Improving Outcomes in COPD

Updates 2018

Neil MacIntyre MD
Duke University
Durham NC

Improving Outcomes in COPD

• COPD – pathophysiology, clinical picture/impact
• Diagnosis and staging
• Evidence based management guidelines
• Barriers to implementation

COPD spectrum

- Proximal predominant (large airways)
  - mucus gland hypertrophy (cough/sputum)
  - reduced respiratory drive
  - airway hyper-reactivity
- Distal predominant (small airways/alveoli)
  - dyspnea - active respiratory drive
  - reduced DLCO

COPD: the clinical spectrum

- Emphysema
- Bronchitis

COPD is a systemic disease

- Chronic airway inflammation “spills” inflammatory cytokines into the circulation
  - ASCVD
  - Renal insufficiency
  - Neuro-myoopathy
  - Osteoporosis
- Cachexia, debility may be product of this

COPD natural history depends on tobacco exposure/sensitivity

- Expiratory Flow Limitation
- Air Trapping
- Hyperinflation
- Exacerbations
- Dyspnea
- Deconditioning
- Reduced Exercise Endurance
- Inactivity
- Poor Health-Related Quality of Life
COPD Projected to Be the Third-Leading Cause of Death by 2020

Coronary Heart Disease Stroke Other CVD COPD All Other Causes

COPD Projected to Be the Third-Leading Cause of Death by 2020

Mortality and Mortality: 2002 Chart Book on Cardiovascular, Lung, and Blood Diseases. NIH/NHLBI. May 2002

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Diagnostic of COPD

EXPOSURE TO RISK FACTORS

SYMPTOMS
- sputum
- cough
- dyspnea
- wheezing

SPIROMETRY

Spirometry

Spirometry

COPD: the spirogram

Normal
Obstructed
Restricted

Global Initiative for Chronic Obstructive Lung Disease teaching slide kit. Available at: www.goldcopd.com/slides/download.ppt.

Proportion of 1965 Rate
Percentage Change in Age-Adjusted Death (US)

1.0 1.5 2.0 2.5 3.0

0.0 0.5 1.0 1.5 2.0

Nursing Home Care
Home Health Care
Physician Services
Hospital Care
Prescription Drugs


†

John Hutchinson
January 22nd 1846
Global Obstructive Lung Disease (GOLD) Consortium Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>FEV(_1)/FVC (%)</th>
<th>FEV(_1) (L)</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: Mild</td>
<td>None</td>
<td>&gt;70</td>
<td>&gt;80</td>
<td>No chronic symptoms</td>
</tr>
<tr>
<td>II: Moderate</td>
<td>50 ≤ FEV(_1)/FVC &lt; 70%</td>
<td>50 ≤ FEV(_1) &lt; 80%</td>
<td>With or without symptoms</td>
<td></td>
</tr>
<tr>
<td>III: Severe</td>
<td>FEV(_1)/FVC &lt; 50%</td>
<td>FEV(_1) &lt; 50%</td>
<td>With or without symptoms</td>
<td></td>
</tr>
<tr>
<td>IV: Very Severe</td>
<td>FEV(_1)/FVC &lt; 30%</td>
<td>FEV(_1) &lt; 30%</td>
<td>With or without symptoms</td>
<td></td>
</tr>
</tbody>
</table>

www.goldcopd.com

Spirometry can miss emphysema

In COPDgene, 357 of 858 smokers with normal spirometry had emphysema on CT

Symptoms/function as important as FEV\(_1\) on survival

BODE: Dyspnea, 6MWT, BMI, FEV\(_1\)

GOLD 2017: Combined Assessment of COPD

- Diagnose COPD
  - Spirometry not enough
  - Radiology (hyperinflation, emphysema) and DLCO alternate diagnostic tools
- Two components determine severity of disease
  - Symptom assessment
  - Risk of exacerbations

GOLD Classification of Airflow Limitation

Risk (Exacerbation history)

Risk (GOLD Chronic Obstructive Lung Disease)

Symptoms

mMRC 0-1 CAT < 10

mMRC ≥ 2 CAT ≥ 20

GOLD 2017

1) Diagnose  2) Obstruction Severity  3) Impact

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GOLD Guidelines 2017
Guided by impact – not physiology

Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Non-pharmacologic

Patient Group | Essential | Recommended | Depending on local guidelines
---|---|---|---
A | Smoking cessation (can include pharmacologic treatment) | Physical activity | Flu vaccination, Pneumococcal vaccination
B, C, D | Smoking cessation (can include pharmacologic treatment) | Physical activity | Flu vaccination, Pneumococcal vaccination

Current Inhaled Medications for COPD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand</th>
<th>Usual Starting Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta-Agonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol</td>
<td>ProAir, Proventil, Ventolin</td>
<td>2 puffs q 4-6 hrs PRN</td>
<td>4-6 h</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>Xopenex HFA</td>
<td>2 puffs q 4-6 hrs PRN</td>
<td>4-6 h</td>
</tr>
<tr>
<td>Pirbuterol</td>
<td>Maxair Autohaler</td>
<td>2 puffs q 4-6 hrs PRN</td>
<td>5 h</td>
</tr>
<tr>
<td>Long-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formoterol</td>
<td>Foradil, Aerolizer, Perforomist, Brossura</td>
<td>1 inhaled capsule bid</td>
<td>12+ h</td>
</tr>
<tr>
<td>Indacaterol</td>
<td>Arcapta Neohaler</td>
<td>1 inhaled capsule daily</td>
<td>24+ h</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Serevent Diskus</td>
<td>1 puff bid</td>
<td>12+ h</td>
</tr>
</tbody>
</table>

**Anticholinergics**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand</th>
<th>Usual Starting Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium bromide</td>
<td>Atrovent</td>
<td>2 puffs qd</td>
<td>8-8 h</td>
</tr>
<tr>
<td>Long-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tiotropium bromide</td>
<td>Spiriva Handihaler</td>
<td>1 inhaled capsule daily</td>
<td>24+ h</td>
</tr>
</tbody>
</table>

**Combination Bronchodilators**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand</th>
<th>Usual Starting Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol/Ipratropium</td>
<td>Combivent</td>
<td>2 puffs q 4-6 hrs PRN</td>
<td>4-6 h</td>
</tr>
<tr>
<td>Umeclidinium/Vilanterol</td>
<td>Anoro Ellipta</td>
<td>1 puff daily</td>
<td>24 h</td>
</tr>
</tbody>
</table>

* NEW: Tiotropium/olodaterol (*Stiolto*)

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<th>Brand</th>
<th>Usual Starting Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled Corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide</td>
<td>Pulmicort Flexhaler</td>
<td>1-2 puffs bid</td>
<td>12 h</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>Flovent HFA</td>
<td>1-2 puffs bid</td>
<td>12 h</td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>QVAR</td>
<td>1-2 puffs bid</td>
<td>12 h</td>
</tr>
<tr>
<td>Combination Inhalers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formoterol/Budesonide</td>
<td>Symbicort</td>
<td>2 puffs bid</td>
<td>12 h</td>
</tr>
<tr>
<td>Fluticasone/Salmeterol</td>
<td>Advair Diskus</td>
<td>1 puff bid</td>
<td>12 h</td>
</tr>
<tr>
<td>Fluticasone/Vilanterol</td>
<td>Bren Ellipta</td>
<td>1 puff daily</td>
<td>24 h</td>
</tr>
</tbody>
</table>

Combination Inhalers:
- Formoterol/Budesonide: Symbicort 2 puffs bid 12 h
- Fluticasone/Salmeterol: Advair Diskus 1 puff bid 12 h
- Fluticasone/Vilanterol: Bren Ellipta 1 puff daily 24 h

Combination Inhalers:
- Formoterol/Budesonide: Symbicort 2 puffs bid 12 h
- Fluticasone/Salmeterol: Advair Diskus 1 puff bid 12 h
- Fluticasone/Vilanterol: Bren Ellipta 1 puff daily 24 h

HFA = hydrofluoroalkane; PDE4 = phosphodiesterase 4.

The latest compounds and formulations - 2017

- LABAs
  - Oladaterol SMI (Stiverdi)
- LAMAs
  - Glycopyronium DPI (Seebri)
  - Umeclidium DPI (Incruse)
- LABA/ICS
  - Formoterol/beclamethasone MDI and DPI (Fostair)
  - Formoterol/mometasone MDI (Dulera)

The latest compounds and formulations - 2018

- LAMA/LABA
  - Formoterol/acilidinium DPI (Genuair)
  - Formoterol/glycopyronium MDF (Bevespi)
  - Indacaterol/glycopyronium DPI (Ultibo)
  - Oladaterol/tiotropium SMI (Stiolto)

- LAMA/LABA/ICS
  - “Stay tuned” – Trelegy Ellipta

HFA = hydrofluoroalkane; PDE4 = phosphodiesterase 4.

Current Oral Medications for COPD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand</th>
<th>Usual Starting Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>4-48mg/day depending on disease and response</td>
<td>12-24 h</td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5-60mg/day depending on disease and response</td>
<td>12-24 h</td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>5-60mg/day depending on disease and response</td>
<td>12-24 h</td>
<td></td>
</tr>
<tr>
<td>PDE4 Inhibitor</td>
<td>Daliresp</td>
<td>One 500 mcg tablet daily</td>
<td>17+ h</td>
</tr>
</tbody>
</table>

Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recommended First Choice</th>
<th>Alternative Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SAMA prn or SABA prn</td>
<td>LAMA or LABA or SABA and SAMA</td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>LAMA and LABA</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA and LABA or PDE4-ih or LABA and PDE4-ih</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA or LAMA</td>
<td>ICS + LABA and LAMA or ICS-LABA and PDE4-ih or LABA and PDE4-ih</td>
</tr>
</tbody>
</table>

Other Management Issues

- Oxygen
  - Rest/episodic
  - Targets? SpO2>88% correct?
- Nocturnal NIV for hypercapnia (high pressure)
  - Lancet Resp Med 2014; Sept 2: 298
  - JAMA 2017;317:2177
- Lung volume reduction procedures
  - Surgery vs bronchoscopic
- Action plan for AECOPD
  - Bronchodilators/antibiotics/steroids/hot line
Improving Outcomes in COPD

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Barriers

- Clinician barriers
  - Proper diagnosis/staging/prescribing per guidelines
- Patient barriers
  - Understanding complex medication regimens
  - Adherence to treatment plans (both pharmaceutical and non-pharmaceutical)
- System barriers
  - Costs of medications
  - Clinical support structures

Clinical COPD Is Just The Tip Of The Iceberg

2 Million "severe"
10 Million Dx
2 Million at risk

COPD Often Unrecognized During Hospitalization.

Percentage Correctly Diagnosed With Obstructive Lung Disease

Mild
Moderate
Severe
Very Severe

SPR Performance 2006-2012

PCE Performance 2008–2012

PCE Performance 2008–2012

Pharmacotherapy: Bronchodilators (HMO)

- Commercial
- Medicaid
- Medicare

2008 2009 2010 2011 2012

Barriers

- Clinician barriers
  - Proper diagnosis/staging/prescribing per guidelines
- Patient barriers
  - Understanding complex medication regimens
  - Adherence to treatment plans (both pharmaceutical and non-pharmaceutical)
- System barriers
  - Costs of medications
  - Clinical support structures

LABA Adherence

- N = 1014 COPD in health plan given new LABA
- Prescription filling over 1 year:
  - >80% 26%
  - 60-70% 14%
  - 40-50% 20%
  - 20-30% 21%
  - <20% 19%

Why aren’t patients adherent?

- Lack of understanding of importance
  - Maintenance vs rescue
- Ineffective use of devices
  - Breathing maneuvers, device operation
- Costs
  - The “donut hole” and drugs running several hundred $/month

Cost Differences Between Baseline and Follow-up

Barriers

- Clinician barriers
  - Proper diagnosis/staging/prescribing per guidelines
- Patient barriers
  - Understanding complex medication regimens
  - Adherence to treatment plans (both pharmaceutical and non-pharmaceutical)
- System barriers
  - Costs of medications
  - Clinical support structures
System Barriers

- Access to clinicians
  - Priority scheduling
  - Hot lines
  - Home visits
  - Education

- Discharge planning
  - Medications
  - Follow-up plans

- Pulmonary rehabilitation centers

Barriers to pulm rehab

- Less than 2% of COPD patients use PR (COPD 2014; July 1)

- Why not more?
  - Limited number of programs
  - Cost/reimbursement issues (now CMS reimbursed)
  - Logistics (transport, timing)
  - Motivation

Clinical Support Structure

- Access to clinicians
  - Hot lines
  - Home visits
  - Education

- Discharge planning
  - Medications
  - Follow-up plans

- Rehabilitation centers

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