STABLE AND EXACERBATION OF COPD (ECOPD)

Based on the 2025 Global Initiative for Chronic Obstructive Lung Disease (GOLD) report and best practice review published in *Am J Respir Crit Care Med* 2024

DEFINITION

COPD is clinically characterized by chronic respiratory symptoms (dyspnea, cough or sputum production, and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and or alveoli (emphysema) that cause persistent and often progressive non-fully reversible air flow obstruction in setting of exposure to risk factors.

ETIOLOGY

- Environmental exposure
    - Cigarette smoking - by far the most common cause of COPD (70% in developed countries). Other smoking include pipe, cigars, vaping, marijuana
    - Household and pollution exposure- dusts, vapors, fumes, chemicals
- Genetically determined - $\alpha 1$ antitrypsin deficiency (AATD) PiZZ genotype
- Abnormal lung development - low birthweight, prematurity
- Childhood respiratory infections, HIV associated COPD
- Asthma with airway remodeling, asthma-COPD overlap syndrome (ACOS), and bronchiectasis-COPD overlap syndrome (BCOS)
- Unknown cause

DIAGNOSIS

A diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough, a history of recurrent lower respiratory tract infections and/or history of risk factors but spirometry showing post-bronchodilator FEV1/FVC < 0.7 is mandatory to establish the diagnosis of COPD.

- Pre-bronchodilator FEV1/FVC ≥0.7 --> not COPD
- FEV1/FVC <0.7 **-->** measure post-bronchodilator FEV1/FVC
    - FEV1/FVC <0.7 **-->** COPD confirmed
    - FEV1/FVC ≥0.7 **-->** needs follow-up with repeat assessment

Using the post-bronchodilator fixed FEV1/FVC ratio versus the lower limit of normal (LLN) remains controversial and has not been adopted by the ATS criteria.

- Fixed FEV1/FVC ratio may underdiagnose COPD in young subjects
- Subjects classified as normal using LLN criteria but obstructed or restricted using the fixed ratio may have a higher risk of mortality.

GOLD 2025 continues recommending the ABE classification to guide treatment in patients with stable COPD.

- While post-bronchodilator spirometry is required for the diagnosis and assessment of COPD, it is not necessary to stop inhaled medications before spirometry during follow-up of patients.

ABE classification

Groups based on symptoms and frequency of exacerbation

A Dyspnea mMRC 0-1 with no exacerbation leading to hospitalization or 1 moderate exacerbation not leading to hospitalization

B Dyspnea mMRC ≥2 with no exacerbation leading to hospitalization or 1 moderate exacerbation not leading to hospitalization

E One or more exacerbations leading to hospitalization or ≥2 moderate exacerbations not leading to hospitalization

Grades based on spirometry values

Mild	FEV1 ≥80
Mod	FEV1 50 to 80
Severe	FEV1 30 to 50
Very severe	FEV1 <30

Pre-COPD

Patients with symptoms, structural and/or physiological lung abnormalities without airflow obstruction (post-bronchodilator FEV1/FVC ≥ 0.7.

- Emphysema
- Decreased FEV1 or rapid decline, air trapping, hyperinflation, or reduced lung diffusing capacity

PRISm (Preserved Ratio Impaired Spirometry)

Spirometric pattern characterized by FEV1/FVC ≥ 0.70 and post-BD FEV1 < 80% predicted.
Potential causes may include:

- PRISm is associated with increased risk of developing airway obstruction, respiratory symptoms, hospitalization, and mortality

Patients with Pre-COPD or PRISm are at risk of developing airflow obstruction over time, but not all of them do but they should be considered “patients” because they are symptomatic and/or have functional and/or structural abnormalities and, as such, they deserve care and treatment. The challenge is that there is no evidence of what the best treatment for these patients is yet.

ECOPD is defined as an event characterized by increased dyspnea and/or cough and sputum that worsen in <14 days which may be accompanied by tachypnea and/or tachycardia and is often associated with increased local and systemic inflammation.

MANAGEMENT OF STABLE COPD

INITIAL ASSESSMENT

Once the diagnosis is confirmed by spirometry, the following five aspects should be assessed to guide COPD treatment:

- ABE classification to assess:
  - Severity of airway obstruction
  - Nature and magnitude of current symptoms
  - Previous history of moderate and severe exacerbations
- Absolute blood eosinophil count (AEC)
- Associated comorbidities

TREATMENT

1. Appropriate vaccination
2. Initial inhaled medications

3. Follow-up pharmacological management
4. Determine the appropriateness of supplemental oxygen
5. Consideration of pulmonary rehabilitation
6. Consideration for lung structural related therapies - interventional procedures
7. Other supportive measures
8. Preoperative evaluation

1. Appropriate vaccination

All patients with COPD should receive:

- Influenza and RSV vaccines yearly
- Covid vaccine following CDC recommendations
- Pneumococcal: one dose conjugate vaccine PCV21 (Prevnar) or PCV15 followed by PPSV23 if they have never received a pneumococcal conjugate vaccine previously, or if their previous pneumococcal vaccination history is unknown
    - Adults who have only received PPSV23 may receive a PCV (either PCV21 or PCV15) ≥ 1 year after their last PPSV23 dose
- Zoster vaccine

2. Initial inhaled medications

Long-acting bronchodilators (LAMA or LABA) for maintenance and short acting (SABA) as needed

- Should be prescribed to ameliorate symptoms and reduce probability of exacerbations. They may maintain or improve lung function.
- GOLD 2025 continues recommending blood absolute eosinophil count (AEC) to guide the use of inhaled corticosteroids (ICS)
    - Group A: a bronchodilator, either LAMA or LABA or SABA (long acting preferred except is patient only occasional dyspnea
    - Group B: LAMA + LABA
    - Group E: LAMA + LABA
    - Triple inhaled therapy (LAMA + LABA + adding ICS):
        - Strongly recommended
            - Group E and AEC ≥300
            - ACOS (asthma-COPD overlap syndrome)
        - Favors use
            - Groups E and B with AEC >100 and not clinical improvement despite dual therapy with LABA + LAMA
            - One moderate ECOPD per year and AEC 100 to <300
        - Against use:
            - Recurrent PNA
            - AEC <100
            - History of mycobacterial infections
    - Concomitant asthma and COPD
        - For all COPD GOLD groups, they should be treated like patients with asthma including the use of an ICS

3. Follow-up pharmacological management

Patients with not improving dyspnea or exercise tolerance

- On LAMA **or** LABA **-->** LAMA + LABA
- On LAMA **+** LABA
    - Consider switching inhaler device or molecules
    - Consider adding Ensifentrine*
    - Investigate and treat if applicable other causes of dyspnea

Patients with recurrent exacerbations despite triple therapy or double therapy not candidate for ICS, consider:

- Roflumilast (PDE-4 inhibitor) if FEV1 <50% and chronic bronchitis
- Azithromycin 250 mg/d or 500 mg x3 weekly, preferentially in former smoker
- Biologics – Dupilumab* for patients treated with triple therapy with no clinical improvement or recurrent exacerbations, chronic bronchitis, and blood AEC >300

*Ensifentrine (bronchodilator and anti-inflammatory) is a selective dual inhibitor of PDE3 and PDE4 that combines effect on airway small muscles and inflammation

- FDA approved in 2024 for maintenance management of COPD, asthma, and cystic fibrosis
- ENHANCE-1 and ENHANCED-2 multicenter RTC trials in patient with symptomatic, moderate to severe COPD (GOLD group B with moderate to severe airway obstruction)
    - 3 mg/2.5 ml by nebulization q12h demonstrated improvement in symptoms, lung function, and COPD exacerbations
    - Effects were consistent in patient with and without chronic bronchitis in contrast to oral PDE-4 inhibitors
    - The effect on exacerbations has not ben evaluated

*Dupixent (dupilumab) is the first biologic therapy approved by the FDA in 2024 to treat COPD as an add-on maintenance treatment for patients with inadequately controlled COPD and an eosinophilic phenotype

- Reduce acute exacerbations of COPD, improve lung function, quality of life, and respiratory symptoms

Patient is on treatment with LABA + ICS

If patient with COPD and no features of asthma has been treated - for whatever reason - and is well controlled in terms of symptoms and exacerbations, continuation with LABA + ICS is an option, however, if the patient has:

- Further exacerbation: escalate to LAMA + LABA + ICS if AEC ≥100 or switch to LAMA + LABA if AEC <100
- Major symptoms: change to LAMA + LABA or LAMA + LABA + ICS depending on previous treatment response to ICS

4. Determine the appropriateness of supplemental oxygen

Supplemental O2 targeting O2Sat ≥90% for resting or severe exercise chronic hypoxemia

- Severe resting chronic hypoxemia:
    - SaO2 at or below 88% or PaO2 at or below 55 mmHg with or without hypercapnia confirmed twice over a three-week period

    - SaO2 of 88% or PaO2 between 55 mmHg and 60 mmHg if there is evidence of pulmonary hypertension, congestive cardiac failure, or polycythemia (hematocrit > 55%)
- Severe exercise chronic hypoxemia
    - SaO2 <80% on 6MWT
- However, individual patient factors must be considered when evaluating the patient's need for supplemental O2.
- Patients should be reevaluated in 60 – 90 days to determine if O2 is still indicated.

Supplemental O2 for air-travel

- Most patients with O2 Sat >95% and 6MWT O2Sat >84% may travel without further assessment
    - Careful consideration for patients with cardiac conditions or severe anemia
- Resting SpO_2 <92% on RA should receive in-flight supplemental oxygen

5. Consideration of pulmonary rehabilitation

Pulmonary rehabilitation is one of the most cost-effective treatment strategies in patients with stable COPD and should be considered part of the integrated management in patient's groups B and E.

6. Consideration for lung structural related therapies - interventional procedures

Generally associated with symptoms and lung function improvement and in very selected cases, survival improvement.

- Refractory dyspnea
    - Emphysema
        - Endobronchial valve therapy (EBV - if intact fissure between the treated and non-treated lobe or absence of collateral ventilation), EBV, coil, lung sealants, thermal vapor ablation, LVRS, or lung transplantation
    - Giant bulla
        - Bullectomy
    - Tracheobronchomalacia or excessive dynamic airway collapse of the posterior membrane (EDAC)
        - Large airway stenting and/or tracheobronchoplasty
- Refractory chronic bronchitis
    - Nitrogen cryotherapy
    - Rheoplasty
        - Both presently being evaluated attempting to reduce mucus hypersecretion by eliminating airway cells goblet cell hyperplasia and submucosal glands in patients with chronic bronchitis
- Recurrent exacerbations
    - Acute and chronic bronchitis, emphysema, tracheobronchomalacia
        - Targeted lung denervation
            - Intended to disrupt the parasympathetic nerve transmission resulting in decrease mucous production and bronchoconstriction

Criteria for endoscopic lung volume reduction (ELVR endobronchial valve therapy-EBV if intact fissure between the treated and non-treated lobe or absence of collateral ventilation), lung coils, or thermal ablation

- Post-bronchodilator FEV1 between 15% to 45% along with hyperinflation

Low volume reduction surgery (LVRS) – it has been progressive by replaced by ELVR

- Severe upper lobe predominance of emphysema
- Hyperinflation
- Low exercise capacity after pulmonary rehabilitation

Criteria for lung transplant referral to improve quality of life and functional capacity

- Progressive disease, BODE index >7 and not candidates for lung volume reduction with at least one of the following:
  - Hospitalization for exacerbation with acute hypercapnia (PaCO2 > 50 mmHg)
  - FEV1 < 20% and either DLco <20% or homogeneous emphysema
  - Pulmonary hypertension and/or cor pulmonale despite O2 therapy

7. Other supportive measures

a. Smoking cessation

- Counseling
- Pharmacological treatment (at least one of these medications should be prescribed in the absence of contraindications)
  - Aimed at achieving long term abstinence
    - Varenicline, bupropion, and nicotine patch
  - Aimed to relieve withdrawal symptoms

    Short acting nicotine (gum, inhaler, nasal spray, sublingual tablets, or lozenge)
- E-cigarettes as a bridge for smoking cessation
  - GOLD 2025 continues not to recommend e-cigarettes due to the lack of knowledge about the long-term effects of e-cigarettes on respiratory health (independent risk factors for COPD and/or lung cancer).
  - Literature favoring e-cigarettes for smoking cessation as a bridge
    - *N Engl J Med 2024; 390:601-610.* Electronic Nicotine-Delivery Systems for Smoking Cessation.
    - *Cochrane review 2024.* Electronic cigarettes for smoking cessation

b. Noninvasive ventilation (NIV)

In patients with prolonged daytime hypercapnia (PaCO2 >53 mmHg) and a history of hospitalization for acute respiratory failure, long-term non-invasive ventilation may decrease mortality and prevent re-hospitalization.

c. Management of mucous hypersecretions

Overall, there are no clear benefits using mucolytics but can be effective in selected groups (NAC, carbocysteine and erdosteine), oscillating positive expiratory pressure (OPEP) therapy, or nebulized hypertonic saline.

- Limited evidence suggesting mild improvement in mucous mobilization and symptoms in selected cases with severe chronic bronchitis
- New classes of mucolytics (CFTR potentiator icenticaftor) and surgical-bronchoscopic interventions to reduce mucus hypersecretion by eliminating airway cells goblet cell hyperplasia and submucosal glands (nitrogen cryospray and rheoplasty) are presently being evaluated.

- Consideration for large airway stenting and/or tracheoplasty for patients with moderate to severe excessive dynamic airway collapse of the posterior membrane (EDAC) or tracheobronchomalacia

d. ATT augmentation

- α1 antitrypsin deficiency and FEV1 ≤65%
- Consider ATT augmentation if progressive disease with FEV1>65%

e. CT chest indications

- Frequent exacerbations with productive cough raising concern for bronchiectasis or atypical infections
- Symptoms out of proportion of severity of airway obstruction (CT + echocardiogram + 6MWT)
- Consideration for lung structural related therapies - interventional procedures
- LDCT for patients meeting criteria
    - Aged 50 to 80 years who have a 20 pack-year smoking and currently smoke or have quit within the past 15 years

8. Preoperative evaluation

Key factor that can contribute to increased risk for atelectasis, lung infections and/or increased airflow obstruction which all potentially result in acute respiratory failure and aggravation of COPD:

- Smoking
- Poor general health status
- Age
- Obesity
- Associated cardiac comorbidities
- Thoracic or abdominal surgery
- COPD severity

Most evidence conclude that epidural or spinal anesthesia have lower risk than general anesthesia.

MANAGEMENT OF EXACERBATION OF COPD (ECOPD)

A. Evaluation to diagnose and establish the cause
B. Assessment of severity
C. Treatment

A. EVALUATION TO DIAGNOSE AND ESTABLISH THE ECOPD CAUSE

- Approximately 70% of ECOPD are triggered by viral and bacterial infections. Other causes include poor treatment adherence, environmental pollution, and excess heat that can initiate and/or amplify an ECOPD. In some cases cannot be determined.
- Eosinophil levels have not been used for ECOPD diagnosis.

- In many patients, the signs and symptoms of an exacerbation are not specific, and COPD patients are at increased risk of other respiratory and nonrespiratory concomitant diseases that may mimic and/or aggravate its clinical presentation (see figure below):
    - Acute decompensated heart failure
    - Pneumonia
    - Pulmonary embolism
    - Other conditions

Acute decompensated heart failure (ADHF)

- Chest pain/discomfort, fluid retention, or irregular pulse suggest a cardiovascular cause as an alternative or contributing diagnosis to an ECOPD.
- Some of these clinical findings can make distinguishing ECOPD from ADHF difficult. In addition, COPD is present in up to 50% of patients ADHF, and ADHF occurs in roughly 20% of individuals with COPD because of overlapping risk factors (aging and smoking).
- Hypoxemia and tachycardia in ECOPD can promote ADHF, whereas pulmonary fluid retention in ADHF can worsen airway obstruction. In addition, wheezing is common in acute ADHF.

Pulmonary embolism (PE)

- The prevalence of PE in patients with ECOPD ranges from 3% to 30%, being more common in patients with atypical or unexplained ECOPD.
- Given the high mortality with PE, evidence supports CTPA imaging in patients with a high clinical PE pretest probability and an atypical clinical presentation for ECOPD, with no need to assess D-dimer.
- If the pretest probability is low/intermediate and a D-dimer is normal (less than 500 ng/ml or less than age x10 for patients older than 50 years) would support ECOPD as the diagnosis and help avoid imaging testing (CTPA, V/Q scan or Doppler/US).

Pneumonia (PNA)

- Because a diagnosis of COPD increases PNA risk and the symptoms of PNA and ECOPD are similar (worsened cough, sputum production, dyspnea, and fever), PNA should always be considered in the differential diagnosis of patients with symptoms of ECOPD.
- Although most patients without severe ECOPD can be safely treated on the basis of chest X-ray results alone, opacities not visible on a chest X-ray may be seen with more sensitive CT scans (CXR negative, CT positive PNA).

Other conditions that may mimic or contribute to the clinical presentation

Bronchiectasis

- The diagnosis of COPD is primarily physiological, whereas that of bronchiectasis is radiological. However, patients with severe and/or extensive bronchiectasis can have poorly-reversible airflow obstruction, meeting spirometric criteria for COPD.
- Diagnostic criteria for bronchiectasis COPD overlap syndrome (BCOS) include appropriate ROSE (radiology, airflow obstruction, symptoms, and exposure). In these patients, it is impossible to differentiate exacerbation of the bronchiectasis from ECOPD.

Asthma exacerbation

- No publication has addressed whether exacerbations in patients with asthma and COPD overlap syndrome (ACOS) are different from exacerbations of asthma or ECOPD, and guidelines define asthma exacerbations and ECOPDs similarly.

- The management of concomitant COPD and asthma is similar to that of asthma.

ILD

- Some patients may present with combined pulmonary fibrosis and emphysema. When these patients experience an exacerbation, it may be difficult to differentiate an ECOPD from an ILD exacerbation.
    - The presence of new widespread groundglass infiltrates in a patient with symptoms consistent with ECOPD supports an important role of an ILD exacerbation in the patient's event.
- A group of patients may have emphysematous/cystic changes and reticular subpleural infiltrates without classic fibrosis (no traction bronchiectasis nor honeycombing) referred as alveolar enlargement or interstitial fibrosis smoking related.

Anxiety-panic attacks

- Concomitant anxiety-depression and COPD is common
- Panic attacks and anxiety may cause tachypnea that, in COPD, may result in hyperinflation and culminate in acute hypercapnic respiratory failure. Furthermore, hypercapnia triggers panic attacks because of the activation of specific brainstem reflexes, causing hyperventilation, hyperinflation, and aggravating panic symptoms
    - In patients with COPD who have a panic attack, the lack of increase in cough and sputum in the absence of either an inflammatory burst or another explanatory morbidity for dyspnea and tachypnea can help establish a diagnosis

Pneumothorax

- It is a potentially life-threatening event that occurs in some patients with COPD, resembles an ECOPD

Pleural effusion

- Large pleural effusions may contribute to worsening dyspnea in patients with COPD. Echocardiogram, BNP, CRP, PCT and clinical history are helpful in the differential. Common causes include:
    - HF
    - Parapneumonic
    - Cancer

Anemia

- Polycythemia can indicate untreated hypoxemia
- Whereas anemia, a frequent concomitant morbidity in stable COPD, may contribute to breathlessness

B. ASSESSMENT OF ECOPD SEVERITY:

According to the GOLD report, the ABE classification is useful to guide pharmacologic treatment in stable patients but not during an actual episode ECOPD.

In patients with ECOPD, it is necessary to separate the physiological classification of exacerbations intended to guide treatment at the point of care from the site of care (outpatient or inpatient)

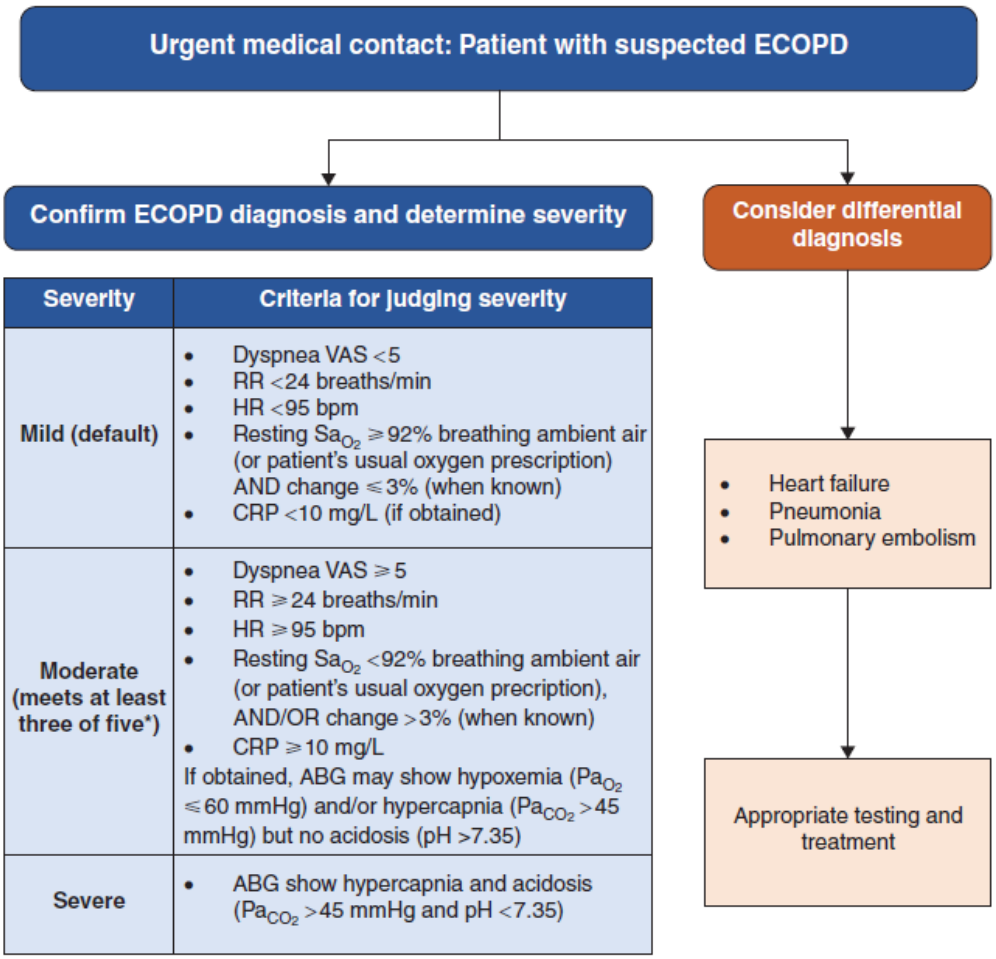
1. At the point of care.

GOLD 2025 continues to propose the use of the Rome classification to guide the treatment of the actual exacerbation episode

Rome proposal classification: integration of five easy-to-evaluate parameters and ABGs as a sixth variable:

- Dyspnea, RR, HR, O2 Sat, and serum CRP
    - Dyspnea assessed by the visual analog scale (VAS)
        - On a numerical scale from 0 to 10, circle 0 for no SOB and 10 for maximal shortness of breath ever experienced
- ABGs must indicate the presence of hypercapnia (PaCO2 >45 mm Hg) and respiratory acidosis (pH <7.35)

Based on above variables ECOPD is classified as mild, moderate or severe (moderate criteria + ABGs criteria):



Severity	Criteria for judging severity
Mild (default)	• Dyspnea VAS <5 • RR <24 breaths/min • HR <95 bpm • Resting Sa_{O_2} ⩾92% breathing ambient air (or patient's usual oxygen prescription) AND change ⩽3% (when known) • CRP <10 mg/L (if obtained)
Moderate (meets at least three of five*)	• Dyspnea VAS ⩾5 • RR ⩾24 breaths/min • HR ⩾95 bpm • Resting Sa_{O_2} <92% breathing ambient air (or patient's usual oxygen precription), AND/OR change >3% (when known) • CRP ⩾10 mg/L If obtained, ABG may show hypoxemia (Pa_{O_2} ⩽60 mmHg) and/or hypercapnia (Pa_{CO_2} >45 mmHg) but no acidosis (pH >7.35)
Severe	• ABG show hypercapnia and acidosis (Pa_{CO_2} >45 mmHg and pH <7.35)

2. In hospitalized patients.

The severity of the exacerbation should be based on the patient's clinical signs and GOLD 2024 continues recommending the following classification:

- *Without respiratory failure:*
    - Respiratory rate: ≤ 24 breaths per minute
    - Heart rate < 95 beats per minute
    - No use of accessory respiratory muscles

    - No changes in mental status
    - Hypoxemia improved with supplemental oxygen given at 24-35% inspired oxygen (FiO2)
    - No increase in PaCO2
- *With acute respiratory failure – non-life-threatening:*
    - Respiratory rate > 24 breaths per minute
    - Using accessory respiratory muscles
    - No change in mental status
    - Hypoxemia improved with supplemental oxygen > 35% FiO2
    - Hypercarbia i.e., PaCO2 increased compared with baseline or elevated 50-60 mmHg
- *With acute respiratory failure – life-threatening:*
    - Respiratory rate > 24 breaths per minute
    - Using accessory respiratory muscles
    - Acute changes in mental status
    - Hypoxemia not improved with supplemental oxygen requiring FiO2 > 40%
    - Hypercarbia i.e., PaCO2 increased compared with baseline or elevated > 60 mmHg or the presence of acidosis (pH ≤ 7.25)

C. TREATMENT OF ECOPD

The goals of treatment for ECOPD are to minimize the negative impact of the current exacerbation and prevent the development of subsequent events.

- General measures
- Pharmacologic therapy
- Respiratory support
- Hospital discharge and follow-up

1. General measures

At all times, patients should receive:

- VTE prophylaxis
- Fluid balance monitoring
- Evaluation for possible aggravating conditions such as PNA, ADHF, and PE
- Smoking cessation when applicable
- Update vaccination

2. Pharmacologic therapy

Inhaled short-acting bronchodilators

- SABA with or without short-acting anticholinergics (SAMA) are recommended as the initial bronchodilators to treat ECOPD.
- It is recommended that patients do not receive continuous nebulization but use the MDI inhaler two puffs or nebulizer every one hour for two or three doses and then every four hours based on the patient's response.

Long-acting bronchodilators and inhaled steroids

- Although there are no clinical studies evaluating the use of long-acting bronchodilators (LABA or LAMA or combinations) with ICS, the 2025 GOLD report recommend continuation of these treatments during ECOPD or to start them as soon as possible before hospital discharge.

Systemic glucocorticoid

- The optimal dose and duration of systemic glucocorticoids in ECOPD is not clearly established but the evidence favors using a moderate, rather than high doses.
    - A dose of 40 mg prednisone per day for 5 days is recommended
    - Higher doses and extended treatment up to 14 days may be used in patients with impending or actual respiratory failure
        - Methylprednisolone 60 mg/IV q12 as starting dose with frequent reassessment
        - Therapy with oral prednisone is equally effective to intravenous administration once GI absorption is of no concern

Antibiotics

- Should be given to patients with ECOPD who have any of the following:
    - Have the three cardinal symptoms: increase in dyspnea, sputum volume, and sputum purulence
    - Have two of the cardinal symptoms, if increased purulence of sputum is one of the two symptoms
    - Require mechanical ventilation (invasive or noninvasive)
- Usually, initial empirical treatment is an aminopenicillin with clavulanic acid, macrolide, ceftriaxone, or tetracycline. The recommended length of antibiotic therapy is 5-7 days.
- For patients with PNA at risk for pseudomonas or MRSA, cefepime or piperacillin/tazobactam with vancomycin or linezolid are indicated.
    - Risk factors for Pseudomonas or MRSA:
        - Previous infection with Pseudomonas or MRSA or known colonization
        - Recent hospitalization within 90 days and use of IV antibiotics
        - Cavitary or necrotizing pneumonia or empyema
        - Underlying immunosuppression
        - ESRD for MRSA and structural lung disease i.e., bronchiectasis for pseudomonas

Vitamin D

- It is recommended that all patients hospitalized for exacerbations should be assessed and investigated for severe deficiency (<10 ng/dl or <25 Nm) followed by supplementation if required.
    - Vitamin D has an immune-modulating role and has been implicated in the pathophysiology of exacerbations
    - As with many chronic diseases vitamin D levels are lower in COPD than in health
    - Some, but not all studies have shown that supplementation in people with severe deficiency results in a 50% reduction in episodes and hospital admission

Treatments without clear benefit

Mucoactive agents, methylxanthines, and mechanical techniques to augment sputum clearance have not been shown to confer benefit for ECOPD.

3. Respiratory support

Oxygen therapy

- Supplemental O2 should be titrated to improve hypoxemia targeting O2 Sat >90% to prevent worsened hypercapnia.

Noninvasive ventilation (NIV)

- It should be the first mode of ventilation because it improves gas exchange, reduce work of breathing and the need for intubation, decreases hospitalization duration, and improves survival

- Indications - at least one of the following:
    - Respiratory acidosis with PaCO2 >45 mmHg and pH <7.35
    - Severe dyspnea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both such as use of accessory muscles, paradoxical abdominal movement, or retraction of the intercostal spaces
    - Persistent hypoxemia despite supplemental O2 therapy

Invasive mechanical ventilation (IMV)

- It should be initiated without delay when patients fail, do not tolerate, or have contraindications to NIV.
- Indications:
    - Unable to tolerate NIV or NIV failure
    - Status post respiratory or cardiac arrest
    - Diminished consciousness, agitation inadequately controlled by sedation
    - Massive aspiration or persistent vomiting
    - Persistent inability to remove respiratory secretions
    - Severe hemodynamic instability without response to IVF and vasoactive drugs
    - Severe ventricular and supraventricular arrhythmias
    - Severe hypoxemia in patients unable to tolerate NIV

4. Hospital discharge and follow-up

- Recurrent exacerbations leading to short term readmissions and increased all-cause mortality are associated with initial hospitalization for acute episode of deterioration.
    - Associated comorbidities, previous exacerbations and hospitalization, and increased length of stay are significant risk factors for 30-90 days all-cause readmission with an ECOPD
    - The introduction of care bundles at hospital discharge aimed to decrease the rate of short term readmissions have been recommended (see below).
        - However, there is insufficient data they influence either readmission rates or short-term mortality and there is little evidence of cost-effectiveness
        - Nevertheless, It remains good clinical practice to cover these issues before discharge with an approach that includes motivational coaching.

Discharge criteria and recommendations for follow-up

1. Full review of all clinical and laboratory data
2. Check maintenance therapy and understanding
3. Reassess inhaler technique
4. Ensure understanding of withdrawal of acute medications (steroids and/or antibiotics)
5. Assess need for continuing any oxygen therapy
6. Provide management plan for comorbidities and follow-up
7. Ensure follow-up arrangements: early follow-up < 4 weeks, and late follow-up < 12 weeks as indicated
8. All clinical or investigational abnormalities have been identified

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