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Chronic Obstructive Pulmonary Disease: Insights into Pathophysiology and Treatment

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition characterized by persistent airflow obstruction, chronic inflammation, and episodes

of acute exacerbations. Common clinical findings include dyspnea, wheezing, cough, increased sputum production, and reduced lung function. Risk factors encompass smoking, air pollution exposure, genetic factors, and impaired lung growth during childhood. Diagnosis involves patient history, physical examination, pulmonary function tests, and imaging studies. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) classifies COPD severity into four stages based on airflow limitation. Management of COPD exacerbations requires a personalized, multifaceted approach tailored to the patient's clinical characteristics and comorbidities. Pharmacological treatments include bronchodilators (beta-2 agonists and antimuscarinics), corticosteroids, and antibiotics. Non-invasive and invasive ventilation strategies are employed to optimize oxygenation and ventilation. Smoking cessation remains the most effective intervention to alter disease progression and improve survival. Oxygen therapy, pulmonary rehabilitation, immunization with pneumococcal vaccines, and appropriate discharge planning are essential components of comprehensive COPD management. In severe cases, lung volume reduction surgery and lung transplantation may be considered. Despite advancements in treatment, COPD remains a significant global health burden, necessitating ongoing research and development of innovative therapies to improve disease management and patient outcomes.

Keywords: Chronic Obstructive Pulmonary Disease, COPD

Introduction

Chronic obstructive pulmonary disease (COPD) is a largely preventable and treatable condition characterized by persistent airflow obstruction, chronic inflammation, and progressive deterioration of lung function. COPD encompasses emphysema and obstructive bronchiolitis, and patients may present with either or both conditions simultaneously. Previously, chronic bronchitis was considered a subtype of COPD but has since been replaced by obstructive bronchiolitis in classification (Erhabor et al., 2021). COPD is a progressive disease marked by episodes of acute exacerbations where respiratory symptoms worsen beyond the usual daily variability. These exacerbations have a cumulative impact on respiratory system function (Lareau et al., 2019). They are associated with hospitalizations, accelerated lung function decline, and increased mortality rates. According to the World Health Organization (WHO), COPD was the third leading cause of death globally in 2019, accounting for 3.23 million deaths [3]. By 2030, it is anticipated to become the leading cause of death worldwide [4]. Effective management of COPD exacerbations is therefore vital for improving patient quality of life and reducing disease burden. Although various guidelines and recommendations exist for managing these exacerbations, the optimal approach remains a topic of ongoing discussion. COPD exacerbation management requires a personalized and multifaceted approach tailored to the patient's clinical characteristics and associated comorbidities.

COPD predominantly affects individuals aged 40 and older, particularly smokers [5]. Diagnosis often occurs late when significant damage to the airways has already developed. Common clinical findings in COPD patients include the following:

A) Shortness of breath (dyspnea): Patients often experience breathlessness,

particularly during physical activity or exertion. During respiratory distress episodes, patients typically adopt a forward-leaning sitting posture with hands on their knees, referred to as the tripod position. This posture alleviates dyspnea by stabilizing and lifting the shoulder girdle, optimizing accessory muscle function, restoring diaphragmatic shape, reducing recruitment of specific muscles, and enhancing thoracoabdominal movement [6]. However, a 2009 study reported no significant difference in outcomes for COPD patients in the tripod position compared to sitting or supine positions [7].

B) Wheezing: A high-pitched, whistling sound during breathing caused by airway narrowing. Unforced wheezing has a likelihood ratio of 2.6 for diagnosing COPD [6].

C) Cough: A persistent, productive cough with sputum or phlegm is commonly observed in COPD.

D) Increased sputum production: Patients may produce excess mucus, complicating breathing. This increased sputum contributes to temporary respiratory infections and the progression of respiratory conditions, worsening COPD outcomes.

E) Cyanosis: Discoloration of the skin, lips, or fingernails (bluish or grayish) occurs due to low blood oxygen levels.

F) Barrel-shaped chest: A rounded, bulging chest appearance results from air trapping in the lungs. Accompanying features include dorsal kyphosis, horizontal rib orientation, prominent sternum, raised clavicles, shortened neck, and widened intercostal spaces. A barrel-shaped chest is more common in severe emphysema, although age-related changes may produce a similar deformity without lung disease.

G) Use of accessory muscles: Neck, shoulder, and chest muscles may be used to assist breathing, particularly during exertion. Despite airflow limitations, patients employ both expiratory and sternomastoid muscles, though expiratory muscles cannot significantly reduce lung volume due to airflow constraints.

H) Reduced breath sounds: Air trapping in the lungs can diminish or silence breath sounds at the mouth. In emphysema, breathing sounds at the mouth are often quiet, as the disease does not typically cause bronchial narrowing.

I) Decreased lung function: Pulmonary function tests (PFTs) often show reduced lung function, including declines in forced expiratory volume in one second (FEV1) and forced vital capacity (FVC). Studies indicate that consistent treatment during periods of remission and exacerbation can significantly slow declines in FEV1 and FVC (Cukic et al., 2013).

Not all COPD patients will exhibit these findings, and additional symptoms or signs may appear based on disease severity. Diagnosis typically involves a combination of patient history, physical examination, PFTs, and imaging studies. As per the 2023 Global Initiative for Chronic Obstructive Lung Disease (GOLD) report, confirmation of COPD diagnosis requires evidence of irreversible airflow limitation on spirometry, with a post-bronchodilator FEV1/FVC ratio of less than 0.7. The GOLD criteria classify obstruction severity into four stages: GOLD 1 (Mild; FEV1 ≥80% predicted), GOLD 2 (Moderate; 50% ≤ FEV1 <80% predicted), GOLD 3 (Severe; 30% ≤ FEV1 <50% predicted), and GOLD 4 (Very severe; FEV1 <30%

predicted).

COPD is often underdiagnosed, and the disease may progress undetected before clinical diagnosis. Spirometry can identify COPD before symptom onset [13]. Additional lung function assessments, such as peak expiratory flow (PEF) tests, fractional exhaled nitric oxide (FeNO) measurements, and arterial blood gas (ABG) analysis, may also be used. Imaging modalities, including chest X-rays and computed tomography (CT) scans, support diagnosis. Epidemiological studies estimate that 20–40% of COPD patients worldwide have never smoked, emphasizing the role of non-smoking-related risk factors in disease development (Agustí et al., 2020). Key risk factors for COPD include:

A) Smoking: The most significant risk factor, accounting for 85–90% of COPD cases. A 2021 study in India showed that smokers exhibited greater dyspnea, more advanced COPD, reduced post-bronchodilator FEV1, and more emphysematous changes on imaging compared to non-smokers (Shah et al., 2021).

B) Exposure to air pollution: Outdoor air pollutants contribute to lung function decline, increased respiratory symptoms, more frequent COPD exacerbations, and higher mortality (Hansel et al., 2016).

C) Temperature: Extreme temperatures, both hot and cold, are associated with increased respiratory morbidity in COPD (Hansel et al., 2016).

D) Passive smoking: Second-hand smoke induces inflammation and reactive oxygen species production, damaging alveolar walls and potentially causing emphysema (Salvi, 2014).

E) Genetic alpha-1 antitrypsin deficiency: A hereditary condition causing liver and lung damage. Blood tests are recommended in patients with liver damage and COPD symptoms to rule out this deficiency.

F) Impaired lung growth during childhood: Early-life exposures, including tobacco exposure in utero, may impair lung development and increase COPD risk later in life.

G) Gender: Women tend to develop emphysema-related symptoms earlier and with less tobacco exposure than men, potentially contributing to disease progression.

H) Non-adherence to treatment: Poor compliance with medications, oxygen therapy, or pulmonary rehabilitation increases exacerbation risk.

I) Respiratory infections: Viral and bacterial infections exacerbate COPD symptoms through increased inflammation.

Despite ongoing research, significant advancements in disease-modifying therapies for COPD are limited. Smoking cessation remains the only intervention proven to alter disease progression and improve survival.

Pharmacological Treatments

The primary aim of pharmacological management in COPD is to enhance exercise

capacity, alleviate symptoms, improve overall health status, and reduce the frequency and severity of exacerbations. In a hospital setting, the key pharmacological treatments for acute exacerbations of COPD include bronchodilators, systemic corticosteroids, and antibiotics.

Bronchodilators

Bronchodilators are fundamental in the treatment of COPD, regardless of disease severity (Dixit et al., 2015). This class of drugs comprises beta-2 agonists and antimuscarinics.

Beta-2 Agonists

Beta-2 agonists help mitigate COPD symptoms and enhance FEV1 by activating beta-2 adrenergic receptors. This activation relaxes airway smooth muscles, increases cyclic adenosine monophosphate (cAMP), and counteracts bronchoconstriction. These drugs are categorized into short-acting beta-2 agonists (SABAs) and long-acting beta-2 agonists (LABAs). SABAs include medications such as salbutamol (albuterol), levalbuterol, terbutaline, and fenoterol. LABAs, such as formoterol and salmeterol, reduce dyspnea severity, decrease exacerbation rates, and minimize hospitalizations. Drugs like indacaterol, olodaterol, and vilanterol have a longer duration of action (24 hours) and require once-daily administration. However, these medications do not impact mortality or the progression of lung function decline. Despite their benefits, beta-2 agonists may cause adverse effects, including sinus tachycardia, palpitations, somatic tremors, fluctuations in blood pressure, hypokalemia, and increased oxygen consumption (Celli et al., 2004).

Antimuscarinics

Antimuscarinics induce bronchodilation by inhibiting acetylcholine's action on M3 muscarinic receptors in airway smooth muscle (Melani, 2015). Short-acting antimuscarinics (SAMAs), such as ipratropium and oxitropium, can also inhibit M2 muscarinic receptors, contributing to vagally induced bronchoconstriction. Long-acting muscarinic antagonists (LAMAs) like tiotropium, glycopyrronium bromide, aclidinium, and umeclidinium prolong bronchodilator effects through sustained binding to M3 receptors and rapid dissociation from M2 receptors. These drugs are associated with fewer side effects, such as dry mouth, urinary symptoms, and a bitter taste. For initial COPD exacerbation management, SABAs, with or without SAMAs, are highly recommended, although evidence from randomized controlled trials is limited. According to the GOLD 2023 report, the role of LABAs, with or without LAMAs, in acute exacerbations remains unclear. However, initiating these drugs during exacerbations or before hospital discharge is recommended. Combination LABA and LAMA therapies are preferred for moderate-to-severe exacerbations or hospitalized patients. A Cochrane review and network meta-analysis identified LABA and LAMA combination therapy as the most effective in reducing COPD exacerbations.

Beta Blockers

Beta blockers, which counteract beta-receptor activation by beta agonists, are classified into cardioselective and non-selective subtypes. Non-selective beta

blockers, such as propranolol and carvedilol, act on both beta-1 and beta-2 receptors, while cardioselective beta-1 blockers, such as atenolol, bisoprolol, and metoprolol, exhibit a higher affinity for beta-1 receptors, making them less likely to induce bronchoconstriction (Li & Mao, 2020). Although beta-1 blockers are often avoided in respiratory diseases, evidence suggests they do not impair the efficacy of beta agonists or exacerbate COPD symptoms. Observational studies demonstrate that beta blockers reduce hospital admissions, mortality rates, emergency room visits, and exacerbations in COPD patients, regardless of the presence of cardiovascular disease (CVD). Despite these benefits, the GOLD 2023 report recommends cardioselective beta-1 blockers only for COPD patients with coexisting CVD.

Ventilation: Non-invasive and Invasive

Ventilation aims to optimize oxygen delivery and carbon dioxide elimination. It is crucial in preventing cardiorespiratory deterioration, which may manifest as increased respiratory rate, asynchronous breathing patterns, altered mental status, persistent hypoxemia, hypercapnia, respiratory acidosis, or circulatory instability (Popat & Jones, 2016). Modern ventilators regulate inspiration and expiration using adjustable parameters known as triggers, targets, and termination.

1. **Trigger:** Determines whether the ventilator delivers a breath based on a set rate (ventilator-initiated/mandatory breaths) or patient effort (patient-initiated/spontaneous breaths).
2. **Target:** Specifies airflow into the lungs, either at a fixed rate (volume control) or pressure (pressure control; pressure support; bi-level).
3. **Termination:** Indicates the transition from inspiration to expiration through signals based on volume, time, or flow criteria.

Non-invasive Ventilation (NIV)

NIV provides respiratory support without requiring tracheal intubation, thus avoiding complications such as sedation, hemodynamic compromise, delirium, and hospital-acquired infections. The American Thoracic Society (ATS) 2020 guidelines recommend noninvasive positive pressure ventilation (NPPV) in specific acute respiratory failure scenarios, including:

- Use of bilevel positive airway pressure (BiPAP) for acute or chronic respiratory acidosis ($pH \leq 7.35$) due to COPD exacerbations.
- BiPAP for stable patients to avoid invasive ventilation.
- BiPAP or continuous positive airway pressure (CPAP) for cardiogenic pulmonary edema.

Conditional recommendations include early NIV for immunocompromised patients with acute respiratory failure, postoperative respiratory failure, dyspnea in terminal conditions (e.g., cancer), chest trauma, and high-risk post-extubation patients.

Invasive Ventilation

Invasive ventilation involves tracheal access, typically via an endotracheal tube. Despite its associated risks, including infection and the need for sedation, its indications are stringent and essential for specific life-threatening conditions.

Different Modes of Ventilation

The selection of a mechanical ventilation mode should prioritize safety, which is achieved by optimizing ventilation-perfusion matching efficiency and the pressure-volume mechanics of the lungs (Mireles-Cabodevila et al., 2013). In intensive care units (ICUs), the assist-control (AC) mode is one of the most utilized methods of mechanical ventilation. A key feature of the AC mode is volume cycling, meaning a predetermined volume is consistently delivered. Lung compliance significantly influences the pressure generated; for instance, high compliance generates low plateau pressures, whereas low compliance (stiff lungs) results in high pressures, as seen in conditions such as acute respiratory distress syndrome (ARDS), pulmonary edema, fibrosis, and pneumonia. This understanding helps mitigate risks like barotrauma through appropriate adjustments.

Benefits of the AC Mode:

- The capacity to trigger breaths as required enhances patient comfort.
- Respiratory imbalances such as alkalosis and acidosis can be corrected by adjusting CO_2 levels.
- This mode reduces the work of breathing for the patient.

Drawbacks of the AC Mode:

- Barotrauma is a notable concern, especially in stiff lungs, given the volume-cycled nature of this system, but monitoring plateau pressures can help avoid it.
- Breath stacking, leading to auto-positive end-expiratory pressure (PEEP), may occur if insufficient exhalation time is provided, as in tachypnea cases. Air accumulation in the lungs increases intrathoracic and plateau pressures, potentially causing hypotension. This issue is managed by removing the patient from the ventilator to allow proper exhalation and readjusting settings.
- Voluntary breath control may lead to respiratory alkalosis due to hyperventilation, which can be resolved with adequate sedation.

Advancements in ventilator technology have introduced new modes to address some AC mode limitations:

- **Neurally Adjusted Ventilator Assist (NAVA):** This mode uses sensors to match the timing and intensity of the ventilator to diaphragmatic activity, minimizing barotrauma risk (Saddy et al., 2014).
- **Adaptive Support Ventilation (ASV):** It achieves a target minute ventilation by automatically adjusting inspiratory pressure and respiratory rate, reducing

patient effort (Kirakli et al., 2015).

- **Airway Pressure Release Ventilation (APRV):** In this pressure-cycled mode, air is delivered at a fixed pressure for a set time, followed by a brief deflation period to prevent alveolar damage. APRV is especially useful when AC mode is contraindicated due to elevated plateau pressures and poor oxygenation (González et al., 2010).

Clinical Outcomes

A prospective randomized study conducted in the pulmonology ICU of a civil hospital in Jamshoro, Pakistan, included COPD patients admitted with acute respiratory failure between January and December 2018. Patients exhibiting hypercapnic (partial pressure of arterial carbon dioxide ($PaCO_2$) > 50 mmHg, pH < 7.30) and hypoxemic (partial pressure of oxygen (PaO_2) < 60 mmHg) respiratory failure were included. Decisions regarding non-invasive positive pressure ventilation (NIPPV) or invasive positive pressure ventilation (IPPV) were based on biochemical abnormalities and clinical presentations, as determined by treating pulmonologists and critical care specialists.

Devi et al. evaluated several outcomes, including ventilation duration, ICU stay length, overall hospital stays, ICU mortality, post-ICU mortality, and NIPPV failure necessitating IPPV initiation.

In the NIPPV group, no statistically significant reduction in $PaCO_2$ was observed after 24 hours of ventilation ($p=0.28$), whereas the reduction in the IPPV group was significant ($p=0.08$). Conversely, PaO_2 significantly improved in the NIPPV group ($p=0.009$) but not in the IPPV group ($p=0.23$). NIPPV significantly improved respiratory rate ($p=0.008$), unlike IPPV. Notable and significant improvements in heart rate were observed in the NIPPV group ($p<0.0001$). Both groups experienced reduced systolic blood pressure, while diastolic blood pressure reduction occurred only in the NIPPV group.

The NIPPV group demonstrated shorter ventilation durations, ICU stays, and overall hospital stays. ICU mortality in the NIPPV group was 13.3%, compared to 40% in the IPPV group ($p=0.01$). Post-ICU mortality rates were 6.7% for NIPPV versus 16% for IPPV, with no statistically significant difference. No deaths occurred within the first 24 hours of hospitalization. NIPPV failure necessitated IPPV for 20% of patients ($n=6$), three of whom died in the ICU, while the remaining three recovered and were discharged. No ICU readmissions or re-ventilation needs were reported post-extubation (Devi et al., 2018).

NIPPV has demonstrated significant patient outcome improvements even in ARF secondary to non-COPD causes. A meta-analysis of 13 observational studies on immunocompromised ICU patients with ARF revealed NIPPV significantly reduced in-hospital mortality (odds ratio (OR): 0.43, $p=0.007$) and 30-day mortality (OR: 0.34). Another meta-analysis involving over 2000 patients with do-not-intubate (DNI) orders indicated a combined survival rate of 56% upon hospital discharge and 32%

one year later. In COPD patients with DNI orders, NIPPV yielded a 68% hospital survival rate (Wilson et al., 2018).

Smoking Cessation

COPD is characterized by increased airflow resistance in the small conducting airways, heightened lung compliance, air trapping causing irreversible obstruction, and a hyperinflammatory response in the small airways. This hyperinflammatory response is an adaptive mechanism to long-term exposure to harmful particles and gases, such as cigarette smoke. It leads to hypersecretion (chronic bronchitis), lung tissue destruction (emphysema), and defense mechanism impairment, resulting in further inflammation and fibrosis (bronchiolitis).

Inflammation in the small airways is present in all smokers and becomes amplified in those with COPD, causing structural changes that persist even after smoking cessation. The pathological processes of COPD, including inflammation, the protease-antiprotease imbalance, and oxidative stress, are interlinked with cigarette smoke exposure [86]. Smoking is the primary exacerbating factor for COPD progression, making cessation vital. Quitting smoking effectively limits disease progression, leading to benefits such as reduced dyspnea, fewer exacerbations and hospitalizations, slower lung function decline, and lower mortality.

Strategies for Smoking Cessation

Smoking cessation strategies can be pharmacological or non-pharmacological. The initial step involves identifying whether the patient is an active or passive smoker. A thorough medical assessment followed by consistent follow-up is crucial to achieving cessation goals. The "brief advice" strategy encourages patients to quit smoking through a single intervention, resulting in a higher frequency of quit attempts than no intervention. Evidence indicates that behavioral support yields better outcomes than medication alone (García-Gómez et al., 2019).

The **"5 A's Approach"** for providing brief advice includes:

1. **Ask:** Inquire about smoking status and tobacco use.
2. **Assess:** Determine the patient's willingness to quit and evaluate nicotine dependence.
3. **Advise:** Provide strong, clear guidance to quit smoking.
4. **Assist:** Develop a cessation plan, discuss pharmacological options for nicotine-dependent patients, motivate, and provide necessary support.
5. **Arrange:** Schedule follow-ups around the quit date, monitor progress, and address issues.

Studies show that light smokers (smoking fewer than 10 cigarettes daily) may not require pharmacotherapy, but many still fail to quit without additional support. Non-pharmacological approaches include one-on-one counseling, individual or group cognitive-behavioral therapy (CBT), telephone counseling, and mobile apps designed for smoking cessation. Evidence suggests individual behavioral interventions significantly aid cessation efforts.

Pharmacological Approaches for Smoking Cessation

- **Varenicline:** The most effective pharmacological option for smoking cessation. However, adverse effects often lead to discontinuation and failure. Unlike nicotine replacement therapy (NRT), varenicline is not associated with increased depression risk and is suitable for COPD patients.
- **Nicotine Replacement Therapy (NRT):** Reduces withdrawal symptoms. Studies reveal that combining rapid-delivery forms (e.g., gum, lozenges, nasal sprays) with slow-release patches is more effective than using a single form.
- **Bupropion:** The first FDA-approved non-nicotinic drug for smoking cessation. It achieves higher long-term abstinence rates and is a first-line treatment. Compared to varenicline and NRT, bupropion has slightly lower cessation rates.
- **Cytisine:** A plant-derived alkaloid acting as a selective partial agonist at nicotinic acetylcholine receptors, similar to varenicline. While cytisine shows similar cessation rates, it has fewer adverse effects, such as abnormal dreams and nausea, compared to varenicline.
- **Vaccines:** Aim to induce antibodies that bind nicotine and reduce its effects. They are intended for individuals who have failed other cessation methods. Nicotine vaccine development is ongoing, with modifications to enhance antibody affinity under investigation.
- **Electronic Cigarettes:** E-cigarettes containing nicotine increase cessation rates compared to placebos or nicotine patches. However, concerns about additional chemicals, potential lung irritants, unknown long-term effects, and lack of FDA approval limit their use as a primary treatment (Sealock & Sharma, 2024).
- **Combined Treatments:** Combining psychological interventions with pharmacological treatments enhances cessation success. Trials demonstrate that gradual cessation produces better outcomes than abrupt quitting. Moreover, adherence to cessation treatment significantly improves efficacy.

Oxygen Prescription

Oxygen therapy systems for COPD are classified into low-flow and high-flow devices.

Low-Flow Devices

Low-flow oxygen delivery methods include:

1. **Nasal Cannula**: A traditional method utilizing nasal cannula prongs available in various sizes and styles. The device employs an elastic band designed to fit over the patient's ears for stability.

2. **Simple Mask**: This method is used when delivering a higher fraction of inspired oxygen (FiO2) is necessary. The mask fits snugly over the bridge of the nose and is secured by an elastic band around the head.
3. **Non-Rebreather Mask**: This device is similar to the simple mask but includes a reservoir bag attached to the mask via a valve.
4. **Venturi Mask**: This mask enables precise control over the delivery of a predetermined FiO2.

Modern oxygen therapy often incorporates noninvasive ventilation (NIV) systems such as CPAP and BPAP. Continuous Positive Airway Pressure (CPAP) therapy delivers a continuous positive end-expiratory pressure (PEEP) during both inspiration and expiration, increasing functional residual capacity (FRC). On the other hand, Bilevel Positive Airway Pressure (BPAP) therapy uses a pressure-cycling mode for NIV delivery.

High-Flow Devices

High-flow oxygen devices include:

1. **Optiflow™ (Fisher & Paykel Healthcare)**: This system mixes 100% oxygen with room air to generate the required FiO2 while delivering humidified gas at high flow rates. It has demonstrated a reduced risk of intubation in COPD patients experiencing acute exacerbations (AECOPD).
2. **Airvo™ 2 (Fisher & Paykel Healthcare)**: This device includes a humidifier with an integrated flow generator, delivering warmed and humidified gases to spontaneously breathing patients. It enhances mucociliary clearance of secretions. Notably, high-flow systems are non-inferior to NIV in reducing PaCO2 within two hours of treatment and exhibit good tolerance in AECOPD patients with sputum stasis.

Immunization with the Pneumococcal Vaccine

Among the bacterial and viral causes of AECOPD, *Streptococcus pneumoniae* is significant, necessitating pneumococcal vaccination. Vaccines such as pneumococcal polysaccharide vaccine 23 (PPSV23) and pneumococcal conjugate vaccine 13 (PCV13) are recommended for COPD patients as prophylactic measures. The capsular polysaccharide, a virulence factor of pneumococci, serves as the basis for vaccine serotyping and formulation (Shoji et al., 2018).

Initially, the 7-valent pneumococcal conjugate vaccine (PCV7) was used in children, later replaced by PCV13 in 2010, which reduced invasive pneumococcal infections in both children and adults. PCV13 was incorporated into the vaccination schedule for children under five years in 2017 and is recommended for high-risk adults with a PPSV23 booster two months later. Generally, PPSV23 is recommended for adults.

For COPD patients, pneumococcal vaccine efficacy is higher in those with severe airflow obstructions and individuals under 65 years. Studies comparing PCV13 and PPSV23 demonstrate that while both provide protection in the first 1–2 years post-vaccination, PCV13 ensures higher protection over five years. PPSV23, in contrast,

shows a greater risk of complications after two years (Ignatova et al., 2021). Current guidelines recommend the sequential administration of PCV13 and PPSV23 for adults over 65 years and high-risk individuals over 19 years, such as those with immunocompromised conditions, cerebrospinal fluid leaks, or cochlear implants.

Hospital Discharge

The discharge plan following a COPD exacerbation should be tailored based on the severity of the exacerbation and the patient's GOLD classification. Components of this plan include optimizing bronchodilation, managing comorbidities, administering pneumococcal vaccination, encouraging smoking cessation, and initiating pulmonary rehabilitation.

Inhalers Prescribed at Discharge

Inhaled bronchodilators, vital for symptom management, are prescribed to prevent or reduce symptoms. These include:

- Single therapy (long-acting beta-agonist [LABA] or long-acting muscarinic antagonist [LAMA])
- Dual therapy (LABA/LAMA or LABA/inhaled corticosteroids [ICS])
- Triple therapy (LABA/LAMA/ICS).

Patients with moderate to severe exacerbations are typically discharged on dual or triple therapy. A combination of ICS and LABA is more effective than monotherapy in reducing exacerbation rates, improving health status, and enhancing lung function. For severe cases with frequent exacerbations (≥2/year) and eosinophil counts ≥300 cells/μL, triple therapy is recommended, as it reduces exacerbation frequency and severity. However, ICS must be used cautiously due to potential adverse effects such as pneumonia, cataracts, oropharyngeal candidiasis, and osteoporosis risk.

Pulmonary Rehabilitation

Pulmonary rehabilitation is a critical aspect of COPD management alongside pharmacological interventions. Rehabilitation programs, delivered by multidisciplinary teams, encompass exercise training, education, nutritional guidance, and psychosocial support. This approach significantly enhances exercise tolerance, reduces dyspnea, and improves health status across all COPD severity levels, with the strongest evidence in moderate to severe cases (Sahin et al., 2016).

Post-exacerbation rehabilitation notably reduces hospital readmissions and improves mortality rates when initiated during hospitalization or within four weeks of discharge. Large cohort studies support these findings, demonstrating lower mortality rates among COPD patients undergoing rehabilitation within 90 days of discharge (Seymour et al., 2010).

Oxygen Therapy Acute hypoxic and hypercapnic respiratory failure due to exacerbated COPD often results from worsened ventilation-perfusion mismatch. The

target oxygen saturation during exacerbations is 88%-92%, or an arterial oxygen pressure (PaO2) of 60–70 mmHg, to mitigate the risk of hypercapnia. Studies comparing oxygen saturation targets found a lower mortality risk with a target of 88%-92% than with liberal oxygen supplementation.

Devices used to deliver oxygen in these scenarios include:

- **Nasal Cannula**: Flow rates up to 6 L/min with an FiO2 of 40%.
- **Venturi Mask**: FiO2 values of 24%-60%, suitable for hypercapnic respiratory failure.
- **Simple Face Mask**: Provides FiO2 up to 55% with 6–10 L/min flow rates.
- **Non-Rebreathing Mask**: Offers up to 90% FiO2, though rarely needed in COPD exacerbations.
- **High-Flow Nasal Cannula (HFNC)**: Delivers adjustable FiO2 at flow rates up to 60 L/min, though its role in COPD exacerbation requires further research.

Before discharge, patients should be assessed for home oxygen requirements, often determined by resting oxygen saturation or a six-minute walk test. Long-term oxygen therapy (LTOT), defined as oxygen use for ≥15 hours/day, is indicated for chronic severe hypoxemia (oxygen saturation <88%, PaO2 <55 mmHg, or PaO2 56%-59% with complications such as cor pulmonale or hematocrit >55%).

LTOT should only be prescribed when hypoxia is chronic and persistent, and the patient is clinically stable on COPD-specific therapies. Trials such as the Nocturnal Oxygen Therapy Trial (NOTT) and the Medical Research Council (MRC) trial confirm that LTOT improves survival in severe chronic hypoxemia due to COPD. Conversely, studies on nocturnal oxygen therapy (NOT) and long-term oxygen therapy for moderate hypoxemia found no survival benefit.

Patients prescribed long-term oxygen therapy (LTOT) should be reassessed after three months to determine the continued need for LTOT and subsequently monitored at intervals of six to twelve months (Suntharalingam et al., 2017). Ambulatory oxygen therapy, defined as oxygen supplementation during physical activities or exercise for individuals experiencing exertional hypoxemia, is recommended by the American Thoracic Society (ATS) for patients with significant exertional hypoxemia. However, the British Thoracic Society (BTS) does not support the use of ambulatory oxygen therapy solely for exertional hypoxemia but suggests it be prescribed to individuals eligible for LTOT if they are ambulatory outdoors.

Extracorporeal Membrane Oxygenation

Extracorporeal life support is utilized for temporary management in cases of respiratory failure and/or cardiac failure, particularly when standard treatments have proven ineffective (Pagani et al., 2001). One of the primary extracorporeal support systems is extracorporeal membrane oxygenation (ECMO). In cases of respiratory failure where cardiac function remains intact, venovenous ECMO is the preferred configuration. In contrast, venoarterial ECMO (VA-ECMO) is employed in instances

of cardiac failure, irrespective of lung function status. The ECMO circuit generally includes a drainage cannula for venous blood removal, which is subsequently pumped to the oxygenator. The oxygenated blood is then returned to the patient via an artery (venoarterial ECMO) or vein (venovenous ECMO). The circuit is equipped with pressure and flow sensors, medication and fluid infusion access points, and laboratory sampling ports for continuous monitoring.

Lung Volume Reduction Surgery (LVRS)

Lung volume reduction surgery (LVRS) is a potential treatment option for patients with severe emphysema or chronic obstructive pulmonary disease (COPD). The National Emphysema Treatment Trial (NETT), a multicenter randomized study conducted in 2003, established the role of LVRS in improving survival rates and quality of life for selected patients. Despite its success, further investigations are ongoing to assess long-term outcomes, cost-effectiveness, its potential as a precursor to lung transplantation, and the relative efficacy of unilateral versus bilateral procedures.

Several bronchoscopic lung reduction methods are available, including foam sealants, metallic coils, airway bypass stents, endobronchial valves, and vapor thermal ablation. Among these, coils have shown particular utility for patients with severe emphysema and hyperinflation. Endobronchial valves, such as the Zephyr valve (Pulmonx) and the Spiration valve (Spiration/Olympus), prevent air from re-entering the affected emphysematous regions, leading to atelectasis and functional lung volume reduction. The Endobronchial Valve for Emphysema Palliation (VENT) trial reported modest improvements in FEV1, dyspnea severity, exercise capacity, and quality of life. However, compared to standard care, this intervention was linked to a higher incidence of complications like pneumonia and pneumothorax.

Lung Transplantation

For patients with severe and advanced lung disease who have a limited life expectancy, lung transplantation remains an option. Double lung transplantation is commonly performed for severe COPD. The International Society for Heart and Lung Transplantation (ISHLT) has established referral criteria for COPD patients, which include FEV1 $\leq$ 30% despite optimized medical and non-pharmacological therapy (e.g., bronchodilators, smoking cessation, oxygen therapy, and pulmonary rehabilitation) and a BMI, Obstruction, Dyspnea, and Exercise Capacity (BODE) index >5. The BODE index also serves as a predictor of mortality in COPD patients.

Although COPD patients may not experience the same survival benefits as individuals undergoing transplantation for other conditions like idiopathic pulmonary fibrosis, cystic fibrosis, or primary pulmonary hypertension, they benefit significantly in terms of improved respiratory function, exercise capacity, and overall quality of life. A study by Hartman et al. included 1,471 patients, predominantly female (63%), with a mean age of 61 years, a 40-pack-year smoking history, severe FEV1 impairment (30%), significant hyperinflation with residual volume (221% predicted), an

emphysema destruction score of 36.8% (−950 Hounsfield Units), and a total St. George's Respiratory Questionnaire (SGRQ) score of 59 units.

Conclusion

Chronic Obstructive Pulmonary Disease (COPD) represents a significant global health challenge, characterized by persistent airflow obstruction and exacerbations that severely impact patients' quality of life. This paper has explored the multifaceted nature of COPD, including its pathophysiology, risk factors, diagnostic criteria, and management strategies. The importance of tailored treatment approaches that consider individual patient characteristics and comorbidities has been emphasized, particularly in managing acute exacerbations. Despite advancements in pharmacological treatments and non-invasive ventilation techniques, challenges remain in achieving optimal outcomes for patients with COPD. Continuous research and development of innovative therapies are crucial to improve disease management and patient prognosis.

In conclusion, addressing the burden of COPD requires a comprehensive understanding of its complexities and a commitment to personalized care strategies. Future efforts should focus on enhancing early diagnosis, promoting smoking cessation, and developing effective interventions to mitigate exacerbations and improve overall lung health.

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