Interventions that Improve Outcomes of COPD

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Disclosures

• Consultant Sunovion, BI, Forest, Meda
• Reference to studies of drugs not approved for COPD exacerbation
Interventions that Improve Outcomes of COPD

Objectives:
1. Recognize the COPD risk factors that lead to hospital admission
2. Discuss the evidence-based hospital protocols to improve symptoms and other outcomes of the COPD exacerbation
3. Identify the high risk co-morbidities of COPD that may lead to a COPD readmission
4. List the reasons for poor adherence to therapy and how to improve low adherence rates
Interventions that Improve Outcomes of COPD

1. Identify the High Risk Patient
Interventions that Improve Outcomes of COPD:
1. Identify the High Risk Patient

- Severity of airway obstruction (FEV\textsubscript{1} impairment)
- Chronic bronchial mucous hypersecretion (productive cough)
- Poor health-related quality of life
- Increased age and duration of COPD
- Prior use of medications for COPD, especially PO steroids
- Bacterial colonization
- Comorbid conditions (e.g., cardiovascular disease)
- Antibiotic or systemic corticosteroid use in the past year
- Pulmonary Artery to Aorta ratio (PA:A) > 1
- Failure to use Oxygen (LTOC) when needed
- Poor Adherence to medication
Interventions that Improve Outcomes of COPD

1. Identify the High Risk Patient
2. Use evidence-based hospital protocols
Which of the following has been shown to reduce the risk re-exacerbation within 30 days?

a. Course of prednisone for 2 weeks
b. Dietary protein supplementation
c. Home-based pulmonary rehabilitation
d. Nocturnal BiPAP ventilation
Evidence-Based Hospital Protocols

- Assess severity of symptoms, blood gases, chest radiograph
- Give supplemental O2 therapy; obtain serial ABG measurements
- Give Bronchodilators
- Add oral or intravenous corticosteroids
- Consider antibiotics (oral or occasionally intravenous) when signs of
- Consider noninvasive mechanical ventilation
- At all times:
  - Monitor fluid balance and nutrition
  - Consider subcutaneous heparin or low molecular weight heparin
  - Identify and treat associated conditions (e.g., heart failure, arrhythmias)
  - Closely monitor condition of the patient

Evidence-Based Hospital Protocols

- Short-acting inhaled beta2-agonists with or without short-acting anticholinergics are usually the preferred bronchodilators- **Evidence C** (no controlled trials)
- No difference MDI + spacer vs. nebulizers
- Methyl Xanthines- ?? **Evidence B**
- Corticosteroids **Evidence A**
- Antibiotics
  - Three cardinal symptoms – (**Evidence B**);
  - Two cardinal symptoms with purulent sputum (**Evidence C**)
  - Mechanical ventilation (invasive or noninvasive) (**Evidence B**)
  - Length of antibiotic therapy is usually 5-10 days (**Evidence D**).
IV Corticosteroids for Treatment of Exacerbations- 1999

Outpatient Corticosteroids to Prevent Relapse of Exacerbations

40 mg Prednisone vs PBO: Probability of Remaining Relapse Free for 30 Days

\[ P = .04 \text{ by the log-rank test.} \]

Short-term vs Conventional Glucocorticoid Therapy in Exacerbations: the REDUCE Study

$P=0.006$ for non-inferiority

<table>
<thead>
<tr>
<th>Percent with Exacerbation within 180 Days</th>
<th>5-day Glucocorticoids (n=156)</th>
<th>14-day Glucocorticoids (n=155)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>35.9%</td>
<td>36.8%</td>
</tr>
</tbody>
</table>

Corticosteroids for COPD Exacerbations for ICU Patients

**Group I (2/3)**

> 240 mg/day

Common Dosage:
125 mg methyl-prednisolone
Q 6 hours

**Group II (1/3)**

≤ 240 mg/day

Common Dosage:
60 mg methylprednisolone
Q 6 hours

Kiser TH et al. AJRCCM 2014;189:1052-1064
Corticosteroids for COPD Exacerbations for ICU Patients

• Low Dose vs. High Dose: No difference in mortality

• With Low Dose Corticosteroids:
  – Reduced ICU length of stay $P<0.01$
  – Reduced Hospital length of stay $P<0.01$
  – Reduced Hospital costs $P=0.01$
  – Reduced time of the ventilator $P=0.01$
  – Reduced insulin need $P<0.01$
  – Reduced fungal infections (antifungal treatment) $P<0.01$

Kiser TH et al. AJRCCM 2014;189:1052-1064
Which of the following has been shown to reduce the risk of a re-exacerbation within 30 days?

a. **Course of prednisone for 2 weeks**
b. Dietary protein supplementation
c. Home-based pulmonary rehabilitation
d. Nocturnal BiPAP ventilation
Checklist for Time of Discharge

• Assurance of effective home maintenance pharmacotherapy regimen
• Reassessment of inhaler technique
• Education regarding role of maintenance regimen
• Instruction regarding completion of steroid therapy and antibiotics, if prescribed
• Assess need for long-term oxygen therapy
• Assure follow-up visit in 4-6 weeks 7 days
• Provide a management plan for comorbidities and their follow-up

High-Risk Period for Recurrent Exacerbation Was 8 Weeks After First Exacerbation

- 633 exacerbations between weeks 3 and 8; 103 (19.4%) more than predicted ($P=0.040$)

The most common reason for a 30 day readmission after an admission for a COPD exacerbation is:

a. Pneumonia
b. Acute myocardial infarction
c. Congestive heart failure
d. COPD exacerbation
## Most Frequent Medical Reasons for Rehospitalization, According to Condition at Index Discharge (Medicare Claims Data)

<table>
<thead>
<tr>
<th>Condition at Index Discharge</th>
<th>30-Day Rehospitalization Rate (%)</th>
<th>Reasons for Rehospitalization (%)</th>
<th>5th to 10th Most Frequent</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>21.0</td>
<td>Most Frequent</td>
<td>5th to 10th Most Frequent</td>
</tr>
<tr>
<td>Heart failure</td>
<td>26.9</td>
<td>Heart failure</td>
<td>GI problems, nutrition-related or metabolic issues, septicemia, GI bleeding, renal failure, urinary tract infection (17.0)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>20.1</td>
<td>Pneumonia (29.1)</td>
<td>Acute MI, COPD, arrhythmias, circulatory disorders, GI bleeding, GI problems (14.0)</td>
</tr>
<tr>
<td>COPD</td>
<td>22.6</td>
<td>COPD (36.2)</td>
<td>Respiratory or ventilation problems, GI problems, nutrition-related or metabolic issues, arrhythmias, GI bleeding, acute MI (12.5)</td>
</tr>
<tr>
<td>Psychoses</td>
<td>24.6</td>
<td>Psychoses (67.3)</td>
<td>Chest pain, nutrition-related or metabolic issues, depression, GI problems, COPD, organic mental conditions (7.0)</td>
</tr>
<tr>
<td>GI problems</td>
<td>19.2</td>
<td>GI problems (21.1)</td>
<td>Major bowel surgery, urinary tract infection, septicemia, GI bleeding, COPD, chest pain (13.4)</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease; GI = gastrointestinal; MI = myocardial infarction

The most common reason for a 30 day readmission after an admission for a COPD exacerbation is:

a. Pneumonia
b. Acute myocardial infarction
c. Congestive heart failure
d. COPD exacerbation
Interventions that Improve Outcomes of COPD

1. Identify the High Risk Patient
2. Use evidence-based hospital protocols
3. Consider assessment of high risk co-morbidities
   1. Pneumonia
   2. Heart Failure
   3. Myocardial infarction
   4. Arrhythmias
   5. GI bleed
Interventions that Improve Outcomes of COPD

1. Identify the High Risk Patient
2. Use evidence-based hospital protocols
3. Consider assessment of high risk co-morbidities
4. Assess for poor adherence to therapy
Which of the following is the most common reason for poor adherence with COPD medication?

a. Can’t afford the medication
b. Adverse side effects
c. Felt good and decided not to dose
d. Confusion about proper dose
Underutilization of Long term Oxygen Therapy is Associated with Higher Risk of Hospitalization

- In a multivariate model, under use of $O_2$ when indicated was associated with:
  - Three or more COPD admissions in the previous year, (OR 6.21 P=0.008)

- Underprescription of LTOT has a higher risk of admission for a COPD exacerbation (OR 22.64) P=0.007

Persistence with All Commonly Used COPD Medications is Poor

The Most Common Reason for Nonadherence in COPD Patients Is Lack of Symptoms

- Family problems interfered
- Insufficient funds to purchase medications
- Confused over schedule and decided not to dose
- Socially inconvenient
- Believed medication was not effective or did not …
- Believed immune to medication: decided not to dose
- Ran out of medicine
- Side effects
- Change in normal routine: unexpected
- Change in normal routine: planned
- Interrupted prior to doing and forgot
- Absorbed in activity and forgot
- Felt good and forgot to dose
- Felt good and decided not to dose

Which of the following is the most common reason for poor adherence with COPD medication?

a. Can’t afford the medication
b. Adverse side effects
c. Felt good and decided not to dose
d. Confusion about proper dose
What therapies are effective to prevent exacerbations?
Non-Pharmacologic Evidence-Based Measures That Reduce COPD Exacerbations

- Smoking cessation
- Immunizations
- Pulmonary rehabilitation
Reduce Exacerbation Risk Factors: Influenza Vaccination

- Evidence from randomized clinical trials indicates that inactivated influenza vaccine reduces exacerbation rates in COPD patients
- The magnitude of this benefit is similar to that seen in large observational studies and was due to a reduction in “late” exacerbations occurring 3 or more weeks after vaccination and due to influenza
- A mild increase in transient local adverse effects with vaccination is observed, but there was no evidence of an increase in exacerbations occurring within 2 weeks of vaccination

Reduce Exacerbation Risk Factors: Pulmonary Rehabilitation

<table>
<thead>
<tr>
<th>Study</th>
<th>Length of follow-up</th>
<th>Risk ratio (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behnke (14/12)</td>
<td>18 months</td>
<td>0.29 (0.10 - 0.82)</td>
<td>37%</td>
</tr>
<tr>
<td>Man (20/21)</td>
<td>3 months</td>
<td>0.17 (0.04 - 0.69)</td>
<td>44%</td>
</tr>
<tr>
<td>Murphy (13/13)</td>
<td>6 months</td>
<td>0.40 (0.09 - 1.70)</td>
<td>19%</td>
</tr>
<tr>
<td>Overall (47/46)</td>
<td></td>
<td>0.26 (0.12 to 0.54)</td>
<td></td>
</tr>
</tbody>
</table>

Chi-Squared 0.70, P=0.71

Risk of unplanned hospital admission

ICS Decrease COPD Exacerbation Risk

Annual Exacerbation Rate

* \( P=0.026 \) versus placebo

Fluticasone: 0.99
Placebo: 1.32

TORCH STUDY

Lower Exacerbation Rate With LABA Plus ICS

UPLIFT Study –
Effects on Exacerbations

Hazard ratio = 0.86,
(95% CI = 0.81, 0.91)

P<0.0001 (log-rank test)

Tiotropium

Control

0.85/yr

0.73/yr; P<0.001
(14% reduction)

Macrolides Prevent COPD Exacerbations

Median time to 1st exacerbation
271 days Macrolide; 89 days Placebo

Proportion of Participants Free from Acute Exacerbations of COPD for 1 Year

Seemungal TAR, et al. AJRCCM 2008

Albert RK et al. NEJM 2011
Reduction in Moderate or Severe Exacerbations- Roflumilast

Trials 5 & 6 (Pooled Data)

\[ \Delta = -17\% \]  
\( (P<0.0003) \)

Mean Rate of Exacerbations Per Patient Per Year

Placebo (N=1554)  
1.37

DALIRESP (N=1537)  
1.14

Number Needed to Treat (NNT) to prevent 1 moderate or severe exacerbation per year:

5.29 in Trial 5
3.64 in Trial 6

Higher Adherence to Therapy Lowers Risk for Hospitalization in COPD

Rate of Hospitalisation (per patient year)

≥80% Percent of Days Covered with Prescribed Medication

0.88

<80%

1.13

P<0.05*

* based on 95% CI for relative risk

Thanks for your attention!