AECOPD Session: Risk Factors for Poor Outcomes in COPD

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Faculty Disclosures

- Investigator/Grants/Research/Continuing Education:
  - Federal: National Institute of Health; Veterans Affairs
  - State: University of Texas System (Patient Safety Education Grant)
  - Private/Non-profit: Chest Foundation (GSK Distinguished Scholar Award)
  - Pharmaceutical: AstraZeneca Pharmaceuticals LP; Bayer Pharmaceuticals; Boehringer Ingelheim Pharmaceuticals; Inc; Centocor Inc; GlaxoSmithKline; Novartis Pharmaceuticals; Pfizer Inc; Schering-Plough

- Advisor/Speaker’s Bureau/Consultant/Stocks:
  - None

- Other:
  - President of the not-for-profit entity entitled The WipeDiseases Foundation
Overall Learning Objectives

At the completion of this activity, the participants should be able to:

• Identify and address risk factors for complications of COPD in a clinical scenario
• Count the risk factors in the following case...
Mrs. S.

• 54 year-old woman (accountant) with hypertension, anxiety, gastroesophageal reflux disease, and “very bad COPD” referred to your Pulmonary clinic for further evaluation.
• She has had two emergency department visits and one hospitalization in the last year for “bronchitis”
• She admits to a “smoker’s cough” (white sputum), dyspnea at 50 meters, reflux symptoms daily, and episodes of severe anxiety
• Medications: angiotensin converting enzyme inhibitor, short-acting beta_2_ agonist (currently using two puffs every four hours), and over-the-counter antacids (currently using 8-10 tablets/day)
Mrs. S. (Continued)

• Continues to smoke one to two packs per day for the last 34 years
• Physical examination is significant for the following:
  – Body Mass Index (BMI) = 18m/kg²
  – Pulse 110/minute, Respiratory Rate 22/minute, Blood Pressure 156/92
  – Lungs: diffuse expiratory wheezing and bibasilar crackles
  – Heart: Tachycardic, but regular rhythm, increased P2
  – Extremities: 1+ edema, no clubbing
• No prior measurement of spirometry or oxygen saturation
Mrs. S. (Continued)

- **Spirometry:**
  - Pre-bronchodilator:
    - FEV₁/FVC = 58%
    - FEV₁ = 1.20 L (48% predicted)
  - Post-bronchodilator:
    - FEV₁/FVC = 62%
    - FEV₁ = 1.46 L (60% predicted)
      (+22% improvement)

- **Lung Volumes:**
  - TLC = 140% predicted
  - RV = 280% predicted

- **Diffusion Capacity:**
  - DL$_{CO}$ = 18% predicted

- Saturation by pulse oximetry = 86% (room air at rest)
How many risk factors for complications of COPD did you count in this particular patient (Mrs. S)?

1. <5
2. 5-9
3. 10-14
4. >15
What is an independent risk factor for mortality in this particular patient with COPD?

1. Heavy tobacco use (50+ pack-years)
2. Body mass index (18m/kg^2)
3. Spirometry values (FEV\textsubscript{1}/FVC of 62%)
4. Abnormal lung examination (wheezing)
Muscle Wasting / Atrophy / Cachexia
Pulmonary Cachexia Syndrome

- Body mass index < 20kg/m²
- 25-35% of patients with moderate to severe COPD have malnutrition
- Associated with worse outcomes:
  - Accelerated decline in functional status
  - Increased risk for admission for exacerbation of COPD
  - Independent predictor of mortality

Body Mass Index is an Independent Predictor of Mortality in COPD

BMI = body mass index

Follow-up (months)

Survival

BMI > 29 kg/m²
BMI 24-29 kg/m²
BMI 20-24 kg/m²
BMI < 20 kg/m²

Risk Factor for Admission for COPD Exacerbation: **Low** Body Mass Index (BMI)

Cause of Death in COPD Patients

- Most patients (50-75%) will die with COPD, not of COPD
Causes of Death in COPD: TORCH Study

- Cardiovascular disease: 27%
- Pulmonary disease: 35%
- Cancer: 21%
- Other: 17%

Cardiovascular Disease in COPD Patients vs. Controls

MI = myocardial infarction; CHF = congestive heart failure; CVD = cardiovascular disease
Between-group differences $p<0.05$.

Cardiovascular Disease

• For every 10% decrease in FEV$_1$
• Cardiovascular mortality increases by about 28%

Which characteristic is associated with the **highest** risk of this patient having a hospitalization for an acute exacerbation of COPD within the next year?

1. Prior exacerbations
2. Uncontrolled gastroesophageal reflux
3. Active smoking
4. Significant bronchodilator response
Probability of COPD Hospitalization within 6 months

Factors used for calculation of COPD hospitalization risk:
- Older age
- FEV₁ percentage of predicted
- Oral steroids at entry
- Cardiovascular comorbidity
- Unscheduled visits in prior year
- Hospital admission in prior year

Trial of tiotropium (N=1829), 551 with one or more exacerbation, 151 with hospitalization due to exacerbation.


FEV₁=forced expiratory volume in one second
Risk Factors for Exacerbations
ECLIPSE: 3-Year Study

Hospitalized for Exacerbation in Year 1 (considered “severe”)
Frequent Exacerbations (≥2 during the year)

ECLIPSE = Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints, GOLD = Global Initiative for Chronic Obstructive Lung Disease
Hurst JR et al. NEJM. 2010;363(12):1128-1138
## Risk Factors for Exacerbations

**ECLIPSE: N=2138**

<table>
<thead>
<tr>
<th>Factor</th>
<th>AECOPD: ≥2 vs. 0</th>
<th>AECOPD: 1 vs. 0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Exacerbation in previous year (any vs. none)</td>
<td>5.72 (4.47-7.31)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV$_1$ per 100-ml decrease</td>
<td>1.11 (1.08-1.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SGRQ, per 4-point increase</td>
<td>1.07 (1.04-1.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of reflux or heartburn (yes vs. no)</td>
<td>2.07 (1.58-2.72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White-cell count, per 1×10$^3$/mm$^3$ increase</td>
<td>1.08 (1.03-1.14)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

ECLIPSE = Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints, AECOPD = Acute Exacerbations of COPD, FEV$_1$=forced expiratory volume in one second, CI=confidence interval, SGRQ=Saint George’s Respiratory Questionnaire

Hurst JR et al. *NEJM*. 2010;363(12):1128-1138
Chronic Bronchitis
Distinct Healthcare Issue

Cough and Sputum Production Indicate Higher Rate of Severe Exacerbation by History (COPDGene)

Pulmonary Artery to Aorta Ratio in the ECLIPSE Validation Cohort (Multivariable Analysis)

<table>
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<th>All Exacerbations (Data from Year 3)</th>
<th>Odds Ratio (95% CI)</th>
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<tr>
<td>Exacerbation in previous year</td>
<td>3.59 (2.76-4.67)</td>
<td>&lt;0.001</td>
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<td>FEV&lt;sub&gt;1&lt;/sub&gt; per percentage-point decrease</td>
<td>1.01 (1.01-1.02)</td>
<td>0.001</td>
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<tr>
<td>SGRQ, per 1-point increase</td>
<td>1.00 (0.99-1.01)</td>
<td>0.17</td>
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<tr>
<td>Gastroesophageal reflux disease</td>
<td>1.69 (1.27-2.23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White-cell count, per 1x10&lt;sup&gt;3&lt;/sup&gt;/mm&lt;sup&gt;3&lt;/sup&gt; increase</td>
<td>1.01 (0.96-1.06)</td>
<td>0.85</td>
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<td>Pulmonary artery to Aorta ratio (PA:A) &gt; 1</td>
<td>6.68 (4.47-9.96)</td>
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ECLIPSE = Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints, FEV<sub>1</sub>=forced expiratory volume in one second, CI=confidence interval, SGRQ=Saint George’s Respiratory Questionnaire. Wells, MJ et al. NEJM. 2012;367(10):913-921
### Pulmonary Artery to Aorta Ratio (PA:A) > 1

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Cl = confidence interval, A = Aorta, PA = Pulmonary Artery

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- Medications: angiotensin converting enzyme inhibitor, short-acting beta₂ agonist (currently using two puffs every four hours), and over-the-counter antacids (currently using 8-10 tablets/day)

No long-acting bronchodilators
Mrs. S. (continued)

- Continues to smoke one to two packs per day for the last 34 years
- Physical examination is significant for the following:
  - Body Mass Index (BMI) = 18m/kg$^2$
  - Pulse 110/minute, Respiratory Rate 22/minute, Blood Pressure 156/92
  - Lungs: diffuse expiratory wheezing and bibasilar crackles
  - Heart: Tachycardic, but regular rhythm, increased P2
  - Extremities: 1+ edema, no clubbing
Mrs. S. (Continued)

- Continuous to smoke one to two packs per day for the last 34 years.
- Physical examination is significant:
  - Body Mass Index (BMI) = 18m/kg
  - Pulse 110/minute, Respiratory Rate 22/minute, Blood Pressure 156/92
  - Lungs: diffuse expiratory wheezing and bibasilar crackles
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Resting tachycardia

Increased second heart sound suggesting possible pulmonary hypertension
Mrs. S. (Continued)

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• Physical examination is significant for the following:
  – Body Mass Index (BMI) = 18m/kg
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??Underlying heart disease
Mrs. S. (Continued)

• **Spirometry:**
  Pre-bronchodilator
  FEV₁/FVC = 58%
  FEV₁ = 1.20 L (48% predicted)

  Post-bronchodilator:
  FEV₁/FVC = 62%
  FEV₁ = 1.46 L (60% predicted)
  (+22% improvement)

• **Lung Volumes:**
  TLC = 140% predicted
  RV = 280% predicted

• **Saturation by pulse oximetry** = 86% (room air at rest)

• **Diffusion Capacity:**
  DLCO = 18% predicted

Significant bronchodilator response
Mrs. S. (Continued)

• **Spirometry:**
  Pre-bronchodilator
  \[ \text{FEV}_{1}/\text{FVC} = 58\% \]
  \[ \text{FEV}_{1} = 1.20 \text{ L} \ (48\% \text{ predicted}) \]
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• **Lung Volumes:**
  \[ \text{TLC} = 140\% \text{ predicted} \]
  \[ \text{RV} = 280\% \text{ predicted} \]

• **Saturation by pulse oximetry:**
  = 86\% (room air at rest)

• **Diffusion Capacity:**
  \[ \text{DL}_{CO} = 18\% \text{ predicted} \]
  Severely reduced diffusion capacity
Mrs. S. (Continued)

- **Spirometry:**
  
  Pre-bronchodilator
  
  \[
  \text{FEV}_1 / \text{FVC} = 58\%
  \]
  
  \[
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  \]

  Post-bronchodilator:
  
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  \]

**Resting hypoxemia**
What is an independent risk factor for mortality in this particular patient with COPD?

1. Heavy tobacco use (50+ pack-years)
2. Body mass index (18m/kg²)
3. Spirometry values (FEV₁/FVC of 62%)
4. Abnormal lung examination (wheezing)
Which characteristic is associated with the highest risk of this patient having a hospitalization for an acute exacerbation of COPD within the next year?

1. Prior exacerbations
2. Uncontrolled gastroesophageal reflux
3. Active smoking
4. Significant bronchodilator response
How many risk factors for complications of COPD did you count in this particular patient (Mrs. S)?

1. <5
2. 5-9
3. **10-14**
4. >15

- **Multiple morbidities:**
  - Hypertension
  - Undiagnosed cardiovascular disease
    - Crackles on lung examination (?congestive heart failure)
    - Tachycardia at rest
    - Peripheral edema
    - Increased P2 (?pulmonary hypertension)
  - Anxiety
  - Gastroesophageal reflux (uncontrolled)
  - Pulmonary cachexia syndrome (low BMI)
- Prior exacerbations
- Chronic bronchitis
- Limited exercise capacity / significant dyspnea
- No long-acting / maintenance inhalers
- Hyperinflation and air trapping
- Very low diffusion capacity
- Resting hypoxemia
Thank you for your attention!