COPD

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Disclosures

• Hill-Rom, Inc.
• Integrated Diagnostics
• ResMed
Objectives

• Diagnose and characterize COPD
• Recognize symptoms and exacerbations
• Manage stable COPD patients
  – non-pharmacologic and
  – pharmacologic treatment
• Manage Acute Exacerbations of COPD
Guidelines

- GOLD
- ACP/ACCP/ATS/ERS
  - (American College of Physicians, American College of Chest Physicians, American Thoracic Society, European Respiratory Society)
My COPD Guidelines

• Make sure it's COPD
• Make sure COPD fully explains the issues
• Eliminate/reduce exposures
• Vaccinate
• If symptoms/flare, treat with meds and rehab
• More symptoms/flare, more treatment
• If there are other problems, treat those too
• Consider surgery/procedures
• The best treatments are the ones patients can afford and are willing/able to use
Global Initiative for Chronic Obstructive Lung Disease

- 2017 Guidelines (4th major version)
- International consensus
- Evidence based
  - A: RCTs; rich body of evidence
  - B: RCTs; important limitations
  - C: Non randomized and Observational studies
  - D: Panel judgement
COPD Definition: GOLD 2017

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

- Dyspnea
- Cough
- Phlegm
- Can’t breathe
- Can’t take a deep breath
- Wheeze
COPD Risk Factors

• Smoking
  – Most common cause, but as many of 1 out of 4 people with COPD never smoked

• Environmental / Occupational exposure
  – Chemicals, dusts, fumes
  – Secondhand smoke, pollutants, particulate matter, bio-mass fuels

• Genetic Factor
  – Alpha-1 antitrypsin (AAT) deficiency
CELLULAR MECHANISMS OF COPD

Barnes PJ: Nat Immunol 2008

Epithelial cells

Cigarette smoke (and other inhaled irritants)

Macrophage

CCR3

Eosinophil

CCL5 (IL-4, IL-5)

TGF-β

CXCL9,10,11

CXCL1

CXCL8

CCL2

CCR2

Monocyte

Th1 cell

Tc1 cell

CXCR3

CXCR2

Neutrophil

Fibroblast

Fibrosis (Small airways)

Alveolar wall destruction (Emphysema)

Neutrophil elastase

MMP-9

Mucus hypersecretion

PROTEASES

Professor Peter J. Barnes, MD
National Heart and Lung Institute, London UK
Diagnosis of COPD

**SYMPTOMS**
- shortness of breath
- chronic cough
- sputum

**EXPOSURE TO RISK FACTORS**
- tobacco
- occupation
- indoor/outdoor pollution

**SPIROMETRY:** Required to establish diagnosis

Global Strategy for Diagnosis, Management and Prevention of COPD
Spirometry

• Most reproducible and objective measurement of airflow limitation
• Non invasive
• Readily available
• Volume of air forcibly exhaled from maximum inspiration (FVC)
• Volume of air exhaled during 1st second (FEV1)
• Done before and after bronchodilator
Spirometry: Obstructive vs Restrictive Pattern

<table>
<thead>
<tr>
<th>Volume, liters</th>
<th>Time, seconds</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
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<td>3</td>
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<td>5</td>
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Obstructive
Restrictive
Normal
Spirometric criteria for airflow limitation

- FEV1/FVC <0.70
  - Small risk of misclassification
  - Overtreatment risk low given other clinical criteria for diagnosis and treatment
  - Simple for busy clinician
- LLN (lower limit of normal)
- Global lung initiative equations
• Based upon symptoms and risk for exacerbations

• Lung function no longer used

GOLD ABCD categories

Exacerbation history

Symptoms

Airflow obstruction

(C) MMRC 0-1 CAT <10  
(D) MMRC ≥2 CAT ≥10

GOLD guidelines, goldcopd.org, updated 2017.
## Modified Medical Research Council Questionnaire (MMRC)

<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 when walking at my own pace</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

- 9 questions about symptoms (0-5):
  - Cough
  - Phlegm
  - Chest tightness
  - Breathlessness walking up a hill
  - Activity limitation
  - Confidence leaving home
  - Sleep
  - Energy

- GOLD symptoms >= 10
Assessment of exacerbation risk

- Acute worsening of respiratory symptoms that result in additional therapy
- 2 or more past year
- Use history, not FEV1
- Serum eosinophils may predict
GOLD ABCD categories

- Based upon symptoms and risk for exacerbations
- Lung function no longer used

Exacerbation history

Airflow obstruction

Symptoms

- MMRC 0-1
- CAT <10
- MMRC ≥2
- CAT ≥10

GOLD guidelines, goldcopd.org, updated 2017.
Management of Stable COPD

• Based on individual assessment of symptoms and exacerbation risk

• Treat to:
  – Reduce symptoms
  – Minimize risk of future exacerbations
## Non-pharmacologic Care

<table>
<thead>
<tr>
<th>PATIENT GROUP</th>
<th>ESSENTIAL</th>
<th>RECOMMENDED</th>
<th>DEPEND ON LOCAL GUIDELINES</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SMOKING CESSATION (include pharma treatment)</td>
<td>Physical activity</td>
<td>Flu vaccine Pneumococcal vaccine</td>
</tr>
<tr>
<td>B, C, D</td>
<td>Same as above plus Pulmonary Rehab</td>
<td>Same as above</td>
<td>Same as above</td>
</tr>
</tbody>
</table>
Identify and Reduce Exposure to Risk Factors

• Smoking cessation (Evidence A)
  – Counseling
  – Pharmacotherapies (NRT, varenicline, bupropion)

• Efficient ventilation, non-polluting cook stoves (Evidence B)

• Advise to avoid continued exposures to potential irritants (Evidence D)
Vaccines

• Influenza (Evidence A)
• Pneumococcal (PPSV23) < 65 yo, FEV1 <40% (Evidence B)
• Pneumococcal (PCV13) >=65 yo (Evidence B)

• I like to offer Pertussis as well
Oxygen
(Evidence A)

- PaO2 < 55 mmHg or SaO2 < 88%, or
- PaO2 < 60 mmHg with RHF or ↑RBC
- Reassess in 60-90 days
- Don’t routinely treat lesser desats or exercise desat
Pulmonary Rehabilitation

• Tailored after evaluation
• Includes:
  – Exercise training
  – Education
  – Self management intervention targeting behavior change
• Typically 6-8 weeks +
Pulmonary Rehabilitation Benefits

• Improves dyspnea, health status and exercise tolerance in stable patients (Evidence A)
• Reduces hospitalization if recent exacerbation (<= 4 weeks) (Evidence B)
Interventional Therapy

- **Lung Volume Reduction Surgery**: Improved survival with upper lobe predominant emphysema and low exercise capacity after rehab (Evidence A)
- **Bullectomy**: Selected patients associated with improved dyspnea, lung function, exercise tolerance (Evidence C)
- **Lung transplant**: Very severe, selected. Improved QOL and functional capacity (Evidence C)
- **Bronchoscopic valves and coils**: Selected patients, advance emphysema; improves exercise, health status and lung function (Evidence B)
Medication terminology

• SABA: Short-acting Beta$_2$ Agonist
• SAMA: Short-acting Muscarinic Antagonist
  – AKA: Anticholinergic
• LABA: Long-acting Beta$_2$ Agonist
• LAMA: Long-acting Muscarinic Antagonist
• ICS: Inhaled Corticosteroid
• OCS: Oral Corticosteroid
Key points for inhaled drugs

• Choice based on access, cost, prescriber, patient ability and preference
• Essential to provide instructions and demonstration
• Re-check at each visit
Key points: Bronchodilators

• LABAs and LAMAs preferred over short acting, unless only occasional dyspnea (Evidence A)
• Start on 1 or 2 agents. Escalate to 2 if 1 is not enough (Evidence A)
• Inhaled not oral (Evidence A)
• Theophylline only if others not available or affordable (Evidence B)
Key points: Anti-inflammatories

• ICS monotherapy not recommended (Evidence A)
• Consider ICS with LABA if exacerbations despite use of BD (Evidence A)
• Long term oral steroids not recommended (Evidence A)
Key points: Not recommended

- Antitussives (Evidence C)
- Drugs approved for PPH in patients with PH from COPD (Evidence B)
- Statin therapy to prevent exacerbations (Evidence A)
GOLD ABCD categories

Exacerbation history

Symptoms

- MMRC 0-1
- MMRC ≥2
- CAT <10
- CAT ≥10

GOLD guidelines, goldcopd.org, updated 2017.
Pharmacologic Therapy: Group A (Low symptoms, Low risk)

- Offer a bronchodilator
- Either short or long acting
- Continue if symptom benefit
Pharmacologic Therapy: Group B
(High symptoms, Low risk)

• Start a bronchodilator
• Long acting superior to short acting
• Either LAMA or LABA
• If symptoms still, add other class
• If severe symptoms, can start on LAMA/LABA
Pharmacologic Therapy: Group C (Low symptoms, High risk)

• Start a long acting bronchodilator
• LAMA preferred
• If exacerbations still:
  – LAMA/LABA, or
  – LABA/ICS
• Pneumonia risk in some with ICS
Pharmacologic Therapy: Group D
(High symptoms, High risk)

• Start LABA/LAMA
• LABA/LAMA preferred over LABA/ICS (unless asthma overlap or serum eosinophils)
• If exacerbations still:
  – LABA/LAMA/ICS, or
  – LABA/LAMA
• If exacerbations on LABA/LAMA/ICS:
  – Roflumilast (FEV1 <50% and chronic bronchitis)
  – Macrolide (Azithromycin)
Eosinophilia and response to inhaled corticosteroids

- Post-hoc analysis of data from 2 RCTs, including 3177 patients total
- Vilaanterol alone vs varying doses of fluticasone
- Stratified by eosinophilia
- Significant reduction in exacerbations for all groups with ICS in the group with eosinophilia
- In vilaanterol only group there was increase in rate of exacerbations with increasing eosinophil percentage
Azithromycin for “frequent exacerbators”

- Dose: 250mg daily
- RCT of 1,577 participants (enriched for exacerbations)
- Risk for exacerbation in azithro group lower vs placebo (HR 0.73)
- SGRQ score improved more in azithro group: 2.8 +/- 12.1
Titrate down when possible

- GOLD propose “a personalization of initiating and escalating/de-escalating treatment”
- “Only partially from evidence generated in randomized controlled trials.”
Withdrawal of ICS

- 12-month RCT of 2,485 patients on “triple therapy”
- Moderate to severe COPD with exacerbation in past year
- Non-inferiority study, margin set at HR 1.20 (arbitrary)
- Non-inferiority met for primary outcome, HR 1.06 (0.94-1.19)

Magnussen et al. NEJM, 2015.
Withdrawal of ICS

• Some benefit noted for quality of life outcomes and lung function in group continuing ICS

Magnussen et al. NEJM, 2015.
Management of Exacerbations

• Acute worsening of respiratory symptoms
• Goals are to minimize impact and prevent future events
Frequent Exacerbator phenotype

- 2+ exacerbations per year
- Triggers for exacerbations: Bacteria, viruses, irritants
- Have higher burden of comorbidities, esp CV
- Outcomes:
  - Poorer QOL and health status
  - Faster FEV1 decline
  - More healthcare utilization
  - Higher mortality

How Your Lung Function Changes as You Age

Lung Function (% Predicted)

Faster decrease in lung function with COPD because of flare-ups

General decrease in lung function with COPD because of smoking

Impact of quitting smoking

FEV₁, Forced Expiratory Volume in one second

Age (Years)

Key Points: Management of Exacerbations

• SABA +/- SAMA initially (Evidence C)
• Systemic Corticosteroids improve lung function, shorten recovery and hospitalization (Evidence A)
  – 5-7 days Prednisone 40 mg
• Antibiotics can shorten recovery, reduce risk of relapse, treatment failure (Evidence B)
• Non-invasive ventilation for acute respiratory failure (Evidence A)
Bronchodilators

• No high quality RCT evidence
• MDI same as nebulized
• One puff every hour X 2-3
• Then every 2-4 hours
• Continue or start long acting agents
Systemic Corticosteroids

• Shorten recovery time and improve lung function and oxygenation
• Prednisone 40 mg X 5 days
• Oral same as IV
Antibiotics

• Still controversial
• Give if 2 or 3 of these:
  – Increased dyspnea
  – Increase sputum volume
  – Sputum purulence
• Treat 5-7 days
• Many choices of agent
Non-invasive Ventilation

• Indications
  – Respiratory acidosis
  – Severe dyspnea with signs of muscle fatigue and/or increased work of breathing
  – Refractory hypoxemia
COPD and Co-Morbidity

• Common to have other health conditions
• Look out for:
  – Cardiovascular disease
  – Depression and anxiety
  – Osteoporosis
  – Metabolic disorders
  – Lung Cancer
• Treat per other care guidelines
• Consider pharmacist input
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