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Dispelling Myths and Misconceptions about Chronic Obstructive Pulmonary Disease

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease is one of the major causes of disability and mortality in the world. Despite better efforts to understand this disease, there are still multiple misconceptions regarding the evaluation and management of these complex patients.

Purpose: The purpose of this review article is to utilize four hypothetical patient case presentations to dispel common myths regarding the evaluation and management of patients with chronic obstructive pulmonary disease.

Hypothetical Case Presentations: Natasha, Kevin, Joe and Mary are hypothetical patients with chronic obstructive pulmonary disease, whose cases were developed based on clinical experiences and a literature review in order to discredit common myths and misconceptions among clinicians and patients.

Common Myths and Misconceptions: Four common myths and misconceptions about patients with chronic obstructive pulmonary disease include: myth #1 symptoms of dyspnea are always reported, myth #2 prolonged cough following an upper respiratory infection is trivial, myth #3 therapy with inhaled corticosteroid plus a long-acting beta 2 agonist is ideal for all newly diagnosed patients, and myth #4 all patients with chronic obstructive pulmonary disease have exacerbations without serious consequences. Throughout this article, we will apply the 2024 Global initiative for chronic Obstructive Lung Disease recommendations to these hypothetical patients to debunk each of these myths and misconceptions.

Conclusions and Clinical Implications: Throughout this article, we have applied information from the literature and 2024 Global initiative for chronic Obstructive Lung Disease report to dispel common myths and misconceptions. The reality is that symptoms of chronic obstructive pulmonary disease are variable and not all patients report dyspnea. In addition, initial therapy should include dual long-acting bronchodilator therapy, but inhaled corticosteroids may be added in specific situations, such as patients with documented eosinophilia. Finally, acute exacerbations of this disease often have serious consequences and should be methodically prevented and aggressively treated.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a chronic lung disease that is one of the major causes of mortality and disability worldwide. In 2020, it was considered the 6th leading cause of mortality in the world. Chronic obstructive pulmonary disease can present as variable respiratory symptoms with or without exacerbation. Despite extensive studies and efforts to better understand this disease, there are still many myths and misconceptions about COPD among clinicians and patients. In this review article, we created hypothetical case presentations based on our literature review and clinical experiences in order to make key points about each of the four myths listed below. We utilize these cases to address these common misconceptions by summarizing and applying the Global Initiative for Obstructive Lung Disease (GOLD) recommendations to each hypothetical case.

Myths and Misconceptions about Chronic Obstructive Pulmonary Disease:

1. Patients with chronic obstructive pulmonary disease (COPD) consistently report some shortness of breath. NOT True!!!
2. A prolonged, "lingering" cough following an upper respiratory infection is "no big deal". False!!!
3. Therapy with an inhaled corticosteroid/ long-acting beta-2 agonists (ICS/LABA) combination agent is the best initial therapy for a patient with newly diagnosed symptomatic COPD. False!!!
4. Acute exacerbations of COPD are inevitable and without serious consequences. Absolutely NOT True!!!

Definition of Chronic Obstructive Pulmonary Disease:

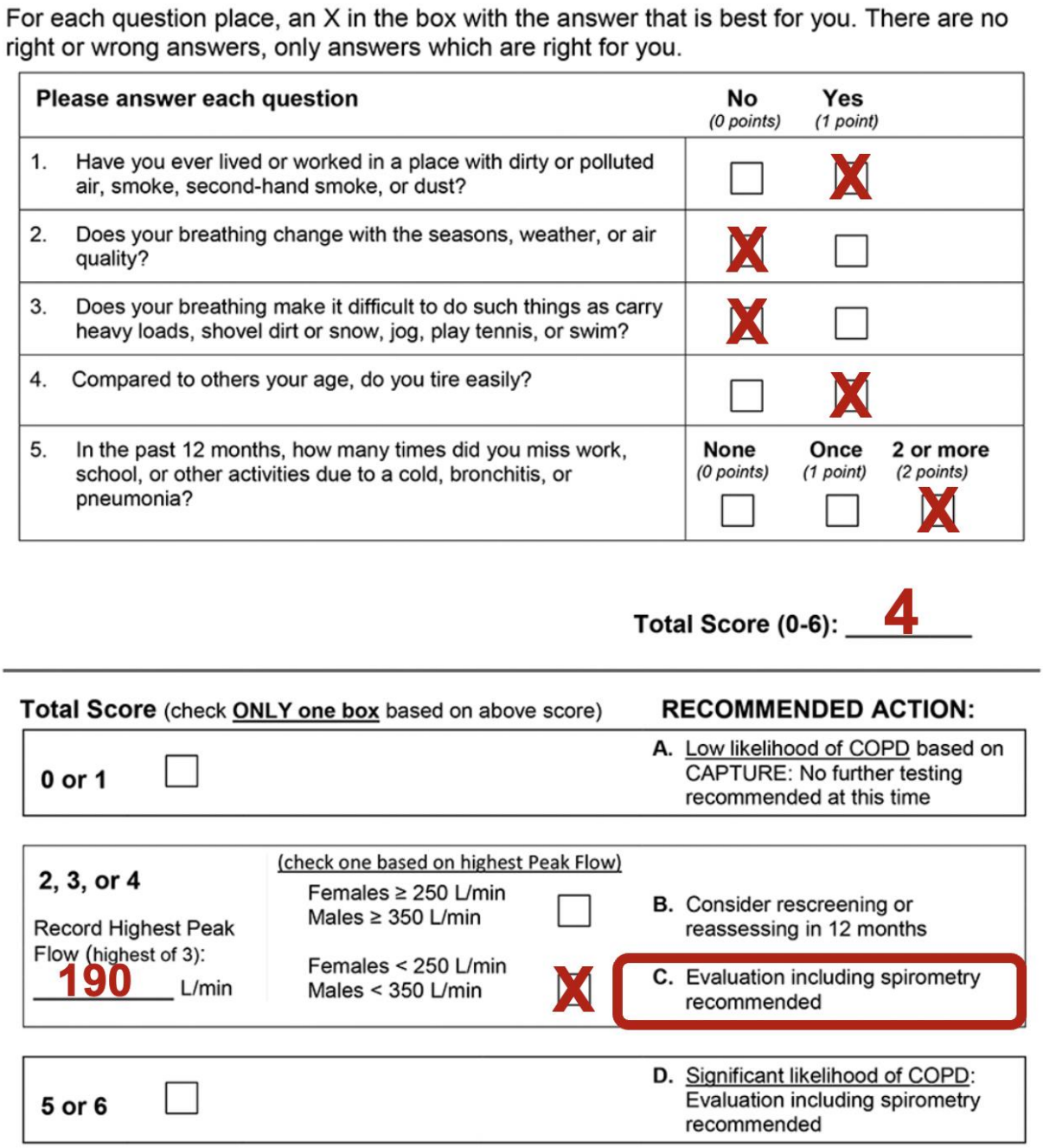
Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition, usually characterized by chronic respiratory symptoms, with or without exacerbations, as well as structural lung abnormalities and progressive, airflow obstruction[1,2,3]. The chronic respiratory symptoms may include dyspnea and/or cough and/or reduced activity levels. The cough may be productive or nonproductive. Structural lung abnormalities may affect the airways in the form of bronchitis or bronchiolitis and/or the alveoli in the form of emphysema.

Let's review a hypothetical clinical case to highlight typical versus subtle symptoms of COPD, as well as clinical clues, features, and studies to confirm the diagnosis of COPD.

Hypothetical Case #1: Natasha is a 56-year-old woman without any previous medical history who presents with progressive fatigue, particularly when shopping and cleaning her home. This fatigue has progressively worsened over the last 8-10 months. She reports a chronic cough with "a bit" of white sputum on most days for the last 3-4 years, but she denies shortness of breath. She was treated with antibiotics for acute bronchitis twice over the last year following a viral upper respiratory infection in which the cough "lingered" for over 8 weeks and her sputum became purulent (green). She continues to smoke cigarettes daily (5-6 cigarettes/day since age 14 years old). Her physical examination is unremarkable, with clear lungs, regular heart rhythm, and no lower extremity edema. Her **C**OPD **A**ssessment in **P**rimary **C**are **T**o identify **U**ndiagnosed **R**espiratory disease and Exacerbation risk (**CAPTURE**)[4] score is 4 (Figure 1.), her peak expiratory flow rate is 190 L/min; therefore, further evaluation with spirometry is recommended.

Misconception 1: Patients with COPD consistently report shortness of breath. **NOT TRUE!!** Natasha reduced her activity level to avoid dyspnea, which commonly occurs in people whose dyspnea occurs insidiously. She likely reduced her activities subconsciously to avoid the uncomfortable sensation of shortness of breath. She may also withdraw from social situations and feel isolated. The functional decline and avoidance of activities, which results in dyspnea, often occurs gradually and may be misinterpreted as feeling "tired" or "fatigued" with minimal exertion[5].

Figure 1. CAPTURE tool with scoring and clinical action recommendations[4].



For each question place, an X in the box with the answer that is best for you. There are no right or wrong answers, only answers which are right for you.

Please answer each question	No (0 points)	Yes (1 point)
1. Have you ever lived or worked in a place with dirty or polluted air, smoke, second-hand smoke, or dust?	☐	X
2. Does your breathing change with the seasons, weather, or air quality?	X	☐
3. Does your breathing make it difficult to do such things as carry heavy loads, shovel dirt or snow, jog, play tennis, or swim?	X	☐
4. Compared to others your age, do you tire easily?	☐	X
5. In the past 12 months, how many times did you miss work, school, or other activities due to a cold, bronchitis, or pneumonia?	None (0 points) ☐	Once (1 point) ☐
		2 or more (2 points) X

Total Score (0-6): 4

Total Score (check **ONLY one box** based on above score)

RECOMMENDED ACTION:

0 or 1 ☐

A. Low likelihood of COPD based on CAPTURE: No further testing recommended at this time

2, 3, or 4

Record Highest Peak Flow (highest of 3): 190 L/min

(check one based on highest Peak Flow)

Females ≥ 250 L/min
Males ≥ 350 L/min ☐

B. Consider rescreening or reassessing in 12 months

Females < 250 L/min
Males < 350 L/min X

C. Evaluation including spirometry recommended

5 or 6 ☐

D. Significant likelihood of COPD: Evaluation including spirometry recommended

Misconception 2: A prolonged, "lingering" cough following an upper respiratory infection (URI) is "no big deal". FALSE!!! These types of episodes of "acute bronchitis", which progress and "go into the chest" may actually represent acute exacerbations of COPD (ECOPD). These episodes should prompt clinicians to strongly consider a diagnosis of COPD, particularly in a person with significant exposure history (e.g., tobacco, combustible fuels, wood-burning stoves, and/or environmental pollution) whose symptoms progress to prolonged congestion and cough, which is often purulent.

Diagnosis of Chronic Obstructive Pulmonary Disease:

Patients with COPD might complain of dyspnea, chronic cough and/or many other respiratory symptoms, but physical examination is normal in the vast majority of patients. Therefore, to establish a COPD diagnosis, spirometry with a post-bronchodilator forced expiratory volume in one second (FEV_1) / forced vital capacity (FVC) ratio should be <0.70 (70%) and confirms the presence of airflow limitation that is not completely reversible[3]. In COPD, the FEV_1/FVC ratio does not

fully correct with a bronchodilator challenge with albuterol +/- ipratropium. A persistently low ratio is not specific for COPD and can be present in other diseases as well.

Hypothetical Case #2: Kevin is 58-year-old man with current tobacco use (30 pack years), who presents to his primary care clinician with dyspnea, predominantly with exertion, that developed 4 months ago. Although he reports his dyspnea does not limit his activities, he is now more aware of his breathing. He denies any other symptoms such as seasonal allergies or acid reflux symptoms. He denies any history of childhood asthma. Due to his smoking history and dyspnea, his primary care clinician ordered pre- and post-bronchodilator spirometry. This revealed a post-bronchodilator FEV_1 of 67% predicted, FVC 76% predicted, FEV_1/FVC 77% with no significant bronchodilator response.

Is this COPD? If not, what would you call it? Let's go over the next concept to determine the proper diagnosis.

Nomenclatures of Chronic Obstructive Pulmonary Disease:

As the COPD definition evolved over the years, the 2023 and 2024 Global Initiative for Obstructive Lung Disease (GOLD) report proposed various definitions to minimize terminology confusion[3].

Early COPD: This phrase was established by the GOLD committee to refer to the "biological" early stages of the disease, which represents the initial mechanisms, ultimately leading to COPD. This should be differentiated from the "clinically" early presentation, which represents the first observation of symptoms, functional limitations, and/or radiographic abnormalities noticed.

Mild COPD: The GOLD committee suggests the term "mild" only be used to characterize the degree of spirometrically-assessed airflow obstruction. Mild COPD refers to severity; however, early refers to time. Mild COPD can begin at any age and may or may not worsen over time.

Young COPD: Young COPD refers to the chronological age of the patient. The GOLD committee suggests for patients with COPD between the ages of 20-50 years to be classified as having young COPD. Family history of respiratory diseases or early life medical incidents (e.g., pre-term birth, etc.) are remarkable in most of those with young COPD.

Pre-COPD: This term describes individuals of any age experiencing respiratory symptoms and displaying detectable structural (e.g., emphysema on chest computed tomography) and/or functional abnormalities (e.g., air trapping/hyperinflation, decreased diffusion capacity of carbon monoxide, etc.), in the absence of fixed airflow limitation on spirometry. The progression of these patients towards developing COPD is uncertain and may or may not occur over time.

Preserved ratio with impaired spirometry (PRISm): As the name describes, this phrase can be used to characterize those with a post-bronchodilator FEV_1/FVC ≥ 0.7 and an FEV_1 <80% of reference following administering one or more short-acting bronchodilators. PRISm is more common among those who are currently or have previously smoked. These patients may progress to obstructive or restrictive physiology.

Kevin has PRISm and is at increased risk of complications, accelerated rates of lung function decline, and higher mortality rates relative to other current and former smokers with normal spirometry (GOLD 0)[6,7]. Individuals with PRISm often progress to a diagnosis of COPD, particularly in those who continue to smoke or have a marginal FEV_1/FVC (close to 0.70)[10]. Therefore, it is reasonable to follow Kevin regularly and be sure to implement all possible preventative strategies (e.g., vaccinations, smoking cessation support, pulmonary rehabilitation, etc.) and therapy for symptoms. More data and studies are still needed to determine the best management strategies for patients with PRISm.

Hypothetical Case #3: Joe is a 62-year-old man with moderate COPD (not on supplemental home oxygen therapy) and a history of cigarette smoking (25 pack-years), who presents to the clinic for COPD management. Joe reports that he has not improved since diagnosis and initiating treatment last year. He experienced an exacerbation, which required hospitalization and treatment for a bacterial pneumonia. His modified Medical Research Counsel dyspnea scale score[9] is 2. Joe reports consistent adherence with his combination ICS/LABA inhaler and demonstrates proper inhaler technique. He denies seasonal nasal allergies and reports acid reflux symptoms are well controlled with life-style modifications and antacid therapy. His physical examination is unremarkable. His blood tests reveal a normal white blood cell count with an eosinophil count of 50 cells/μL.

Misconception 3: Therapy with an ICS/LABA combination agent is the best initial therapy for a patient with newly diagnosed symptomatic COPD. Not True!!!

The reality is that ICS/LABA is no longer recommended as a therapeutic option by the 2024 GOLD committee[3]. Adding an ICS to the long-acting bronchodilators is only indicated in certain situations of patients with COPD (see below) and is associated with an increased risk of pneumonia[24].

Chronic Obstructive Pulmonary Disease Managements:

Pharmacological Treatments

For the initial pharmacological therapy in patients in GOLD Group A, with minimal symptoms, the GOLD committee recommends monotherapy with a long-acting bronchodilator[3]. In contrast, dual long-acting bronchodilator therapy, including a long-acting beta 2 agonist and long-acting muscarinic antagonist (LABA + LAMA), is now recommended for more symptomatic patients in Group B[22]. Dual long-acting bronchodilator therapy is also recommended as the first line of treatment for patients in Group E[23]. However, if the blood eosinophil count is ≥300 cells/μl, initiating triple inhaled therapy (LABA + LAMA + inhaled corticosteroids [ICS]) in a single inhaler is preferred[25].

Dyspnea and the occurrence of exacerbations are the treatable traits recommended by the GOLD committee to guide follow up therapy. For patients with persistent dyspnea on monotherapy, escalation to dual therapy with LABA+LAMA is recommended. LABA+ICS is no longer recommended by the GOLD committee[24]. For patients with persistent dyspnea on dual with long-acting bronchodilators therapy, the treating clinician should assess inhaler techniques and consider the type of device being used. For patients with exacerbations on monotherapy, escalation of therapy is recommended. Triple therapy (preferably in a single device) is recommended in patients with an eosinophil count ≥300 cells/μl[25]. For patients with exacerbations on triple therapy or patients on LABA+LAMA with eosinophil count <100 cells/μl, adding roflumilast and/or a macrolide should be considered. As with adding any additional medications, clinicians and patients should carefully weigh the potential risks and side effects vs. the potential benefits. Shared decision making is crucial in these situations. For symptomatic COPD patients in GOLD Groups A, B, and E with eosinophil counts at least 100 cells/μl, but <300 cells/μl, the potential risks vs. potential benefits of adding ICS to the LABA+LAMA therapy should be considered and discussed. Finally, there is absolutely no role for chronic systemic/oral corticosteroids for patients with stable, i.e., non-exacerbating, COPD[27].

Non-Pharmacological Therapy

In managing COPD, several non-pharmacological strategies should be discussed. Patients should receive education regarding COPD and its treatment options. In addition, patients should be evaluated for signs and symptoms of anxiety and depression. Smoking cessation support must be available for all who continue to smoke[15]. Vaccinations against various respiratory illnesses including influenza,

pneumococcus, COVID-19, pertussis, and respiratory syncytial virus (RSV) should be offered[14]. Herpes Zoster vaccination is encouraged, when age appropriate. Promoting an active lifestyle is essential for patients with COPD. Pulmonary Rehabilitation (PR) programs are recommended for all symptomatic patients and in addition, PR is an effective way to manage anxiety and depression in these patients those at risk for exacerbations[16]. Supplemental oxygen therapy and ventilatory support should be provided when necessary. Surgical or endoscopic lung volume reduction may be considered for patients meeting specific criteria, including severe hyperinflation unresponsive to traditional therapy. Lung transplantation is also an option for select patients with advanced COPD who are otherwise healthy. Finally, palliative care services should be offered to help optimize symptoms and facilitate end-of-life discussions for the patients and their families.

Hypothetical Case #3 (continued): Because regularly using ICS in patients with COPD is a risk factor for pneumonia, Joe is a candidate for withdrawal of ICS. This is particularly important with low blood eosinophils and a hospitalization for bacterial pneumonia. Due to his high symptom burden and the fact that he is classified as GOLD Group E, treating with a combination LABA/LAMA inhaler is the optimal choice.

Hypothetical Case #4: Mary is a 68-year-old woman with COPD, diabetes mellitus, hyperlipidemia, and hypertension who presented to the emergency department (ED) due to progressively worsening shortness of breath for the past five days. Mary mentioned that she had nasal congestion, rhinorrhea, sore throat, and low-grade fevers prior to developing dyspnea. She reported using her rescue inhaler more than five times per day due to worsening dyspnea. She also complained of increased cough productive of green sputum. When asked about medication adherence, she reported not using her maintenance inhaler regularly, because she believes COPD is "no big deal and flares are inevitable". Her physical examination upon arrival was remarkable for tachypnea, tachycardia, hypoxia, moderate respiratory distress, bilateral reduced air entry, and diffuse inspiratory and expiratory wheezes. Initial blood gas was remarkable for acute respiratory acidosis. Due to the patient's underlying diagnosis of COPD, her non-adherence to inhalers, clinical presentation, physical examination, and initial blood gas values, the ED clinician ordered nebulized bronchodilator therapy, a systemic corticosteroid, and non-invasive positive pressure ventilation (NIV) with supplemental oxygen while awaiting further diagnostic evaluation. The patient's breathing and respiratory acidosis improved significantly within the next two hours and the patient was admitted to the medical floor for monitoring and further therapy.

But what if this ED provider/team had not acted quickly and appropriately? What if they had waited for the results of the entire work up before starting treatment for a COPD exacerbation? What if they had ordered supplemental oxygen therapy without NIV?

Mary likely could have become more distressed with worsening respiratory acidosis, and hypercapnic encephalopathy, which might have progressed, necessitating admission to the intensive care unit for endotracheal intubation and mechanical ventilation. Early therapy with bronchodilators and NIV, reduces the risk of intubation, mechanical ventilation, and mortality[3,18].

Misconception 4: Acute exacerbations of COPD are inevitable and without serious consequences. Absolutely NOT True!!! As we can see from Mary's comorbidities, she has multiple risk factors for coronary artery disease. If she presented with chest pain, there would no hesitation to suspect a myocardial infarction and to act quickly to aggressively evaluate and treat her for this potential cardiac complication. We should act with the same urgency when a patient with COPD presents with acute symptoms suggesting a COPD exacerbation. These exacerbations are serious and

often have significant complications. Therefore, some refer to a COPD exacerbation as a "lung attack". COPD exacerbations are preventable with adherence to appropriate medical therapy, by remaining physically active, obtaining preventative strategies such as recommended vaccinations, and aggressively managing comorbidities. As healthcare professionals, it is our role to understand and convey to our patients the seriousness of the disease and its complications. In addition, there is significant evidence that patients with COPD exacerbations are at an increased risk for cardiovascular events and mortality[11].

Exacerbations of Chronic Obstructive Pulmonary Disease

The GOLD committee found that the previous definition of exacerbations of COPD (ECOPD) lacked specificity and was not sufficient to consistently guide therapy. Therefore in 2023, the GOLD committee introduced a new definition for ECOPD, proposed by Rome consensus, to address these limitations. The current GOLD committee defines ECOPD as an event with increased dyspnea and/or cough and sputum worsening over <14 days[3]. It may include tachypnea and/or tachycardia and is often associated with local and systemic inflammation.

Management of Exacerbations of Chronic Obstructive Pulmonary Disease

Exacerbations of Chronic Obstructive Pulmonary Disease (ECOPD) can be managed in the inpatient or outpatient setting based on the severity of the exacerbation. Therefore, as an initial step, the severity of the exacerbation should be assessed and determined to be mild, moderate, or severe. Multiple clinical variables were included in the *Rome Proposal* [2]. Such clinical variables include intensity of dyspnea using a visual analogue scale, respiratory rate, heart rate, oxygen saturation level, C-reactive protein levels, and arterial blood gases.

Pharmacological treatment includes inhaled short-acting beta-2-agonist with or without a short-acting muscarinic antagonist, administered via metered dose inhaler with a valved holding chamber or via nebulizer. The GOLD 2024 committee recommends continuing long-acting bronchodilators throughout the exacerbation.

A systemic glucocorticoid, specifically a 5-day course of 40mg of prednisone per day, improves lung function and oxygenation. In addition, this short course of oral prednisone reduces the risk of relapse and the duration of hospitalization in patients with COPD exacerbations. Longer courses of systemic corticosteroids should be avoided due to an increased risk of pneumonia and mortality[13].

Antibiotics are indicated for ECOPD patients with increased sputum volume, sputum purulence, and those requiring mechanical ventilation[21]. Recommended therapy duration is generally 5–7 days with initial empiric antibiotic therapy guided by local bacterial resistance patterns. Aminopenicillins with clavulanic acid is the usual initial choice for patients with frequent exacerbations or severe airflow obstruction. However, obtaining respiratory cultures is important in this population.

Consider adjunct therapies for fluid balance, comorbidity treatment, and nutritional monitoring. We should also emphasize smoking cessation, evaluating for acute venous thromboemboli (VTE), and implementing VTE prophylaxis during hospitalization[19].

Clinicians should titrate supplemental oxygen to achieve a target saturation of 88–92% and monitor blood gases in severe ECOPD. Venturi masks offer accurate and controlled oxygen delivery, so as to not provide too much oxygenation. High-Flow Nasal Therapy (HFNT) delivers heated and humidified air–oxygen blends and has shown benefits in some COPD patients[17]. However, the suboptimal quality of many of these studies and the heterogeneous patient populations make it difficult to determine the value of HFNT in the general COPD patient population[3]. Therefore, more trials and data are

needed to appropriately define the role of HFNT in ECOPD.

Currently, ventilatory support is recommended before HFNT in hypercapnic exacerbations. Ventilatory support in COPD exacerbations can be noninvasive positive pressure ventilation (NIV) or invasive mechanical ventilation. NIV may be initiated with a nasal or facial mask and improves outcomes, including reducing the need for invasive mechanical ventilation, length of stay, and mortality[18]. Invasive ventilation is a rescue therapy for NIV failure, influenced by event reversibility, patient characteristics (e.g., hemodynamic instability, obtunded mental status, etc.), preferences, and needs, as well as facility availability.

Conclusion

As we've discussed throughout this review article, there are many myths and misconceptions regarding COPD. Patients with COPD do not all consistently report dyspnea, but may report fatigue, social isolation, and/or reductions in activity levels. In a patient at risk for COPD, prolonged, "lingering" cough following an upper respiratory infection may actually represent an acute exacerbation of COPD. Therapy with long-acting bronchodilators, including a LABA/LAMA combination inhaler is the best initial therapy for a patient with newly diagnosed symptomatic COPD. In general, patients with COPD should not be started on an ICS unless they have elevated blood eosinophil levels, a documented history of asthma, or other characteristics suggestive of asthma. If an ICS is needed, it should only be used in patients with COPD as combination therapy with LABA/LAMA/ICS. Finally, acute exacerbations of COPD have serious consequences and should be methodically prevented and aggressively treated.

Optimal Management of Exacerbations of Chronic Obstructive Pulmonary Disease in Hospitalized Patients

Do's (Clearly Useful)	Not Harmful, May be helpful	Don'ts (Potentially Harmful)
Bronchodilators (usually nebulized or may give high-dose via MDI with VHC) SABA +/- SAMA ++Long-acting (LABA/LAMA)[29]	Oscillatory, flutter valve or vibratory airway clearance device (Aerobika, Acapella, Vibrapep, etc.)[30]	Aggressive manual chest physiotherapy (may result in rib fractures – particularly in underweight patients)[1]
Antibiotics: if sputum purulence or anyone requiring MICU care (monitor and prescribe based on local resistance patterns unless patient has risk factors or history of resistant organism, e.g., pseudomonas, MRSA, etc.)[21,31]	Smoking cessation counseling[32]	In the MICU, procalcitonin to withhold antibiotics (procalcitonin should not be used to withhold antibiotics in patients in the MICU → should give antibiotics based on clinical characteristics) procalcitonin algorithm was associated with increased mortality – multicenter RCT[12]
Systemic corticosteroids (oral route is preferred unless unable to absorb → gut edema, NPO, etc.): Prednisone 40mg x 5 days is preferred. High-dose nebulized budesonide may be an alternative in some non-critically ill patients[28]	Inhaler demonstration / education with return demonstration[1]	Benzodiazepines in patients with severe to very severe COPD or $PaCO_2$ retention (may result in excessive sedation and worsening of respiratory acidosis)[33]
Oxygen if hypoxic to maintain saturations between 88-92% (should target >95% if concern/documentation of cardiovascular disease) May use HFNT (high flow nasal therapy) if increased work of breathing or significant hypoxia[34,35]	One-time measurement of spirometry / Peak Expiratory Flow Rate (definitely not useful for serial measurements)[36]	Methylxanthines should not be used due to increase risk and side effect profiles[1]
NIV (noninvasive positive pressure ventilation) if increased work of breathing/distress +/- if acute, or	Oral expectorant +/- cough suppressant for	Nebulized N-acetylcysteine is often associated with severe bronchospasm in

acute on chronic, respiratory acidosis, +/- persistent hypoxemia despite supplemental oxygen[37,38]	symptom management[1]	patients with obstructive lung diseases and is not recommended during ECOPD[1]
Intubation and invasive mechanical ventilation if profoundly altered mental status with failure +/- inability to clear secretions +/- hemodynamic instability +/- arrhythmias or anyone who fails a trial of NIV[40]		Pulmonary rehabilitation during the acute phase of illness is associated with worse outcomes – but outpatient pulmonary rehabilitation following ECOPD hospitalization is helpful![41]
Chest imaging (PE in 10-30%) with VTE prophylaxis unless contraindicated[42]		

Abbreviation key (alphabetical):

HFNT: high flow nasal therapy; LABA: long-acting beta agonist; LAMA: long-acting muscarinic antagonist; MDI: metered dose inhaler; MICU: medicine intensive care unit; MRSA: methicillin-resistant *Staphylococcus aureus*; NIV: noninvasive positive pressure ventilation; NPO: nothing by mouth; $PaCO_2$: partial pressure of carbon dioxide; PE: pulmonary emboli; RCT: randomized controlled trial; SABA: short-acting beta agonist; SAMA: short-acting muscarinic antagonist; VHC: valved holding chamber; VTE: venous thromboemboli

Conflicts of Interest:

Dr. Oweis has no conflicts of interest to report
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JO and SGA are the guarantors of the manuscript and take responsibility for the content and data within this manuscript.

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