4:45 – 5:30pm

Advances in Managing COPD Patients

SPEAKER
Nicola Hanania, MD, FCCP, FRCP, FACP

Presenter Disclosure Information

The following relationships exist related to this presentation:

► Nicola Hanania, MD, FCCP, FRCP, FACP: Contractor and research support from GSK, Mylan, BI, Sunovion, Pearl, Novartis, Pfizer; Speaking and teaching honorarium for Genentech; Honorarium as a consultant for Genentech, Novartis, Pfizer, BI, GSK, Sunovion.

Off-Label/Investigational Discussion

► In accordance with pmCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Nicola A. Hanania, MD, MS, FCCP
Associate Professor of Medicine
Pulmonary and Critical Care Medicine
Director, Asthma Clinical Research Center
Baylor College of Medicine,
Ben Taub General Hospital
Houston, TX

Case Presentation: Betty
A Classic Scenario

• Betty is 52-year-old woman who smoked for about 15 years, but stopped 20 years ago.
• Presents with increasing shortness of breath on exertion over the past 2 years. Suffers from hypertension and osteoporosis.
• Reports that she used to walk 9 holes of golf with her women's group every Wednesday morning, but has needed to use a golf cart over the past year. She attributed this to getting old.
• Was told 3 years ago that she had “a touch of asthma” and was given a short-acting inhaler to use when she was symptomatic.
• During the past 6 months, she has gone to the emergency department three times for “acute bronchitis.”
• Spirometry shows a post-bronchodilator FEV1 of 62% predicted and an FEV1/FVC of 58%.

Objectives

• Discuss the Impact of COPD
• Review the pathophysiology of COPD
• Outline guidelines’ recommendations for assessment of COPD
• Discuss non-pharmacologic and pharmacologic management strategies of COPD

GOLD: Global Initiative for Chronic Obstructive Lung Disease

GOLD definition of COPD1
- Common, preventable, treatable—partially reversible
- Characterized by persistent airflow limitation
- Usually progressive and disabling
- Associated with enhanced chronic inflammatory response in airways/lung to noxious particles or gases

COPD is heterogeneous2
- Multiple risk factors, phenotypes, comorbidities
- Exacerbations and comorbidities contribute to severity

The New Look of COPD

- Epidemiology
- Pathophysiology
- Diagnosis and Assessment
- Management

COPD: The Old Look

Perception

COPD is a disease of the elderly
COPD is a disease of men

COPD in Younger Patients and Women is on the Rise

Reality

COPD affects the working-age population.
COPD is also a disease of women.

The Impact of COPD in the United States

- 10.3 million physician office visits/y
- 1.5 million ED visits
- 699,000 hospital discharges
- Costly
  - Direct: ≈ $27 billion/y
  - Indirect: ≈ $20 billion/y
- 3rd leading cause of death
- 4th leading cause of hospital readmissions

Risk Factors for COPD

- Exposure to inhaled particles:
  - Tobacco smoke (active and passive)
  - Occupational dusts, organic and inorganic
  - Indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings
  - Outdoor air pollution
- Susceptibility genes
- Poor lung growth and development
- Oxidative stress
- Female gender
- Age
- Respiratory infections
- Low socioeconomic status
- Poor nutrition
- Co-morbidities
COPD: Oxidative Stress is Central to the Destruction of Pulmonary Tissue

- Cigarette Smoke
- Inflammatory cells (neutrophils, macrophages)
- Activation of Nuclear Factor κB
- TNF-α
- IL-1
- Neutrophil Recruitment
- Isoprostanes
- ROS
- Anti-Proteases
- α1-anti-trypsin and secretory leukoprotease inhibitor
- Corticosteroid Resistance
- Mucus Secretion
- Bronchoconstriction
- Plasma Leak

ROS = Reactive Oxygen Species


Emphysema and Small Airways Disease Contribute to Total Airflow Limitation in COPD

- Normal
- COPD
- Disrupted alveolar attachments (emphysema)
- Mucosal inflammation, fibrosis
- Mucus hypersecretion and inflammatory exudate
- Airway obstructed by:
  - Loss of alveolar attachments
  - Mucosal inflammation and fibrosis
  - Luminal obstruction with inflammatory exudate and mucus


Pathophysiology of COPD

- Hypersomnia
- Airflow obstruction
- Exacerbations
- Tachypnea
- Ventilatory requirement
- Air trapping
- Hyperinflation
- Activity limitation
- Dyspnea
- Poor health-related quality of life


The New Look of COPD

- Epidemiology
- Pathophysiology
- Diagnosis and Assessment
- Management

Key Indicators for COPD Diagnosis

- Consider a diagnosis of COPD, and perform spirometry, if any of these indicators are present in an individual >40 years of age
  - Exertional dyspnea
  - Chronic cough
  - Chronic sputum production
  - History of exposure to risk factors (eg, tobacco smoke)
- Spirometry is required to make the diagnosis
  - Post-bronchodilator FEV1/FVC <0.70 confirms persistent airflow limitation and COPD diagnosis


Natural History of COPD

Significant Drops in Lung Function Are Often Required for Patients to Become Severely Symptomatic

- Dyspnea, Cough
- Exercise Intolerance
- Exacerbations
- Hospitalizations
- Systemic Effects
- Respiratory Failure
- Pulm Hypertension

Age (years)

FEV1 (% predicted at age 25 years)

0 25 50 75

25 50 75

100 75 50 25

Dyspnea, Cough
Exercise Intolerance
Exacerbations
Hospitalizations
Systemic Effects
Respiratory Failure
Pulm Hypertension
Global Strategy for Diagnosis, Management and Prevention of COPD: Assessment of COPD

- Assess symptoms
- Assess degree of airflow limitation using spirometry
**Assessment of COPD: Lung Function**

In patients with post-bronchodilator FEV1/FVC < 0.70:

- **GOLD 1: Mild** \( \text{FEV}_1 \geq 80\% \text{ predicted} \)
- **GOLD 2: Moderate** \( 50\% \leq \text{FEV}_1 < 80\% \text{ predicted} \)
- **GOLD 3: Severe** \( 30\% \leq \text{FEV}_1 < 50\% \text{ predicted} \)
- **GOLD 4: Very Severe** \( \text{FEV}_1 < 30\% \text{ predicted} \)

*Based on Post-Bronchodilator FEV1

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**Global Strategy for Diagnosis, Management and Prevention of COPD:**

- Assess symptoms
- Assess degree of airflow limitation using spirometry
- Assess risk of exacerbations

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**The ‘frequent exacerbator phenotype’:**

Parameters associated with exacerbation in year 1 (multivariate analysis)

- FEV1 (per 100mL decrease)
- SGRQ score (per 4-point increase)
- Positive history of reflux or heartburn
- White Cell Count (per increase of 1000/mL)

Analysis by GOLD Stage showed similar results: The best predictor of future exacerbation is a history of previous exacerbations.


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**Frequent Exacerbations Drive Disease Progression**

Patients with frequent exacerbations

- Lower quality of life
- Increased mortality rate
- Increased inflammation
- Increased risk of recurrent exacerbations
- Increased likelihood of hospitalization
- Faster disease progression


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**GOLD 2014: Combined COPD Assessment**

Assessment Using Symptoms, Breathlessness, Spirometric Classification, and Risk of Exacerbations

- **Risk:**
  - **C:** High risk, Less symptoms
  - **D:** High risk, More symptoms
  - **A:** Low risk, Less symptoms
  - **B:** Low risk, More symptoms

- **Exacerbations/Year:**
  - 4
  - 3 or 2 leading to hospital admission
  - 1 (not leading to hospital admission)

- **Symptoms:**
  - CAT < 10
  - mMRC 0-1

- **Breathlessness:**
  - mMRC > 2

*When assessing risk, choose the highest risk according to GOLD grade or exacerbation history.
Comorbidities of COPD

- Anemia, depression
- Pulmonary hypertension
- Cardiovascular disease
- Peripheral muscle wasting and dysfunction
- Osteoporosis
- GI complications
- Peptic ulcers
- Cachexia

Nonpharmacologic Therapy To Manage COPD

- Smoking Cessation
- Patient Education
- Vaccination
- Oxygen Therapy
- Pulmonary Rehabilitation
- Surgical and Non-surgical Alternatives

Components of Pulmonary Rehabilitation Programs

- Exercise Training: Involves the measurement of a number of physiologic variables, including maximum oxygen consumption, maximum heart rate, and maximum work performed.
- Nutrition Counseling: Important determinant of symptoms, disability, and prognosis in COPD; a reduction in BMI is an independent risk factor for mortality in patients with COPD.
- Education: Specific contributions of education to the improvements seen after pulmonary rehabilitation remain unclear.
- Assessment and Follow-up:
  - BMI=body mass index.
  - Global Initiative for Chronic Obstructive Lung Disease (GOLD).

Outcomes of Pulmonary Rehab in COPD

- Reduces dyspnea
- Improves deconditioning, muscle fatigue
- Increases exercise capacity
- Improves quality of life
- Improves depression
- Reduces acute exacerbations
- Reduces hospitalizations
- May reduce mortality
- Does not improve PFTs or ABGs

Pharmacological Management of COPD

- Guideline-recommended COPD treatment
  - Improves lung function
  - Minimizes symptoms
  - Improves QoL
  - Prevents exacerbations
- Wide variety of options including new agents
  - Appropriate treatment selection hinges on GOLD staging
  - Before stepping up/modifying treatment, re-evaluate
    - Treatment goals
    - Clinical phenotype
    - Comorbidities
    - Adherence

COPD Pharmacological Agents Approved in the U.S.

- Bronchodilators
  - Short-acting β-Agonists (SABA)
    - Albuterol
    - Pirbuterol
    - Levalbuterol
  - Long-acting β-Agonists (LABA)
    - Salmeterol
    - Formoterol
    - Arformoterol
    - Indacaterol
  - Anticholinergic (SAMA)
    - Ipratropium
  - Bronchodilators (LAMA)
    - Tiotropium
    - Aclidinium
    - Umeclidinium
    - LABA +LAMA
    - LAMA +Umeclidinium
    - LABA +Umeclidinium +Vilanterol
    - Theophylline

- Anti-Inflammatory
  - ICS+LABA
  - Fluticasone + Salmeterol
  - Budesonide + Formoterol
  - Fluticasone Fuorate + Vilanterol
  - PDE-4 Inhibitors
  - Roflumilast
  - Methylprednisolone

Rationale for Early Treatment in COPD

- The effect of treatment on lung function may be more marked in patients who are younger and in those with less severe disease1-4
- Lung function deteriorates more rapidly during the less severe, early stages of COPD5
- LABA and LAMA are recommended initial maintenance therapy for patients who are symptomatic but at low risk of exacerbations6
- Lack of data in treatment-naïve patients with mild or moderate airflow limitation7

Improving Outcomes in COPD

- Early diagnosis and accurate assessment
  - Identifying patients at risk
  - Using appropriate diagnostic approaches, ruling out other mimickers
  - Early treatment
- Implementing optimal management
  - Reducing exposures to risk factors and triggers
  - Non-pharmacological approaches
  - Pharmacological treatments
- Incorporating self-management skills through education and collaboration with a health care team
  - Improve adherence

Inhaler Devices Available in the U.S.

A large proportion (49-76%) of patients use their inhalers incorrectly.
GOLD guidelines recommend rechecking inhaler technique at each patient visit.

Summary

- COPD continues to be a major public health problem
- The pathophysiology of COPD involves chronic airway inflammation and lung destruction driven by several inflammatory cells and mediators
- COPD is a heterogenous disease with multiple phenotypes
  - Phenotypic characterization of COPD will improve personalized approach the disease

Summary

- Clinical approach to COPD includes assessment of symptoms, lung function, exacerbation risk and comorbidities
- Several non-pharmacological and pharmacological interventions are available which should be implemented according to disease severity
- Multiple novel targets of therapy are being evaluated and may be available in the future