COPD

Thomas M. Roy, MD, FCCP

Disclosure Statement of Financial Interest

• I, (Thomas M. Roy, MD), DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Disclosure Statement of Financial Interest

• I, (Thomas M. Roy, MD), DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation, they are:

  Affiliation/Financial Interest: Name of Organization(s):
  Grant/Research Support: ___
  Consultant: ___
  Speaker's Bureau: ___
  Major Stock/Shareholder: ___
  (excluding mutual funds)
  Advisory Board: ___
Disclosure Statement of Unapproved/Investigative Use

I, (Thomas M. Roy, MD), DO NOT anticipate discussing the unapproved/investigative use of a commercial product/device during this activity or presentation.

Chronic Obstructive Lung Diseases

Epidemiology
- 11.2 million Americans have COPD
- ~24 million are estimated to have evidence of impaired lung function
- COPD is the 4th leading cause of death
  - Claims the lives of 120,000 Americans annually
- By 2020, COPD will become the 3rd leading cause of death worldwide
  - Increasing epidemic of smokers
  - Change in demographics, people living longer
**Risk Factors for COPD**

- Susceptibility genes
- Exposure to inhaled particles
  - Tobacco smoke (active and passive)
  - Occupational dust, organic and inorganic agents
  - Indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings
  - Outdoor air pollution
- Female gender
- Age
- Respiratory infections
- Poor lung growth and development
- Oxidative stress
- Poor nutrition
- Low socioeconomic status
- Comorbidities

*Cumulative exposure to noxious particles is the key risk factor for COPD*

*From the Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Global Initiative for Chronic Obstructive Lung Disease 2015-2016. Analysts from www.goldcopd.org*
COPD

- COPD should be suspected in persons presenting with cough, dyspnea, or increased sputum production, especially those with a history of smoking
- GOLD Stage 0 – At risk

Diagnosis

- Appropriate symptoms in the setting of risk factors +/- exposures:
  - symptoms begin in middle (40’s-50’s) and slowly progress
  - consider diagnosis with cough, dyspnea and the risk factor of smoking
- PFT confirmation:
  - Most reproducible, standardized, objective
  - Airflow limitation is not fully reversible with bronchodilator testing
  - Severity is based on FEV₁
PFTs - The Essentials

![Diagram of lung function tests]

Expiratory Flows

- FEV1/FVC < 70% defines Obstruction
  - FVC – the maximal amount of air that can be forcibly exhaled
  - FEV1 – the volume exhaled during the first second of a forced vital capacity (FVC)

COPD

Spirometry should be performed in patients 45 years or older who smoke and have a persistent cough

- Identify the at risk population
- Diagnosis and stage COPD
- Plan therapy
Asymptomatic smokers

- Health assessment - “know your flow”
- FEV1 Decrease 30mL/yr is normal
- 50-80mL/yr in susceptible smokers COPD

Stages of COPD

- Post-bronchodilator FEV1 is recommended for the diagnosis and assessment of COPD

<table>
<thead>
<tr>
<th>FEV1 (L)</th>
<th>Staging</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 80% of predicted</td>
<td>Mild</td>
</tr>
<tr>
<td>50% ≤ FEV1 &lt; 80%</td>
<td>Moderate</td>
</tr>
<tr>
<td>30% ≤ FEV1 &lt; 50%</td>
<td>Severe</td>
</tr>
</tbody>
</table>

- FEV1/FVC < 0.70

Low Risk

- Post-bronchodilator FEV1 > 50% of predicted
- Exacerbations < 2 per year
- Symptoms
  - Moderate
  - Severe

High Risk

- Post-bronchodilator FEV1 < 50% of predicted
- Exacerbations < 2 per year
- Symptoms
  - Moderate
  - Severe

GROUP A: [low risk of exacerbation, less symptoms]
GROUP B: [low risk of exacerbation, more symptoms]
GROUP C: [high risk of exacerbation, less symptoms]
GROUP D: [high risk of exacerbation, more symptoms]
Smoking cessation

- The most important (and cost-effective) intervention
- The only intervention able to reduce the progression of COPD
  - patients who quit smoking experience less respiratory symptoms and hyper-responsiveness than those who continue to smoke
Smoking Cessation

- Approximately 20.8% (45.3 million) American adults currently smoke
- Most effective way to reduce COPD
- Cost effective
- Brief (3 minute) counseling results in 5-10% of smoking cessation

<table>
<thead>
<tr>
<th>ASK with each visit.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVISE quitting.</td>
</tr>
<tr>
<td>ASSESS willingness to quit.</td>
</tr>
<tr>
<td>ASSIST with quit plan.</td>
</tr>
<tr>
<td>ARRANGE follow up.</td>
</tr>
</tbody>
</table>

Smoking cessation

- The largest improvements in lung function and symptoms occur within the first year after cessation
- The rate of decline in lung function is slower among persons who quit smoking
- 10 years after quitting: The lung cancer death rate is about half that of a continuing smoker’s
Smoking cessation

- With good smoking cessation programs, 20 to 40 percent of participants are able to quit for at least one year

- Brief clinical interventions by health care providers can increase the chances of successful cessation, as can counseling and behavioral cessation therapies

- The use of a pharmaceutical product in concert with counseling doubles a person’s chances of success

Smoking Cessation Therapy

1. Antidepressant: bupropion
2. New medications—varenicline
3. Nicotine replacement (use 2 simultaneous therapies): patch, gum, oral inhaler, nasal spray, lozenges
4. Counseling at every physician visit

Optimal approach simultaneously combines various therapies


Smoking cessation

- Although as many as 69% of smokers want to quit, only 3% to 5% of unaided cessation attempts succeed.

- Changes in societal norms that are a result of strict public health policies (such as banning smoking in the workplace) have helped decrease the percentage of smokers from 42% in 1965 to 19% today
Vaccines

- Influenza vaccine
  - Reduces mortality
  - Reduces hospitalization rate for pneumonia and influenza
- Pneumococcal vaccine
  - Research pending
- GOLD guidelines recommend vaccination but conclude that there is not enough data to recommend widespread, general use of vaccines for COPD patients

Recent Guideline Recommendations for ICS Use in COPD

Consistent message: ICS for FEV₁ < 50% predicted and/or recurrent exacerbations


Never mind how serious it is... how expensive is it?

LABA and LAMAs in development for combination therapies

<table>
<thead>
<tr>
<th>Therapy</th>
<th>LABA</th>
<th>LAMA</th>
<th>Doseage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indacaterol</td>
<td>LABA</td>
<td>Once daily</td>
<td>Ombrez</td>
</tr>
<tr>
<td>Indacaterol</td>
<td>LABA</td>
<td>Once daily</td>
<td>Accepta</td>
</tr>
<tr>
<td>Olodaterol</td>
<td>LABA</td>
<td>Once daily</td>
<td>Striverdi</td>
</tr>
<tr>
<td>Ventalerol</td>
<td>LABA</td>
<td>Once daily</td>
<td>Breo Ellipta</td>
</tr>
<tr>
<td>Aclidinium</td>
<td>LAMA</td>
<td>Twice daily</td>
<td>Tudorza</td>
</tr>
<tr>
<td>Tiotropium</td>
<td>LAMA</td>
<td>Once daily</td>
<td>Spiriva</td>
</tr>
<tr>
<td>Umeclidinium</td>
<td>LAMA</td>
<td>Once daily</td>
<td>Ellipta</td>
</tr>
<tr>
<td>Umeclidinium/ Vilanterol</td>
<td>LABA/LABA</td>
<td>Once daily</td>
<td>Anoro</td>
</tr>
</tbody>
</table>
COPD Treatment

COPD

• None of the existing medications for COPD have yet been shown prospectively to modify the long-term decline in lung function

• Pharmacotherapy is used to decrease symptoms and reduce complications such as acute exacerbations

Possible Causes of Worsening Symptoms in COPD

• Progression of disease
• Acute exacerbation of COPD
• Comorbidity, such as cardiovascular disease
• Nonadherence to treatment
• Incorrect use of inhaler(s)
• COPD trigger, such as smoking
Incorrect inhaler technique is common among patients with asthma or COPD.

This could result in suboptimal disease control, raising the risk of absences from work or school, unnecessary increases in medication dosage, exacerbations requiring oral corticosteroid treatment, and potential side-effects.

Published studies from around the world suggest that as many as 25% of patients with asthma or COPD have never received verbal inhaler technique instruction.

When given, instruction is often rushed, poor quality and not reinforced.

Only an estimated 11% of patients receive follow-up assessment and education on their inhaler technique.
• “Can you show me how you use your inhaler?”

• In an Australian study, 75% patients using an inhaler for an average of 2–3 years reported they were using their inhaler correctly but, on objective checking, only 10% demonstrated correct technique.

• Inhaler technique must be rechecked and education must be reinforced regularly in order to maintain correct technique, as inhaler technique deteriorates again after education.

• Older patients may be particularly prone to losing technical skills over time.

Potential Inhaler Problems

• Inability to coordinate activation with inhalation
• Failure to hold breath for a sufficient time
• Multiple actuations without waiting or shaking in between doses
• Incorrect position of inhaler
• Difficult for people with osteoarthritis affecting hands
• May be unsuitable for patients with severe COPD with poor inspiratory flow rate
Theophylline

• Theophylline remains an option for COPD care, but is usually reserved for late-stage add-on therapy in patients with severe COPD who are already using or have not responded to all other available therapy.

• The adverse effects of theophylline are dose-related, and low doses may be used without blood level monitoring.

• Even at low doses theophylline has significant drug interactions with other frequently used medications including digitalis and warfarin.

Theophylline

• A methylxanthine (theophylline) could be used in addition to these treatments or as an alternative in patients intolerant of β2-agonist adverse effects.

• Mechanism for improvement is not solely bronchodilation from phosphodiesterase inhibition.
Theophylline

- The doses currently recommended (approximately 300 mg once daily at bedtime or 200 mg every 12 hours) are unlikely to carry a risk of toxicity
- Narrow therapeutic range/toxicity
- 8-13 mcg/ml
- > 20 mcg/ml considered toxic level
- Monitoring blood levels at low dosages (plasma concentrations of 5-10 mg/L) is not necessary.

Theophylline

Decreases level
- Rifampin
- Dilantin
- Phenobarbital
- Carbamazepine
- Smoking

Increases level
- Acyclovir
- Cimetidine*
- Macrolides
- Fluoroquinolones
- Propranolol*
- Allopurinol
- Zafirlukast

Theophylline

- Theophylline use may decrease serum levels of:
  - Lithium
  - Phenytoin
COPD - roflumilast

- Common side effects of roflumilast include diarrhea, weight loss, nausea, headache, backache, decreased appetite, dizziness, and occasionally neuropsychiatric symptoms such as depression and suicidality.
- Roflumilast is expensive and should be considered as add-on therapy in highly selected patients. (only chronic bronchitis)

COPD

- Roflumilast is an oral phosphodiesterase-4 inhibitor recently approved for use in patients with severe and very severe COPD associated with chronic bronchitis and a history of frequent exacerbations.

Emphysema

- Emphysema is the permanent enlargement of the airspace distal to the terminal bronchioles with destruction of the alveolar septa
- Destruction is due to imbalance between proteases and antiproteases
  - Increased protease activity
    - proteolytic elastase from neutrophils (tobacco smoke)
  - Decreased antiprotease
    - Alpha-1-antitrypsin deficiency
COPD

• 3-5% of Emphysema is genetic
• Due to a severe hereditary deficiency of alpha1-antitrypsin

• Most common in Caucasians
  – 96% of AAT deficiency patients have a ZZ genotype

Emphysema

Panacinar
• 3%-5% of emphysema from alpha-1 deficiency
• Smoking exacerbates emphysema formation in A1A deficiency
• Alpha-1-antitrypsin deficiency: bullae in the lung bases rather than apices
• Onset in late 30’s rather than late 40’s

COPD

• GOLD recommends α1-antitrypsin screening in white patients who develop COPD before the age of 45 years or in those with a strong family history of COPD
Alpha-1 antitrypsin level

• Assess for deficiency in settings of clinical suspicion:
  – age 45 or less,
  – absence of other risk factors or severity of disease
    out of proportion to risk factors
  – prominent basilar lucency
  – family history
  – bronchiectasis.

Pulmonary rehabilitation

• All patients with COPD benefit from exercise
  training programs (pulmonary rehabilitation)

• Reduces dyspnea, anxiety and depression,
  improves exercise capacity and quality of life

• May reduce hospitalizations

COPD

• Current recommendations recommend
  pulmonary rehabilitation for patients with
  symptomatic COPD who have an FEV1 less
  than 50%
Pulmonary rehabilitation

• Does not change Pulmonary function measurements
• Does not change ABGs
• Does not decrease mortality

Oxygen

• Long-term oxygen administration (>15 h per day) has been shown to improve survival in patients with chronic respiratory failure

• It is the only therapy that increases their life span

Chronic O$_2$ use in COPD

• Criteria for chronic (continuous) O$_2$ use:
  • Resting $\text{PaO}_2 < 55$ or $\text{O}2 \text{ sat} < 88\%$
  • $\text{PaO}_2 < 59 \text{ mmHg or Sat 89%} \text{ with evidence of cor pulmonale or erythrocytosis (hct } > 55\%)$
  • Patients who qualify as above should be on oxygen 24 hours a day
Chronic O₂ use in COPD

- Some patients desaturate with exercise or while sleeping
- **Survival benefit is unproven**
- If prescribe supplemental O₂ in the hospital you should re-evaluate the continued need after 2 months
  - Rule of 21

COPD

- **Lung volume reduction surgery** is an extensive surgical procedure in which parts of the lung are resected, leading to reduction of hyperinflation, improvement of mechanical efficiency of respiratory muscles, and improvement of expiratory flow rate
- It is recommended only in highly selected patients with COPD.

Lung Volume Reduction Surgery

- LVRS should be considered in patients with severe COPD on maximal medical therapy who have completed pulmonary rehabilitation and meet the following criteria:
  - presence of homogeneous bilateral emphysema on CT scan
  - Post bronchodilator total lung capacity greater than 150% and residual volume greater than 100% of predicted
  - Maximum FEV₁, no greater than 45% of predicted
  - Arterial PCO₂ no more than 60 mm Hg and arterial PO₂ of at least 45 mm Hg breathing ambient air.
Lung Transplantation

- Patients with homogenous emphysema, an FEV₁ not greater than 20% of predicted, and DLCO not greater than 20% of predicted have a median survival of 3 years and should be considered for lung transplantation.
- This patient is a candidate for transplantation.
- Functional capacity and quality of life are improved after lung transplantation, but the effect on overall survival is mixed.

BODE index

- BODE index assessment may be used to determine prognosis for severe disease, but is usually deferred to referral specialists.
  - Body-mass index,
  - Airflow obstruction [% of predicted FEV₁],
  - Dyspnea using the modified Medical Research Council dyspnea scale
  - Exercise capacity [distance walked in 6 minutes]
Possible Causes of Worsening Symptoms in COPD

- Progression of disease
- Acute exacerbation of COPD
- Comorbidity, such as cardiovascular disease
- Nonadherence to treatment
- Incorrect use of inhaler(s)
- COPD trigger, such as smoking

Treatment Options for Worsening Symptoms

- Oral corticosteroids if the patient is having an exacerbation
- Adding a second long-acting bronchodilator
- Changing the medication delivery device, such as adding a spacer to a metered-dose inhaler (MDI), or using a dry-powder inhaler (DPI) or a nebulizer

Take-Home Messages

- When a patient presents with worsening symptoms, carefully evaluate the many possible causes.
- Closely and regularly assess the patient’s inhaler technique.
- For patients who have difficulty using an MDI, consider a spacer, a DPI, or a nebulizer.
- Consider patient preference when choosing a delivery system.