340 cells/microL)
- Theophylline therapy
- Presence of one or more comorbidities (eg, ischemic heart disease, heart failure, or diabetes mellitus)

- Women are slightly more likely to experience a COPD exacerbation than men

- In general, worsening airflow limitation FEV1, is associated with an increasing risk of COPD exacerbation, although airflow limitation alone does not provide a good assessment of exacerbation risk

Severity of COPD and history of prior exacerbations

In the prospective Evaluation of COPD ,2138 patients with moderate to severe COPD (Global Initiative for Chronic Obstructive Lung Disease [GOLD] stages 2, 3, or 4 were followed for three years .

The single best predictor of exacerbations was a history of prior exacerbations, regardless of COPD severity

The GOLD guidelines suggest using a combination of

- an individual's FEV1 ,
- history of exacerbations,
- history of hospitalization for exacerbation,
- and symptoms to assess the exacerbation risk

THE REFINED ABCD ASSESSMENT TOOL

Spirometrically Confirmed Diagnosis

Post-bronchodilator $FEV_1/FVC < 0.7$

Assessment of airflow limitation

Grade	FEV_1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

Assessment of symptoms/risk of exacerbations

Moderate or Severe Exacerbation History

≥2 or ≥ 1 leading to hospital admission

0 or 1 (not leading to hospital admission)

C	D
A	B

mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10

Symptoms

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Gastroesophageal reflux disease

GERD may be an additional risk factor for COPD exacerbations.

In the ECLIPSE study noted above, the occurrence of two or more exacerbations in a year was associated with a history of GERD or heartburn.

A similar observation was made in a case-control study that assessed the presence of GERD symptoms and frequency of COPD exacerbations in 80 patients with COPD.

The presence of GERD symptoms was associated with an increased risk of COPD exacerbations (RR 6.55, 95% CI 1.86-23.11).

However, in an observational study of 638 patients with stable COPD, therapy with proton pump inhibitors did not decrease the risk for severe exacerbations.

Pulmonary hypertension

Secondary pulmonary hypertension may be an additional risk factor for COPD exacerbations, possibly as an indicator of disease severity. In a follow-up to the ECLIPSE study, chest computed tomography scans were used to compute the ratio of the diameter of the pulmonary artery to the diameter of the aorta. In the study, a PA:A ratio greater than 1 was an independent risk factor for a future severe

Physical findings

often include wheezing and tachypnea and may include features of respiratory compromise.

Patients should be examined for physical findings, such as fever, hypotension, bibasilar fine crackles and peripheral edema, which might suggest a comorbidity or alternate diagnosis

Triggers

- Respiratory infections, most commonly viral (eg, rhinovirus) or bacterial, are estimated to trigger approximately 70 percent of COPD exacerbations ,atypical bacteria are a relatively uncommon cause.
- The remaining 30 percent are due to environmental pollution,
- pulmonary embolism,
- or have an unknown etiology

Hospitalizations for COPD exacerbation were associated with exposure to poor outdoor air quality, such as higher levels of ozone, carbon monoxide, particulate matter (up to 10 microns), and nitrogen dioxide.

Increased ambient levels of fine particulate matter [≤2.5 microns] are associated with an increase in hospitalization and mortality in COPD

The relationship between COPD exacerbation and pulmonary embolism was illustrated by a meta-analysis of five observational studies. Among the 550 patients having a COPD exacerbation, the prevalence of pulmonary embolism was 20 percent. The prevalence was even higher (25 percent) among those hospitalized

CLINICAL MANIFESTATIONS

range from a mild increase in dyspnea, cough that is productive or nonproductive to respiratory failure with acute respiratory acidosis and/or hypoxemia.

goals of the evaluation of a suspected exacerbation of COPD are:

- to confirm the diagnosis,
- identify the cause (when possible),
- assess the severity of respiratory impairment and contribution from comorbidities,
- and exclude alternate diagnostic possibilitie

For patients with a mild exacerbation (absence of resting dyspnea or respiratory distress, preserved ability to perform activities of daily living), who do not require emergency department treatment, the evaluation may be limited to clinical assessment and possibly pulse oxygen saturation.

For patients who require emergency department care, the evaluation should generally include the following :

- Assessment of pulse oxygen saturation
- A chest radiograph to exclude pneumonia, pneumothorax, pulmonary edema, pleural effusion

Laboratory studies (eg, complete blood count and differential, serum electrolytes and glucose)

- Arterial blood gas analysis is obtained if acute or acute-on-chronic respiratory acidosis is suspected or if ventilatory support is anticipated.
- We do not use procalcitonin or C-reactive protein to determine the need for antibiotics in COPD exacerbations

Severity of exacerbation(GOLD)

- Mild – Only one of three cardinal symptoms are present. Treatment with short-acting bronchodilators is sufficient.
- Moderate – At least two of three cardinal symptoms are present. Treatment includes short-acting bronchodilators plus antibiotics and/or oral glucocorticoids
- Severe – Patient requires emergency room treatment or hospitalization for severe symptoms (eg, sudden worsening of dyspnea, high respiratory rate, decreased oxygen saturation, confusion, drowsiness), insufficient response to initial short-acting bronchodilators, and presence of all three cardinal symptoms

Treatment includes short-acting bronchodilators, antibiotics, and oral or intravenous glucocorticoids. Severe exacerbations may be associated with respiratory failure and require noninvasive or invasive ventilation

DIFFERENTIAL DIAGNOSIS

- Heart failure
- Cardiac arrhythmias
- Pneumonia
- Pneumothorax
- Pulmonary embolism
- Inappropriate oxygen therapy

Strategies to Reduce Frequency of Exacerbations

Long-acting muscarinic antagonists (LAMA, including aclidinium, glycopyrrolate, tiotropium, and umeclidinium) improve symptoms and reduce exacerbations.

In a large randomized clinical trial, there was a trend toward reduced mortality rate in tiotropium-treated patients that approached statistical significance.

Side effects are minor; dry mouth is the most frequent side effect.

Long-acting beta2 agents (LABA) provide symptomatic benefit and reduce exacerbations, though to a lesser extent than a LAMA.

Currently available long-acting inhaled β agonists are arformoterol, formoterol, indacaterol, olodaterol, salmeterol, and vilanterol.

The main side effects are tremor and tachycardia

Combinations of Beta Agonist — Muscarinic Antagonist The combination inhaled β agonist and muscarinic antagonist therapy has been demonstrated to provide improvement in lung function that is greater than either agent alone and reduces exacerbations

Antibiotics There are strong data implicating bacterial infection as a precipitant of a substantial portion of exacerbations. A randomized clinical trial of azithromycin, chosen for both its anti- inflammatory and antimicrobial properties, administered daily to subjects with a history of exacerbation in the past 6 months demonstrated a reduced exacerbation frequency and longer time to first exacerbation

- Inhaled Corticosteroids The main role of ICS is to reduce exacerbations.

- Their use has been associated with increased rates of oropharyngeal candidiasis and pneumonia and in some studies an increased rate of loss of bone density.

- A trial of ICS should be considered in patients with frequent exacerbations, defined as two or more per year, and in patients with features of asthma, such as eosinophilia.

- In stable patients, ICS withdrawal may be considered

The selective phosphodiesterase 4 (PDE4) inhibitor roflumilast has been demonstrated to reduce exacerbation frequency in patients with severe COPD, chronic bronchitis, and a prior history of exacerbations;