New Insights Into COPD Management
November 3, 2017

John G. Mastronarde, M.D., M.Sc.
Garnjobst Chair, Department of Medical Education
Portland Providence Medical Center

Pulmonary/Critical Care/Sleep Medicine Staff Physician
The Oregon Clinic

Conflicts

• None
Outline/Objectives

- Case
- Definition
- Prevalence
- Etiology
- Pathogenesis
- Clinical Assessment
- Phenotypes
- Therapy

B.B. is a 61 yr old AA Female Referred for Dyspnea

- Symptoms began 1-2 years ago
- Shortness of breath especially with stair climbing or carrying things
- Will cough at times, not sure about wheezing
- No sputum since stopped smoking 1 year ago, but when smoking had morning cough with sputum
- Used asthmatic son’s SABA which helps but still with dyspnea
- 40 pack year tobacco history
- 0 hospital stays
- 2 ED visits for respiratory issues in past year
- Hx of GERD, rhinitis
- Exam mild end expiratory wheeze
- CXR normal
- Spirometry with moderate obstruction, not reversible with albuterol
- Baseline labs done 3 months prior unremarkable
COPD Definition

Global Strategy for the Diagnosis, Management and Prevention of COPD (GOLD 17)

*COPD is a common, preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases*

COPD is Common

- Currently 3rd leading cause of death in USA
- Death rate has doubled since 1969
- Death rate has declined for men but not women
Etiology

• Worldwide cigarette smoking is leading risk factor (50%)
• Biomass fuel exposure, air pollution, occupational exposures
• Genetic factors:
  – Alpha one anti trypsin deficiency
  – ?others
• Host factors:
  – Lung growth
  – Childhood environmental exposures
  – SES status

Pathogenesis

• COPD is an inflammatory lung disease
• Exposure to toxic fumes/particles leads to a dysregulated inflammatory response
• Inflammation results in parenchymal destruction and small airway fibrosis leading to airflow limitation and air trapping
• Mucous hypersecretion present in some but not all
COPD Clinical Assessment

COPD is likely in a patient with exposure to known risk factors with the following symptoms, especially in combination

• Dyspnea that is progressively worsened over time and persistent and worse with exercise especially increased work (carrying things)
• Sputum daily or intermittently
• Frequent lower respiratory track infections
• Family history of COPD

Symptom Questionnaires

Modified British Medical Research Council (mMRC)

| mMRC Grade 6 | I only get breathless with strenuous exercise. |
| mMRC Grade 5 | I get short of breath when hurrying or on the level or walking up a slight hill. |
| mMRC Grade 4 | I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level. |
| mMRC Grade 3 | I stop for breath after walking about 100 meters or after a few minutes on the level. |
| mMRC Grade 2 | I am too breathless to leave the house or I am breathless when dressing or undressing. |

- Well established
- Simple
- Single metric
- >1 abnormal
- ≥2 correlates with all cause mortality
Questionnaires

COPD Assessment Test

- Multi system
- Different but not superior to mMRC
- Cut point of 10
- *Cut Point of 17 correlates better with mortality
- GSK trademarked


Questionnaires

- So which to use?
- Personal preference
- I prefer the mMRC
- Good for trending especially after medication changes
- The other aspects of the COPD Assessment Test are important to document:
  - Sleep
  - Limitations from COPD and expectations with treatment
  - Mental Health issues
COPD Assessment

- Spirometry is required for diagnosis
- Spirometry is required for diagnosis
- Spirometry is required for diagnosis
  - Newer data suggests some people who smoke have COPD symptoms prior to onset of obstruction, so what do they have? Lots of debate right now with little clarity

2017: Not all COPD is alike
COPD is not a single disease
Phenotypes

- Tobacco Use
  - Active Smoker
  - Ex Smoker
  - Never Smoker
- Air flow obstruction
  - Fixed
  - Reversible
  - Normal
- Sputum
  - Frequent
  - Never
- Exacerbation History
  - Frequent (>2/yr or 1 hospitalization/yr)
  - Few
- Other toxic exposures
- Peripheral eosinophilia
- Asthma COPD Overlap
- Other
  - Symptoms with no obstruction
  - Obstruction with no symptoms
  - Chest CT changes with no symptoms

Therapy
Pulmonary Rehabilitation

- Underutilized
- May be the most effective therapy we have and is also cost effective
- Consider it for all patients if available
- Access is main limitation
- Advocate locally if possible

<table>
<thead>
<tr>
<th>Table 3.8. Pulmonary rehabilitation, self-management and integrative care in COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary rehabilitation</td>
</tr>
<tr>
<td>• Pulmonary rehabilitation improves dyspnea, health status and exercise tolerance in stable patients (Evidence A)</td>
</tr>
<tr>
<td>• Pulmonary rehabilitation reduces hospitalizations among patients who have had a recent exacerbation (≤ 4 weeks from prior hospitalization) (Evidence B)</td>
</tr>
</tbody>
</table>

GOLD 17

Vaccines

www.uptodate.com
Tobacco Cessation

- MD counselling can make a difference
- eCigarettes, it is unclear if help or not
- Oregon Health Authority Program:
  - [https://www.quitnow.net/oregon/](https://www.quitnow.net/oregon/)

<table>
<thead>
<tr>
<th>Table 3.1. Brief strategies to help the patient willing to quit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASK:</strong> Systematically identify all tobacco users at every visit. Implement an office-wide system that ensures that, for EVERY patient at EVERY clinic visit, tobacco-use status is queried and documented.</td>
</tr>
<tr>
<td><strong>ADVISE:</strong> Strongly urge all tobacco users to quit. In a clear, strong, and personalized manner, urge every tobacco user to quit.</td>
</tr>
<tr>
<td><strong>ASSESS:</strong> Determine willingness and rationale of patient's desire to make a quit attempt. Ask every tobacco user if he or she is willing to make a quit attempt at this time (e.g., within the next 30 days).</td>
</tr>
<tr>
<td><strong>ASSIST:</strong> Aid the patient in quitting. Help the patient with a quit plan; provide practical counseling; provide intra-treatment social support; help the patient obtain extra-treatment social support; recommend use of approved pharmacotherapy except in special circumstances; provide supplementary materials.</td>
</tr>
<tr>
<td><strong>ARRANGE:</strong> Schedule follow-up contact. Schedule follow-up contact, either in person or via telephone.</td>
</tr>
</tbody>
</table>

Pharmacotherapies
Phenotypic Therapy

• Mild symptoms (mMRC 0-1) SOB walking up hill or with fast exertion
  – Prn short acting bronchodilator (albuterol) or Long Acting Muscarinic Antagonist (LAMA) or Long Acting Beta Agonist (LABA)
  – LAMA preferred over LABA as it reduces exacerbations

Phenotypic Therapy

• Symptoms continue or worsen (mMRC >2, have to stop and catch breath) or > 2 exacerbation(s) despite bronchodilator:
  – Combination therapy with LAMA/LABA
  – Note if you are treating symptoms or exacerbations
Phenotypic Therapy

• Combination of Long acting bronchodilators
  – Long Acting Muscarinic Antagonist (LAMA) + Long Acting Beta Agonist (LABA)
• Now preferred over combination of inhaled corticosteroid + LABA (ICS/LABA)
• Improved outcomes and ongoing concern of pneumonia in COPD with ICS

Phenotypic Therapy

• Symptoms persist and/or more exacerbations
• Symptoms
  – Can add ICS (triple inhaler)
    • Not for everyone, PNA risk seems real
    • Chronic bronchitis and/or (+) BD
    • Smoking status
    • F/up for effect and d/c if none
    • ?Eo’s
  – Double down on rehab, adherence, Co morbidities
• Exacerbations
  – ICS (ditto above)
  – Ex smoker, macrolide
    • Azithro 500 mg MWF
  – Roflumilast
  – NAC
Frequent Exacerbation Phenotype
Macrolide

- Data has been mixed due to heterogeneity in severity of COPD, definition of exacerbation prone and regimen of azithromycin
- Meta Analysis suggests a modest reduction in exacerbations overall with improvement in time to next exacerbation and quality of life with no impact on mortality
- Sub group analysis suggests smoking history may confound results with active smokers and those <65 years not as responsive

Wedzicha, et al ERJ 2017

Macrolide

- Data on resistance to azithromycin has been inconsistent and thus far not proven to be valid issue
- QT prolongation with lots of press but actually rare
- Need to be attentive to other meds that can increase QT and avoid if baseline EKG reveals a prolonged QTc (>450 ms or 500 ms)
- Hearing loss also inconsistent in studies but reasonable to inform patients about potential and d/c if occurs
**Roflumilast**

- Roflumilast is a phosphodiesterase-4 inhibitor
- Some data support use in severe COPD to reduce exacerbations
- Expensive
- Lots of side effects especially GI which can lessen with time but limit patient acceptance

**Other Agents**

- Mucolytics/Antioxidants may reduce symptoms and hospitalizations in some patients with moderate – severe COPD
  - NAC 600 mg bid most common one used
- Daily oral steroids are not beneficial and harmful for stable COPD
- Oral steroids help with AECOPD with short courses often enough (30 mg-40 mg x 5-7 days)
- Antibiotics appear useful for AECOPD especially with signs of infection
  - “ID bundles” may impact this in the future
An Oldie but ? Goodie

- GOLD 17 doesn’t like theophylline, but I do
  - Conflicting data on efficacy but some supportive
  - No good phenotypic specific data
  - ? Smokers
  - I trial 300 XL q day for some who either fail inhalers or can’t afford them or smoke
  - It is cheap, minimal toxicity at that dose

Failure to Improve

- Adherence
  - Motivation/knowledge “Tell me when you take your inhalers”
  - Cost “Can you afford your medicines?”
  - Community Resources/Case Management
- Inhaler technique
  - “Show my how you take your inhaler”
- Environmental issues in home/work
- Other medications (beta blocker, ACEi, et.)
- Herbs, supplements, marijuana
- Maximize Co Morbidities
  - Don’t forget about Pulmonary Hypertension
Asthma COPD Overlap

- Prevalence of smoking amongst asthmatics 20%-30%
- Recognition some people may have features of both asthma & COPD
- Patients with features of both asthma and COPD have worse outcomes than those with asthma or COPD alone
  - Frequent exacerbations
  - Poor quality of life
  - More rapid decline in lung function
  - Higher mortality
  - Greater health care utilization
- Reported prevalence of overlap varies by definitions used
  - Concurrent doctor-diagnosed asthma and COPD are found in 15–20% of patients with chronic airways disease
  - Prevalence varies by age and gender
Asthma COPD Overlap

- Need much more data but likely will hear more about this
- For now think just be aware and consider as you phenotype
- These may be the COPD patients who actually benefit from ICS

Non Pharmacologic Therapies
Who needs oxygen?

Multi Center NIH trial
- Enrolled 738 people with COPD with:
  - SpO2 89%-93% at rest or
  - SpO2 < 90% for > 10 secs but remaining
    > 80% for > 5 minutes with exercise
- Mean follow up 18 months
- Primary Outcome was death or time to initial hospitalization
  - Found no difference with oxygen Rx
- Secondary outcomes of all hospitalizations, exacerbations, QOL, lung function, 6 minute walk, depression also no difference
- Did not include:
  - Nocturnal desaturations
  - Dyspnea with exercise that improves on oxygen
  - Co morbidities not factored in

Who needs oxygen?

- Previous data is from 1970s and not well done by current standard
- Criticisms appear weak given robust findings and issues with previous data
  - Pt’s who “feel better” on oxygen? Athletes on sidelines feel better too
- How clinicians adopt new evidence into their practice will be interesting
- Oxygen is expensive for third party payers

<table>
<thead>
<tr>
<th>Table A.10. Oxygen therapy and ventilatory support in stable COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen therapy</td>
</tr>
<tr>
<td>The long-term administration of oxygen increases survival in patients with severe chronic resting arterial hypoxemia (Evidence A).</td>
</tr>
<tr>
<td>In patients with stable COPD and moderate resting or exercise-induced arterial desaturation, prescription of long-term oxygen does not lengthen time to death or first hospitalization or provide sustained benefit in health status, lung function, and 6-minute walk distance (Evidence A).</td>
</tr>
</tbody>
</table>

GOLD 17
Non Invasive Mechanical Ventilation

• Standard now for acute exacerbations in ED
• Ongoing debate on use in “stable” COPD
• Some data suggests those with elevated pCO2 may benefit but there is conflicting data and nothing is definitive
Interventional options

Shared decision making key at this stage and goals of care should be clarified

Table 3.11. Interventional therapy in stable COPD

- Lung volume reduction surgery
  - Lung volume reduction surgery improves survival in severe emphysema patients with an upper-lobe emphysema and low post-rehabilitation exercise capacity (Evidence A).
- Bullectomy
  - Bullectomy is associated with decreased dyspnea, improved lung function and exercise tolerance (Evidence C).
- Transplantation
  - In appropriately selected patients with very severe COPD, lung transplantation has been shown to improve quality of life and functional capacity (Evidence C).
- Bronchoscopic interventions
  - In selected patients with advanced emphysema, bronchoscopic interventions reduce end-expiratory lung volume and improve exercise tolerance, health status and lung function at 6-12 months following treatment. Endobronchial valves (Evidence B); Luna coils (Evidence B).

GOLD 17

Not Recommended

- Mono therapy with ICS
- Daily oral steroids
- Montelukast or any leukotriene modifier
- Anti Tussives
- Statins
- Vasodilators for Pulmonary Hypertension
B.B. is a 60 yr old AA Female Referred for Dyspnea

- Symptoms began 1-2 years ago
- Shortness of breath especially with stair climbing or carrying things
- Will cough at times, not sure about wheezing
- No sputum since stopped smoking 1 year ago, but when smoking had morning cough with sputum
- 0 hosp stays
- 0 ED visits or unscheduled health care visits in past year
- Used asthmatic son’s SABA which helps but still with dyspnea
- Hx of GERD
- Exam mild end expiratory wheeze
- CXR normal
- Spirometry with moderate obstruction, not reversible with albuterol
- Baseline labs done 3 months prior unremarkable

Therapy
- LAMA with pulmonary rehabilitation/vaccines and SABA prn
- Fails then LAMA/LABA
- Fails then need to consider other factors to choose next agent
  - Exacerbations
  - ?Eo’s

Summary

- Document phenotype and spirometry on diagnosis
- Pulmonary Rehab, Vaccines, Tobacco Cessation for all
- Consider patient’s phenotype as select agents
- Symptoms
  - LAMA + Pulmonary Rehab
- Ongoing Symptoms/Exacerbations
  - LAMA + LABA
  - Adherence, co morbidities (old and new)
- Fails to improve or worsens
  - Asthma like or chronic bronchitis: ICS (follow up closely)
  - Exacerbations: ICS or macrolide or PDE (-)
  - Oxygen assessment
  - Considerations: theophylline, NAC
  - Severe: LVRS, Bullectomy, Transplant
References

• GOLD 2017: www.goldcopd.org

Lets go Bucks!