UPDATE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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- No disclosures
Objectives

■ Review GOLD classification by symptom and its guidance for treatment
■ Explore new studies released on triple inhaler therapy
■ Review newest data on chronic azithromycin and roflumilast
We have more than inhalers!
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Diagnostic considerations

GOLD

FEV1/FVC ratio < 70

ATS

FEV1/FVC ratio < 5th percentile of predicted value or LLN

### In patients with $\text{FEV}_1/\text{FVC} < 0.70$:

<table>
<thead>
<tr>
<th>GOLD 1:</th>
<th>Mild</th>
<th>$\text{FEV}_1 \geq 80%$ predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 2:</td>
<td>Moderate</td>
<td>$50% \leq \text{FEV}_1 &lt; 80%$ predicted</td>
</tr>
<tr>
<td>GOLD 3:</td>
<td>Severe</td>
<td>$30% \leq \text{FEV}_1 &lt; 50%$ predicted</td>
</tr>
<tr>
<td>GOLD 4:</td>
<td>Very Severe</td>
<td>$\text{FEV}_1 &lt; 30%$ predicted</td>
</tr>
</tbody>
</table>

The MRC Breathlessness Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Degree of breathlessness related to activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not troubled by breathlessness except on strenuous exercise</td>
</tr>
<tr>
<td>2</td>
<td>Short of breath when hurrying on the level or walking up a slight hill</td>
</tr>
<tr>
<td>3</td>
<td>Walks slower than most people on the level, stops after a mile or so, or stops after 15 minutes walking at own pace</td>
</tr>
<tr>
<td>4</td>
<td>Stops for breath after walking about 100 yds or after a few minutes on level ground</td>
</tr>
<tr>
<td>5</td>
<td>Too breathless to leave the house, or breathless when undressing</td>
</tr>
</tbody>
</table>

Exacerbation risk

Low risk
0 to 1 exacerbations (no hospitalizations)

High risk
2 exacerbations or >1 exacerbation leading to hospitalization

Spirometrically confirmed diagnosis → Assessment of airflow limitation → Assessment of symptoms/risk of exacerbations

Exacerbation history

<table>
<thead>
<tr>
<th>FEV1 (% predicted)</th>
<th>≥ 2 or ≥ 1 leading to hospital admission</th>
<th>0 or 1 (not leading to hospital admission)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1</td>
<td>≥ 80</td>
<td></td>
</tr>
<tr>
<td>GOLD 2</td>
<td>50–79</td>
<td></td>
</tr>
<tr>
<td>GOLD 3</td>
<td>30–49</td>
<td></td>
</tr>
<tr>
<td>GOLD 4</td>
<td>&lt; 30</td>
<td></td>
</tr>
</tbody>
</table>

Symptoms

- mMRC 0–1
- CAT < 10

C

D

A

B
What’s the point?
Treatment guidance

Prediction of risk of exacerbation?

Goossens et al. Does the 2013 GOLD classification improve the ability to predict lung function decline, exacerbations and mortality: a post-hoc analysis of the 4-year UPLIFT trial. *BMC Pulmonary Medicine* 2014; 14:163.
Mortality prediction?

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Inclusion Criteria

• Age > 40 years
• FEV1/FVC ratio < 70%, FEV1 < 50%
• Long acting therapy for 2 months
• Symptomatic

Exclusion Criteria

• COPD exacerbation in last 4 weeks
• Allergy or atopy
• Severe cardiac disease

Main outcomes

- Triple therapy had more effect on 2 hour post dose FEV1
- 23% lower rate of exacerbation with triple therapy
- No difference in breathlessness
- Improvement in QOL

Problems

- Didn’t address LABA and LAMA combination
- Low baseline exacerbation rate
- Do you need a triple inhaler or triple therapy

What about pneumonia during ICS use?
IMPACT trial

Outcomes

■ Significantly lower rates of moderate or severe COPD exacerbations, better lung function, QOL than any other dual therapy

■ ICS-LABA combination superior with rates of exacerbations compared to LABA-LAMA, contrast to FLAME trial.

■ All cause mortality?

SUNSET Trial

Can you safely withdraw ICS in patient on long-term triple therapy without frequent exacerbations?

SUNSET Trial

Sunset Trial - Outcomes

- Significant decrease in FEV1
- No difference in moderate to severe COPD exacerbation except in patient group with > 300 eosinophils.

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Do macrolides truly reduce the risk of exacerbations?
<table>
<thead>
<tr>
<th>Year</th>
<th>Journal</th>
<th>Study Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>NEJM</td>
<td>Compared azithromycin 250mg daily to placebo. Less exacerbations and increased QOL.</td>
</tr>
<tr>
<td>2018</td>
<td>CHEST</td>
<td>Long term efficacy and safety. Retrospective analysis. Reduction in exacerbations. Increase in resistant infection and pseudomonas infections.</td>
</tr>
</tbody>
</table>
Roflumilast
Roflumilast

Diagram showing the conversion of cAMP to AMP with Roflumilast inhibiting PDE4.
REACT Trial

- First large trial with roflumilast
- Compared patients with severe COPD using roflumilast versus placebo
- 14.2% decrease in moderate to severe exacerbation in 1 year of use

When do you add on roflumilast?

- Maximal inhaler therapy
- History of multiple exacerbations
- Chronic systemic corticosteroids
- Caution side effects

What’s new with roflumilast?

Severe COPD
> 2 exacerbation in the past year

ICS/LABA + Placebo
ICS/LABA + Roflumilast

## Main outcomes

| Decreased overall exacerbations | Greatest decrease in hospitalized patients | Decrease in death and hospitalization related to severe exacerbations |

Summary

- Consider using symptoms based model for classification and treatment guidance
- New triple inhaler therapy trials show a reduction in COPD exacerbation rates
- Inhaler therapy can be de-escalated safely in patients on triple therapy with good control
- Newer data on chronic azithromycin in COPD suggests that there is long term reduction in exacerbations but increased rates of infection
- Newer data on roflumilast suggests that patients who have been hospitalized for COPD exacerbation have the greatest decrease in rates of exacerbation
References


Goossens et al. Does the 2013 GOLD classification improve the ability to predict lung function decline, exacerbations and mortality: a post-hoc analysis of the 4-year UPLIFT trial. BMC Pulmonary Medicine 2014; 14:163.


