COPD, ACOS and device considerations

COI

- AstraZeneca Consultant
- Teva Advisory Board; Speaker

Us prevalence of COPD is 6.3%
Diagnosis and Initial Assessment

**Key Indicators for Considering a Diagnosis of COPD**

- **Progressive Shortness of Breath:**
  - Persistent.
- **Chronic Cough:**
  - May be intermittent and may be productive.
  - Reversed wheezes.
- **Chronic Sputum Production:**
  - Any pattern of chronic sputum production may indicate COPD.
- **Recurrent Lower Respiratory Tract Infections:**
- **History of Risk Factors:**
  - Herd factors (such as genetics factors, congenital abnormality, abnormalities, etc.).
  - Tobacco smoke (including passive local preparation).
  - Inside home: second-hand smoking, and heating fuels.
  - Occupational dust, fumes, fumes, and other chemicals.
- **Family History of COPD and/or Childhood Factors:**
  - For example low birthweight, childhood respiratory infections, etc.

---

**Key considerations in diagnosing COPD**
Etiology, pathobiology & pathology of COPD leading to airflow limitation & clinical manifestations

Diagnosis and Initial Assessment

PATHWAYS TO THE DIAGNOSIS OF COPD

1. Symptoms
   - Chronic cough
   - Expectoration

2. Risk Factors
   - Tobacco smoking
   - Occupational factors
   - Air pollution
   - Genetic factors

3. Spirometry: Confirm the diagnosis

GOLD 2019 Report: Chapters

1. Definition and Overview
2. Diagnosis and Initial Assessment
3. Evidence Supporting Prevention & Maintenance Therapy
4. Management of Stable COPD
5. Management of Exacerbations
6. COPD and Comorbidities
Once COPD has been diagnosed, effective management should be based on an individualized assessment to reduce both current symptoms and future risks of exacerbations.

**GOALS FOR TREATMENT OF STABLE COPD**
- Alleviate Symptoms
- Improve Exercise Tolerance
- Improve Health Status
- Avoid Further Exacerbations
- Prevent Disease Progression
- Prevent and Treat Exacerbations
- Reduce Mortality

**ABCD assessment tool**

<table>
<thead>
<tr>
<th>Grade</th>
<th>FEV1</th>
<th>Symptom Score</th>
<th>Exacerbation History</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1</td>
<td>&gt; 80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOLD 2</td>
<td>50-79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOLD 3</td>
<td>30-49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOLD 4</td>
<td>&lt; 30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Symptom Score**
- 0: None
- 1: Occasional
- 2: Frequent
- 3: Daily

**Exacerbation History**
- 0: None
- 1: 1 or 2 exacerbations per year
- 2: 3 or more exacerbations per year

**Classification**
- A: Symptom Score 0, Exacerbation History 0
- B: Symptom Score 0, Exacerbation History 1
- C: Symptom Score 1-2, Exacerbation History 0
- D: Symptom Score 1-2, Exacerbation History 1-2

**Figure 2.6**

© 2019 Global Initiative for Chronic Obstructive Lung Disease
COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

- Classified as:
  - Mild (treated with SABDs only)
  - Moderate (treated with SABDs plus antibiotics and/or oral corticosteroids) or
  - Severe (patient requires hospitalization or visits the emergency room). Severe exacerbations may also be associated with acute respiratory failure.
- Blood eosinophil count may also predict exacerbation rates (in patients treated with LABA without ICS).
Treatment of stable COPD

**INITIAL PHARMACOLOGICAL TREATMENT**

Group A

► All Group A patients should be offered bronchodilator treatment based on its effect on breathlessness. This can be either a short- or a long-acting bronchodilator.

► This should be continued if benefit is documented.

Group B

► Initial therapy should consist of a long acting bronchodilator (LABA or LAMA).

► Long-acting inhaled bronchodilators are superior to short-acting bronchodilators taken as needed i.e., *pro re nata* (prn) and are therefore recommended.
Initial therapy should consist of a single long acting bronchodilator.

In two head-to-head comparisons the tested LAMA was superior to the LABA regarding exacerbation prevention therefore we recommend starting therapy with a LAMA in this group.

**INITIAL PHARMACOLOGICAL TREATMENT**

- LABA
- LAMA
- A Bronchodilator
- A Long-Acting Beta-2 Agonist (LABA) + LAMA

*Figure 4.3*
In general, therapy can be started with a LAMA as it has effects on both breathlessness and exacerbations.

For patients with more severe symptoms (order of magnitude of CAT™ ≥ 20), especially driven by greater dyspnea and exercise limitation, LAMA/LABA may be chosen as initial treatment based on studies with patient reported outcomes as the primary endpoint where LABA/LAMA combinations showed superior results compared to the single substances.

An advantage of LABA/LAMA over LAMA for exacerbation prevention has not been consistently demonstrated, so the decision to use LABA/LAMA as initial treatment should be guided by the level of symptoms.

> INITIAL PHARMACOLOGICAL TREATMENT

► Following implementation of therapy, patients should be reassessed for attainment of treatment goals and identification of any barriers for successful treatment (Figure 4.2).

► Following review of the patient response to treatment initiation, adjustments in pharmacological treatment may be needed.

Group D

► In general, therapy can be started with a LAMA as it has effects on both breathlessness and exacerbations.

► For patients with more severe symptoms (order of magnitude of CAT™ ≥ 20), especially driven by greater dyspnea and exercise limitation, LAMA/LABA may be chosen as initial treatment based on studies with patient reported outcomes as the primary endpoint where LABA/LAMA combinations showed superior results compared to the single substances.

► An advantage of LABA/LAMA over LAMA for exacerbation prevention has not been consistently demonstrated, so the decision to use LABA/LAMA as initial treatment should be guided by the level of symptoms.

Treatment of stable COPD

► Following implementation of therapy, patients should be reassessed for attainment of treatment goals and identification of any barriers for successful treatment (Figure 4.2).

► Following review of the patient response to treatment initiation, adjustments in pharmacological treatment may be needed.

> MANAGEMENT CYCLE

► Initial treatment includes: LAMA or LABA (if exacerbations)

► Follow-up pharmacological treatment

► Dyspnea

► Exacerbations

> FOLLOW-UP PHARMACOLOGICAL TREATMENT
Pharmacological therapy

**OTHER PHARMACOLOGICAL TREATMENTS**

**α-1-ANTITRYPSIN DEGRADATION THERAPY**
- Intermittent augmentation therapy may slow the progression of emphysema (Evidence B).

**Bronchodilators**
- There is no conclusive evidence of a beneficial role of anticholinergics in patients with COPD (Evidence C).

**Antidigoxins**
- Antidigoxins do not improve outcomes and may worsen exacerbations (Evidence B).

| TABLE 5.7 |

Management of Exacerbations

- **Bronchodilators**
  - Although there is no high-quality evidence from RCTs, it is recommended that short-acting inhaled beta₂-agonists, with or without short-acting anticholinergics, are the initial bronchodilators for acute treatment of a COPD exacerbation.

- **Corticosteroids**
  - Data from studies indicate that systemic glucocorticoids in COPD exacerbations shorten recovery time and improve lung function (FEV₁). They also improve oxygenation, the risk of early relapse, treatment failure, and the length of hospitalization.

- **Antibiotics**
  - Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should be 5–7 days.

Management of Exacerbations

<table>
<thead>
<tr>
<th>Interventions that reduce the frequency of COPD exacerbations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchodilators</td>
</tr>
<tr>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Antithrombotics</td>
</tr>
<tr>
<td>Vaccines</td>
</tr>
<tr>
<td>Long-term antibiotics</td>
</tr>
<tr>
<td>Inhaled corticosteroids</td>
</tr>
<tr>
<td>Nebulizers</td>
</tr>
<tr>
<td>Systemic corticosteroids</td>
</tr>
<tr>
<td>Smoke cessation</td>
</tr>
</tbody>
</table>

| TABLE 5.7 |

© 2019 Global Initiative for Chronic Obstructive Lung Disease

© 2017 Global Initiative for Chronic Obstructive Lung Disease
Inhaler technique and spacers

In-check Dial

Device used to check inhaler technique

Billable teaching

Should be used at every visit to confirm proper inhaler technique
Spacers and VHCs

Increases medication delivery to the lower airways by reducing oral deposition and by enhancing hand-mouth coordination

Spacer is a generic term for any open tube placed on the MDI mouthpiece to extend its distance from the mouth

VHCs are manufactured with a one-way valve that prevents exhalation into the device

Activate only once into VHC/spacer

Rinsing with diluted household detergents should prevent static electricity and enhance delivery to lungs (or use anti-static device)

Valved Holding Chamber vs. Spacer

VHC
- Has one way valve to hold medication in place
- Eliminates need to coordinate inhalation with actuation
- Improves deposition of respirable particles in the airways

Spacer only provides space between MDI mouthpiece and patient’s mouth
- Does not hold medication in spacer
- Patient must still inhale in time with actuation to get medication
- No data to show improvement of respirable particles

Spacers and Inhaled Drug Delivery

O'Callaghan, Thorax 1993; 48:603

Courtesy R. Pleasants
Respiratory and non-respiratory diseases use inhalational therapy

Requires treatment by inhalation to deliver to the lungs (max benefits) with least side effects

Technically possible by modulating particle size through inhaler design, and by adjusting excipients and propellants.

Respiratory Tract Deposition

Courtesy R. Pleasants
Excipient

Peanut can cross-react with soy but not enough to cause reaction

Lecithin is no longer used as an emulsifier in Atrovent

Dry Powder Inhalers

Formulation  Metering  Dispersion  Oropharyngeal Deposition  Pulmonary Delivery


Pressurized Metered-Dose Inhaler Technique
Respiratory and non-respiratory diseases use inhalational therapy

Asthma & COPD
Requires treatment by inhalation to deliver to the lungs (max benefits) with least side effects
Technically possible by modulating particle size through inhaler design, and by adjusting excipients and propellants

HFA propellant allows for smaller particle size

If prescribing nebulized medications know which nebulizers are recommended for long term use

Patients still ask for nebulizers!

If prescribing nebulized medications know which nebulizers are recommended for long term use
Montreal Protocol on Substances that Deplete the Ozone Layer

International treaty designed to protect the ozone layer by phasing out the production of substances responsible for ozone depletion

Chlorofluorocarbons (CFCs) Phase-out
First universally ratified treaty in UN history
Ratified by 197 parties in 1987 only 14 years after hole discovered

Amounts of CFCs exempted, used, on hand at the end of each year (tons), 1996-2014

Carbon footprint
Carbon footprint is the amount of CO₂ and other carbon compounds emitted by a particular person, group, or product
CFCs had a larger carbon footprint
HFCs have a much smaller carbon footprint
Metered dose inhalers and the Montreal Protocol

In 2008 CFCs were replaced with HFCs (HFCs)
98% use HFC-134a
2% use HFC-227ea

Not on the label
6-12g for albuterols
12-20g for inhaled steroids
Formulations w/alcohol as a cosolvent have half the GWP as MDIs w/only HFCs (e.g., Proair and Proventil; not Ventolin)

Estimated relative carbon dioxide emissions of everyday items compared with asthma inhalers

<table>
<thead>
<tr>
<th>Item</th>
<th>CO2 eq/dose or serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFC-113 crosses</td>
<td>High</td>
</tr>
<tr>
<td>CFC-11 crosses</td>
<td>High</td>
</tr>
<tr>
<td>CFC-12 crosses</td>
<td>Moderate</td>
</tr>
<tr>
<td>CFC-125 crosses</td>
<td>High</td>
</tr>
<tr>
<td>CFC-22 crosses</td>
<td>Moderate</td>
</tr>
<tr>
<td>CFC-23 crosses</td>
<td>Moderate</td>
</tr>
<tr>
<td>CFC-2100 crosses</td>
<td>High</td>
</tr>
<tr>
<td>CFC-227ea crosses</td>
<td>Low</td>
</tr>
<tr>
<td>CFC-3100 crosses</td>
<td>Low</td>
</tr>
<tr>
<td>CFC-124a crosses</td>
<td>Low</td>
</tr>
<tr>
<td>CFC-134a crosses</td>
<td>Moderate</td>
</tr>
<tr>
<td>CFC-1241mzea/14mzfa beacon</td>
<td>Low</td>
</tr>
<tr>
<td>CFC-1241mzea/14mzfa</td>
<td>Low</td>
</tr>
<tr>
<td>CFC-1241mzfa</td>
<td>Low</td>
</tr>
<tr>
<td>CFC-1241mzfa</td>
<td>Low</td>
</tr>
<tr>
<td>CFC-1241mzfa</td>
<td>Low</td>
</tr>
</tbody>
</table>

- CO2 eq = Carbon Dioxide Equivalent
Proportions of doses delivered by MDIs and DPIs in different regions, 2012

Sweden is 90% DPI

PRESSAIR-TUDOZA (ACLIDINUM BROMIDE)

Remove the inhaler cap by pressing the arrows on the sides and pulling it off.

Press the button all the way down and release it.

Breathe out completely through the mouth, away from the inhaler.

Place the mouthpiece in the mouth and tighten the lips around it.

Breathe in quickly and deeply through the mouth, until the lungs are filled.

Remove the inhaler from the mouth.

Hold the breath for as long as is comfortably possible.

Replace the cap.
SABA/SAMA and LABA/LAMA combinations

Medications for long-term control

PDE4 inhibitors

Recommended for patients with severe airflow limitation, symptoms of chronic bronchitis, and a history of exacerbations whose disease is not adequately controlled by long-acting bronchodilators

Albeit safe, its significant side effects (diarrhea, nausea, weight loss) make it intolerable in some patients

Complementary action of bronchodilators
Asthma and COPD Overlap (ACO)

ACO is identified in clinical practice by features that it shares with both asthma and COPD.

ACO is characterized by persistent airflow limitation with severe features, associated with asthma and several features usually associated with COPD.

ACO identified by the features shared with asthma and COPD.

ACO includes several different clinical phenotypes and different underlying mechanisms.

Stepwise approach to ACOS diagnosis and initial treatment

For an adult who presents with respiratory symptoms:
1. Does the patient have chronic airways disease?
2. Syndromic diagnosis of asthma, COPD and ACO
3. Spirometry
4. Commence initial therapy
5. Referral for specialized investigations (if necessary)

GINA 2016, Box 5-4