COPD: Pathophysiology, Disease Process, and Outcomes
Michael Smith, Pharm D, BCPS, CACP

Disclosure:
• Dr Smith has no actual or potential conflict of interest associated with this presentation.

Grant recognition:
• This activity was funded by an independent professional education grant from Pfizer.

Learning Objectives
- Identify risk factors that contribute to the development and exacerbation of COPD
- Describe the progression of COPD from diagnosis to end-stage disease
- Discuss outcomes associated with COPD management

Why COPD?
• Highest risk of readmission at Backus Hospital
• Chronic disease
• Medication therapy is a cornerstone of treatment
• Proper treatment will decrease morbidity and mortality

Chronic Obstructive Pulmonary Disease is....
“a common ___①___ and ___②___ disease, is characterized by ___③___ airflow limitation that is usually ___④___ and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gasses.”

• Word Bank:
  – treatable, progressive, persistent, preventable

Global Initiative for Chronic Obstructive Lung Disease
www.goldcopd.org
COPD
Chronic Obstructive Pulmonary Disease is...
“a common preventable and treatable disease, is characterized by persistent 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

Two Major Subtypes

<table>
<thead>
<tr>
<th>Chronic Bronchitis</th>
<th>Emphysema</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mucoid sputum production, decreased ciliary activity, impaired resistance to infection.</td>
<td>• Permanent, parenchymal destruction</td>
</tr>
<tr>
<td>• Irreversible narrowing of airways associated with increased resistance to airflow.</td>
<td>• Loss of alveolar attachments</td>
</tr>
<tr>
<td>• Blue Blower</td>
<td>• Reduced lung elastic recoil causing airway collapse.</td>
</tr>
</tbody>
</table>

No longer differentiated in the GOLD guidelines

Figure 1: Mechanisms of Airflow Limitation in Chronic Obstructive Pulmonary Disease.

In the peripheral airways of patients with chronic obstructive pulmonary disease, as compared with normal peripheral airways, inhaled air has to travel a variable distance of less alveolar attachments, resulting in the development of small airways, and ultimately obstructive airways.

Figure 2: Risk Factors for COPD.

Risk Factors
• Genetics
• Smoking
• Occupational dust—Farming, mining, cement
• Indoor air pollution
• Outdoor air pollution
• Age
• Gender
• Early respiratory infections
• Socioeconomic status
• Asthma
• Chronic Bronchitis

WWW.GOLD COPD.ORG
**COPD**

**Smoking**
- Cause of COPD in 80-90% of patients
- 100-200% increase in the rate of FEV1 decline
- 2-20 fold increase in the risk of death from COPD
- Never smokers account for only 23% of COPD
- Impairs ciliary movement
- Inhibits alveolar macrophages
- Encourages hypertrophy and hyperplasia of mucus glands
- Acutely increases smooth muscle contraction

**Air pollution**
- Increased incidence and higher mortality rates of COPD in industrialized urban areas.
- Exacerbations linked to periods of heavy sulfur dioxide pollution
- 2-20 fold increase in the risk of death from COPD
- Never smokers account for only 23% of COPD
- Impairs ciliary movement
- Inhibits alveolar macrophages
- Encourages hypertrophy and hyperplasia of mucus glands
- Acutely increases smooth muscle contraction

**Occupational Dust**
- 10% prevalence of COPD in farm workers
- Most common respiratory syndrome in agricultural workers

**Infection**
- Severe viral pneumonia in childhood may lead to small airways obstruction (SAO)
- Mortality, morbidity, and frequency of respiratory infections are increased in patients with chronic bronchitis

**Genetic**
- Protease/antiprotease
  - Alpha-1-antitrypsin/elastase imbalance
  - Increased degradation of elastin
- TNF-alpha gene polymorphism
  - May influence immune response, increase inflammatory damage

**Epidemiology**
- COPD is a leading cause of morbidity and mortality worldwide.
- Caused 5% of all deaths in 2005
- In the US, age-adjusted mortality due to COPD doubled from 1970-2002
- Rate has stabilized/declined in many nations, skyrocketing in underdeveloped lands.
- Projected to be the #3 world-wide killer by 2020

**World Wide Projected Cause of Death**

- Ischemic heart disease
- CVD disease
- Lower respiratory infection
- Diarrhoeal disease
- Perinatal disorders
- COPD
- Tuberculosis
- Measles
- Road traffic accident
- Lung cancer

1990 | 2020
---|---
Stomach cancer | HIV
HIV | Suicide

1/28/2013
COPD Diagnosis

- Diagnosis should be considered in any patient with hallmark symptoms - dyspnea, chronic cough, chronic sputum production, especially with exposure to risk factors (smoking)
- Dyspnea: Progressive, persistent and characteristically worse with exercise
- Chronic Cough: May be intermittent and may be unproductive
- Chronic Sputum Production: common symptom

COPD Spirometry

- FEV1/FVC < 0.7 = COPD*
  - Forced Vital Capacity
    - Max volume exhaled after max inhalation
  - Forced Expiratory Volume in 1 second

* need to take in consideration of normal age related decline

COPD Classification of Severity

- GOLD 1: Mild  FEV1 ≥ 80% predicted
- GOLD 2: Moderate 50% ≤ FEV1 < 80% predicted
- GOLD 3: Severe 30% ≤ FEV1 < 50% predicted
- GOLD 4: Very Severe FEV1 < 30% predicted; or <50% plus respiratory failure.

*Based on Post-Bronchodilator FEV1

Risk of exacerbations:
- Two or more exacerbations within the past year or GOLD 2,3,4 severity = "High Risk"
COPD

Modified Medical Research Council (mMRC) Dyspnea Scale

- Breathless measurement that predicts future mortality risk

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description of Breathlessness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I only get breathless with strenuous exercise.</td>
</tr>
<tr>
<td>1</td>
<td>I get short of breath when hurrying on level ground or walking up a slight hill.</td>
</tr>
<tr>
<td>2</td>
<td>On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath a few times on level ground.</td>
</tr>
<tr>
<td>3</td>
<td>I stop for breath after walking about 100 yards or after a few minutes on level ground.</td>
</tr>
<tr>
<td>4</td>
<td>I am too breathless to leave the house or I am breathless when dressing.</td>
</tr>
</tbody>
</table>


COPD Assessment Test (CAT)

- 8 item measurement of health status impairment
- www.catestonline.org

“The COPD Assessment Test (CAT) is a new questionnaire for people with COPD. It is designed to measure the impact of COPD on a person’s life, and how this changes over time. The CAT is very simple to administer, and aims to help clinicians manage a patient’s COPD better.”

www.catestonline.org

COPD Combined Assessment

When assessing risk, choose the highest risk according to GOLD grade or exacerbation history

<table>
<thead>
<tr>
<th>Patient</th>
<th>Characteristic</th>
<th>Spirometric Classification</th>
<th>Exacerbations per year</th>
<th>mMRC</th>
<th>CAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low Risk</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>0-1</td>
<td>&lt;10</td>
</tr>
<tr>
<td>B</td>
<td>More Symptoms</td>
<td>GOLD 1-2</td>
<td>≥ 1</td>
<td>≥2</td>
<td>≥10</td>
</tr>
<tr>
<td>C</td>
<td>High Risk</td>
<td>GOLD 3-4</td>
<td>≥2</td>
<td>0-1</td>
<td>&lt;10</td>
</tr>
<tr>
<td>D</td>
<td>More Symptoms</td>
<td>GOLD 3-4</td>
<td>≥2</td>
<td>≥2</td>
<td>≥10</td>
</tr>
</tbody>
</table>

www.goldcopd.org

COPD Prognosis

The Body-mass index (B), the degree of airflow Obstruction (O) and Dyspnea (D), and Exercise capacity (E) BODE index — developed to assess an individual’s risk of death from COPD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points on BODE Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (% predicted)</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>6-Minute Walk Test (meters)</td>
<td>≤66 66-133 133-200 200-266</td>
</tr>
<tr>
<td>mMRC Dyspnea Scale</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>&gt;21 ≤21</td>
</tr>
</tbody>
</table>

Celli BR. NEJM 2004;350:1005

COPD Prognosis

Quartile 1: BODE 0-2
Quartile 2: BODE 2-4
Quartile 3: BODE 4-6
Quartile 4: BODE 6-10

Celli BR. NEJM 2004;350:1005
Goals of Therapy

Reduce Symptoms
- Relieve symptoms
- Improve exercise tolerance
- Improve health status

Reduce Risk
- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

COPD

Goals of Therapy

- Appropriate pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.
- None of the existing medications for COPD has been shown conclusively to modify the long-term decline in lung function.

COPD

Avoidance of risk factors

- Smoking cessation
- Reduction of indoor pollution
- Smoking cessation
- Reduction of occupational exposure
- Smoking cessation
- Influenza vaccination

COPD

Quit Smoking
- Most effective (and cost-effective) intervention to slow progression
- Ask
- Advise
- Assess
- Assist
- Arrange

Pulmonary Rehab

ATS/ERS:
- Evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities.
- Pulmonary rehabilitation is designed to reduce symptoms, optimize functional status, increase participation, and reduce health care costs by stabilizing or reversing systemic manifestations of the disease.

Effect of pulmonary rehabilitation on dyspnea

Effect of exercise training on dyspnea compared with bronchodilators and oxygen.

Data from Am J Respir Crit Care Med 1999; 159:321.
COPD

- RS is a 66yo male with who was diagnosed with COPD 2 years ago (FEV1= 70% of predicted). He continues to smoke and is poorly compliant with his medications. He has hypertension, hyperlipidemia and anxiety. He has been walking nightly with his wife to lose weight. His chief complaint today is that when he walks with his wife he easily gets short of breath on small hills. He had 2 COPD exacerbations last year.
- What GOLD patient category does he fall into?

COPD

**Combined Assessment**

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Spirometric Classification</th>
<th>Exacerbations per year</th>
<th>mMRC</th>
<th>CAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Low Risk Less Symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>0-1</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>B Low Risk More Symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>≥ 2</td>
<td>≥ 10</td>
</tr>
<tr>
<td>C High Risk Less Symptoms</td>
<td>GOLD 1-4</td>
<td>≥ 2</td>
<td>0-1</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>D High Risk More Symptoms</td>
<td>GOLD 1-4</td>
<td>≥ 2</td>
<td>≥ 2</td>
<td>≥ 10</td>
</tr>
</tbody>
</table>

Spirometry assessment = GOLD 2; Exacerbations = 2; mMRC = 1

COPD Exacerbation

“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.”

COPD

**Exacerbations**

- Diagnosis based on the presentation of the patient complaining of an acute change of symptoms that is beyond normal day-to-day variation.
- The goal of treatment is to minimize the impact of the current exacerbation and to prevent the development of subsequent exacerbations.

COPD

**Combined Assessment**

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Spirometric Classification</th>
<th>Exacerbations per year</th>
<th>mMRC</th>
<th>CAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Low Risk Less Symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>0-1</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>B Low Risk More Symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>≥ 2</td>
<td>≥ 10</td>
</tr>
<tr>
<td>C High Risk Less Symptoms</td>
<td>GOLD 1-4</td>
<td>≥ 2</td>
<td>0-1</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>D High Risk More Symptoms</td>
<td>GOLD 1-4</td>
<td>≥ 2</td>
<td>≥ 2</td>
<td>≥ 10</td>
</tr>
</tbody>
</table>

Spirometry assessment = GOLD 2; Exacerbations = 2; mMRC = 1

COPD Exacerbation

“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.”

COPD

**Exacerbations**

- Diagnosis based on the presentation of the patient complaining of an acute change of symptoms that is beyond normal day-to-day variation.
- The goal of treatment is to minimize the impact of the current exacerbation and to prevent the development of subsequent exacerbations.
COPD

Treatment of Exacerbations

- Increase dose or frequency of current medications
- Consider adding bronchodilator agents
- Systemic steroids
- Antibiotics should be given to patients if:
  - Dyspnea and cough are increased AND sputum is purulent and increased in volume

COPD

A Systemic Inflammatory Disease?

COPD patients are at high risk for:

- Cardiovascular diseases
- Osteoporosis
- Respiratory infections
- Anxiety and Depression
- Diabetes
- Lung cancer
- These conditions should be actively investigated and aggressively treated as if the patient did not have COPD

COPD

A Systemic Inflammatory Disease?

- Cardiovascular disease is a major comorbidity in COPD and probably both the most frequent and most important disease coexisting with COPD.
- Cardioselective beta-blockers are not contraindicated in COPD.

- Osteoporosis and anxiety/depression: often under-diagnosed and associated with poor health status and prognosis.
- Lung cancer: frequent in patients with COPD; the most frequent cause of death in patients with mild COPD.
- Serious infections: respiratory infections are especially frequent.
- Diabetes: more frequent in COPD and is likely to impact on prognosis.