Chronic Obstructive Pulmonary Disease (COPD)

- COPD is currently the fourth leading cause of death in the world.\(^1\)
- COPD is projected to be the 3rd leading cause of death by 2020.\(^2\)
- More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally.
- Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population.


This Lecture will cover......

1. Definition and Overview
2. Diagnosis and Initial Assessment
3. Evidence Supporting Prevention & Maintenance Therapy
4. Management of Stable COPD
5. Management of Exacerbations

COPD Definition

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.
OVERALL KEY POINTS (1 of 2):

► Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

► The most common respiratory symptoms include dyspnea, cough and/or sputum production. These symptoms may be under-reported by patients.

► The main risk factor for COPD is tobacco smoking but other environmental exposures such as biomass fuel exposure and air pollution may contribute.

OVERALL KEY POINTS (2 of 2):

► Besides exposures, host factors predispose individuals to develop COPD. These include genetic abnormalities, abnormal lung development and accelerated aging.

► COPD may be punctuated by periods of acute worsening of respiratory symptoms, called exacerbations.

► In most patients, COPD is associated with significant concomitant chronic diseases, which increase its morbidity and mortality.

Prevalence

Prevalence of COPD

► Estimated 384 million COPD cases in 2010.

► Estimated global prevalence of 11.7% (95% CI 8.4%–15.0%).

► Three million deaths annually.

► With increasing prevalence of smoking in developing countries, and aging populations in high-income countries, the prevalence of COPD is expected to rise over the next 30 years.

► By 2030 predicted 4.5 million COPD related deaths annually.
Economic and Social Burden

Economic burden of COPD

- COPD is associated with significant economic burden.
- COPD exacerbations account for the greatest proportion of the total COPD burden.

European Union:
- Direct costs of respiratory disease ~6% of the total healthcare budget
- COPD accounting for 56% (38.6 billion Euros) of the cost of respiratory disease.

USA:
- Direct costs of COPD are $32 billion
- Indirect costs $20.4 billion.

Global Burden of Disease (GBD) study

- Disability-Adjusted Life Year (DALY) = sum of years lost because of premature mortality and years of life lived with disability, adjusted for the severity of disability.
- COPD is an increasing contributor to disability and mortality around the world.
- In 2013 COPD was 5th leading cause of DALYs lost.
- In the United States, COPD is the second leading cause of reduced DALYs, trailing only ischemic heart disease.

Factors that influence disease progression

- Genetic factors
- Age and gender
- Lung growth and development
- Exposure to particles
- Socioeconomic status
- Asthma & airway hyper-reactivity
- Chronic bronchitis
- Infections
OVERALL KEY POINTS (1 of 2):

► COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.

► Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation.

► The goals of COPD assessment are to determine the level of airflow limitation, the impact of disease on the patient’s health status, and the risk of future events (such as exacerbations, hospital admissions, or death), in order to guide therapy.

OVERALL KEY POINTS (2 of 2):

► Concomitant chronic diseases occur frequently in COPD patients, including cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression, anxiety, and lung cancer. These comorbidities should be actively sought and treated appropriately when present as they can influence mortality and hospitalizations independently.
Diagnosis and Initial Assessment

Symptoms of COPD
- Chronic and progressive dyspnea
- Cough
- Sputum production
- Wheezing and chest tightness
- Others – including fatigue, weight loss, anorexia, syncope, rib fractures, ankle swelling, depression, anxiety.

Other causes of chronic cough
- Asthma
- Lung cancer
- Tuberculosis
- Meningitis
- Left heart failure
- History of lung disease
- Cystic fibrosis
- Bronchiectasis
- Heart failure
- Post nasal drip syndrome (PND)
- Upper Airways/Cough Syndromes (UACS)
- Psychosocial origins
- Medication (e.g., ACE inhibitors)
Medical History

- Patient's exposure to risk factors
- Past medical history
- Family history of COPD or other chronic respiratory disease.
- Pattern of symptom development
- History of exacerbations or previous hospitalizations for respiratory disorder
- Presence of comorbidities
- Impact of disease on patient's life
- Social and family support available to the patient
- Possibilities for reducing risk factors, especially smoking cessation.

Diagnosis and Initial Assessment

Table 2.5: Considerations in performing spirometry

<table>
<thead>
<tr>
<th>Spirometry</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>Forced expiratory volume in 1 second</td>
</tr>
<tr>
<td>FVC</td>
<td>Forced vital capacity</td>
</tr>
<tr>
<td>Ratio</td>
<td>FEV1/FVC</td>
</tr>
</tbody>
</table>

Classification of severity of airflow limitation

Table 2.6: Classification of airflow limitation severity in COPD (based on post-bronchodilator FEV1) (In patients with FEV1/FVC < 0.70)

- **GOLD 1**: Mild, FEV1 > 80% predicted
- **GOLD 2**: Moderate, 50% ≤ FEV1 ≤ 80% predicted
- **GOLD 3**: Severe, 30% ≤ FEV1 < 50% predicted
- **GOLD 4**: Very Severe, FEV1 < 30% predicted

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Assessment of Exacerbation Risk

► 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).

Summary

Table 2-4. Role of spirometry

- Diagnosis
- Assessment of severity of airflow obstruction (for prognosis)
- Follow-up assessment
  - Respiratory infections
  - History of smoking in residents (e.g., differences between spirometry and level of symptoms)
- Deliberate alternative diagnoses (when symptoms are disproportionate to degree of airflow obstruction)
- Non-pharmacological (e.g., bronchoscopic procedures)
- Identification of mild disease

Alpha-1 antitrypsin deficiency (AATD)

AATD screening

► The World Health Organization recommends that all patients with a diagnosis of COPD should be screened once especially in areas with high AATD prevalence.
► AATD patients are typically < 45 years with parlobular basal emphysema
► Delay in diagnosis in older AATD patients presents as more typical distribution of emphysema (centriobular apical).
► A low concentration (< 20% normal) is highly suggestive of homozygous deficiency.
OVERALL KEY POINTS (1 of 3):
► Smoking cessation is key. Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates.
► The effectiveness and safety of e-cigarettes as a smoking cessation aid is uncertain at present.
► Pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.
► Each pharmacologic treatment regimen should be individualized and guided by the severity of symptoms, risk of exacerbations, side-effects, comorbidities, drug availability and cost, and the patient’s response, preference and ability to use various drug delivery devices.
► Inhaler technique needs to be assessed regularly.

OVERALL KEY POINTS (2 of 3):
► Influenza vaccination decreases the incidence of lower respiratory tract infections.
► Pneumococcal vaccination decreases lower respiratory tract infections.
► Pulmonary rehabilitation improves symptoms, quality of life, and physical and emotional participation in everyday activities.
► In patients with severe resting chronic hypoxemia, long-term oxygen therapy improves survival.
► In patients with stable COPD and resting or exercise-induced moderate desaturation, long-term oxygen treatment should not be prescribed routinely. However, individual patient factors must be considered when evaluating the patient’s need for supplemental oxygen.
Evidence Supporting Prevention & Maintenance Therapy

OVERALL KEY POINTS (3 of 3):

► In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, long-term non-invasive ventilation may decrease mortality and prevent re-hospitalization.

► In select patients with advanced emphysema refractory to optimized medical care, surgical or bronchoscopic interventional treatments may be beneficial.

► Palliative approaches are effective in controlling symptoms in advanced COPD.

Smoking Cessation

► Smoking cessation has the greatest capacity to influence the natural history of COPD.

► If effective resources and time are dedicated to smoking cessation, long-term quit success rates of up to 25% can be achieved.

Vaccination

► Influenza vaccination can reduce serious illness (such as lower respiratory tract infections requiring hospitalization) and death in COPD patients.

► Pneumococcal vaccinations, PCV13 and PPSV23, are recommended for all patients ≥ 65 years of age.
Bronchodilators in Stable COPD

1. Long-acting bronchodilators are effective in improving lung function, dyspnea, health status, and exercise tolerance in patients with COPD.
2. Combination therapy with a LABA and a LAMA is associated with a greater improvement in FEV1, FEF25-75, and bronchodilator responsiveness compared to monotherapy with either drug.
3. Regular and as-needed use of SABA and SAMA improves FEV1 and symptoms. (Evidence A)
4. Combination therapy with a LABA and a LAMA significantly improves lung function, dyspnea, health status, and exercise tolerance compared to monotherapy with either drug. (Evidence A)
5. Asthma and COPD are distinct diseases, but there is overlap in clinical presentation. (Evidence A)

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Anti-inflammatory Therapy in Stable COPD

Table 1: Anti-Inflammatory Therapy in Stable COPD

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Inhaled corticosteroids</td>
<td>A</td>
</tr>
<tr>
<td>COPD</td>
<td>Systemic corticosteroids</td>
<td>A</td>
</tr>
</tbody>
</table>

The Inhaled Route

Table 3A: The Inhaled Route

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Choose an inhaled route. Ensure proper technique is demonstrated.</td>
</tr>
<tr>
<td>2</td>
<td>Instruct the patient on how to use the inhaler.</td>
</tr>
<tr>
<td>3</td>
<td>Monitor patient's adherence to therapy.</td>
</tr>
</tbody>
</table>

Other Pharmacologic Treatments

Table 3B: Other Pharmacologic Treatments

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airway hyperreactivity</td>
<td>Long-acting anticholinergics</td>
<td>A</td>
</tr>
<tr>
<td>Airway hyperreactivity</td>
<td>Long-acting beta-2 agonists</td>
<td>A</td>
</tr>
</tbody>
</table>

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Oxygen Therapy & Ventilatory Support in Stable COPD

During exacerbations of COPD, Noninvasive ventilation (NIV) in the form of noninvasive positive pressure ventilation (NPPV) is the standard of care for decreasing morbidity and mortality in patients hospitalized with an exacerbation of COPD and acute respiratory failure.

Table 3.6: Oxygen therapy and ventilatory support in stable COPD

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Description</th>
</tr>
</thead>
</table>
| Oxygen therapy | Long-term oxygen therapy in patients with severe chronic obstructive pulmonary disease (COPD) and hypoxemia. (Evidence A).
| Ventilatory support | Noninvasive ventilatory support in selected patients after recent hospitalization, particularly those with pulmonary hypertension (PH). (Evidence C).
**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 symptomatic benefit is documented.

**Group B**
- Initial therapy should consist of a long-acting bronchodilator. Long-acting inhaled bronchodilators are superior to short-acting bronchodilators taken as needed i.e., pro re nata (prn) and are therefore recommended.
- There is no evidence to recommend one class of long-acting bronchodilators over another for initial relief of symptoms in this group of patients. In the individual patient, the choice should depend on the patient's perception of symptom relief.
- For patients with persistent breathlessness on monotherapy the use of two bronchodilators is recommended.

**Group B (continued)**
- For patients with severe breathlessness initial therapy with two bronchodilators may be considered.
- If the addition of a second bronchodilator does not improve symptoms, we suggest the treatment could be stepped down again to a single bronchodilator.
- Group B patients are likely to have comorbidities that may add to their symptomatology and impact their prognosis, and these possibilities should be investigated.
Pharmacologic treatment algorithms

**Group C**
- 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.
- Patients with persistent exacerbations may benefit from adding a second long acting bronchodilator (LABA/LAMA) or using a combination of a long acting beta2-agonist and an inhaled corticosteroid (LABA/ICS). As ICS increases the risk for developing pneumonia in some patients, our primary choice is LABA/LAMA.

**Group D**
- We recommend starting therapy with a LABA/LAMA combination because:
  - In studies with patient reported outcomes as the primary endpoint, LABA/LAMA combinations showed superior results compared to the single substances. If a single bronchodilator is chosen as initial treatment, a LAMA is preferred for exacerbation prevention compared to LABAs (for details see GOLD 2017 Chapter 3).
  - LABA/LAMA combination was superior to a LABA/ICS combination in preventing exacerbations and other patient reported outcomes in Group D patients (for details see GOLD 2017 Chapter 3).
  - Group D patients are at higher risk of developing pneumonia when receiving treatment with ICS.

**Group D (continued)**
- In some patients, initial therapy with LABA/ICS may be the first choice. These patients may have a history and/or findings suggestive of asthma-COPD overlap. High blood eosinophil counts may also be considered as a parameter to support the use of ICS, although this is still under debate (for details see Chapter 2 and Appendix).
- In patients who develop further exacerbations on LABA/LAMA therapy, we suggest two alternative pathways:
  - Escalation to LABA/LAMA/ICS. Studies are underway comparing the effects of LABA/LAMA vs. LABA/LAMA/ICS for exacerbation prevention.
  - Switch to LABA/ICS. However, there is no evidence that switching from LABA/LAMA to LABA/ICS results in better exacerbation prevention. If LABA/ICS therapy does not prevent further exacerbations or patients experience symptoms, a LAMA can be added.
Pharmacologic treatment algorithms

**Group D (continued)**

If patients treated with LABA/LAMA/ICS still have exacerbations the following options may be considered:

- Add roflumilast. This may be considered in patients with an FEV1 < 50% predicted and chronic bronchitis, particularly if they have experienced at least one hospitalization for an exacerbation in the previous year.
- Add a macrolide. The best available evidence exists for the use of azithromycin. Consideration to the development of resistant organisms should be factored into decision making.
- Stopping ICS. A reported lack of efficacy, an elevated risk of adverse effects (including pneumonia) and evidence showing no significant harm from withdrawal supports this recommendation (see Chapter 3 for further details).

Non-Pharmacologic Treatment

**Education and self-management**

Self-management education and coaching by healthcare professionals should be a major component of the "Chronic Care Model" within the context of the healthcare delivery system.

The aim of self-management education is to motivate, engage and coach the patients to positively adapt their health behavior(s) and develop skills to better manage their disease.

<table>
<thead>
<tr>
<th>Non-Pharmacologic management of COPD</th>
<th>Recommended</th>
<th>Depending on local guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient group: Essential</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A Smoking cessation (non-pharmacologic)</td>
<td>Physical activity</td>
<td>Blood sampling, blood pressure monitoring</td>
</tr>
<tr>
<td>B-2 Smoking cessation (non-pharmacologic)</td>
<td>Physical activity</td>
<td>Blood sampling, physical examination</td>
</tr>
<tr>
<td></td>
<td>Pulmonary rehabilitation</td>
<td></td>
</tr>
</tbody>
</table>

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Oxygen therapy

Long-term oxygen therapy is indicated for stable patients who have:

► PaO2 at or below 7.3 kPa (55 mmHg) or SaO2 at or below 88%, with or without hypercapnia confirmed twice over a three week period; or

► PaO2 between 7.3 kPa (55 mmHg) and 8.0 kPa (60 mmHg), or SaO2 of 88%, if there is evidence of pulmonary hypertension, peripheral edema suggesting congestive cardiac failure, or polycythemia (hematocrit > 55%).
**Monitoring and Follow-up**

**Monitoring disease progression and development of complications and/or comorbidities**

- **Measurements.** Decline in FEV₁ can be tracked by spirometry performed at least once a year.
- **Symptoms.** At each visit, information on symptoms since the last visit should be collected, including cough and sputum, breathlessness, fatigue, activity limitation, and sleep disturbances.
- **Exacerbations.** The frequency, severity, type and likely causes of all exacerbations should be monitored.
- **Imaging.** If there is a clear worsening of symptoms, imaging may be indicated.
- **Smoking status.** At each visit, the current smoking status and smoke exposure should be determined followed by appropriate action.

**Pharmacotherapy and other medical treatment**

In order to adjust therapy appropriately as the disease progresses, each follow-up visit should include a discussion of the current therapeutic regimen.

Monitoring should focus on:

- Dosages of prescribed medications.
- Adherence to the regimen.
- Inhaler technique.
- Effectiveness of the current regime.
- Side effects.

Treatment modifications should be recommended.
OVERALL KEY POINTS (1 of 3):

► An exacerbation of COPD is defined as an acute worsening of respiratory symptoms that results in additional therapy.
► Exacerbations of COPD can be precipitated by several factors. The most common causes are respiratory tract infections.
► The goal for treatment of COPD exacerbations is to minimize the negative impact of the current exacerbation and to prevent subsequent events.
► Short-acting inhaled beta₂-agonists, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat an acute exacerbation.

OVERALL KEY POINTS (2 of 3):

► Maintenance therapy with long-acting bronchodilators should be initiated as soon as possible before hospital discharge.
► Systemic corticosteroids can improve lung function (FEV₁), oxygenation and shorten recovery time and hospitalization duration. Duration of therapy should not be more than 5-7 days.
► 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.
► Methylxanthines are not recommended due to increased side effect profiles.

OVERALL KEY POINTS (3 of 3):

► Non-invasive mechanical ventilation should be the first mode of ventilation used in COPD patients with acute respiratory failure who have no absolute contraindication because it improves gas exchange, reduces work of breathing and the need for intubation, decreases hospitalization duration and improves survival.
► Following an exacerbation, appropriate measures for exacerbation prevention should be initiated (see GOLD 2017 Chapter 3 and Chapter 4).
Management of Exacerbations

COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

- They are classified as:
  - Mild (treated with short-acting bronchodilators only, SABDs)
  - 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.

Classification of hospitalized patients

**No respiratory failure:**
Respiratory rate: 20-30 breaths per minute; no use of accessory respiratory muscles; no change in mental status; hypoxemia improved with supplemental oxygen given via Venturi mask 28-35% inspired oxygen (FiO₂); no increase in PaCO₂.

**Acute respiratory failure — non-life-threatening:**
Respiratory rate: > 30 breaths per minute; using accessory respiratory muscles; no change in mental status; hypoxemia improved with supplemental oxygen via Venturi mask 25-30% FiO₂; hypercarbia i.e., PaCO₂ increased compared with baseline or elevated 50-60 mmHg.
Classification of hospitalized patients

Acute respiratory failure — life-threatening:
Respiratory rate: > 30 breaths per minute; using accessory respiratory muscles; acute changes in mental status; hypoxemia not improved with supplemental oxygen via Venturi mask or requiring FiO₂ > 40%; hypercarbia i.e., PaCO₂ increased compared with baseline or elevated > 60 mmHg or the presence of acidosis (pH < 7.25).

Table 6.1: Potential indicators for hospitalisation assessment
- Fever; symptoms such as sudden worsening of shortness of breath, high respiratory rate, increased oxygen saturation, confusion, dizziness.
- Acute exacerbation failure.
- Other causes of abnormal lung sounds (e.g., pneumonia, pulmonary edema).
- Failure of an exacerbation to respond to initial medical management.
- Presence of serious co-morbidities (e.g., heart failure, newly occurring arrhythmias, etc.).
- Inadequate home support.

Table 6.2: Management of acute but not life-threatening exacerbations
- Administer supplemental oxygen therapy, obtain serial arterial blood gases, perform capillary oximetry measurements.
- Bronchodilators:
  - Increase dose and/or frequency of bronchodilators.
  - Use nebulizers and long-acting bronchodilators when patient remains stable.
- Consider oral corticosteroids.
- Consider antibiotics if bronchial infection is present.
- Consider noninvasive mechanical ventilation (NIV).
- At all times:
  - Monitor fluid balance.
  - Consider supplementary oxygen or low endotracheal oxygen for initial ventilation therapy.
  - Identify and treat associated conditions (e.g., cyanotic fever, arrhythmias, pulmonary embolism, etc.).

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Pharmacologic treatment

The three classes of medications most commonly used for COPD exacerbations are:

► 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

Respiratory support

Table 4.4: Indications for respiratory or medical (intensive care unit admittance)

- Oxygen therapy (inhaled or nasal cannula), intubation, renal, or mechanical ventilation
- Respiratory failure, respiratory acidosis, respiratory alkalosis, metabolic acidosis, metabolic alkalosis
- Respiratory failure, metabolic acidosis, respiratory acidosis

Table 4.5: Indications for noninvasive mechanical ventilation (NIV)

- Respiratory acidosis, respiratory alkalosis, metabolic acidosis, metabolic alkalosis
- Respiratory failure, respiratory acidosis, respiratory alkalosis, metabolic acidosis, metabolic alkalosis
- Respiratory failure, respiratory acidosis, respiratory alkalosis, metabolic acidosis, metabolic alkalosis
- Respiratory failure, respiratory acidosis, respiratory alkalosis, metabolic acidosis, metabolic alkalosis
- Respiratory failure, respiratory acidosis, respiratory alkalosis, metabolic acidosis, metabolic alkalosis

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Management of Exacerbations

Respiratory support

<table>
<thead>
<tr>
<th>Table 1: Indications for intubation and mechanical ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unable to tolerate NIPPV or HFOV.</td>
</tr>
<tr>
<td>• Severe pain or respiratory or cardiac arrest.</td>
</tr>
<tr>
<td>• Uncontrolled somnolence, psychomotor agitation inadequately controlled by sedation.</td>
</tr>
<tr>
<td>• Medication-resistant respiratory acidosis.</td>
</tr>
<tr>
<td>• Persistent inability to receive respiratory ventilations.</td>
</tr>
<tr>
<td>• Severe tachypnoea and hypoxia requiring mechanical ventilation.</td>
</tr>
<tr>
<td>• Severe ventilator or non-ventilator barotrauma.</td>
</tr>
<tr>
<td>• Uncontrolled hypoxemia in patients unable to tolerate NIPPV.</td>
</tr>
</tbody>
</table>

Table 2: Treatment options and recommendations for follow-up

<table>
<thead>
<tr>
<th>Treatment Options</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Oxygen therapy</td>
<td>Continuous low-flow oxygen.</td>
</tr>
<tr>
<td>• Bronchodilators</td>
<td>Medium-dose inhaled bronchodilators.</td>
</tr>
<tr>
<td>• Antibiotics</td>
<td>Intravenous broad-spectrum antibiotics.</td>
</tr>
<tr>
<td>• Corticosteroids</td>
<td>Intravenous corticosteroids.</td>
</tr>
<tr>
<td>• Long-term oxygen</td>
<td>Long-term oxygen therapy.</td>
</tr>
<tr>
<td>• Smoking cessation</td>
<td>Smoking cessation.</td>
</tr>
<tr>
<td>• Vaccinations</td>
<td>Pneumococcal vaccination.</td>
</tr>
<tr>
<td>• Pulmonary rehab</td>
<td>Pulmonary rehabilitation.</td>
</tr>
</tbody>
</table>

Table 3: Interventions that reduce the frequency of COPD exacerbations

<table>
<thead>
<tr>
<th>Intervention Class</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled corticosteroids</td>
<td>LABA + ICS</td>
</tr>
<tr>
<td>Long-acting bronchodilators</td>
<td>LABA + ICS</td>
</tr>
<tr>
<td>Azithromycin monotherapy</td>
<td>Azithromycin</td>
</tr>
<tr>
<td>Vaccinations</td>
<td>Pneumococcal vaccination.</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>Smoking cessation.</td>
</tr>
<tr>
<td>Pulmonary rehabilitation</td>
<td>Pulmonary rehabilitation.</td>
</tr>
<tr>
<td>Long-term oxygen therapy</td>
<td>Long-term oxygen therapy.</td>
</tr>
</tbody>
</table>