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Principles and Practice of Hospital Medicine

Second Edition

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CHAPTER 232

Chronic Obstructive Pulmonary Disease

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1. What conditions mimic an acute exacerbation of chronic obstructive pulmonary disease (COPD) and require different diagnostic and treatment modalities?
2. What inpatient therapeutic modalities reduce mortality or length of stay for patients with exacerbation of COPD?
4. What are the indications for noninvasive ventilation for patients with an acute exacerbation of COPD?
5. Explain the therapeutic interventions that you would consider and discuss with a patient at the time of discharge following an acute exacerbation of COPD?

INTRODUCTION

■ DEFINITION AND BACKGROUND

Chronic obstructive pulmonary disease (COPD) is a group of clinical and pathological pulmonary disorders that are preventable and treatable and are characterized by airflow limitation that is not fully reversible. The most common phenotypes of COPD are emphysema and chronic bronchitis. Emphysema is generally defined as irreversible enlargement of the airways and loss of elastic recoil. Clinically, emphysema presents with dyspnea along with clinical findings of an expanded chest, decreased breath sounds, radiographic lucency, and flattening of the diaphragms. Chronic bronchitis is defined by the finding of cough and sputum production on most days of at least 3 months per year for two consecutive years. Pathologically, the hallmarks of chronic bronchitis are large airway inflammation and the hypertrophy and hyperplasia of the mucous-secreting goblet cells. COPD is diagnosed after demonstrating airflow limitation by spirometry (at a time free of exacerbation) that is not fully reversible in patients who exhibit cough, sputum production, dyspnea or other appropriate risk factors. The severity of COPD is classified by the degree of limitation in the forced expiratory volume in 1 second (FEV_1) as well as by the frequency of exacerbations (0-1 vs $\geq$ 2 per year) and patient reported symptoms using validated questionnaires (**Tables 232-1** and **232-2**).

Hospitalists often manage patients presenting with new symptoms consistent with COPD, patients with acute exacerbations of underlying COPD, and patients whose COPD complicates the course of other medical conditions. In this chapter, we will review best practices for each of these scenarios and solutions for optimizing care of these patients as they transition out of the acute care setting.

■ RISK FACTORS

Tobacco smoking is the single most important risk factor for the development of COPD. Cigarette, pipe, and cigar smoking account for more than 90% of cases of COPD; yet, clinically important disease is only found in 10% to 20% of smokers. Clearly there are other predisposing factors because dose-dependent exposure to tobacco does not wholly determine the onset or severity of disease in COPD. Additional factors that lead to the onset (or accelerate the progression) of COPD include exposure to second-hand smoke, environmental irritants and pollutants (including biomass), occupational exposures, malnutrition, childhood pulmonary infections, HIV infection, and genetic predisposition. The role of genetics is incompletely understood, but COPD is more common in the relatives of those with COPD.

■ PATHOGENESIS

Tobacco smoke and other exposures trigger inflammatory, biochemical and anatomic changes that account for the symptoms, limitations, and complications of COPD (Figure 232-1). These airway irritants activate the airway epithelium as well as alveolar macrophages to release chemokines that attract a host of inflammatory cells into the airway including neutrophils and monocytes. Production of IL-6 and TNF-α magnify this inflammatory response. These cells, in concert with the airway epithelium produce metalloproteinases responsible for the degradation of elastin resulting in emphysema. Neutrophil elastase stimulates mucous hypersecretion

TABLE 232-1 GOLD Spirometry Criteria for Chronic Obstructive Pulmonary Disease Severity

GOLD Stage	Severity	Spirometry
I	Mild	$FEV_1/FVC < 0.7$ and FEV_1 80% predicted
II	Moderate	$FEV_1/FVC < 0.7$ and 50% FEV_1 < 80% predicted
III	Severe	$FEV_1/FVC < 0.7$ and 30% FEV_1 < 50% predicted
IV	Very severe	$FEV_1/FVC < 0.7$ and FEV_1 < 30% predicted or FEV_1 < 50% predicted with respiratory failure or signs of right heart failure

FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

TABLE 232-2 GOLD Grading Criteria for Chronic Obstructive Pulmonary Disease

Grade	Spirometry	Yearly Exacerbation Rate	Symptom Score
A	Stage 1 or 2	≤1 exacerbation not leading to a hospitalization	CAT <10 or mMRC 0-1
B	Stage 1 or 2	≤1 exacerbation not leading to a hospitalization	CAT ≥10 or mMRC ≥2
C	Stage 3 or 4	≥2 exacerbations or ≥1 exacerbation leading to hospitalization	CAT < 10 or mMRC 0-1
D	Stage 3 or 4	≥2 exacerbations or ≥1 exacerbation leading to hospitalization	CAT ≥10 or mMRC ≥2

Severity is determined by a combination of symptom scores and either number of yearly exacerbations or spirometry stage. CAT, COPD assessment test; mMRC, modified Medical Research Council questionnaire for assessing the severity of breathlessness.

while epithelial cells produce TGF-β and fibroblast growth factors causing small airway fibrosis. When taken together, these insults lead to loss of elastic recoil, airflow limitation and impaired gas exchange characteristic of COPD.

EPIDEMIOLOGY

■ PREVALENCE AND EXACERBATIONS

Estimates of the incidence of COPD in the United States and worldwide vary, but data are consistent that the disease burden is large and COPD is underdiagnosed. COPD is the third leading cause of death in the United States. An estimated 12.7 million adults carried the diagnosis of COPD in 2011. COPD was listed as the leading diagnosis in 715,000 hospital discharges in 2010 and accounted for 133,965 deaths in 2009 according to the American Lung Association.

■ COPD COMPLICATING OTHER DISEASES

There is increasing evidence that patients with COPD have high rates of morbidity and mortality caused by extrapulmonary conditions. Patients with COPD have been found to have higher rates of cardiovascular, gastrointestinal and psychiatric illnesses, among

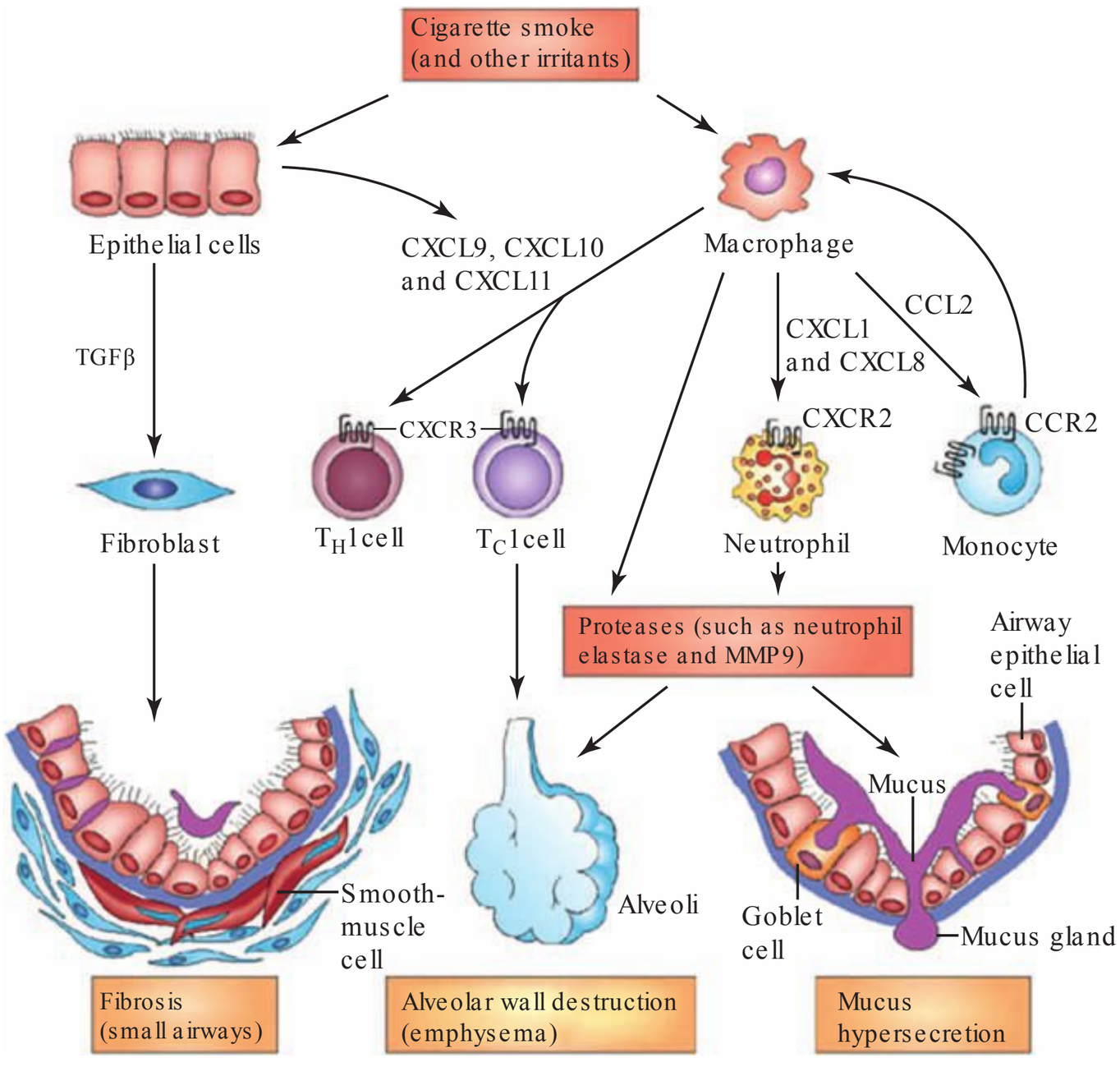

Figure 232-1 Pathogenesis of chronic obstructive pulmonary disease. (From Barnes PJ. Immunology of asthma and chronic obstructive pulmonary disease. Nat Rev Immunol. 2008;8[3]:183-192. Reprinted by permission from Macmillan Publishers Ltd.)

others. It is estimated that COPD is a primary or contributing cause of almost 10% of all admissions to the hospital. Cardiovascular morbidity and mortality might be even higher than that of lung disease and respiratory failure.

COPD EXACERBATION: DIFFERENTIAL AND EVALUATION

An acute exacerbation of COPD (AECOPD) is defined as a change in the baseline symptoms of dyspnea, cough and/or sputum color or volume that necessitates a change in management. When a patient with COPD or risk factors for COPD presents with any of these complaints, the diagnosis of AECOPD must be considered against a number of other diagnoses that may mimic an AECOPD. Once a diagnosis of AECOPD is reached, issues of causation of the exacerbation and level of severity need to be addressed. There is no single agreed-upon system to rank severity of exacerbations, but broadly categorizing among three levels has been suggested: (1) home management, (2) hospital management, and (3) respiratory failure.

■ ETIOLOGY AND DIFFERENTIAL DIAGNOSIS OF AECOPD

AECOPD has many different potential causes and the specific trigger for any one event is sometimes never elucidated. It is commonly agreed, however, that various triggers cause acute inflammation superimposed on the chronic inflammation of the underlying disease. During an AECOPD, inflammatory cells of many inflammatory pathways can be found in sputum and blood. Together, all infectious agents (bacteria, virus, and other) account for up to 80% of acute exacerbations.

The differential diagnoses to consider as triggers in patients that have underlying COPD and an acute respiratory decompensation are extensive (Table 232-3). Many of these triggers incite the inflammatory pathway at the root of an AECOPD, but they may also require other specific therapy. When a trigger is not immediately obvious from history and physical examination, there are certain other diagnoses that must be considered. An autopsy study of patients that were diagnosed as having an AECOPD and that died within 24 hours of admission showed that 37% of these deaths were due to heart failure and 21% due to pulmonary embolism. Patients admitted with otherwise unexplained exacerbations of COPD are often found to have pulmonary emboli when this diagnosis is pursued.

TABLE 232-3 Precipitants of Acute Exacerbation of Chronic Obstructive Pulmonary Disease: Differential Diagnosis

Pneumonia
Upper respiratory tract infection
Pulmonary embolism
Reactive airways disease or allergens
Congestive heart failure
Pneumothorax (trauma, rib fracture)
Arrhythmia
Myocardial infarction
Upper airway obstruction
Sleep disordered breathing
Sedating medications
Medication nonadherence
Environmental irritants (smoke, smog, workplace irritants)
Thickened bronchial secretions (eg, dehydration)

DIAGNOSTIC EVALUATION

For patients with known or suspected COPD, any complaint consistent with a COPD exacerbation warrants thorough investigation. The degree of diagnostic evaluation should be determined by the patient's subjective degree of discomfort, physical examination abnormalities, alterations in vital signs and/or diagnostic studies. Careful consideration of any conditions in the differential diagnosis of AECOPD (Table 232-3) must be undertaken.

■ KEY HISTORY AND PHYSICAL EXAMINATION

Questions regarding dyspnea, cough, sputum volume or color and rescue bronchodilator use may establish a change in symptoms from the patient's baseline. The history may also provide clues to other diagnoses or triggers (Table 232-3) for patients suspected of having an AECOPD.

AECOPD is associated with increased dyspnea, sputum purulence, wheezing, constitutional symptoms (fever, malaise, myalgias), and cough. Other past medical history and comorbid conditions can affect overall mortality and may influence patient triage for monitoring and therapy.

For patients with suspected AECOPD, but without a diagnosis of COPD, questioning regarding age, smoking status, exercise tolerance and other respiratory exposures can help increase or decrease the suspicion of COPD as the underlying disease.

The physical examination may help identify undiagnosed COPD, exclude other diagnoses in patients with known COPD, and help triage the severity of a diagnosed AECOPD. For evaluating the severity of an exacerbation, ominous physical examination findings portending higher risk and poorer outcomes include altered mentation (agitation and/or obtundation), respiratory muscle retraction, paradoxical abdominal movement, cyanosis and diaphoresis. These findings necessitate higher levels of monitoring and expedited care. Other findings that are consistent with an AECOPD include wheezing, cough, hyper-resonance to percussion and diffusely decreased breath sounds.

■ LABORATORY EVALUATION

In the initial evaluation of AECOPD, pulse oximetry O_2 saturation > 89% is evidence of acceptable oxygenation.

- An arterial blood gas should be rapidly obtained to evaluate any patient with an AECOPD considered for hospital admission, as recommended by international guidelines.

Arterial blood gases (ABGs) are able to more accurately determine the derangement of gas exchange by calculating an alveolar-arterial gradient, and may detect worse hypoxia than expected or evidence of hypercarbia. Importantly, the pH from the ABG may also provide valuable information helping direct management (eg, consideration of noninvasive ventilation). Arterial blood gas interpretation must take into account the patient's baseline status. Patients with more severe disease are likely to have elevated partial pressure of carbon dioxide (PCO_2) with a relatively preserved pH as the kidneys compensate for chronic hypoventilation. Ominous findings include elevated PCO_2 with a decreased pH (indicating an acute onset or worsening of hypoventilation), low partial pressures of oxygen, and a severely elevated PCO_2.

Guidelines recommend hematology and basic chemistry panels in the evaluation of COPD. These tests may show polycythemia associated with chronic COPD, or conversely, anemia. These basic

labs are most valuable in identifying other diagnoses to be considered or comorbid conditions that may require parallel treatment. Patients receiving theophylline therapy should have the serum level measured.

Routine collection of sputum for Gram stain and culture is not recommended in the management of COPD exacerbation. Sputum Gram stain and culture may play a role in the laboratory evaluation of patients that do not respond to initial therapy and/or have evidence of pneumonia.

■ RADIOGRAPHY AND ELECTROCARDIOGRAPHY

Chest radiography is indicated for evaluation of AECOPD. Findings on the radiograph may influence the type of care if there are findings such as pneumothorax, atelectasis, focal infiltrate or pulmonary edema. About 20% of patients thought to have an AECOPD have chest radiograph findings that influence management.

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Patients with dyspnea and other chest complaints need electrocardiography (ECG) evaluation to identify relevant findings including coronary ischemia or arrhythmias. The irregular rhythm of multifocal tachycardia (MAT) that is found frequently in COPD patients may be difficult to distinguish from atrial fibrillation without ECG. MAT responds to the treatment of the underlying lung disease and rate control whereas atrial fibrillation requires additional therapeutic approaches.

■ SPIROMETRY

Spirometry, while a core diagnostic tool for the evaluation of outpatient stable COPD, does not have a role in the evaluation of COPD exacerbations. In fact, national and international guidelines recommend against the use of spirometry in the setting of AECOPD.

TRIAGE: DETERMINING SEVERITY, INDICATIONS FOR ADMISSION, AND LEVEL OF CARE

■ DETERMINING SEVERITY OF AN EXACERBATION

No single system exists to classify patient severity of illness once they are identified as having an AECOPD. The American Thoracic Society and European Respiratory Society (ATS/ERS) guidelines define severity based upon where the exacerbation is managed (home versus inpatient versus ICU) requiring clinicians evaluating patients for AECOPD to rely on previously mentioned risk factors for mortality and clinical acumen to best triage patients.

■ CRITERIA FOR ADMISSION

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) and ATS/ERS guidelines for management of COPD provide criteria for hospitalization in AECOPD (Table 232-4). Certain findings may predict the success or failure of outpatient management. Older age, lower baseline FEV_1, hypoxemia, previous recent exacerbations and extensive comorbidities can increase risk of mortality or relapse exacerbation.

■ CRITERIA FOR INTENSIVE CARE UNIT ADMISSION

The best location to manage any patient with an AECOPD will vary based on individual hospital resources and staffing, with differences in the availability of specified inpatient respiratory units, step-down or intermediate care units and personnel. Therefore, criteria for intensive care unit (ICU) admission are often institution specific. Nonetheless, some guidelines suggest criteria for ICU admission (Table 232-5).

TABLE 232-4 Indications for Hospitalization of Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

1. High-risk comorbid conditions (heart failure, renal disease, liver failure, pneumonia)
2. Failure of outpatient management
3. Inability to perform activities of daily living (eating, sleeping, etc)
4. Unremitting dyspnea
5. Worsening hypercapnea, hypoxemia
6. Altered mental status
7. Diagnostic uncertainty

MANAGEMENT OF AN ACUTE EXACERBATION OF COPD

■ INITIAL HOSPITAL TREATMENT

Bronchodilators

Short-acting β-agonists such as albuterol are a mainstay of outpatient management of stable COPD and play a key role in the treatment of AECOPD for improving symptoms and FEV_1. β-agonists induce airway smooth muscle relaxation via increased cyclic adenosine monophosphate and have their largest effect on peripheral airways. Their onset of action occurs within minutes, peak at 30 minutes, and last for several hours. β-agonists should be given every 2 hours for initial treatment of a patient being admitted to a general medical floor, but may be given as frequently as every 20 minutes or continuously for patients in extremis. Levalbuterol, a pure R isomer of albuterol (albuterol is a 1:1 mixture of the R and S isomers) may produce better bronchodilation in asthma exacerbations, but this effect has not been shown in COPD. There is also some thought that levalbuterol may cause less tachycardia when compared to racemic albuterol, but scarce evidence supports this effect or its clinical significance. Based on the multitude of conflicting data surrounding the use of levalbuterol, it is difficult to recommend its routine use, but it may be reasonable in patients that appear to have an adverse effect from albuterol or for a short time while frequent dosing of a β-agonist is needed.

Short-acting anticholinergics, including ipratroprium, should be used in concert with β-agonists to treat acute exacerbations. They bronchodilate via inhibition of muscarinic pulmonary acetylcholine esterase receptors and have their largest effects on central airways.

TABLE 232-5 Indications for Intensive Care Unit Admission of Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

1. Severe dyspnea that responds inadequately to initial emergency therapy
2. Confusion, lethargy, or respiratory muscle fatigue (the last characterized by paradoxical diaphragmatic motion)
3. Impending respiratory failure
4. Hemodynamic instability
5. Persistent or worsening hypoxemia despite supplemental oxygen or severe/worsening respiratory acidosis (pH < 7.30)
6. Assisted mechanical ventilation, either intubation or noninvasive positive pressure ventilation

The onset of action is slower than that of β-agonist with an onset of approximately 15 minutes, a peak effect at 60 to 90 minutes, and duration of 4 to 6 hours.

The optimal dose of albuterol is 2.5 to 5.0 mg via nebulizer or six to eight puffs (90 mcg each) via metered dose inhaler (MDI). For ipratroprium, the optimal dose is 0.5 mg via nebulizer or four to eight puffs of an MDI (at 17 mcg per puff). Inhalational technique varies widely from patient to patient, especially in times of respiratory distress. However, evidence supports delivery of drug via MDI with a spacer for equivalent results at a lower cost compared to a nebulizer. Long-acting bronchodilators, including long-acting β-agonists (eg, salmeterol) and long-acting anticholinergics (eg, tiotropium) have no role in the management of AECOPD. Oral and injection bronchodilators are not as effective as inhaled route and should be avoided.

Corticosteroids

Systemic steroids are indicated for the treatment of AECOPD requiring hospitalization. More controversial, however, is the optimal route of administration and dose.

- Systemic steroids have been shown to speed recovery of FEV_1, lower the number of treatment failures and shorten hospital length of stay. A 5-day course of oral steroids has been shown to be noninferior to longer durations.

Steroids have significant side effects, including hyperglycemia, which is the most common acute side effect. Higher doses and longer duration of exposure increase these risks. The initial dose and route of administration of steroids should be tailored to the patient. Patients requiring hospitalization but without impending respiratory failure may be started at a dose of prednisone 30 to 40 mg (or equivalent) daily to maximize benefit and minimize risk, whereas use of higher doses and IV route should be considered for patients in acute distress or respiratory failure. Recent literature has shown that a 5-day course of oral prednisone (40 mg) is noninferior to 2 weeks of therapy. No data supports use of inhaled steroids in AECOPD.

Antibiotics

Bacterial infections play an important role in AECOPD. Guideline recommendations encourage the use of empiric antibiotics for patients with moderate to severe AECOPD that have suspected infection. Antibiotics should be tailored to the patient risk factors as well as to community and hospital specific microbial patterns, but should always include coverage for the most common causal pathogens (ie, Haemophilus infuenzae, Streptococcus pneumonia, and Moraxella catarrhalis). For patients with very severe airflow limitation, extended spectrum coverage should be considered as more resistant bacteria (ie, Pseudomonas, other Gram-negative rods) can cause exacerbations.

Oxygen and noninvasive ventilation

Oxygen level monitoring and supplemental oxygen provision are often necessary for patients with AECOPD (Figure 232-2). Early and

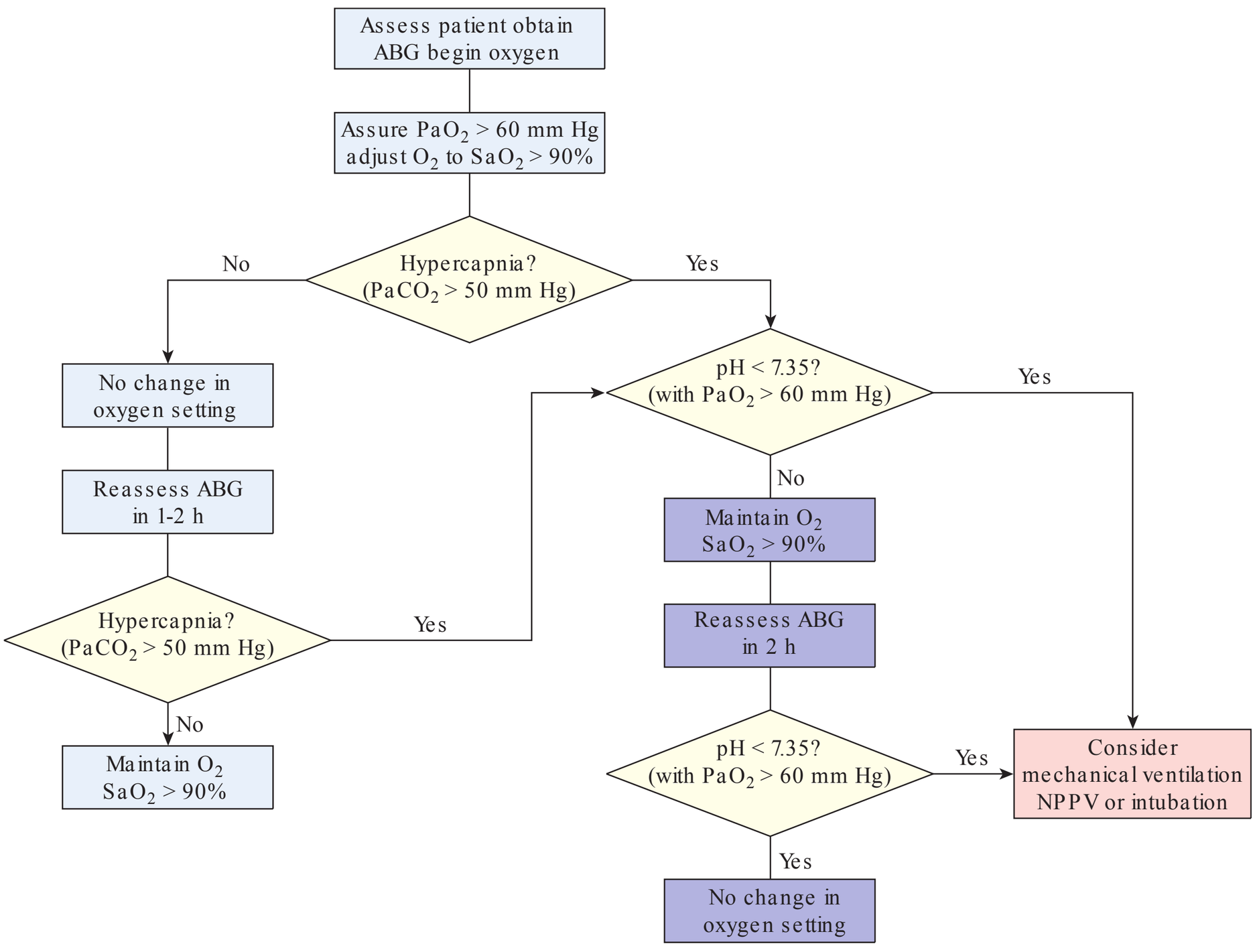

Figure 232-2 Algorithm *for* oxygen and carbon dioxide assessment during an acute exacerbation *of* chronic obstructive pulmonary disease. ABG, arterial blood gas; O_2, oxygen; $PaCO_2$, partial pressure *of* carbon dioxide in arterial blood; PaO_2, partial pressure *of* oxygen in arterial blood; SaO_2, saturation level *of* oxygen in hemoglobin.

frequent assessment of blood oxygen levels (via arterial blood gases or pulse oximetry) is critical for patients with an AECOPD. Oxygen can be supplied via nasal cannula, simple face masks, nonrebreather masks or high-flow oxygen masks. For patients with respiratory distress and increased work of breathing, rapid inspiration may overcome the reservoir of a nonrebreather mask. In this situation, oxygen delivered by high-flow masks yields the greatest percentage of inspired oxygen. The goal of oxygen supplementation should be to achieve a goal SpO_2 of 88% to 92% and/or a PaO_2 of > 60. Care must also be taken to provide adequate but not excessive levels of oxygen for patients that have baseline hypercapnea to avoid exacerbating carbon dioxide retention. Carbon dioxide binds reversibly to reduced hemoglobin, but oxygen drives the reaction to release carbon dioxide, a phenomenon known as the Haldane effect. Patients receiving supplemental oxygen need frequent assessment of blood oxygen and carbon dioxide levels in addition to a clinical assessment of alertness. The GOLD guidelines recommend rechecking an arterial blood gas 30 to 60 minutes after initiation of oxygen therapy.

Positive pressure ventilation

Noninvasive positive pressure ventilation (NIPPV) has been shown to benefit some patients with an AECOPD and should be considered for patients with mild to moderate acidemia, increased work of breathing and hypercapnea. Special consideration should be given for patients with a pH between 7.2 and 7.35, as this patient population has the most evidence supporting benefit.

- Positive pressure ventilation applied at two levels during the respiratory cycle (bi-level ventilation) has been shown to decrease mortality, the need for intubation, and the length of hospital stay for patients with an AECOPD.

Absolute contraindications to NIPPV include immediate need for intubation, untreated tension pneumothorax and a comatose state. Relative contraindications for use of NIPPV include severity of disease, likelihood of failure and anatomical risks (Table 232-6). If NIPPV is selected, patients require frequent reassessment and close observation. An ABG should be rechecked 30 minutes to 1 hour from the time of NIPPV initiation. Within the first 1 to 2 hours, there should be a clear trend toward improvement in clinical and laboratory (pH, PCO_2) parameters. Without rapid improvement, strong consideration must be given to intubation and mechanical ventilation.

TABLE 232-6 Relative Contraindications for Use of Noninvasive Positive Pressure Ventilation

1. Craniofacial abnormality or trauma
2. Respiratory arrest/apnea/refractory hypoxemia
3. Cardiac arrest/unstable cardiac arrhythmia
4. Hemodynamic instability
5. Inability to tolerate aerophagia (swallowing too much air), eg, recent gastrointestinal surgery
6. Inability to cooperate or protect airway
   a. Severe encephalopathy
   b. Severe upper gastrointestinal bleed
   c. High risk for aspiration

Invasive mechanical ventilation is sometimes required to treat severe exacerbations of COPD. The decision to intubate and mechanically ventilate a patient with an AECOPD is ultimately clinical, but guideline statements offer possible indications for intubation that include severe dyspnea, respiratory rate > 35, somnolence, severe acidosis (pH < 7.25), refractory hypoxemia and complications of comorbidities. Predictors of poor outcomes with intubation and mechanical ventilation include a baseline FEV_1 <30% predicted, nonrespiratory comorbidities and poor functional capacity prior to intubation.

■ OTHER THERAPIES

Methylxanthines such as theophylline and aminophylline have been used to treat COPD (both stable and during exacerbations) for decades. A systemic review of methylxanthines in AECOPD did not find significant benefits but did describe increased side effects, including palpitations and arrhythmias. While guidelines do list methylxanthines as alternate therapies for patients that do not respond to first-line therapies, they should be considered later-line therapy. If methylxanthines are used, they require monitoring for side effects and toxicity. Serum levels should be monitored every several days, and daily after a dose change until levels are relatively stable. Acute illness and medication changes at the time of admission can affect metabolism and serum levels of methylxanthines. If theophylline is used, drug levels should be adjusted to 8 to 12 mg/mL.

Other therapies that have been used to treat AECOPD include mucolytic therapy, postural drainage and chest physiotherapy. These modalities may improve symptoms, but have not been shown to improve outcomes. Guidelines do not recommend pulmonary rehabilitation during treatment for an AECOPD, but early ambulation and physical and/or occupational therapy for patients that are not in respiratory failure is advisable (Table 232-7).

■ TRIGGERS FOR CONSULTATION

Management of an AECOPD may have varying levels of complexity. The decision to consult a pulmonary or critical care specialist will be determined by hospital and referral resources, as well as the experience level of clinicians caring for these patients. For the inpatient

TABLE 232-7 Evidence for Specific Therapies in Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Therapy	Outcomes Improved
Antibiotics	Decreased treatment failure in the ICU Decreased in-hospital mortality while in the ICU
Oral corticosteroids	Decreased treatment failure Decreased hospital LOS Increased FEV_1 after 3 d
Bronchodilators	Increased FEV_1
Noninvasive positive pressure ventilation	Decreased need for intubation Decreased in-hospital mortality Decreased hospital LOS
Pulmonary rehabilitation (following recovery)	Decreased readmissions Decreased mortality in follow-up Increased quality of life in questionnaires Increased exercise capacity in 6MWT

6MWT, 6-minute walk test; FEV_1, forced expiratory volume in 1 s; LOS, length of stay.

management of an acute exacerbation, acuity of illness, hemodynamic compromise and poor response to therapy should be the overriding considerations for consultation. The ATS/ERS guidelines for the management of COPD list the following factors as indication for outpatient specialist consultation: age of COPD onset < 40 years old, two or more exacerbations per year (despite adequate outpatient management), rapidly progressive disease, severe disease (FEV_1 < 50% predicted), need for long-term oxygen therapy, onset of comorbid illness (osteoporosis, heart failure, bronchiectasis, lung cancer) and/or evaluation for surgery. A consultant may also help with discharge planning and follow-up care for patients after their acute illness. Outpatient specialty referral may be indicated for most patients once they have completed their inpatient treatment.

OUTPATIENT THERAPEUTICS AND REGIMEN AUGMENTATION

■ SUPPLEMENTAL OXYGEN

If patients remain hypoxemic at the time of discharge, they will require home oxygen therapy. To meet the Centers for Medicare and Medicaid Services (CMS) criteria for 24 hours per day long-term home oxygen therapy, patients must have resting, room air PaO_2 of 55 mm Hg or less or PaO_2 of 59 mm Hg or less with coexisting congestive heart failure, peripheral edema, hematocrit > 56%, or cor pulmonale (Table 232-8). Alterations of oxygen levels during sleep and/or exercise can also qualify patients for supplementation during those activities. Hypoxemia at hospital discharge following AECOPD may represent a prolonged recovery from an acute illness, a new baseline, or new recognition of a chronic problem. Regardless, long-term oxygen therapy improves mortality for COPD patients that have resting hypoxemia. Patients that have a new prescription for home oxygen should be reassessed with an arterial blood gas within 3 months to determine the ongoing need for supplemental oxygen.

■ ORAL STEROIDS

Systemic oral steroids are indicated for the treatment of an AECOPD that requires hospitalization. A 5-day course of oral steroids is supported by current evidence. Once the patient has stabilized, there is no indication for long-term treatment with steroids.

TABLE 232-8 Centers for Medicare and Medicaid Services Criteria for Oxygen Supplementation

Group I Coverage
• $PaO_2 \leq 55$ or $SaO_2 \leq 88\%$
ª At rest
ª During sleep
• OR↓ PaO_2 > 10 mm Hg or ↓ SaO_2 5% associated with symptoms or signs of hypoxemia
ª During activity
Group II Coverage
• SaO_2 = 89% (not + 89%)
• Any of the following:
ª Dependent edema
ª Pulmonary hypertension or cor pulmonale
ª Hematocrit > 56%
Requires retesting between 61 and 90 d

PaO_2, partial pressure of oxygen in arterial blood; SaO_2, saturation level of oxygen in hemoglobin.

■ INHALED THERAPIES

Inhaled long-acting bronchodilators (long-acting β-agonists and long-acting anticholinergics) and inhaled corticosteroids (ICS) have a significant role in regimen augmentation when a patient with AECOPD is being discharged. Strong evidence supports that inhaled medications reduce deterioration in health status, improve lung function (FEV_1), and reduce the number of exacerbations per year. All patients who have been hospitalized with AECOPD should be discharged on a combination of a long-acting bronchodilator and ICS, as meta-analysis data suggest mortality reduction with this regimen compared to placebo and other regimens. Additional data indicate that the combination of LABA and ICS plus long-acting anticholinergic for patients with more advanced COPD is associated with additional improvement in quality of life and a reduction in subsequent hospitalizations. Some evidence shows that chronic use of short-acting anticholinergic agents may impart increased cardiovascular risk in COPD patients, while mounting evidence suggests that long-acting anticholinergic agents may not have significant cardiovascular risks. The decisions of which medications to utilize should be made in light of clinical acumen, patient preferences, and patient-provider discussions regarding treatment goals and potential adverse effects.

■ MUCOLYTIC AND MUCOKINETIC AGENTS

Mucolytic agents are sometimes used in the treatment of COPD though they are not recommended in the guidelines. This is an area of active research.

COPD COMPLICATING ADMISSIONS FOR OTHER DIAGNOSES

Underlying COPD may complicate the care of patients admitted for other diagnoses. Complications may result from the underlying compromise of the respiratory symptom or because an exacerbation occurs at the time of, or shortly after, the onset of the original stress. Also, patients hospitalized for any reason are exposed to iatrogenic risks such as resistant microbes, painful procedures (causing splinting), sedative medications (hypoventilation), and decreased physical activity (deconditioning).

The use of β-blockers in COPD has long been a controversial topic. A 2005 Cochrane Review demonstrated that there was no short-term decrease in FEV_1 or responsiveness to inhaled β-agonists for patients that received cardioselective β-blockers, regardless of the severity of COPD. Therefore, cardio-selective β-blocker prescription is reasonable for chronic COPD patients who have a cardiac indication to receive this therapy.

While COPD may complicate any medical or surgical illness, there are certain processes where this occurs more frequently. Patients with heart failure and COPD often present complaining of shortness of breath. It is difficult to decipher if the worsening of the baseline condition is because of cardiac decompensation, pulmonary exacerbation, or both. Normal levels of serum brain natriuretic peptide (BNP) significantly decrease the likelihood of cardiac decompensation, but elevated BNP is less specific and more difficult to interpret. A full physical examination and workup is often necessary and occasionally an empiric trial of treating both conditions is warranted. Patients recovering from surgical procedures need to have special consideration of postoperative activity, pain control (without oversedation) and abdominal processes (such as swelling or ileus).

■ PERIOPERATIVE EVALUATION

Large numbers of patients with recognized or unrecognized COPD may require surgery. Hospitalists are often asked to determine which patients represent undue risk and if there are any measures that can minimize these risks. In general, pulmonary complications are

equal (in prevalence, morbidity, mortality, and length of stay) when compared to cardiac complications for moderate and high-risk surgeries. Perioperative care of COPD patients includes identifying and managing any acute worsening from pulmonary baseline, risk assessment, preoperative risk minimization (ensuring proper preoperative care and medications) and postoperative risk minimization. Separate chapters describe perioperative pulmonary care (Chapters 51 [Preoperative Pulmonary Risk Assessment and Management] and 60 [Management of Postoperative Pulmonary Complications]).

PROGNOSIS AND END-OF-LIFE CARE

■ PROGNOSIS

COPD patients' pulmonary function progressively declines over the course of the disease. Tobacco cessation is the most important factor in slowing the progression of COPD, but even those patients that stop smoking experience continued age-related decline in lung function. Predicting the future health of a patient with COPD is important at the time of discharge to ensure all appropriate treatment modalities are considered as well as ensuring patients have the needed social support to meet the demands of daily life.

Once a patient is admitted for an AECOPD, morbidity and mortality are significantly different when compared to COPD patients that have not been hospitalized previously. The 1-year readmission rate for COPD patients discharged for AECOPD is as high as 59% for patients with severe disease and the 1-year mortality rate is as high as 22%. Two-year mortality approaches 50% for patients admitted with AECOPD and hypercapnea.

Increasing age, male sex, white race, prior hospitalization, weight loss, pulmonary hypertension, hypoxemia, hypercapnea, decreased FEV_1, and decreased diffusing capacity of the lung for carbon monoxide (DLCO) have all been identified as risk factors for death with COPD. Progressive decline in FEV_1 has historically been used as the primary measure of predicting the course of COPD, but it is being replaced by an indexed score, the BODE score. The BODE score (Table 232-9) has the advantage of taking into account multiple factors that have been shown to be predictive of respiratory and all-cause mortality. The BODE index requires a (B) BMI, FEV_1 as a measure of (O) obstruction, degree of (D) dyspnea on the Medical Research Council dyspnea scale, and (E) exercise capacity as measured by a 6-minute walk test. Patients who have a 5 or greater BODE score are appropriate for evaluation for lung transplant and/or other advanced treatment modalities.

■ END-OF-LIFE CARE

For patients that have not previously expressed their desires regarding invasive or life supporting treatments, dif cult decisions have to be made during the time of an acute illness. It is preferable, however, to facilitate patient expression of their end-of-life wishes in a stable and less stressed state. The time of discharge from the hospital can be a "teachable moment" and discussion of what the patient would or would not want in the case of future illness and/or respiratory failure should occur.

For some patients, an emphasis on palliative care (formally or informally) and/or hospice referral may be appropriate. Dyspnea is a key symptom that must be addressed as a source of anxiety and discomfort for the patient. Oxygenation status, respiratory rate, and other objective measures are not good indicators of a patient's perception of breathlessness. When underlying causes of dyspnea can be corrected, that should be the focus of care. When the underlying causes are not reversible, opioids in low-to-moderate doses have good effect in relieving dyspnea. For patients who have a significant component of anxiety along with dyspnea, benzodiazepines may be added to relieve symptoms.

TABLE 232-9 BODE Index Scoring System

	0	1	2	3
FEV_1 (% predicted)	≥ 65	50-64	36-49	≤ 35
6MWT distance	> 350 m	250-349 m	150-249 m	≤ 149 m
mMRC dyspnea scale	0-1	2	3	4
BMI	> 21	< 21		

6MWT, 6-minute walk test; BMI, body mass index; BODE, body mass index, airflow obstruction, dyspnea and exercise capacity; FEV_1, forced expiratory volume in 1 s; mMRC, modified Medical Research Council.

DISCHARGE PLANNING

For the majority of patients admitted with an AECOPD, improvement is noted within a short period from admission. For the minority of patients that do not improve, alternative diagnoses, intensified therapies, and/or palliative measures must be considered. The latter stages of an acute inpatient stay can focus on tapering the frequency of medication dosing, transitioning care to an outpatient setting, patient education, and prevention of future exacerbations.

The GOLD and ATS/ERS guidelines provide lists of criteria that should be met for consideration of discharge home. These include controlling or reversing the reason for admission, hemodynamic stability, return to oxygenation baseline, less frequent need for inhaled bronchodilators, ability to resume ambulating, no parenteral therapy for 12 to 24 hours, ability to eat and sleep without being disturbed by dyspnea, understanding the use of medications, and completion of arrangements for follow-up and/or home care. For patients to meet all of these criteria, length of stay might increase beyond what is reasonable or desirable. While the patient's trend should be back toward baseline, full recovery and baseline oxygenation status might take several weeks and strict adherence to the guidelines may not be practical or feasible.

QUALITY IMPROVEMENT

■ SECONDARY PREVENTION

Smoking cessation

Counseling regarding tobacco cessation for active smokers is essential because tobacco cessation is the best way to slow the decline in lung function. There is some limited data that counseling during an inpatient stay might increase the chance of quitting and more robust evidence that quit rates can be increased by inpatient counseling followed by continued outpatient intervention. Also, several pharmacological strategies have been shown to improve quit rates. Options include nicotine replacement, buproprion (which can be used in conjunction with nicotine replacement) and varenicline. A Cochrane Review compiled several trials of varenicline and found that relative risk of cessation was two to three times greater when compared to placebo, approximately 1.5 times greater when compared to buproprion, and approximately 1.3 times greater when compared to nicotine replacement therapy.

Vaccinations

All patients with COPD should have the 23-valent pneumococcal polysaccharide vaccine, and those patients aged greater than 65 that have not had the vaccine in the last 5 years should have it administered regardless of previous vaccination status. The CDC recommends all adults over the age of 65 receive the pneumococcal

conjugate vaccine (PCV13). The PCV13 and 23-valent should not be administered during the same visit and the minimum time between administration is 8 weeks. Also, all patients with COPD should have the influenza vaccine annually.

■ PATIENT EDUCATION

Efforts toward education are also vital for improving the patient's health after discharge and include education regarding proper inhaler technique, and avoidance of second-hand smoke (and other respiratory irritants). Patient education regarding the ability to recognize the symptoms of an exacerbation should be emphasized.

■ PULMONARY REHABILITATION

Pulmonary rehabilitation is an important part of outpatient COPD care after an admission for AECOPD, and should be considered at the time of discharge for all patients with chronic lung disease with the goal of alleviating symptoms and optimizing functional capacity. Evidence supports that entering pulmonary rehabilitation within 10 days of hospital discharge is safe. Furthermore, patients enrolled in early pulmonary rehabilitation experienced improved exercise tolerance and health status at 3 months. Beyond functional capacity, pulmonary rehabilitation programs often focus on establishing social support and care networks that are most appropriate for the patient and can have quality-of-life benefits beyond physical improvements.

- Evidence supports that entering pulmonary rehabilitation within 10 days of hospital discharge is safe, and patients enrolled in early pulmonary rehabilitation experience improved exercise tolerance and health status at 3 months.

■ SURGICAL TREATMENT OPTIONS AND TRANSPLANT EVALUATION

Surgical treatment options for COPD include lung volume reduction surgery (LVRS), bullectomy, lung transplantation and investigational approaches. LVRS involves bilateral removal of 25% to 30% of total lung volume. The National Emphysema Treatment Trial, published in 2003, demonstrated that LVRS improved exercise capacity but not survival among all patients with severe emphysema. This trial did, however, identify subgroups that had a survival advantage. The best candidates for LVRS are patients with predominantly upper-lobe disease and a low exercise capacity after pulmonary rehabilitation. Bullectomy has not been well studied in randomized trials, but it may be considered for patients with at least one-third of the thorax occupied by bullae.

For patients with advanced disease another therapy to consider is lung transplantation. Lung transplant referral is indicated for younger patients with COPD that have progressive symptoms despite maximal medical therapy, including smoking cessation. Lung transplant for COPD has been shown to improve quality of life, but effect on mortality has not been clearly demonstrated and is more controversial. For further analysis of trials addressing treatment strategies in COPD, please refer to the key references (Table 232-10).

■ TRANSITIONS OF CARE

Patients transitioning from inpatient to outpatient care, whether for an AECOPD or for patients with underlying COPD admitted for other reasons, have many educational and therapeutic needs. Education needs include smoking cessation, inhaler technique and mobility prescriptions. For patients that might still have pain issues or decreased mobility, education regarding incentive spirometry is imperative. Follow-up care should be arranged with a primary care physician, a pulmonary specialist or both. For discharges after an AECOPD, follow-up should be arranged at discharge for the patient to be seen within 2 weeks of discharge or sooner if requiring significant changes to their care regimen. Recent literature has suggested implementing a "COPD care bundle" prior to discharge. This includes specialist notification of patient admissions, smoking cessation assistance, referral to pulmonary rehab, educational literature and proper inhaler teaching. Preliminary data have shown a significant reduction in readmissions for AECOPD following these steps.

■ DISPARITIES IN HEALTH CARE

COPD has long been considered a disease of white, male smokers. Data, however, show that the epidemic is increasing most rapidly for women and African Americans. For over a decade, more women have died of COPD than men annually. The death rate is increasing more rapidly for African Americans as well. To some degree, these changes represent changes in the demographics of cigarette smoking over decades. However, some data suggest that women and African Americans may actually be more susceptible to chronic lung disease when compared to white men. In general, women have smaller caliber central airways than similarly sized men and African Americans have smaller trunk/leg ratios than whites. These differences may explain more clinically significant airflow limitation after exposure to cigarettes or other respiratory toxins. Possible differences in specific genes, proteases, and/or cytokines might also explain some differences in response to exposures.

■ OUTCOMES TO MONITOR

There are many possible outcomes to monitor and measure regarding quality of care for patients admitted with an AECOPD or for patients with COPD treated in the hospital for other issues. The percentage of patients provided with smoking cessation counseling would be appropriate for either group, as would vaccination rates.

For patients treated for an AECOPD, tracking the number of patients referred for pulmonary rehabilitation is another option, as is the short-term readmission rate. Lastly, the percentage of patients with severe COPD that are referred to hospice and/or palliative services could be monitored.

■ COSTS AND RESOURCE UTILIZATION

While only smoking cessation and supplemental oxygen have been proven to have an impact on chronic COPD mortality, there are many other modalities that may improve quality of life and possibly decrease health care costs for patients with COPD.

Smoking cessation programs, health-maintenance caseworkers for patients with COPD and pulmonary rehabilitation programs each offer ways in which large institutions might decrease overall costs for the care of a population of COPD patients. Vaccinations have been shown to have significant cost-savings as well.

Another area of focus for resource utilization is goals of care and end-of-life discussions. A 2006 study found that COPD patients in the last 6 months of life were more likely to be admitted to an ICU and have longer length of stay when compared to patients in the last 6 months of life with lung cancer. Total health care costs were $4000 more per patient during this time frame. Improved communication (preferably before admission, but also possibly at the time of admission) regarding goals of care and realistic expectations could prove to decrease these costs while hopefully improving quality of life for terminal patients and their families.

TABLE 232-10 Evidence-based Medicine: Key References for Chronic Obstructive Pulmonary Disease

Reference	Methodology	Results	Limitations	Bottom Line
Calverely P, et al. N Engl J Med. 2007;356: 775-789. TORCH trial	Randomized, double-blind, placebo-controlled trial of placebo vs salmeterol alone vs fluticasone alone vs salmeterol plus fluticasone inhaled twice daily for 3 y. 6112 patients were active or former smokers with diagnosis of COPD, FEV_1 < 60% predicted and no significant bronchodilator response	Comparing combination therapy to placebo, there was nonstatistically significant reduction in mortality (OR, 0.825; CI 0.681-1.002). Compared to placebo, combination therapy reduced exacerbations. There were higher levels of pneumonia in both groups receiving fluticasone when compared to placebo	There was a large drop-out rate (as might be expected in a COPD trial with a placebo arm)	There is insufficient data to suggest that inhaled corticosteroids decrease mortality in patients with COPD, but addition of inhaled corticosteroid may reduce exacerbations for patients on LABAs that have recurrent exacerbations. For monotherapy in COPD, LABA should be used rather than an ICS
Taskin DP, et al. N Engl J Med. 2008;359: 1543-1554. UPLIFT	Randomized, double-blind, placebo-controlled trial of tiotroprium vs placebo to decrease decline in FEV_1 over time (before and after bronchodilation) in 5993 patients	There was no significant difference in decline in FEV_1 over time in the tiotroprium group as compared to placebo. Tiotroprium did lead to increases in FEV_1 (but not change over time), improved quality-of-life scores, and fewer exacerbations	There was a large drop-out rate and short-acting inhaled anticholinergics were stopped in all patients	Tiotroprium may be prescribed to alleviate symptoms of COPD, but should not be expected to alter progression of disease
Anthonisen NR. JAMA. 1994;272: 1497-1505. Lung Health study	Randomized, placebo-controlled trial comparing no intervention to smoking cessation counseling plus placebo to smoking cessation counseling plus inhaled short-acting anticholinergics in 5887 patients	Participants in both smoking cessation groups experienced smaller declines in FEV_1 over time. Responses to short-acting anticholinergics were not cumulative over time	There was predictably low adherence to prescribed inhalers	Smoking cessation counseling can lead to declines in rates of smoking, and FEV_1 decline was mitigated amongst patients who received counseling, and the effect was strongest in those who did abstain
Bronchard L, et al. N Engl J Med. 1995;333: 817-822.	Prospective randomized trial comparing use of NIPPV vs standard care for treating 85 patients admitted to ICU with COPD exacerbation	NIPPV significantly decreased rate of endotracheal intubation, hospital LOS, and in-hospital mortality	Large percentage of patients admitted to ICU with COPD exacerbation were excluded, limiting population of patients to which data can be applied	For selected patients with acute exacerbations of COPD, application of NIPPV can prevent need for endotracheal intubation and speed recovery
NETT Research Group. N Engl J Med. 2003;348: 2059-2073. NETT trial	Randomized trial of 1218 patients with severe emphysema to receive lung volume reduction surgery vs continued medical care. Overall mortality and maximal exercise capacity were compared as primary outcomes	In entire study group, there was no difference in overall mortality. Surgery group had significantly higher percentage of patients who improved maximal exercise capacity when compared to nonsurgery group. In subgroup analysis, patients with mostly upper-lobe disease and low exercise capacity after pulmonary rehabilitation, there was a mortality benefit from surgery. Amongst subgroup of nonupper-lobe emphysema and high exercise capacity, mortality was higher in surgery group. Interim analysis identified group of patients with high risk of surgical death	No difference in mortality overall. Caution must be used when results of subgroup analysis are applied	Lung volume reduction surgery may be indicated for specific group of patients who have predominantly upper-lobe emphysema and low exercise capacity after pulmonary rehabilitation. Risks and benefits must be weighed against options of doing nothing vs lung transplant. Patients with $FEV_1 \leq 20\%$ predicted and either homogenous emphysema or DLCO $\leq 20\%$ predicted are at high risk of death from lung-volume reduction surgery
Leuppi JD. JAMA. 2013;309: 2223-2231. REDUCE trial	Randomized, noninferiority trial comparing use of 5 d vs 14 d of corticosteroids in 314 patients with COPD exacerbation	No significant difference in rates of re-exacerbation at 6 mo between treatment arms (37.2% in the short term treatment group vs 38.4% in the long-term treatment group)	The study used an absolute difference of 15% to show noninferiority which may miss smaller treatment differences between treatment arms	To reduce the overall exposure to steroids, limit treatment to a total of 5 d of prednisone for acute exacerbations of COPD

COPD, chronic obstructive pulmonary disease; DLCO, diffusing capacity of the lung for carbon monoxide; FEV_1, forced expiratory volume in 1 s; ICS, inhaled corticosteroid; ICU, intensive care unit; LABA, long-acting beta-agonist; NIPPV, noninvasive positive pressure ventilation; OR, odds ratio.

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