EB MEDICINE

EMERGENCY MEDICINE PRACTICE

EBMEDICINE.NET

AN EVIDENCE-BASED APPROACH TO EMERGENCY MEDICINE

Diagnosis and Management of Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Abstract

Acute exacerbation of chronic obstructive pulmonary disease (COPD) is a clinical diagnosis that is based on changes in dyspnea, cough, and/or sputum production in a COPD patient; however, patients presenting with an acute exacerbation may be undiagnosed or have a variety of comorbid conditions that can complicate diagnosis. This issue presents strategies and algorithms for the early use of evidence-based interventions, including appropriate use of antibiotics, bronchodilators, and corticosteroids, along with noninvasive ventilation with capnography, to minimize morbidity and mortality associated with this disease.

October 2017
Volume 19, Number 10

Authors

Van Holden, MD
Pulmonary and Critical Care Fellow, Division of Pulmonary and Critical Care Medicine, University of Maryland Medical Center, Baltimore, MD

Donald Slack, III, MD
Pulmonary and Critical Care Medicine, Greater Baltimore Medical Center, Baltimore, MD

Michael T. McCurdy, MD, FCCM, FCCP, FAAEM
Associate Professor, Department of Emergency Medicine and Department of Medicine, Division of Pulmonary and Critical Care; Director, Critical Care Medicine Fellowship Program, University of Maryland School of Medicine, Baltimore, MD

Nirav G. Shah, MD, FCCP
Associate Professor of Medicine, Division of Pulmonary and Critical Care Medicine; Director, Pulmonary and Critical Care Medicine Fellowship Program, University of Maryland School of Medicine, Baltimore, MD

Peer Reviewers

Gabriel Wardi, MD, MPH
Department of Emergency Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, University of California San Diego, San Diego, CA

Geralda Xavier, MD, MPH, FACEP
Department of Emergency Medicine, NYC Health + Hospitals, Kings County Hospital, Brooklyn, NY

Prior to beginning this activity, see "Physician CME Information" on the back page.

Case Presentations

It is change of shift, and you receive sign-out on a 67-year-old gentleman with a history of COPD presenting with 5 days of worsening productive cough, wheezing, and increased albuterol use despite outpatient treatment with prednisone and doxycycline. His oxygen saturation was 86% on arrival, and the nurse placed him on oxygen therapy at 6 L/min via nasal cannula shortly before you arrived. You find the patient sitting on the edge of his bed, tachypneic, with increased work of breathing and audible wheezing on auscultation. He is alert and acknowledges your presence but does not speak. You wonder why he continues to be hypoxic and if there is any other intervention that is indicated . . .

Your next patient is a 57-year-old woman with a history of smoking 2 packs of cigarettes per day. Her husband called 911 because she was having increased difficulty with breathing and productive cough for the previous week. She has no documented pulmonary history. Upon arrival, EMS noted that she could not speak in full sentences, her oxygen saturation was 81% on room air, and she had diffuse end-expiratory wheezing on auscultation. IV access was obtained. She was given continuous albuterol nebulization without relief and started on supplemental oxygen. The chest x-ray does not demonstrate a focal infiltrate; however, her lungs appear hyperinflated, with flattened diaphragms and a small cardiac silhouette. You wonder if she has COPD with an acute exacerbation and whether prednisone and antibiotics are indicated . . .

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of death worldwide. From a financial perspective, COPD exacted a net $36 billion toll in 2010 in the United States, and its costs are expected to continue to rise.[1] Despite decreasing tobacco use nationally, emergency department (ED) visits for COPD-related problems continue to climb, with over 1.7 million in 2011 alone. Moreover, about one-fifth of COPD patients presenting to the ED required hospitalization.[2]

COPD is characterized by a persistent airflow limitation, after administration of bronchodilators, that can be identified on spirometry as a ratio of forced expired volume in 1 second (FEV_1) to forced vital capacity (FVC) that is < 70%. Although COPD is a treatable disease, the airflow limitation is not fully reversible. Previous definitions of COPD have included the terms *emphysema* and *chronic bronchitis*; however, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines do not, and they clarify the distinction: *Emphysema* is a pathological term that refers to the destruction of alveoli, which can be present but is not inherent in patients with COPD. *Chronic bronchitis* is an independent clinical entity characterized by cough and sputum production for at least 3 months in each of 2 consecutive years and can occur without the development of airflow limitation. Guidelines define acute exacerbation of COPD (AECOPD) as an event characterized by a worsening of the patient's respiratory symptoms (dyspnea, cough, and/or sputum production) that is beyond normal day-to-day variations, and that leads to a change in medication.[3,4]

Patients with COPD often have comorbid conditions that may have either resulted from COPD, (eg, pulmonary hypertension or malnutrition) or are simply associated with it (eg, anxiety, cardiovascular disease, sleep apnea, and venous thromboembolism).[5] Because of the myriad presenting features of COPD and/or these comorbidities, diagnostic challenges exist when these patients present to the ED in extremis. This issue of *Emergency Medicine Practice* reviews the most recent evidence-based recommendations for the diagnosis and management of AECOPD, with a focus on tailoring management to the underlying pathophysiology of the disease state.

Selected Abbreviations

AECOPD Acute exacerbation of COPD
ATS American Thoracic Society
BLUE Bedside lung ultrasound in emergency
CAT COPD Assessment Test
CI Confidence interval
COPD Chronic obstructive pulmonary disease
ERS European Respiratory Society
FEV_1 Forced expired volume in 1 second
FVC Forced vital capacity
GOLD Global Initiative for Chronic Obstructive Lung Disease
IPAP Inspiratory positive airway pressure
mMRC Modified Medical Research Council scale
NIPPV Noninvasive positive-pressure ventilation
$PaCO_2$ Arterial partial pressure of carbon dioxide
$PvCO_2$ Venous partial pressure of carbon dioxide
REDUCE Reduction in the Use of Corticosteroids in Exacerbated COPD Trial
RR Relative risk
SpO_2 Oxygen saturation measured by pulse oximetry

Critical Appraisal of the Literature

A literature search was performed in PubMed, with the search terms *COPD*, *chronic obstructive pulmonary disease,* and *acute COPD exacerbation.* The search was limited to articles published within the last 10 years, and studies relating specifically to acute COPD exacerbation (as opposed to stable COPD) were reviewed. In addition, references were appraised for additional relevant articles. A total of 127 articles have been included in this review.

The Cochrane Library was searched for sys-

tematic reviews using the key term *acute COPD exacerbation*, which identified 25 articles. In addition, guidelines from the GOLD, American Thoracic Society (ATS), European Respiratory Society (ERS), American College of Chest Physicians (ACCP), and National Institute for Health and Care Excellence (NICE) were reviewed.

COPD is a composite of heterogenous etiologies that contribute to variations in the presentation in patient populations. For example, it has been increasingly recognized that exposures to substances other than cigarette smoke contribute to the pathophysiology of disease. The asthma-COPD overlap syndrome is a newly identified condition, with varied acceptance in the community, but it illustrates that a history of asthma does not exclude coexisting COPD. Cohorts included in studies are similarly diverse, making the generalizability of results challenging. Clinically, the varied presentation of COPD makes detecting previously undiagnosed patients more difficult; however, these patients may well be the ones seeking care in the ED.

The current state of the literature remains limited mainly by the retrospective observational nature of most studies. There are few randomized controlled trials to direct management of acute COPD exacerbations. Furthermore, existing studies have wide-ranging outcome measures, such as pulmonary function, symptom scores, rate of exacerbation, and short-term mortality. In the absence of high-quality data, some interventions should be directed by prior individual patient response.

Definition

The ATS and ERS produced a consensus document, "Standards for the Diagnosis and Management of Patients with COPD" in 2004 that has not been updated.[3] The GOLD Guidelines, updated in 2016, contain a consensus definition of AECOPD, combined COPD assessment for risk (Groups A-D, see **Table 1**), and evidence-based management strategies for both stable disease and acute exacerbation. The risk model includes the severity of pulmonary obstruction based on FEV_1 and COPD-related symptoms based on the modified Medical Research Council (mMRC) scale or the COPD Assessment Test (CAT). (Note: the CAT is not available in the United States at this time.) The mMRC scale measures breathlessness on a scale of 0 to 4, ranging from breathlessness only with strenuous exercise (mMRC = 0) to breathlessness with dressing (mMRC = 4).[4]

MDCalc link to mMRC scale online tool: www.mdcalc.com/mmrc-modified-medical-research-council-dyspnea-scale

Epidemiology, Etiology, and Pathophysiology

Epidemiology of COPD

In the United States, COPD accounts for nearly 20% of hospitalizations of patients over the age of 65 years, and it is a major cause of morbidity and mortality each year.[6] COPD and other chronic lower respiratory diseases are the third leading cause of death in the United States annually (147,000 deaths/year), and projections over the next several decades suggest an increasing burden of disease.[7,8] One large cohort of COPD patients had an annual mortality rate of approximately 19%, with only 50% survival at 3.6 years after the first hospitalization for AECOPD.[9] A retrospective study published in 2013 estimated 13.8 COPD-related ED visits per 1000 person-years in the United States, with a 7% return visit rate at 30 days and a 28% return rate at 365 days.[10] Because of the frequency of hospitalizations, COPD exacts a significant economic cost to the healthcare system. The National Heart, Lung, and Blood Institute estimated that, in 2010, $49.9 billion in direct and indirect healthcare costs were related to COPD.[11]

Etiology of Acute Exacerbation of COPD

The general consensus is that the majority of acute exacerbations of COPD are caused by upper and lower respiratory tract viral and bacterial infections.[12-15] As with many other chronic lower respiratory diseases, however, these patients are often colonized with known pathogenic bacteria, so it is unclear exactly

Table 1. Model of Symptom/Risk Evaluation of COPD[4]

- **Category A** (low risk, less symptoms): includes patients with an $FEV_1 \geq 50\%$; ***and/or*** ≤ 1 exacerbation per year with no hospitalization for exacerbation; ***and*** CAT score < 10 ***or*** mMRC grade ≤ 1
- **Category B** (low risk, more symptoms): Includes patients with an $FEV_1 \geq 50\%$; ***and/or*** ≤ 1 exacerbation per year with no hospitalization for exacerbation; ***and*** CAT score ≥ 10 ***or*** mMRC grade ≥ 2
- **Category C** (high risk, less symptoms): Includes patients with an $FEV_1 < 50\%$; ***and/or*** ≥ 2 exacerbations per year or ≥ 1 with hospitalization for exacerbation; ***and*** CAT score < 10 ***or*** mMRC grade ≤ 1
- **Category D** (high risk, more symptoms): Includes patients with an $FEV_1 < 50\%$; ***and/or*** ≥ 2 exacerbations per year ***or*** ≥ 1 with hospitalization for exacerbation; ***and*** CAT score ≥ 10 ***or*** mMRC grade ≥ 2

Abbreviations: CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; FEV_1, forced expired volume in 1 second.

From the *Global Strategy for the Diagnosis, Management and Prevention of COPD*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016. Available from: http://goldcopd.org/. Used with permission.

what triggers any particular acute episode, including whether or not the cultured bacterium is a causal factor in any single acute exacerbation. Noninfectious etiologies, such as acute pulmonary embolism and environmental antigens, are less common but well-established triggers, and should be considered. To date, however, studies have had a difficult time showing a link between such pollution and long-term pathophysiologic changes contributing to the ongoing development and progression of COPD.[16-18]

Pathophysiology of COPD

In COPD, there is a progressive decline in FEV_1. The natural history of the disease suggests that this rate of decline accelerates over time. The FVC also declines, due to gas trapping and increased residual volume, but by less than FEV_1. The ratio of these 2 values, the FEV_1/FVC ratio, therefore decreases over time due to the loss of elastic recoil of the lung, a defining feature of COPD. The distal branches of bronchioles are held open due to the radial traction of the surrounding lung tissue. With the development of emphysema, the progressive loss of this radial force leads to closure of these bronchioles earlier in the expiratory phase of a breath and at progressively higher lung volumes. Thus, as this process continues, the effective lumen of these airways becomes smaller, and the degree of bronchial smooth-muscle contraction necessary to induce closure becomes less.[19] It is understandable, then, how an AECOPD may be precipitated by acute infection or environmental antigens that increase mucosal secretions and bronchial smooth-muscle contraction. Air trapping ensues, and patients breathe at higher lung volumes. With less-effective gas exchange, tachypnea often develops, leading to further dynamic hyperinflation, until the patient develops frank exacerbation of the underlying disease.

Differential Diagnosis

The signs and symptoms of many pulmonary disorders overlap, making the differential of AECOPD extensive. In addition, it may be difficult to differentiate AECOPD from a patient's other comorbidities. **(See Table 2.)**

Table 2. Differential Diagnosis of Acute Exacerbation of COPD

- Asthma
- Congestive heart failure
- Central airway obstruction
- Myocardial infarction
- Pneumonia
- Pulmonary embolism
- Bronchiectasis

Abbreviation: COPD, chronic obstructive pulmonary disease.

Prehospital Care

The overall goals of prehospital management of AECOPD include rapid recognition, identifying healthcare proxies and advanced directives, establishing adequate intravenous (IV) access, initiating medical treatment, and providing safe transport to the ED. Obtaining the level of oxygen saturation via pulse oximetry (SpO_2) is an important first step in order to determine the need for supplemental oxygen, with a goal oxygen saturation of 88% to 92%. Excessive oxygen therapy should be avoided; oxygen saturation > 92% in patients with AECOPD has been associated with increased levels of respiratory acidosis upon arrival to the ED, but has not been associated with increased length of stay, need for ventilatory support, or in-hospital mortality.[20,21] We recommend to begin supplemental oxygen therapy with 1 to 3 L/min via nasal cannula, then titrating to 92%.[22] Some patients will need ventilatory assistance or advanced airway management, and a delay in recognition of these patients may result in increased morbidity and mortality. The role of noninvasive positive-pressure ventilation (NIPPV) for AECOPD management in the prehospital arena is not defined; however, if used, precaution should be taken to avoid over-ventilation, as it may result in barotrauma.[23]

Emergency Department Evaluation

The initial approach to patients with AECOPD focuses on the vital signs, mental status, and respiratory effort.

History

The history should establish details surrounding the current ED presentation. Existing medical problems and the duration of the diagnoses, triggers for exacerbations, disease severity (eg, baseline level of dyspnea, number of prior exacerbations, previous endotracheal intubation), and required therapy for prior exacerbations (eg, corticosteroids) should be delineated.

When an underlying diagnosis of COPD is suspected but not reported, screening questions can help determine an individual's likelihood of having the disease. Smoking is the single greatest risk factor for developing COPD, with > 70% of COPD cases developing in current or former smokers,[24] and a history of smoking > 40 pack-years has a likelihood ratio of 8.3 for the diagnosis. In someone without a prior diagnosis, age ≥ 45 years has a likelihood ratio of 1.3 for COPD.[25] Other pertinent historical features that increase the probability of COPD include a history of asthma, many childhood respiratory tract infections, alpha-1 antitrypsin deficiency, and chronic exposures to heating fuels, toxins, dusts, industrial chemicals, wood smoke, or smog.[24] Having a high index of suspicion for COPD can subsequently assist

in directing the clinical care to the underlying etiology for the acute respiratory distress.

History that may help identify triggers for exacerbation and determine the illness severity of the current ED presentation include: noncompliance with or recent changes to COPD medication regimen, cold-like symptoms, dyspnea, cough, and FEV_1/FVC ratio to confirm obstruction. In addition, ascertaining whether the patient had any recent medical care (eg, ED visits, hospital admissions, acute therapies) or history of prior COPD exacerbations, including their frequency and severity, will help to identify the presence and severity of a current acute exacerbation. According to a bronchoscopic study of 40 patients, a self-report of purulent sputum production significantly increased the likelihood (odds ratio, 27) of bacterial infection of the lower airways.[26] The type and quantity of sputum production can vary according to each patient, but those characteristics are highly consistent with a COPD exacerbation.[27]

Physical Examination

Along with the clinical history, the physical examination findings in COPD patients contribute to the emergency clinician's ability to diagnose COPD, assess its chronicity, determine its severity, identify alternate disease processes, and evaluate a patient's response to therapy. Vital sign abnormalities will invariably include tachypnea, tachycardia, and hypoxia, with or without fever. Pulse oximetry is useful for monitoring supplemental oxygen needs, with the goal of maintaining saturation at 88% to 92%.[28] The patient's respiratory rate, in addition to physical examination findings, may indicate impending respiratory failure, while hemodynamic instability designates an increased severity of illness.[4]

Physical examination findings vary with severity and can be divided into those that are present in chronic, severe disease and those that may be more suggestive of an acute exacerbation. Patients with chronic, severe COPD will likely demonstrate pursed-lip breathing, barrel chest, decreased chest expansion, hyperresonance, and cachexia, the most ominous prognostic sign.[29] While not commonly checked or documented, a thoracic index ≥ 0.9[30] (anteroposterior diameter of the thorax divided by the transverse diameter) and excavated supraclavicular fossae[31] may also be present. Physical examination findings that suggest a likely acute exacerbation of COPD include accessory muscle use,[31,32] prolonged expiratory time from baseline,[30,33-36] asymmetric lung sounds, auscultated wheezing, respiratory alternans (paradoxical rib cage and abdomen motion thought to alternate the respiratory load between the inspiratory muscles of the chest and the diaphragm to prevent fatigue), cyanosis, and neck-vein distention during expiration.[37]

Diagnostic Studies

Although the diagnosis of an AECOPD is made clinically, several diagnostic tests are available to evaluate for precipitating disorders, such as an infectious process, and to exclude other conditions with similar presentations. **(See Table 3.)**

Laboratory Testing and Arterial Blood Gas Sampling

A complete blood cell count may identify polycythemia, leukocytosis, or bandemia. Serum drug concentrations can be considered if clinically applicable (such as if the patient is taking theophylline). Serum electrolytes and arterial blood gas sampling in moderate-to-severe cases of COPD exacerbation allow for the determination of the acid-base status. Comparison to prior laboratory measurements of baseline bicarbonate and arterial partial pressure of carbon dioxide ($PaCO_2$) levels can assist in evaluating the acuity of the respiratory distress. If the pH is normal and the $PaCO_2$ is elevated, then the CO_2 retention can be considered chronic.[3] Patients with severe COPD exacerbations may have an acute respiratory acidosis; however, decisions on any intervention must take the clinical status into account and not rely solely on laboratory values.

Table 3. Summary of Diagnostic Testing in Patients With Acute Exacerbation of COPD

- All patients should have pulse oximetry checked to determine the need and response to oxygen therapy
- Most patients with an acute exacerbation of COPD are recommended to have the following tests:
  - Complete blood cell count, serum electrolytes, and renal and liver function tests
  - Chest x-ray to evaluate for infiltrates, lung masses, pneumothoraces, and pulmonary edema
  - Electrocardiogram to assess for arrhythmia and cardiac ischemia
- Patients can be considered for the following tests:
  - Arterial blood gas sampling to determine severity of acute respiratory distress and acid-base status
  - Serum troponin in select situations concerning for acute coronary syndromes
  - Serum BNP or NT-proBNP to assess for decompensated heart failure
  - Sputum Gram stain and culture in patients who have developed respiratory failure, have risk factors for drug-resistant organisms, or have not responded to antibiotics
  - Respiratory viral panel (depending on the time of year)
  - Focused ultrasonography of the heart, lungs, and deep veins

Abbreviations: BNP, b-type natriuretic peptide; COPD, chronic obstructive pulmonary disease; NT-proBNP, N-terminal pro b-type natriuretic peptide.

Obtaining an arterial blood gas sample, complete blood cell count, serum electrolytes, and renal and liver function tests is recommended in patients who require hospitalization or have developed respiratory failure.[3] A study comparing venous to arterial blood gas analysis found good agreement between arterial and venous measures of pH and bicarbonate; however, the $PaCO_2$ values varied by approximately 6 mm Hg.[38] Another study found that a venous partial pressure of carbon dioxide ($PvCO_2$) < 45 mm Hg has a high negative predictive value for arterial hypercapnia.[39] Thus, a venous blood gas sample is reasonable in less severe exacerbations, but an arterial blood gas analysis is still recommended in patients with hypoxemic respiratory failure or patients requiring mechanical ventilation to assess the degree of hypercapnia and/or hypoxemia and the response to treatment.

In these more-ill patients, a $PaCO_2$, along with serum albumin and urea, was used in a clinical algorithm to risk stratify AECOPD admissions into 5 groups of inpatient mortality, ranging from 3% to 23.4%. The highest-risk group had elevated serum urea > 20.6 mg/dL and $PaCO_2$ > 48.4 mm Hg, with normal serum albumin > 3.7 g/dL.[40]

Chest Imaging

At a minimum, a chest radiograph is recommended in patients who require hospitalization or have developed respiratory failure, as it can be used to exclude alternative diagnoses. Typical radiographic findings that can be associated with COPD include over-inflation, flattening of the hemidiaphragms, increased retrosternal air space, bullae, and saber-sheath trachea (an increase in the posterior diameter but narrowing of the lateral diameter).[41] **(See Figure 1.)** While the chest radiograph may show evidence of obstructive lung disease, it is not specific enough to diagnose COPD, as this is still a diagnosis made by history, physical examination, and pulmonary function tests. Computed tomographic (CT) imaging can be performed in selected patients who present with atypical presentations or who have a high probability of pulmonary embolism.

Nevertheless, patients presenting with AECOPD can have incidental radiographic abnormalities including infiltrates, lung masses, pneumothoraces, and pulmonary edema up to one-fourth of the time;[42] thus, studies evaluating the use of selective criteria for obtaining chest radiographs in AECOPD to minimize their use have been unsuccessful.[43,44]

Figure 1. Saber-Sheath Trachea on Computed Tomography

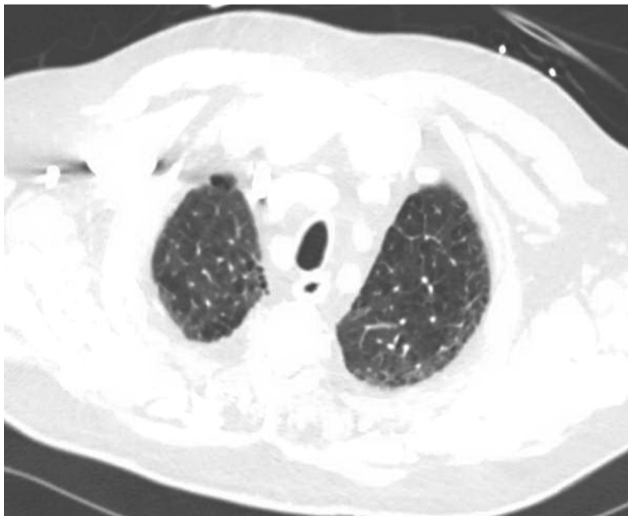
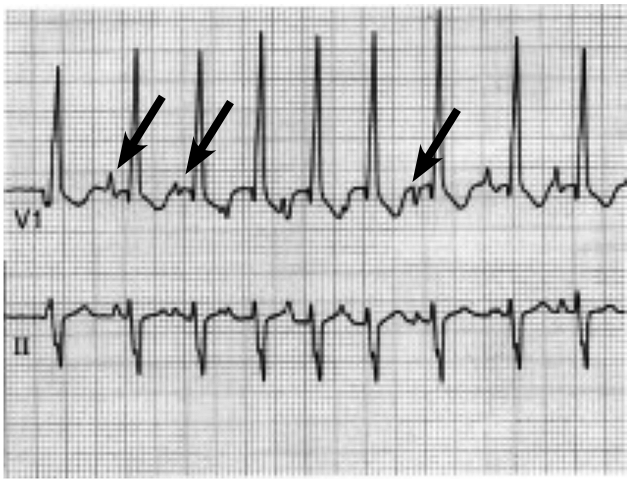


Image courtesy of University of Maryland Medical Center.

Electrocardiogram

An electrocardiogram (ECG) is recommended in patients who present with possible COPD exacerbation, mainly to evaluate for coexisting cardiac problems. About 20% of patients with COPD have a diagnosed cardiovascular comorbidity, and the same percentage of COPD exacerbations are precipitated by acute decompensated heart failure or cardiac arrhythmias.[45] Arrhythmias associated with COPD severity include atrial fibrillation/flutter, nonsustained ventricular tachycardia, and sustained ventricular tachycardia. Multifocal atrial tachycardia, an irregular rhythm with at least 3 distinct P-wave morphologies, is almost exclusively associated with COPD.[46] **(See Figure 2 and Table 4, page 7.)**

Figure 2. Electrocardiogram of Multifocal Atrial Tachycardia



Arrows point out multiple P-wave configurations consistent with multifocal atrial tachycardia.

Reprinted from *Chest*, Volume 113, Issue 1. James McCord, Steven Borzak. Multifocal atrial tachycardia. Pages 203-209. Copyright 1998, with permission from Elsevier.

There are a variety of ECG abnormalities related to COPD. **(See Table 5 and Figure 3.)** The ECG changes may be attributed to associated pulmonary hypertension, hyperinflation causing a shift in the heart's position within the chest, and right ventricular hypertrophy leading to a clockwise rotation of the electrical axis of the heart.[47]

Serum Cardiac Biomarkers

Ischemic changes (Q or QS pattern, ST-segment depression, and T-wave inversions), elevated troponin levels, and chest discomfort are common in patients with COPD, making it difficult to distinguish whether or not acute coronary syndromes (ACS) are present. A systematic review found elevated cardiac troponin levels in 18% to 73% of patients with an AECOPD, and elevated levels were associated with an increased risk for all-cause mortality.[50]

B-type natriuretic peptides (BNP) are released in response to cardiac wall stretch from either volume or pressure overload. Serum BNP and N-terminal pro b-type natriuretic (NT-proBNP) concentrations are often elevated during AECOPD and also predict poor short-term outcomes.[45] A recent systematic review that included 7 studies demonstrated that elevated levels are associated with left ventricular dysfunction in patients with COPD.[51]

Decisions to obtain cardiac biomarkers and how to interpret them need to be made on an individual basis, and abnormal findings taken within the clinical context, including the patient's cardiac risk factors and results of other testing. There are no guidelines that help identify in whom to obtain cardiac biomarkers in this patient population.

Microbiologic Evaluation

The presence of purulent sputum during an exacerbation is sufficient to start treatment with antibiotics; however, if the patient does not respond to the initial treatment, then a sputum culture with sensitivities should be performed.[4] Sputum culture is also recommended in patients with respiratory failure or those who have recently been on antibiotics.[3] One of the main limitations of sputum testing is a patient's inability to expectorate.

Approximately 50% of COPD exacerbations are caused by bacterial infection. The most common bacterial pathogens in COPD are *Haemophilus influenzae, Streptococcus pneumoniae,* and *Moraxella catarrhalis*.[52,53] Isolation of *Pseudomonas aeruginosa* is associated with a greater severity of COPD, particularly in patients with an $FEV_1 < 1$ L.[54,55] However, patients may be chronically colonized with these pathogens; approximately 20% to 30% of patients with stable COPD have positive sputum cultures.[53] The results of a patient's prior sputum cultures can potentially assist with identifying the inciting organism and selecting antibiotics.

AECOPD can also be precipitated by viral infections. A meta-analysis showed that the weighted overall prevalence of respiratory viruses was 39.3% in patients with AECOPD and 13.6% in patients with stable COPD.[56] The most common types of respiratory viruses, in descending order, are rhinovirus, respiratory syncytial virus, and influenza.[56,57] Thus, a respiratory viral panel should be considered as part of the microbiologic evaluation, especially since medications are available to treat influenza. Most respiratory viruses tend to occur in the winter, but rhinovirus circulates mainly in the autumn and spring.[57]

Table 4. Arrhythmias Related to COPD

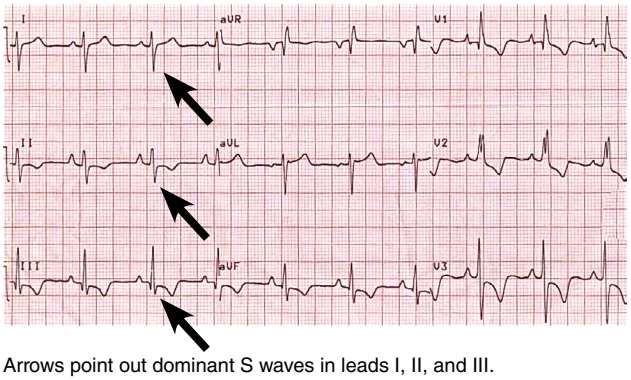
- Atrial fibrillation
- Atrial flutter
- Nonsustained ventricular tachycardia
- Sustained ventricular tachycardia
- Multifocal atrial tachycardia

Table 5. Electrocardiogram Abnormalities Related to COPD

- Right atrial enlargement ("P pulmonale," P wave ≥ 0.25 mV in extremity leads or > 0.15 mV in V_1)
- Vertical P-wave axis (P axis > 60°)
- Right ventricular hypertrophy
- Right or left bundle branch block
- Right or left axis deviation[48,49]
- Low voltage in limb leads
- S1S2S3 pattern

Abbreviation: COPD, chronic obstructive pulmonary disease.

Figure 3. Electrocardiogram of Right Ventricular Hypertrophy



Arrows point out dominant S waves in leads I, II, and III.
Image used by permission of Dr. Johnson Francis by Creative Commons License Attribution 4.0 International.
Available at: https://cardiophile.org/ecg-quiz-28/

Point-of-Care Ultrasound

More emergency medicine physicians are using ultrasonography in their clinical practice since a minimum skill set was incorporated into residency training.[58] The bedside lung ultrasound in emergency (BLUE) protocol established typical ultrasonographic profiles for intensive care unit (ICU) patients with diagnoses of pulmonary edema, COPD or asthma, pulmonary embolism, pneumothorax, and pneumonia based on ultrasonography of the heart, lungs, and deep veins. The thoracic ultrasound included evaluation of A or B lines, lung sliding, and alveolar consolidation and/or pleural effusion. Predominant A lines plus lung sliding indicated, with high sensitivity and specificity, a diagnosis of asthma or COPD. If this profile was seen in addition to a deep venous thrombosis, then it was suggestive of pulmonary embolism. Multiple anterior diffuse B lines with lung sliding was consistent with pulmonary edema, whereas pneumothorax was identified by absent lung sliding with the presence of A lines and lung point. One study found that use of these profiles in patients admitted to the ICU with acute respiratory failure would have provided the correct diagnosis in 90.5% of cases.[59]

A prospective study of 130 patients evaluated the use of cardiopulmonary ultrasound performed by emergency clinicians in patients presenting to the ED with acute dyspnea. Cardiopulmonary ultrasound had a diagnostic accuracy of 90% for acute left-sided heart failure, 86% for pneumonia or pleural effusion, and 95% for decompensated COPD or asthma.[60] Focused cardiopulmonary ultrasonography with limited evaluation of the deep veins is fast (median time of 12 minutes), can identify acute life-threatening conditions in the ED, and expedites establishing the correct diagnosis.[61,62] A limited ultrasonography evaluation can be considered as a supplement to the clinical assessment, depending on its availability and user competency. Limitations to widespread use are the determination of proficiency and high levels of concern about medicolegal liability.[63]

Other Tests

Spirometry is not recommended during an AECOPD because the results may be inaccurate and thus not useful for identifying obstructive ventilatory defects.[4] Using peak expiratory flow rates as a surrogate for FEV_1 in COPD patients has been shown to be unreliable.[64,65] If a patient has had a prior spirometry, it is helpful to understand how severe their obstruction was at baseline; however, it does not need to be repeated in the acute setting.

It is difficult to determine when to evaluate for venous thromboembolism as another cause of dyspnea in patients presenting with presumed AECOPD. The prevalence of pulmonary embolism in hospitalized patients with AECOPD was 24.7%, in one systematic review. In addition, 2 of the included studies did not find any significant differences in symptoms of dyspnea, chest pain, hemoptysis, cough, or palpitations between patients with and without pulmonary embolism.[66] Another recent systematic review that included 880 patients found that patients with unexplained AECOPD who presented with pleuritic chest pain and signs of heart failure and no identified infectious etiology were more frequently found to have a pulmonary embolism. Patients found to have both AECOPD and pulmonary embolism had increased mortality and hospital length of stay.[67] There are no guidelines to suggest when to pursue venous thromboembolism evaluation in patients presenting with AECOPD, and such decisions will need to be made on an individual basis. If an assessment is needed, then the standard diagnostic and treatment algorithms would apply.

Treatment

Supplemental Oxygen

A 2010 prospective randomized trial of 405 patients with AECOPD evaluated the use of nontitrated 6 to 10 L/min supplemental oxygen versus supplemental oxygen titrated to an SpO_2 goal of 88% to 92% in the prehospital and ED setting. The authors observed a 9% versus 4% inhospital mortality for the higher-flow groups versus the titrated-supplemental-oxygen groups, respectively. There was no statistically significant difference between groups regarding SpO_2 at presentation or baseline FEV_1.[28] However, hypoxia may not improve with low-flow oxygen supplementation via nasal cannula when a patient's minute ventilation is significantly greater than the typical 2 to 6 L/min of oxygen supplementation. When this occurs, other devices such as face masks or nonrebreather masks that are capable of delivering oxygen at effectively higher concentrations may be used. Arterial oxygen saturation goals do not differ between supplemental oxygen modalities.

Recent guidelines agree that oxygen supplementation should target an arterial saturation of 88% to 92%. They also recommend pH monitoring to ensure adequate ventilation during ongoing oxygen supplementation. Specifically, GOLD guidelines suggest that pH monitoring should be done within 30 to 60 minutes after the initiation of supplemental oxygen.[68] Oxygen-induced hypercapnia in the setting of AECOPD has long been a concern in the ED. Several proposed mechanisms, including reversal of hypoxic pulmonary vasoconstriction as well as increased dead space with ventilation-perfusion redistribution contribute to this. While these physiologic changes may occur with exposure to high oxygen in acute hypercapnia, at the bedside, it is a rare manifestation of supplemental oxygen, with current standards of care targeting the relatively lower SpO_2 goals noted above.[69]

Bronchodilators

Bronchodilators, including anticholinergics and beta-2 agonists, are a mainstay of the management of AECOPD. Currently, most commonly used medications include inhaled and/or nebulized albuterol with or without ipratropium bromide. Albuterol (a beta-2 agonist) stimulates cyclic adenosine 3′,5′-monophosphate (cAMP), resulting in airway smooth-muscle relaxation. Inhaled ipratropium bromide (an anticholinergic agent derived from atropine) demonstrates limited systemic absorption, thereby maintaining its bronchodilatory and antisecretory effects while minimizing systemic anticholinergic symptoms. Both agents have an onset of action within minutes, although peak effect is slower for ipratropium bromide (at least 60 minutes) compared to that of albuterol (30-60 minutes).

The side-effect profiles for these drugs are quite favorable.[70,71] Albuterol has been associated with hypokalemia, tremulousness, tachycardia, or tachyarrhythmias, and on rare occasion, lactic acidosis (type B) as well as transient worsening of the ventilation-perfusion mismatch, with decreased oxygenation. Anticholinergic agents such as ipratropium bromide, due to low systemic absorption, tend to have minimal side effects. When present, they include urinary retention, tremulousness, and dry mouth. An important side effect of anticholinergic agents noted in a previous review includes inducing mydriasis when in contact with the eye (eg, from the vapor of nebulized ipratropium). This may precipitate acute angle-closure glaucoma in susceptible patients or, in the unconscious patient, mislead the care team into suspecting other acute intracranial pathologies.[72]

Head-to-head studies, including a more recent meta-analysis, of these 2 classes of bronchodilators have not demonstrated clinical superiority of one class over the other in AECOPD. Combination therapy has also not demonstrated improved pulmonary function (specifically FEV_1) in the acute setting compared to monotherapy with either drug.[73] Older data also suggest no difference in clinical outcomes between inhaled use with a spacer and nebulized administration of these agents, and no recently published data have challenged this.[74-76]

Severely ill or frail patients are less likely to use metered-dose inhalers properly and nebulized administration of bronchodilators is probably more effective in these circumstances.

Data on the ideal frequency (continuous versus frequent intermittent dosing) of bronchodilators in AECOPD are also lacking. Unfortunately, there is a paucity of guidance from current consensus statements on the subject. Commonly prescribed starting doses of nebulized bronchodilators include albuterol 2.5 mg and ipratropium bromide 0.5 mg (2.5 mL). Continuous administration of bronchodilators is reasonable if symptoms persist despite frequent intermittent doses. Ultimately, decisions regarding the choice of bronchodilators, frequency, and route of drug delivery for the treatment of AECOPD should take into consideration the patient's symptoms, institutional cost, ease of administration, as well as timely availability of necessary resources for treatment and monitoring.

Corticosteroids

Classically, COPD and the inflammatory pathways involved in its pathophysiology have been thought of as inherently corticosteroid-resistant, compared to asthma.[77,78] Nonetheless, systemic corticosteroids have become a mainstay of therapy in the treatment of AECOPD and are associated with a number of therapeutic benefits, including enhanced bronchodilator response (eg, improvement in FEV_1 and PaO_2), reduced need for admission from the ED, reduced treatment failure when discharged from the ED, and shorter hospital length of stay when admitted.[79-83]

Treatment is certainly not without risk, however, as the side-effect profile of systemic corticosteroids is quite extensive. Short-term exposure lends itself to certain side effects including leukocytosis (due to peripheral neutrophil demargination), hyperglycemia, restlessness, and acute psychosis. Medium- to long-term exposure carries additional inherent risks, such as Cushingoid features, hypernatremia, hypertension, hyperlipidemia, myopathy, diabetes, glaucoma, skin thinning, easy bruising and bleeding, glaucoma, osteoporosis, immunosuppression, and adrenal insufficiency.[83]

The dosage, route of administration, and duration of treatment of corticosteroids continue to be debated. Previous research suggests that oral administration of corticosteroids is noninferior to IV administration in the acute setting and, therefore, in patients who can tolerate it, oral corticosteroid use is appropriate.[84] Most studies agree that treatment with relatively lower doses for shorter periods of time appears to offer therapeutic benefit similar to longer courses of higher doses, while reducing total cumulative doses.[82] This was recently emphasized in the REDUCE trial, which showed that, in patients who presented to the ED for AECOPD (the majority of whom were admitted), 40 mg oral prednisone daily for 5 days compared to 14 days of treatment demonstrated no significant difference in time to re-exacerbation, death, or recovery of lung function.[85]

Consensus guidelines that pre-date the REDUCE trial recommended 30 to 40 mg oral prednisone daily for 10 days.[3,68,86] Given recent trial data, however, the most recent GOLD guidelines recommend 40 mg oral prednisone daily for 5 days.[4] It is notable that critically ill patients requiring mechanical ventilation have not been studied as a specific group, and higher doses with longer courses of therapy are commonly prescribed in this demographic, with limited data to support this

practice. In addition, IV corticosteroids are often administered in critically ill patients when enteral administration cannot be performed or is not available. Some commonly used IV corticosteroids (and their dose equivalence to prednisone 40 mg) are: methylprednisolone (32 mg), dexamethasone (6 mg), and hydrocortisone (160 mg).

Antibiotics

Historically, antimicrobial coverage in AECOPD has been tailored to treat commonly implicated community-acquired pathogens, including *S pneumoniae, M catarrhalis,* and *H influenzae*. In critically ill patients with AECOPD, methicillin-resistant *Staphylococcus aureus* (MRSA), *P aeruginosa, Stenotrophomonas maltophilia,* and *Acinetobacter baumannii* have been cultured, and antimicrobial coverage is often tailored accordingly.[87]

Despite the common use of antibiotics in the treatment of AECOPD, the data supporting this practice are quite varied. A large systematic review and meta-analysis published in 2008, incorporating evidence from 11 studies and over 1000 patients, concluded that antibiotic use in hospitalized patients with AECOPD reduced rates of treatment failure and inhospital mortality. Interestingly, these same benefits were not observed in the ambulatory setting.[88] A similar analysis was performed in 2012 incorporating more recent data by Cochrane Airways (www.airways.cochrane.org). They analyzed data from 16 trials with over 2000 patients across the spectrum of severity of AECOPD and concluded that the strongest evidence for antibiotic use in AECOPD existed for patients admitted to the ICU.[89] Most recently, a 2013 study reviewed 53,900 AECOPD admissions to 410 hospitals. Their results suggested that the addition of antibiotics to a treatment regimen including systemic corticosteroids demonstrated reduced inhospital mortality and 30-day readmission rates.[90]

Consensus statements from major organizations do not appear to limit recommendations to the inpatient setting; instead, their language is focused on symptom severity. GOLD guidelines support antibiotic use for patients with increased dyspnea, sputum volume, and sputum purulence, or in patients who have at least 2 of those 3 symptoms, if increased sputum purulence is 1 of the 2 symptoms. They also support the use of antibiotics in all patients who require mechanical ventilation for AECOPD. While evidence remains limited, they currently recommend a duration of antibiotic therapy of 5 to 7 days.[68] ATS/ERS guidelines state that antibiotics "…may be initiated in patients with altered sputum characteristics" in the outpatient setting and may include cephalosporins, doxycycline, macrolides, or cefdinir.

Suggested antibiotics for inpatient management of AECOPD include amoxicillin/clavulanate, respiratory fluoroquinolones (eg, levofloxacin, moxifloxacin), or broader therapies if *P aeruginosa* or other more resistant organisms are suspected.[3] In the critically ill patient with AECOPD, we suggest that antibiotic treatment covers MRSA, as community-acquired MRSA has become more commonplace in recent years. If available, institutional antibiograms should be consulted to determine the optimal antibiotic therapy based on local resistance patterns. **(See Table 6.)**

The ideal duration of antimicrobial therapy for the treatment of AECOPD remains unclear. Most literature focuses on the use of antibiotics in addition to the usual treatment regimen. Few data exist on the comparison of treatment durations and their effect on clinical outcomes. The GOLD guidelines recommendation of 5 to 7 days of treatment is graded as Evidence Level B, and is consistent with other published guidelines on the subject.[68] Most of the literature cited previously utilized antibiotic treatment durations approximating 7 days; thus, a recommendation of 5 to 10 days of therapy seems appropriate.

Magnesium Sulfate

The use of magnesium sulfate and literature surrounding its modest efficacy stem from its role in the treatment of moderate-to-severe asthma exacerbations. Its safety profile for that use has likely contributed to its extrapolated use by emergency clinicians for AECOPD, for which there is a paucity of data. One study in 2006 examined the impact of 1.5 g IV magnesium sulfate on FEV_1 in the setting of AECOPD in the ED. The authors observed no direct bronchodilatory effect after magnesium sulfate administration alone, but did note an improved

Table 6. Antibiotics to Consider for the Treatment of Acute Exacerbation of COPD[3]

- Outpatient management:
  - Cefdinir: 300 mg by mouth twice daily[a,b] ***or***
  - Doxycycline: 100 mg by mouth twice daily ***or***
  - Azithromycin: 500 mg by mouth daily x 1, ***then*** 250 mg by mouth daily
- Inpatient management
  - Amoxicillin/clavulanate: 875 mg/125 mg extended release by mouth twice daily[a] ***or***
  - Levofloxacin 750 mg by mouth (or IV) daily[a] ***or***
  - Moxifloxacin 400 mg by mouth ***and***
  - Vancomycin[a] or linezolid: dosing should be determined after discussion with pharmacist[c]

[a]Requires dose adjustment for renal impairment.
[b]Alternatives include cefuroxime or cefprozil.
[c]Typically reserved for severe exacerbations requiring intensive care unit admission.

bronchodilatory response when given in conjunction with beta-agonists. Unfortunately, clinical outcomes were not measured in this small study (n = 24).[91] In 2013, a group from New Zealand examined the efficacy of inhaled magnesium sulfate in addition to nebulized beta-agonist and anticholinergic treatments in 161 ED patients with AECOPD. There was no statistical difference in the improvement of FEV_1 in the treatment group compared with placebo.[92]

Consensus guidelines do not address the use of magnesium sulfate in the treatment of AECOPD. Data are scarce, and the quality of existing studies varies in quality. Therefore, the role of magnesium sulfate in the setting of AECOPD remains uncertain. It is our practice to limit the use of magnesium sulfate to asthma exacerbations, and we do not incorporate this treatment into the usual care provided to patients with AECOPD.

Methylxanthines

A 2008 review on COPD in this publication noted the outdated nature of the use of methylxanthines for AECOPD. Without new published data on its effect on clinical outcomes, recommendations have not changed. ATS/ERS guidelines on the management of AECOPD do not comment on methylxanthine therapy. GOLD guidelines state, "intravenous methylxanthines are only to be used in selected cases when there is insufficient response to short-acting bronchodilators," yet literature from the late 1980s to early 1990s is cited, half of which is focused on ambulatory patients with stable disease.[68] It is our opinion that methylxanthines do not play a meaningful role in acute management of AECOPD.

Noninvasive Positive-Pressure Ventilation

NIPPV has been a mainstay of therapy for AECOPD in the ED setting for years. It can be supplied as continuous positive airway pressure (CPAP) or as bilevel positive airway pressure (BiPAP), with a higher inspiratory than expiratory pressure. In most circumstances, BiPAP is utilized for patients with AECOPD because the driving pressure (difference between inspiratory PAP and expiratory PAP) assists with their ventilatory needs and work of breathing. The expiratory PAP is thought to improve gas exchange and dead space by splinting open distal airways. **See Table 7** for NIPPV exclusion criteria and indications for intubation.

GOLD guidelines recommend a trial of NIPPV for patients meeting either of the following criteria: (1) respiratory acidosis (arterial pH < 7.35 or $PaCO_2$ > 45 mm Hg), and/or (2) severe dyspnea with clinical signs suggestive of respiratory muscle fatigue or increased work of breathing.[68] A Cochrane review originally published in 2004 and updated in 2009 concluded that the use of NIPPV as first-line treatment for AECOPD is associated with decreased need for intubation (relative risk [RR], 0.41; 95% confidence interval [CI], 0.33-0.53), shorter hospital length of stay (-3.24 days; 95% CI, -4.42 to -2.06), and mortality (RR, 0.52; 95% CI, 0.35-0.76).[93] While no major guidelines recommend specific settings for initiation of NIPPV, we recommend to start with an inspiratory positive airway pressure (IPAP) of at least 5 cm H_2O greater than the expiratory pressure (commonly started at 8 cm H_2O or less), and to titrate the IPAP in increments of 5 cm H_2O every few minutes over the first hour to a goal of decreased work of breathing and patient comfort. Regular repeat observations of the patient should be made during this initial phase to ensure clinical stability.

In 2005, Merlani et al performed a retrospective analysis of 104 patients placed on NIPPV for AECOPD in the ED. An arterial pH of ≤ 7.35 or a respiratory rate ≥ 20 breaths/min (OR, 3.51; 95% CI, 1.29-9.62; and OR, 1.13-11.20, respectively) after 1 hour of NIPPV were the strongest predictors of treatment failure, defined as subsequent intubation.[94] For more information about NIPPV, see the February 2017 issue of *Emergency Medicine Practice*, "Noninvasive Ventilation for Patients in Acute Respiratory Distress: An Update," available at www.ebmedicine.net/NIPPV.

Mechanical Ventilation

Once the decision is made to intubate, the method of intubation and pharmacologic therapy used should be chosen based upon availability and clinician experience with a given regimen or method.

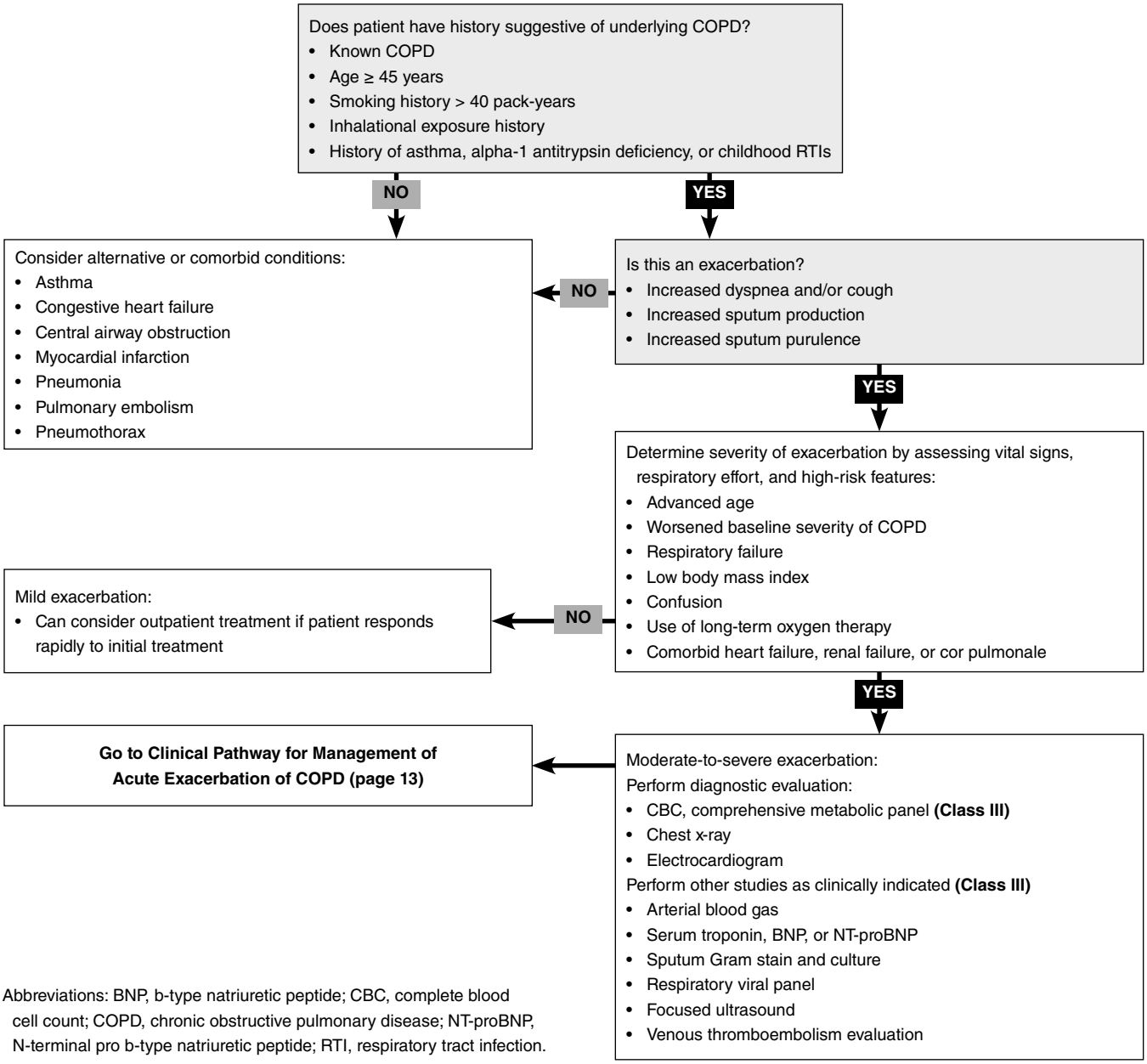
Literature on the use of ketamine in the setting of hypercapnic respiratory failure secondary to status asthmaticus has been extrapolated to patients with AECOPD. Its proposed mechanism is the antimuscarinic effect that may provide some bronchodilatory relief; however, there are no well-designed studies supporting its use in AECOPD, and at this time, there is no definitive recommendation on its use in AECOPD.[95-98]

Intubated patients with AECOPD require attention to ventilator settings in order to avoid breath-

Table 7. Exclusion Criteria for Noninvasive Positive-Pressure Ventilation and Indications for Intubation

- Inability to tolerate a tightly sealed face mask
  - Discomfort
  - Craniofacial abnormalities (eg, trauma, burns, etc)
  - Significant air leak
- Inability to protect airway or coordinate breathing with ventilator
  - Depressed mentation
  - Hemodynamic instability
  - Vomiting or Inability to clear secretions
  - Apnea or respiratory arrest
- Recent gastrointestinal surgery (due to risk of aerophagia)

Clinical Pathway for Diagnostic Evaluation of Acute Exacerbation of COPD



Abbreviations: BNP, b-type natriuretic peptide; CBC, complete blood cell count; COPD, chronic obstructive pulmonary disease; NT-proBNP, N-terminal pro b-type natriuretic peptide; RTI, respiratory tract infection.

Class Of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

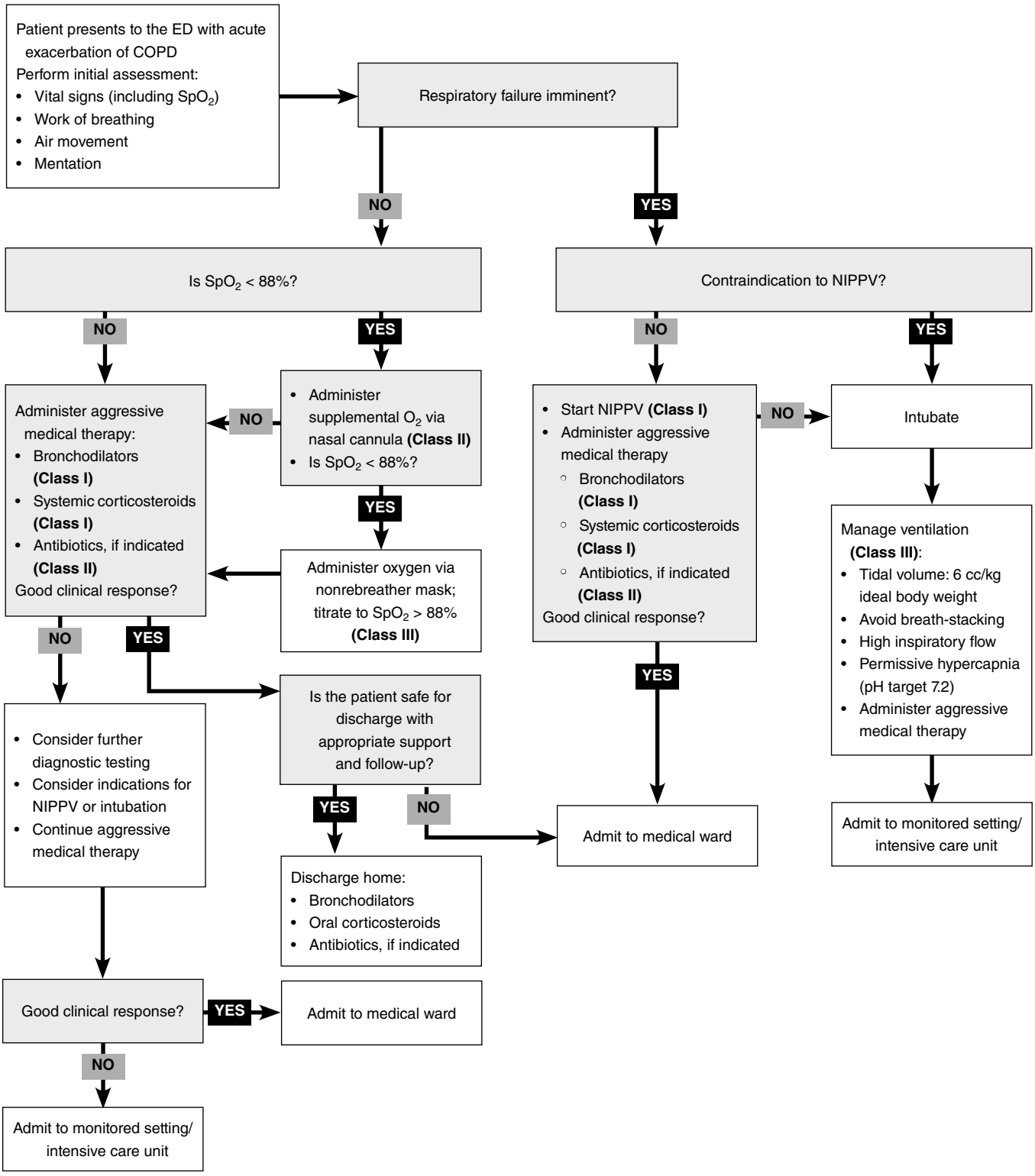
Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Clinical Pathway for Management of Acute Exacerbation of COPD



Abbreviations: COPD, chronic obstructive pulmonary disease; NIPPV, noninvasive positive-pressure ventilation; SpO_2, oxygen saturation measured by pulse oximetry.

For Class of Evidence Definitions, see page 12.

stacking and consequent dynamic hyperinflation. Resulting acute pulmonary barotrauma or volutrauma and high intrathoracic pressures may acutely decrease cardiac preload, leading to hemodynamic collapse. Thus, in the immediate postintubation setting, attention must focus on the respiratory rate, tidal volume, I:E ratio (inspiratory time to expiratory time), and airway resistance to allow for complete exhalation of a given breath in order to avoid hypotension and circulatory collapse.[99] Some centers are gaining experience avoiding intubation for severe COPD exacerbations with the use of extracorporeal CO_2 removal; however, further research is needed in this area.[100]

It has become common practice to allow for some measure of "permissive hypercapnia;" however, there is variability in the degree of acidemia tolerated. There is no consensus on the lower limit of an acceptable pH, and guidelines on the matter offer no meaningful direction. We recommend targeting an arterial pH of 7.2, offering the ability to maintain adequate ventilatory support while avoiding dynamic hyperinflation in the majority of patients. **(See Table 8.)**

Lastly, aggressive medical treatments (ie, frequent; initially, even hourly) with bronchodilator administration, as well as administration of systemic corticosteroids and antibiotics, if indicated, should be continued after intubation to promote secretion clearance, bronchodilation, and to minimize the need for ongoing mechanical ventilation. Adequate analgesia and sedation are important aspects of postintubation care and cannot be emphasized enough. These should be addressed to ensure patient synchrony with the ventilator. For more information on ventilator management in the ED, see the September 2014 issue of *EM Critical Care*, "Ventilator Management and Troubleshooting in the Emergency Department," at www.ebmedicine.net/ventmanagement.

Table 8. Ventilator Setting Recommendations Post Intubation

- Tidal volumes of 6 cc/kg ideal body weight*
- Respiratory rate of 8-12 breaths/min (higher if expiratory flows allow) to minimize breath-stacking or auto-PEEP
- High inspiratory flows to allow for longer expiratory time per breath cycle
- Adjustments to minute ventilation to target an arterial pH of 7.2
- FiO_2 should be adjusted to target SpO_2 > 88%-92%

*May be achieved by a pressure-controlled or volume-controlled mode of ventilation. We prefer a volume-controlled mode to ensure a targeted minute ventilation, at least initially, in these patients.

Abbreviations: FiO_2, fraction of inspired oxygen; PEEP, positive end-expiratory pressure; SpO_2, oxygen saturation measured by pulse oximetry.

High-Flow Nasal Cannula

There are no guidelines that discuss the use of high-flow nasal cannula devices, which can offer gas flow rates up to 60 L/min in the setting of AECOPD. While it is postulated that these devices probably better meet the oxygenation needs of the hypercapnic patient, match their respiratory demands (either objectively or subjectively) with high flow rates, and provide a minimal amount of positive end-expiratory pressure, the role for high-flow nasal cannula in the setting of AECOPD or hypercapnic respiratory failure has not yet been demonstrated in clinical studies. For now, these devices are more appropriately utilized for acute hypoxic respiratory failure. Therapy with high-flow nasal cannula will likely be addressed in future studies.

Controversies and Cutting Edge

Biomarkers

While current recommendations include antibiotic therapy for 5 to 10 days for severe exacerbations requiring intubation, not all patients should be treated in this manner. A recent Danish study of COPD patients determined that point-of-care procalcitonin-guided antibiotic therapy could substantially reduce the overall use of antibiotics among patients hospitalized for AECOPD without increasing harm. While biomarkers are not yet considered standard of care, there is increasing research suggesting that they can help guide therapy and identify patients that may require noninvasive ventilation and/or have a more difficult hospital course.[101]

Heliox

Heliox is a gas mixture of 79% helium and 21% oxygen, resulting in a density that is nearly 6 times lower than atmospheric air and allows improved airflow. It has a strong safety profile and has been studied for various applications. In obstructive lung disease, its use in asthma has been studied extensively; however, it was not until the late 1990s that multiple randomized controlled trials investigated the use of heliox in COPD patients.[102-105] The data demonstrate that heliox, when added to NIPPV, decreases respiratory effort and intrinsic positive end-expiratory pressure, but does not alter or improve clinical outcomes in acute exacerbations. While relatively safe, caution should be exercised in patients with high oxygen requirements, as they may not tolerate this gas mixture. The authors of this review do not typically use heliox in their practice for patients with AECOPD.

Capnography

Measuring the partial pressure of CO_2 in exhaled breath over time and depicting it in graphical form as a capnogram has been increasingly incorporated

into clinical practice over the last decade. Most commonly, we use end-tidal carbon dioxide ($EtCO_2$) monitoring in intubated patients to determine adequacy of ventilation, confirm endotracheal tube placement, and gauge effectiveness of resuscitation efforts in cardiac arrest. Recently, using capnograms from normal subjects, COPD patients, and congestive heart failure patients, automated quantitative analysis was shown to be capable of discriminating between COPD and congestive heart failure—a tool that would be highly useful in the ED.[106] Additionally, the shape of the capnogram can help diagnose obstructive lung disease. The expiratory flow is impaired, and there is an upward slope in the alveolar plateau.[72] **(See Figure 4.)**

If capnography is used to monitor treatment effect and clinical status, $EtCO_2$ must be correlated with $PaCO_2$ from an arterial blood gas measurement, as the gradient between these values may widen the more severe the lung disease is.

Disposition

Outpatient Versus Inpatient Care

There is wide heterogeneity in studies evaluating poor prognostic factors, with a variety of measures, outcomes, and settings assessed. Both short- and long-term outcomes have been evaluated and vary from inhospital morbidity and mortality to patient-reported outcomes such as dyspnea to functional measurements eg, FEV_1 and 6-minute walk test.[107] Thus, it has been difficult to establish a clinical prediction rule for outpatient versus inpatient care. Advanced age, baseline severity of COPD, and the development of respiratory failure have consistently been shown to be prognostic factors of short-term mortality.[108-110] A meta-analysis that included 189,772 COPD patients to assess predictors of mortality identified several additional factors for both short- and long-term mortality.[111] **(See Table 9.)**

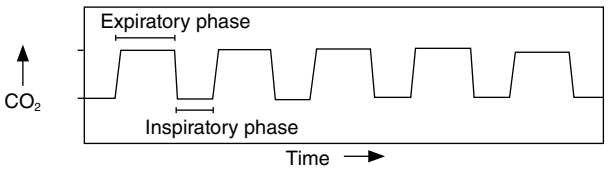
Some of these factors have been incorporated into clinical prediction rules to predict short-term mortality, including the Pneumonia Severity Index (PSI),[112] CURB65,[113] SOFA score,[114] and others.[115-119] Although some of these clinical prediction models have been prospectively validated, the patient population varied in the inclusion or exclusion of those with comorbidities. The models also have varying cut-offs for different risk categories; thus, there is no recommendation to use one clinical prediction rule over another. The decision to admit a patient should take into account the patient's social situation at home, level of support and functional status, and ability to follow up with a physician in a timely manner. The ATS/ERS and GOLD guidelines for hospital admission are shown in **Table 10, page 17**.

Management for Patients Going Home

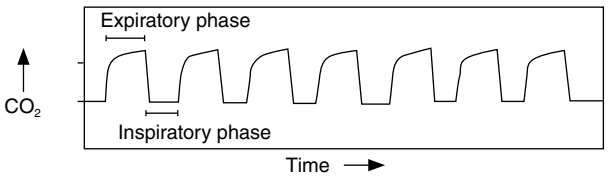
Patients treated as outpatients should receive patient education regarding inhaler techniques and the use of a spacer. Medical management for all patients includes short-acting inhaled beta-2 agonists, with or without short-acting anticholinergics, and a corticosteroid course, such as prednisone 40 mg daily for 5 days. Antibiotics are indicated for patients with a change in their sputum characteristics, and the choice of therapy should be based on local bacterial resistance patterns and the patient's prior culture data. Management should also focus on strategies to prevent further acute exacerbations.

Figure 4. End-Tidal Capnography Tracings[72]

Normal capnography tracing:



Capnography tracing in bronchospasm and obstruction. Note the blunted upslope at the beginning of exhalation due to expiratory airflow limitation:



Gruber P, Swadron S. The acute presentation of chronic obstructive pulmonary disease in the emergency department: a challenging oxymoron. *Emerg Med Pract.* 2008;10(11):1-28. © 2008 EB Medicine.

Table 9. Factors Associated With Risk of Death From COPD Exacerbation[111]

Factors for Short-term and Long-term Mortality
• Advanced age
• Low body mass index
• Cardiac failure
• Long-term oxygen therapy
Factors for Short-term Mortality
• Male sex
• Chronic renal failure
• Confusion
• Lower-limb edema
• GOLD criteria stage 4
• Cor pulmonale
• Acidemia
• Elevated plasma troponin level

Data taken from a meta-analysis of 37 studies (189,772 study subjects) of adults admitted to the hospital with COPD exacerbation.
Abbreviation: GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Risk Management Pitfalls in Managing Acute Exacerbation of COPD

1. **"But the patient said he has asthma."**
   Not all wheezing is asthma, and not all patient-reported histories of asthma are actually asthma. Ensure that the patient's risk factors and history align with the diagnosis.

2. **"I know she has COPD, but I doubt that's what's causing her respiratory distress."**
   Inadequately assessing triggers for AECOPD may lead you down an expensive and ultimately fruitless diagnostic path. A good history can increase efficiency, decrease costs, and most importantly, improve clinical outcomes.

3. **"This COPD patient's respiratory and hemodynamic statuses are simply not improving, despite doing everything by the book. What's going on?"**
   Largely due to the high systemic inflammatory state in individuals with COPD, patients presenting with an AECOPD have a surprisingly high incidence of pulmonary embolism. Be vigilant to ensure that the patient does not have a pulmonary embolism when he fails to respond as expected to the standard interventions for an AECOPD.

4. **"COPD is not possible – I don't hear any wheezing."**
   Although wheezing is often considered a hallmark of COPD, a lack of wheezing can actually signify a loss of effective airflow and can indicate imminent clinical deterioration.

5. **"His COPD exacerbation wasn't that bad – I didn't need to actually measure anything."**
   Much of the physical examination is inherently subjective, which may cause an underappreciation of the severity of a patient's AECOPD. A focused diagnostic assessment can identity poor prognostic markers.

6. **"We need to keep the oxygen saturation as high as possible to make sure that oxygenation remains stable."**
   Not only is there no benefit to maintaining an oxygen saturation in the high 90s in a patient with COPD, it may actually be harmful. Recent guidelines agree on an arterial saturation target of 88% to 92%.

7. **"She looks really sick; let's intubate to assist her breathing now."**
   Many patients can avoid endotracheal intubation with early implementation of NIPPV with bilevel positive airway pressure. Taking into account the absolute contraindications for NIPPV, consider a trial to assist breathing.

8. **"We need to provide high tidal volumes on the ventilator to blow down the CO_2!"**
   Despite a desire to increase minute ventilation to remove CO_2 in a COPD patient, excessive tidal volumes on the ventilator may actually injure the lungs.

9. **"I don't need to give any oral or IV corticosteroids because the patient is already on inhaled ones."**
   Although some systemic absorption of inhaled steroids can occur, it is insufficient to suppress the inflammatory process in the airways during an AECOPD. Therefore, oral or IV steroids are necessary for these circumstances.

10. **"There's no need to tell the patient to stop smoking because it's so obvious and, plus, there's nothing I can do to change that."**
    Smoking cessation can normalize the natural rate of decline in a person's lung function, even in a long-term smoker, and brief clinician advice about the need to stop smoking can actually increase the rate of cessation.

These include smoking cessation, influenza and pneumococcal vaccinations, and treating with long-acting inhaled bronchodilators with or without inhaled corticosteroids.[3,4,120]

Influenza vaccination has been shown to reduce all-cause mortality in COPD patients during influenza seasons.[121] Both the PCV13 and PPSV23 pneumococcal vaccines are recommended in adults aged ≥ 65 years. The PCV13 should be given first, followed by a dose of PPSV23 in 6 to 12 months in adults who have not previously received the pneumococcal vaccine or whose vaccination history is unknown. If a patient has already received the PPSV23 vaccine, then a dose of PCV13 should be given ≥ 1 year afterwards.[122] The pneumococcal vaccines have been demonstrated to reduce the risk of invasive pneumococcal disease and all-cause community-acquired pneumonia in adults ≥ 65 years and pneumococcal pneumonia hospitalizations in patients with COPD.[123-124]

Summary

COPD remains a leading cause of morbidity and mortality, with an increasing prevalence as the population ages. The presentation and risk factors for comorbid diseases will guide the workup. Establishing a diagnosis of COPD and/or early identification of an exacerbation in the ED can improve symptoms, reduce the severity of an exacerbation, and ultimately improve outcomes. AECOPD treatment should consist of supplemental oxygen to target an arterial saturation of 88% to 92%, bronchodilator therapy (beta-2 agonists and anticholinergics), corticosteroids, 5 to 7 days of antibiotic therapy for symptomatic patients, and the early use of NIPPV for patients with respiratory acidosis and/or severe dyspnea with signs of respiratory muscle fatigue or increased work of breathing. Studies have demonstrated varying levels of concordance with guideline-directed diagnostic studies and treatment, suggesting that there is much room for improvement to provide consistent care in order to improve outcomes.

Table 10. Indications for Hospital Admission[3,4]

- Severe underlying COPD
- Onset of new physical signs (eg, cyanosis, peripheral edema, changes in mental status)
- Worsening hypoxemia or hypercapnia
- Failure of an exacerbation to respond to outpatient or initial medical management
- Presence of serious or high-risk comorbidities (eg, pneumonia, cardiac arrhythmia, congestive heart failure, diabetes mellitus, renal or liver failure)
- Frequent exacerbations
- Older age
- Insufficient home support
- Uncertain diagnosis

Abbreviation: COPD, chronic obstructive pulmonary disease.
From the *Global Strategy for the Diagnosis, Management and Prevention of COPD*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016. Available from: http://goldcopd.org/. Used with permission.

Case Conclusions

For the 67-year-old man with COPD, you found his nurse and respiratory therapist and ordered nebulized bronchodilator treatments, IV corticosteroids, sputum culture, a chest x-ray, and NIPPV. He was provided supplemental oxygen to maintain oxygen saturation of 88% to 92%. You reviewed his records and noted that he had grown P aeruginosa *in previous sputum cultures. Based on the sensitivities, IV levofloxacin was ordered. After 3 hours, the patient appeared notably more comfortable while lying in a semirecumbent position in bed. He was now able to speak in full sentences, and his wheezing and work of breathing were improved. His arterial blood gas showed only mild ongoing respiratory acidosis, and his chest x-ray demonstrated hyperinflation only. You called the hospitalist for admission to the medical step-down unit, given his age, clinical status, and need for NIPPV.*

For your second patient with dyspnea and cough, given her history of smoking, physical examination that demonstrated hypoxia, inability to speak in full sentences, and wheezing, plus laboratory data and chest imaging consistent with COPD, a diagnosis of AECOPD was made in the ED. She was admitted to the intermediate care unit, started on NIPPV for respiratory distress, given levofloxacin 750 mg IV and methylprednisolone 40 mg IV, and closely monitored. In 2 hours, her symptoms were not improved; she remained hypercapnic and continued to have respiratory distress and paradoxical breathing. She was intubated, transferred to the ICU, and started on assist control/volume control with a respiratory rate of 10 breaths/min, tidal volume of 380 (6 mL/kg of ideal body weight), positive end-expiratory pressure of 5, and FiO_2 of 50%. Careful attention was given to the settings to avoid dynamic hyperinflation. Over the next 24 to 48 hours, she began to improve, and you confirmed the plan with the team to treat her with oral antibiotics for 7 days and oral corticosteroids for 5 days, based on current data and guidelines.

Time- and Cost-Effective Strategies

- **Use point-of-care ultrasound.** Using ultrasound can quickly narrow down the differential diagnosis for dyspnea, thus expediting appropriate treatment.
  Risk Management Caveat: The use and interpretation of point-of-care ultrasound is operator-dependent. Standards for determining competency may vary from hospital to hospital.
- **Use oral prednisone.** The oral route of corticosteroid administration is appropriate in clinically stable nonsevere AECOPD and is more cost-effective than the IV route.
- **Use NIPPV.** NIPPV may reduce the need for endotracheal intubation in certain patients.
- **Vaccinate.** Influenza and pneumococcal vaccinations can reduce morbidity and mortality associated with the infections.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study is included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) next to the number of the reference.

1. Ford ES, Murphy LB, Khavjou O, et al. Total and state-specific medical and absenteeism costs of COPD among adults aged ≥ 18 years in the United States for 2010 and projections through 2020. *Chest*. 2015;147(1):31-45. **(Retrospective observational study)**
2. Ford ES. Hospital discharges, readmissions, and ED visits for COPD or bronchiectasis among US adults: findings from the nationwide inpatient sample 2001-2012 and Nationwide Emergency Department Sample 2006-2011. *Chest*. 2015;147(4):989-998. **(Retrospective observational study)**
3.* Celli BR, MacNee W, Agusti A, et al. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*. 2004;23(6):932-946. **(Systematic review; consensus guidelines)**
4.* Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016. http://goldcopd.org/. Accessed September 10, 2017. **(Systematic review; consensus guidelines)**
5. Cavailles A, Brinchault-Rabin G, Dixmier A, et al. Comorbidities of COPD. *Eur Respir Rev*. 2013;22(130):454-475. **(Review article)**
6. Mannino D, Watt G, Hole D, et al. The natural history of chronic obstructive pulmonary disease. *Eur Respir J*. 2006;27(3):627-643. **(Review article)**
7. Heron M. Deaths: leading causes for 2014. *Natl Vital Stat Rep*. 2016;65(5):1-96. **(Retrospective observational study)**
8. Mathers C, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLOS Medicine*. 2006;3(11):e442. **(Retrospective epidemiologic study)**
9. Yeatts KB, Lippmann SJ, Waller AE, et al. Population-based burden of COPD-related visits in the ED. *Chest*. 2013;144(3):784-793. **(Retrospective observational study; 97,511 patients)**
10. Mannino DM, Higuchi K, Tzy-Chyi Y, et al. Economic burden of COPD in the presence of comorbidities. *Chest*. 2015;148(1):138-150. **(Retrospective observational study; 183,681 patients)**
11. Suissa S, Dell'Anioello S, Ernst P. Long-term natural history of chronic obstructive pulmonary disease: severe exacerbations and mortality. *Thorax*. 2012;67(11):957-963. **(Prospective observational study; 73,106 patients)**
12. Seemungal T, Harper-Owen R, Bhowmik A, et al. Respiratory viruses, symptoms, and inflammatory markers in acute exacerbations and stable chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2001;164(9):1618-1623. **(Prospective observational study; 83 patients)**
13. Querol-Ribelles J, Molina J, Naberan K, et al. Discrepency between antibiotics administered in acute exacerbations of chronic bronchitis and susceptibility of isolated pathogens in respiratory samples: multicentre study in primary care setting. *Int J Antimicrob Ag*. 2006;28(5):472-476. **(Prospective observational study; 1537 patients)**
14. Monso E, Ruiz J, Manterola J, et al. Bacterial infection in chronic obstructive pulmonary disease. A study of stable and exacerbated outpatients using the protected specimen brush. *Am J Respir Crit Care Med*. 1995;152(4):1316-1320. **(Prospective observational study; 69 patients)**
15. Ko F, Ip M, Chan PK, et al. A 1-year prospective study of the infectious etiology in patients hospitalized with acute exacerbations of COPD. *Chest*. 2007;131(1):44-52. **(Prospective, observational study; 373 patients)**
16. Atkinson RW, Anderson HR, Sunyer J, et al. Acute effects of particulate air pollution on respiratory admissions. *Am J Respir Crit Care Med*. 2001;164(10):1860-1866. **(Retrospective observational study; 79,008 patients)**
17. Peacock JL, Anderson HR, Bremner SA, et al. Outdoor air pollution and respiratory health in patients with COPD. *Thorax*. 2011;66(7):591-596. **(Prospective observational study; 94 patients)**
18. Schikowski T, Mills IC, Anderson HR, et al. Ambient air pollution: a cause of COPD? *Eur Respir J*. 2014(43):250-263. **(Systematic review; 14 studies)**
19. Macklem PT. Therapeutic implications of the pathophysiology of COPD. *Eur Respir J*. 2010;35:676-680. **(Review article)**
20. Cameron L, Pilcher J, Weatherall M, et al. The risk of serious adverse outcomes associated with hypoxaemia and hyperoxaemia in acute exacerbations of COPD. *Postgrad Med J*. 2012;88(1046):684-689. **(Retrospective observational study; 680 patients)**
21. Ringbaek TJ, Terkelsen J, Lange P. Outcomes of acute exacerbations in COPD in relation to pre-hospital oxygen therapy. *Eur Clin Respir J*. 2015;2:10.3402/ecrj.v2.27283. eCollection 2015. **(Retrospective observational study; 405 patients)**
22. Denniston AK, O'Brien C, Stableforth D. The use of oxygen in acute exacerbations of chronic obstructive pulmonary disease: a prospective audit of pre-hospital and hospital emergency management. *Clin Med (Lond)*. 2002;2(5):449-451. **(Prospective observational study; 97 patients)**
23. Mal S, McLeod S, Iansavichene A, et al. Effect of out-of-hospital noninvasive positive-pressure support ventilation in adult patients with severe respiratory distress: a systematic review and meta-analysis. *Ann Emerg Med*. 2014;63(5):600-607. **(Systematic review; 7 studies, 632 patients)**
24. US Preventive Services Task Force (USPSTF), Siu AL, Bibbins-Domingo K, et al. Screening for chronic obstructive pulmonary disease: US Preventive Services Task Force recommendation statement. *JAMA*. 2016;315(13):1372-1377.

(Systematic review; consensus guidelines)
25. Straus SE, McAlister FA, Sackett DL, et al. The accuracy of patient history, wheezing, and laryngeal measurements in diagnosing obstructive airway disease. CARE-COAD1 Group. Clinical assessment of the reliability of the examination-chronic obstructive airways disease. *JAMA*. 2000;283(14):1853-1857. **(Prospective observational study; 309 patients)**
26. Soler N, Agusti C, Angrill J, et al. Bronchoscopic validation of the significance of sputum purulence in severe exacerbations of chronic obstructive pulmonary disease. *Thorax*. 2007;62(1):29-35. **(Prospective observational study; 40 patients)**
27. Seemungal TA, Donaldson GC, Bhowmik A, et al. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2000;161(5):1608-1613. **(Prospective observational study; 101 patients)**
28. Austin MA, Wills KE, Blizzard L, et al. Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial. *BMJ*. 2010;341:c5462. **(Randomized controlled trial; 405 patients)**
29. Gunen H, Hacievliyagil SS, Kosar F, et al. Factors affecting survival of hospitalised patients with COPD. *Eur Respir J*. 2005;26(2):234-241. **(Prospective observational study; 205 patients)**
30. Mattos WL, Signori LG, Borges FK, et al. Accuracy of clinical examination findings in the diagnosis of COPD. *J Bras Pneumol*. 2009;35(5):404-408. **(Prospective case-control study; 98 patients)**
31. Bohadana AB, Mohankumar T. Symptoms and signs in the assessment of chronic airflow obstruction. *Indian J Chest Dis Allied Sci*. 1982;24(2-3):133-142. **(Review)**
32. Fletcher CM. The clinical diagnosis of pulmonary emphysema; an experimental study. *Proc R Soc Med*. 1952;45(9):577-584. **(Retrospective observational study)**
33. Holleman DR Jr, Simel DL, Goldberg JS. Diagnosis of obstructive airways disease from the clinical examination. *J Gen Intern Med*. 1993;8(2):63-68. **(Prospective observational study)**
34. Schapira RM, Schapira MM, Funahashi A, et al. The value of the forced expiratory time in the physical diagnosis of obstructive airways disease. *JAMA*. 1993;270(6):731-736. **(Cross-sectional study; 500 patients)**
35. Marini JJ, Pierson DJ, Hudson LD, et al. The significance of wheezing in chronic airflow obstruction. *Am Rev Respir Dis*. 1979;120(5):1069-1072. **(Prospective observational study; 83 patients)**
36. Straus SE, McAlister FA, Sackett DL, et al. Clinical assessment of the reliability of the examination-chronic obstructive airways disease. Accuracy of history, wheezing, and forced expiratory time in the diagnosis of chronic obstructive pulmonary disease. *J Gen Intern Med*. 2002;17(9):684-688. **(Prospective observational study; 161 patients)**
37. Tokuda Y, Miyagi S. Physical diagnosis of chronic obstructive pulmonary disease. *Intern Med*. 2007;46(23):1885-1891. **(Review article)**
38. McKeever TM, Hearson G, Housley G, et al. Using venous blood gas analysis in the assessment of COPD exacerbations: a prospective cohort study. *Thorax*. 2016;71(3):210-215. **(Prospective observational study; 234 patients)**
39. Kelly AM, Kerr D, Middleton P. Validation of venous pCO_2 to screen for arterial hypercarbia in patients with chronic obstructive airways disease. *J Emerg Med*. 2005;28(4):377-379. **(Prospective observational study; 112 patients)**
40. Asiimwe AC, Brims FJ, Andrews NP, et al. Routine laboratory tests can predict in-hospital mortality in acute exacerbations of COPD. *Lung*. 2011;189(3):225-232. **(Retrospective, observational study; 5985 patients)**
41. Webb WR. Radiology of obstructive pulmonary disease. *AJR Am J Roentgenol*. 1997;169(3):637-647. **(Review article)**
42. Emerman CL, Cydulka RK. Evaluation of high-yield criteria for chest radiography in acute exacerbation of chronic obstructive pulmonary disease. *Ann Emerg Med*. 1993;22(4):680-684. **(Retrospective observational study; 742 patients)**
43. Sherman S, Skoney JA, Ravikrishnan KP. Routine chest radiographs in exacerbations of chronic obstructive pulmonary disease. Diagnostic value. *Arch Intern Med*. 1989;149(11):2493-2496. **(Retrospective observational study; 242 patients)**
44. Tsai TW, Gallagher EJ, Lombardi G, et al. Guidelines for the selective ordering of admission chest radiography in adult obstructive airway disease. *Ann Emerg Med*. 1993;22(12):1854-1858. **(Prospective observational study; 128 patients)**
45. MacDonald MI, Shafuddin E, King PT, et al. Cardiac dysfunction during exacerbations of chronic obstructive pulmonary disease. *Lancet Respir Med*. 2016;4(2):138-148. **(Review article)**
46. McCord J, Barzak S. Multifocal atrial tachycardia. *Chest*. 1998;113(1):202-209. **(Review article)**
47. Goudis CA, Konstantinidis AK, Ntalas IV, et al. Electrocardiographic abnormalities and cardiac arrhythmias in chronic obstructive pulmonary disease. *Int J Cardiol*. 2015;199:264-273. **(Review article)**
48. Vanfleteren LE, Franssen FM, Uszko-Lencer NH, et al. Frequency and relevance of ischemic electrocardiographic findings in patients with chronic obstructive pulmonary disease. *Am J Cardiol*. 2011;108(11):1669-1674. **(Retrospective observational study; 543 patients)**
49. Lazovic B, Svenda MZ, Mazic S, et al. Analysis of electrocardiogram in chronic obstructive pulmonary disease patients. *Med Pregl*. 2013;66(3-4):126-129. **(Retrospective observational study; 110 patients)**
50. Pavasini R, d'Ascenzo F, Campo G, et al. Cardiac troponin elevation predicts all-cause mortality in patients with acute exacerbation of chronic obstructive pulmonary disease: systematic review and meta-analysis. *Int J Cardiol*. 2015;191:187-193. **(Systematic review, 10 studies; meta-analysis, 8 studies)**
51. Buchan A, Bennett R, Coad A, et al. The role of cardiac biomarkers for predicting left ventricular dysfunction and cardiovascular mortality in acute exacerbations of COPD. *Open Heart*. 2015;2(1):e000052. **(Systematic review; 14 studies)**
52. Sethi S, Murphy TF. Infection in the pathogenesis and course of chronic obstructive pulmonary disease. *N Engl J Med*. 2008;359(22):2355-2365. **(Review article)**
53. Sykes A, Mallia P, Johnston SL. Diagnosis of pathogens in exacerbations of chronic obstructive pulmonary disease. *Proc Am Thorac Soc*. 2007;4(8):642-646. **(Review article)**
54. Boixeda R, Almagro P, Diez-Manglano J, et al. Bacterial flora in the sputum and comorbidity in patients with acute exacerbations of COPD. *Int J Chron Obstruct Pulmon Dis*. 2015;10:2581-2591. **(Retrospective observational study; 536 patients)**
55. Larsen MV, Janner JH, Nielsen SD, et al. Bacteriology in acute exacerbation of chronic obstructive pulmonary disease in patients admitted to hospital. *Scand J Infect Dis*. 2009;41(1):26-32. **(Retrospective observational study; 118 patients)**
56. Wu X, Chen D, Gu X, et al. Prevalence and risk of viral infection in patients with acute exacerbation of chronic obstructive pulmonary disease: a meta-analysis. *Mol Biol Rep*. 2014;41(7):4743-4751. **(Systematic review and meta-analysis; 17 studies)**
57. Zwaans WA, Mallia P, van Winden ME, et al. The relevance of respiratory viral infections in the exacerbations of chronic obstructive pulmonary disease-a systematic review. *J Clin Virol*. 2014;61(2):181-188. **(Systematic review; 19 studies, 1728 patients)**

58. Akhtar S, Theodoro D, Gaspari R, et al. Resident training in emergency ultrasound: consensus recommendations from the 2008 Council of Emergency Medicine Residency Directors Conference. *Acad Emerg Med*. 2009;16 Suppl 2:S32-S36. **(Consensus statement)**
59. Lichtenstein DA, Meziere GA. Relevance of lung ultrasound in the diagnosis of acute respiratory failure: the BLUE protocol. *Chest*. 2008;134(1):117-125. **(Prospective observational study; 260 patients)**
60. Gallard E, Redonnet JP, Bourcier JE, et al. Diagnostic performance of cardiopulmonary ultrasound performed by the emergency physician in the management of acute dyspnea. *Am J Emerg Med*. 2015;33(3):352-358. **(Prospective observational study; 147 patients)**
61. Laursen CB, Sloth E, Lambrechtsen J, et al. Focused sonography of the heart, lungs, and deep veins identifies missed life-threatening conditions in admitted patients with acute respiratory symptoms. *Chest*. 2013;144(6):1868-1875. **(Prospective observational study; 139 patients)**
62. Laursen CB, Sloth E, Lassen AT, et al. Point-of-care ultrasonography in patients admitted with respiratory symptoms: a single-blind, randomised controlled trial. *Lancet Respir Med*. 2014;2(8):638-646. **(Prospective randomized trial; 320 patients)**
63. Stolz LA, Stolz U, Fields JM, et al. Emergency medicine resident assessment of the emergency ultrasound milestones and current training recommendations. *Acad Emerg Med*. 2017;24(3):353-361. **(Prospective observational study; 539 patients)**
64. Pothirat C, Chaiwong W, Phetsuk N, et al. Peak expiratory flow rate as a surrogate for forced expiratory volume in 1 second in COPD severity classification in Thailand. *Int J Chron Obstruct Pulmon Dis*. 2015;10:1213-1218. **(Prospective observational study; 300 patients)**
65. Emerman CL, Cydulka RK. Use of peak expiratory flow rate in emergency department evaluation of acute exacerbation of chronic obstructive pulmonary disease. *Ann Emerg Med*. 1996;27(2):159-163. **(Prospective observational study; 199 patients)**
66. Rizkallah J, Man SF, Sin DD. Prevalence of pulmonary embolism in acute exacerbations of COPD: a systematic review and metaanalysis. *Chest*. 2009;135(3):786-793. **(Systematic review and meta-analysis; 5 studies, 550 patients)**
67. Aleva FE, Voets LW, Simons SO, et al. Prevalence and localization of pulmonary embolism in unexplained acute exacerbations of COPD: a systematic review and meta-analysis. *Chest*. 2017;151(3):544-554. **(Systematic review; 7 studies)**
68.* Vestbo J, Hurd SS, Agusti AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med*. 2013;187(4):347-365. **(Consensus statement; guidelines)**
69. Robinson TD, Freiberg DB, Regnis JA, et al. The role of hypoventilation and ventilation-perfusion redistribution in oxygen-induced hypercapnia during acute exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2000;161(5):1524-1529. **(Prospective observational study; 22 patients)**
70. Schreck D. Asthma pathophysiology and evidence-based treatment of severe exacerbations. *Am J Health Syst Pharm*. 2006;63(3). **(Review article)**
71. Karpel JP, Pesin J, Greenberg D, et al. A comparison of the effects of ipratropium bromide and metaproterenol sulfate in acute exacerbations of COPD. *Chest*. 1990;98(4):835-839. **(Prospective randomized trial; 32 patients)**
72. Gruber P, Swadron S. The acute presentation of chronic obstructive pulmonary disease in the emergency department: a challenging oxymoron. *Emerg Med Pract*. 2008;10(11):1-28. **(Review article)**
73. McCrory DC, Brown CD. Anticholinergic bronchodilators versus beta2-symathomimetic agents for acute exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2002(4):CD003900. **(Systematic review; 4 trials)**
74. Turner MO, Patel A, Ginsburg S, et al. Bronchodilator delivery in acute airflow obstruction. A meta-analysis. *Arch Intern Med*. 1997;157(15):1736-1744. **(Systematic review and meta-analysis; 12 studies, 507 patients)**
75. Turner JR, Corkery KJ, Eckman D, et al. Equivalence of continuous flow nebulizer and metered-dose inhaler with reservoir bag for treatment of acute airflow obstruction. *Chest* 1988;93(3):476-481. **(Randomized controlled trial; 75 patients)**
76. Summer W, Elston R, Tharpe L, et al. Aerosol bronchodilator delivery methods. *Arch Intern Med*. 1989;149(3):618-623. **(Randomized controlled trial; 36 patients)**
77. Keatings VM, Jatakanon A, Worsdell YM, et al. Effects of inhaled and oral glucocorticoids on inflammatory indices in asthma and COPD. *Am J Respir Crit Care Med*. 1997;155(2):542-548. **(Prospective crossover study; 15 patients)**
78. Culpitt SV, Maziak W, Loukidis S, et al. Effect of high dose inhaled steroid on cells, cytokines, and proteases in induced sputum in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1999;160(5 Pt 1):1635-1639. **(Randomized controlled trial; 25 patients)**
79. Davies L, Angus RM, Calverley PM. Oral corticosteroids in patients admitted to hospital with exacerbations of chronic obstructive pulmonary disease: a prospective randomised controlled trial. *Lancet*. 1999;354(9177):456-460. **(Randomized controlled trial; 56 patients)**
80. Thompson WH, Nielson CP, Carvalho P, et al. Controlled trial of oral prednisone in outpatients with acute COPD exacerbation. *Am J Respir Crit Care Med*. 1996;154(2 Pt 1):407-412. **(Randomized controlled trial; 27 patients)**
81. Aaron SD, Vandemheen KL, Hebert P, et al. Outpatient oral prednisone after emergency treatment of chronic obstructive pulmonary disease. *N Engl J Med*. 2003;348(26):2618-2625. **(Randomized controlled trial; 147 patients)**
82. Niewoehner DE, Erbland ML, Deupree RH, et al. Effect of systemic glucocorticoids on exacerbations of chronic obstructive pulmonary disease. Department of Veterans Affairs Cooperative Study Group. *N Engl J Med*. 1999;340(25):1941-1947. **(Randomized controlled trial; 271 patients)**
83. Schacke H, Docke W, Asadullah K. Mechanisms involved in the side effects of glucocorticoids. *Pharmacol Ther*. 2002;96(2):23-43. **(Review article)**
84. de Jong YP, Uil SM, Grotjohan HP, et al. Oral or IV prednisolone in the treatment of COPD exacerbations: a randomized, controlled, double-blind study. *Chest*. 2007;132(6):1741-1747. **(Randomized controlled trial; 435 patients)**
85.* Leuppi JD, Schuetz P, Bingisser R, et al. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. *JAMA*. 2013;309(21):2223-2231. **(Randomized controlled trial; 314 patients)**
86. National Institute for Health and Care Excellence (NICE). Chronic obstructive pulmonary disease in over 16s: diagnosis and management. Clinical guideline [CG101]. June 2010. Available at: https://www.nice.org.uk/guidance/cg101. Accessed September 10, 2017. **(Consensus statement; guidelines)**
87. Nseir S, Di Pompeo C, Cavestri B, et al. Multiple-drug-resistant bacteria in patients with severe acute exacerbation of chronic obstructive pulmonary disease: prevalence, risk factors, and outcome. *Crit Care Med*. 2006;34(12):2959-2966. **(Prospective observational study; 857 patients)**
88. Quon BS, Gan WQ, Sin DD. Contemporary management of acute exacerbations of COPD: a systematic review and meta-analysis. *Chest*. 2008;133(3):756-766. **(Systematic review, meta-analysis; 35 trials, 2958 patients)**
89.* Vollenweider DJ, Jarrett H, Steurer-Stey CA, et al. Antibiotics

for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2012;12:CD010257. **(Systematic review and meta-analysis; 16 trials, 2068 patients)**
90. Stefan MS, Rothberg MB, Shieh MS, et al. Association between antibiotic treatment and outcomes in patients hospitalized with acute exacerbation of COPD treated with systemic steroids. *Chest*. 2013;143(1):82-90. **(Retrospective observational study; 53,900 patients)**
91. Gonzalez JA, Garcia CH, Gonzalez PA, et al. Effect of intravenous magnesium sulfate on chronic obstructive pulmonary disease exacerbations requiring hospitalization: a randomized placebo-controlled trial. *Archivos de Bronconeumologia*. 2006;42(8):384-387. **(Randomized controlled trial; 24 patients)**
92. Edwards L, Shirtcliffe P, Wadsworth K, et al. Use of nebulised magnesium sulphate as an adjuvant in the treatment of acute exacerbations of COPD in adults: a randomised double-blind placebo-controlled trial. *Thorax*. 2013;68(4):338-343. **(Randomized controlled trial; 161 patients)**
93.* Ram FS, Picot J, Lightowler J, et al. Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2004;(3)(3):CD004104. **(Systematic review and meta-analysis; 14 studies)**
94. Merlani PG, Pasquina P, Granier JM, et al. Factors associated with failure of noninvasive positive pressure ventilation in the emergency department. *Acad Emerg Med*. 2005;12(12):1206-1215. **(Retrospective observational study; 104 patients)**
95. Allen JY, Macias CG. The efficacy of ketamine in pediatric emergency department patients who present with acute severe asthma. *Ann Emerg Med*. 2005;46(1):43-50. **(Randomized controlled trial; 68 patients)**
96. Hirota K, Lambert D. Ketamine: its mechanism(s) of action and unusual clinical use. *Br J Anaesth.* 1996;77(4):441-444. **(Review article)**
97. Sato T, Hirota K, Matsuki A, et al. The relaxant effect of ketamine on guinea pig airway smooth muscle is epithelium-independent. *Anesthesiol Analges*. 1997;84:641-647. **(Animal study)**
98. Howton JC, Rose J, Duffy S, et al. Randomized, double-blind, placebo-controlled trial of intravenous ketamine in acute asthma. *Ann Emerg Med.* 1996;27(2):170-175. **(Randomized controlled trial; 53 patients)**
99. Parrilla FJ, Moran I, Roche-Campo F, et al. Ventilatory strategies in obstructive lung disease. *Semin Respir Crit Care Med*. 2014;35(4):431-440. **(Review article)**
100. Bonin F, Sommerwerck U, Lund LW, et al. Avoidance of intubation during acute exacerbation of chronic obstructive pulmonary disease for a lung transplant candidate using extracorporeal carbon dioxide removal with the Hemolung. *J Thorac Cardiovasc Surg*. 2013;145(5):e43-e44. **(Case report)**
101. Pazarli AC, Koseoglu HI, Doruk S, et al. Procalcitonin: is it a predictor of noninvasive positive pressure ventilation necessity in acute chronic obstructive pulmonary disease exacerbation? *J Res Med Sci.* 2012;17(11):1047-1051. **(Cross-sectional study; 118 patients)**
102. Hashemian SM, Fallahian F. The use of heliox in critical care. *Int J Crit Illn Inj Sci.* 2014;4(2):138-142. **(Review article)**
103. Hunt T, Williams MT, Frith P, et al. Heliox, dyspnoea and exercise in COPD. *Eur Respir Rev*. 2010;19(115):30-38. **(Systematic review; 8 studies)**
104. Jolliet P, Ouanes-Besbes L, Abroug F, et al. A multicenter randomized trial assessing the efficacy of helium/oxygen in severe exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2016. **(Randomized controlled trial; 445 patients)**
105. Maggiore SM, Richard JC, Abroug F, et al. A multicenter, randomized trial of noninvasive ventilation with helium-oxygen mixture in exacerbations of chronic obstructive lung disease. *Crit Care Med*. 2010;38(1):145-151. **(Randomized controlled trial; 204 patients)**
106. Mieloszyk RJ, Verghese GC, Deitch K, et al. Automated quantitative analysis of capnogram shape for COPD-normal and COPD-CHF classification. *IEEE Trans Biomed Eng*. 2014;61(12):2882-2890. **(Prospective observational trial; 139 patients)**
107. Roche N, Rabbat A, Zureik M, et al. Chronic obstructive pulmonary disease exacerbations in emergency departments: predictors of outcome. *Curr Opin Pulm Med*. 2010;16(2):112-117. **(Review article)**
108. Bustamante-Fermosel A, De Miguel-Yanes JM, Duffort-Falco M, et al. Mortality-related factors after hospitalization for acute exacerbation of chronic obstructive pulmonary disease: the burden of clinical features. *Am J Emerg Med*. 2007;25(5):515-522. **(Retrospective observational study; 763 patients)**
109. Quintana JM, Esteban C, Unzurrunzaga A, et al. Predictive score for mortality in patients with COPD exacerbations attending hospital emergency departments. *BMC Medicine.* 2014;12(1):66. **(Prospective observational study; 2487 patients)**
110. Roche N, Zureik M, Soussan D, et al. Predictors of outcomes in COPD exacerbation cases presenting to the emergency department. *Eur Respir J*. 2008;32(4):953-961. **(Prospective, observational study; 794 patients)**
111. Singanayagam A, Schembri S, Chalmers JD. Predictors of mortality in hospitalized adults with acute exacerbation of chronic obstructive pulmonary disease. *Ann Am Thorac Soc*. 2013;10(2):81-89. **(Systematic review; 37 studies, 189,772 subjects)**
112. Hu G, Zhou Y, Wu Y, et al. The pneumonia severity index as a predictor of in-hospital mortality in acute exacerbation of chronic obstructive pulmonary disease. *PLoS One*. 2015;10(7):e0133160. **(Prospective observational study; 752 patients)**
113. Chang CL, Sullivan GD, Karalus NC, et al. Predicting early mortality in acute exacerbation of chronic obstructive pulmonary disease using the CURB65 score. *Respirology*. 2011;16(1):146-151. **(Prospective observational study; 252 patients)**
114. Xiao K, Guo C, Su L, et al. Prognostic value of different scoring models in patients with multiple organ dysfunction syndrome associated with acute COPD exacerbation. *J Thorac Dis*. 2015;7(3):329-336. **(Retrospective observational study; 153 patients)**
115. Steer J, Gibson J, Bourke SC. The DECAF Score: predicting hospital mortality in exacerbations of chronic obstructive pulmonary disease. *Thorax*. 2012;67(11):970-976. **(Prospective observational study; 920 patients)**
116. Echevarria C, Steer J, Heslop-Marshall K, et al. Validation of the DECAF score to predict hospital mortality in acute exacerbations of COPD. *Thorax*. 2016;71(2):133-140. **(Prospective observational study; 1725 patients)**
117. Steer J, Norman EM, Afolabi OA, et al. Dyspnoea severity and pneumonia as predictors of in-hospital mortality and early readmission in acute exacerbations of COPD. *Thorax.* 2012;67(2):117-121. **(Prospective observational study; 920 patients)**
118. Shorr AF, Sun X, Johannes RS, et al. Validation of a novel risk score for severity of illness in acute exacerbations of COPD. *Chest*. 2011;140(5):1177-1183. **(Retrospective observational study; 34,669 patients)**
119. Esteban C, Arostegui I, Garcia-Gutierrez S, et al. A decision tree to assess short-term mortality after an emergency department visit for an exacerbation of COPD: a cohort study. *Respir Res.* 2015;16:151. **(Prospective observational study; 2487 patients)**
120. Criner GJ, Bourbeau J, Diekemper RL, et al. Prevention of acute exacerbations of COPD: American College of Chest

Physicians and Canadian Thoracic Society Guideline. *Chest*. 2015;147(4):894-942. **(Consensus statement; guidelines)**
121. Schembri S, Morant S, Winter JH, et al. Influenza but not pneumococcal vaccination protects against all-cause mortality in patients with COPD. *Thorax*. 2009;64(7):567-572. **(Retrospective observational study; 177,120 patients)**
122. Tomczyk S, Bennett NM, Stoecker C, et al. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged ≥ 65 years: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep*. 2014;63(37):822-825. **(Consensus statement)**
123. Kraicer-Melamed H, O'Donnell S, Quach C. The effectiveness of pneumococcal polysaccharide vaccine 23 (PPV23) in the general population of 50 years of age and older: a systematic review and meta-analysis. *Vaccine*. 2016;34(13):1540-1550. **(Systematic review, meta-analysis)**
124. Lee TA, Weaver FM, Weiss KB. Impact of pneumococcal vaccination on pneumonia rates in patients with COPD and asthma. *J Gen Intern Med*. 2007;22(1):62-67. **(Retrospective observational study; 34,193 patients)**
125. Lodewijckx C, Sermeus W, Vanhaecht K, et al. Inhospital management of COPD exacerbations: a systematic review of the literature with regard to adherence to international guidelines. *J Eval Clin Pract*. 2009;15(6):1101-1110. **(Systematic review; 7 studies)**
126. Sandhu SK, Chu J, Yurkovich M, et al. Variations in the management of acute exacerbations of chronic obstructive pulmonary disease. *Can Respir J*. 2013;20(3):175-179. **(Retrospective observational study; 293 patients)**
127. Tsai CL, Ginde AA, Blanc PG, et al. Improved care of acute exacerbation of chronic obstructive pulmonary disease in two academic emergency departments. *Int J Emerg Med*. 2009;2(2):111-116. **(Retrospective observational study; 272 patients)**

CME Questions

Current subscribers receive CME credit absolutely free by completing the following test. Each issue includes *4 AMA PRA Category 1 Credits™*, 4 ACEP Category I credits, 4 AAFP Prescribed credits, or 4 AOA Category 2A or 2B credits. Online testing is available for current and archived issues. To receive your free CME credits for this issue, scan the QR code below with your smartphone or visit www.ebmedicine.net/E1017.

1. In addition to cigarette smoking, which of the following is a risk factor for the development of COPD?
a. Obesity
b. Age
c. Low-fiber diet
d. Family history

2. What is the most common cause of AECOPD?
a. Pneumothorax
b. Pulmonary embolism
c. Respiratory bacterial or viral infection
d. Congestive heart failure

3. Most patients with AECOPD who present to the ED should get which one of the following diagnostic tests?
a. Troponin
b. B-type natriuretic peptide
c. Respiratory viral panel
d. Chest x-ray

4. Which diagnostic test should be avoided in AECOPD due to unreliable results?
a. Spirometry
b. Electrocardiogram
c. D-dimer
d. Arterial blood gas

5. What is the target oxygen saturation level for patients with AECOPD?
a. 88%-92%
b. 85%-89%
c. 92%-95%
d. > 97%

6. Based on the results of the REDUCE trial, which dose and duration of corticosteroid treatment is generally recommended?
a. Prednisone 80 mg daily for 7 days
b. Prednisone 40 mg daily for 14 days
c. Prednisone 40 mg daily for 10 days
d. Prednisone 40 mg daily for 5 days

7. Antibiotic therapy is recommended in patients who present with:
a. Chest pain
b. Shortness of breath
c. Purulent sputum
d. Tachypnea

8. Mechanical ventilation management strategies should focus on:
a. Avoiding development of breath-stacking
b. Normalization of pH
c. Use of large tidal volumes
d. Use of very high respiratory rates

9. Which of the following preventive strategies is recommended for patients with AECOPD who are sent home from the ED?
a. Smoking cessation
b. Influenza vaccine
c. Pneumococcal vaccine
d. All of the above

The 2015-2018 Lifelong Learning and Self-Assessment Study Guides Are Available Now

Receive full article reprints, CME, and more when you order yours today!*

$219/volume

Your *Lifelong Learning And Self-Assessment Study Guides* include:

- Full reprints* of the original articles
- A handy summary of the key points
- An in-depth discussion to clarify and elaborate on the key points
- Sample questions to help you quiz yourself on your knowledge of the material
- Print or online formats at the same low price
- 35 *AMA PRA Category 1 Credits™* and 35 ACEP Category I Credits.
- The practical knowledge you need to ace the ABEM LLSA exams

> *"Excellent. I like the format with the synopsis and key points followed by the full article. Easy to read. Easy to navigate."*
>
> **- ANITA L'ITALIEN, MD**

> *"I have been using your LLSA Study Guides for over seven years now. They are concise, thoughtful, and extremely helpful. With the CME credits included for free, it is definitely money well spent."*
>
> **- JAMES ROSBRUGH, MD**

**Due to copyright restrictions, 1 article from the 2016 LLSA, 2 articles and 1 table from the 2017 LLSA, and 1 article from the 2018 LLSA are not included.*

2 Easy Ways To Order:

1. Go online to: www.ebmedicine.net/NKLXT
2. Call 1-800-249-5770 or 678-366-7933

*Use Promotion Code: **NKLXT** at checkout*

Accreditation: EB Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. This activity has been planned and implemented in accordance with the accreditation requirements and policies of the ACCME. **Credit Designation**: EB Medicine designates this enduring material for a maximum of 35 *AMA PRA Category 1 Credits™* per study guide. Physicians should claim only the credit commensurate with the extent of their participation in the activity. **Faculty Disclosure**: It is the policy of EB Medicine to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME-sponsored educational activities. All faculty participating in the planning or implementation of a sponsored activity are expected to disclose to the audience any relevant financial relationships and to assist in resolving any conflict of interest that may arise from the relationship. In compliance with all ACCME Essentials, Standards, and Guidelines, all faculty for this CME activity made a full disclosure statement. This information will be presented as part of the course materials. **Commercial Support:** This activity received no commercial support.

EB MEDICINE

In upcoming issues of *Emergency Medicine Practice....*

- Inflammatory Bowel Disease
- Lower Extremity Dislocations
- Thermal Burns
- Oncologic Emergencies
- Jaundice
- Emerging Infectious Diseases

Physician CME Information

Date of Original Release: October 1, 2017. Date of most recent review: September 10, 2017. Termination date: October 1, 2020.

Accreditation: EB Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. This activity has been planned and implemented in accordance with the accreditation requirements and policies of the ACCME.

Credit Designation: EB Medicine designates this enduring material for a maximum of 4 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ACEP Accreditation: *Emergency Medicine Practice* is approved by the American College of Emergency Physicians for 48 hours of ACEP Category I credit per annual subscription.

AAFP Accreditation: This Enduring Material activity, *Emergency Medicine Practice,* has been reviewed and is acceptable for credit by the American Academy of Family Physicians. Term of approval begins 07/01/2017. Term of approval is for one year from this date. Physicians should claim only the credit commensurate with the extent of their participation in the activity. Approved for 4 AAFP Prescribed credits.

AOA Accreditation: *Emergency Medicine Practice* is eligible for up to 48 American Osteopathic Association Category 2-A or 2-B credit hours per year.

Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals: Upon completion of this activity, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

Objectives: Upon completion of this article, you should be able to: (1) describe the differential diagnosis for patients who present with presumed acute exacerbation of COPD, considering potential comorbid or exacerbating conditions; (2) apply a tailored diagnostic approach based on the severity of the exacerbation; (3) treat COPD aggressively using an evidence-based algorithm; and (4) determine the best disposition option for patients with acute exacerbation of COPD, based on individual risks and benefits.

Discussion of Investigational Information: As part of the journal, faculty may be presenting investigational information about pharmaceutical products that is outside Food and Drug Administration–approved labeling. Information presented as part of this activity is intended solely as continuing medical education and is not intended to promote off-label use of any pharmaceutical product.

Faculty Disclosure: It is the policy of EB Medicine to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME-sponsored educational activities. All faculty participating in the planning or implementation of a sponsored activity are expected to disclose to the audience any relevant financial relationships and to assist in resolving any conflict of interest that may arise from the relationship. In compliance with all ACCME Essentials, Standards, and Guidelines, all faculty for this CME activity were asked to complete a full disclosure statement. **The information received is as follows: Dr. Holden, Dr. Slack, Dr. McCurdy, Dr. Shah, Dr. Wardi, Dr. Xavier, Dr. Mishler, Dr. Toscano, and their related parties report no significant financial interest or other relationship with the manufacturer(s) of any commercial product(s) discussed in this educational presentation. Dr. Jagoda made the following disclosures: Consultant, Daiichi Sankyo Inc; Consultant, Pfizer Inc; Consultant, Banyan Biomarkers Inc; Consulting fees, EB Medicine.**

Commercial Support: This issue of *Emergency Medicine Practice* did not receive any commercial support.

Earning Credit: Two Convenient Methods: (1) Go online to www.ebmedicine.net/CME and click on the title of the article. (2) Mail or fax the CME Answer And Evaluation Form (included with your June and December issues) to EB Medicine.

Hardware/Software Requirements: You will need a Macintosh or PC to access the online archived articles and CME testing.

Additional Policies: For additional policies, including our statement of conflict of interest, source of funding, statement of informed consent, and statement of human and animal rights, visit www.ebmedicine.net/policies.

Direct all inquiries to:
EB Medicine
Phone: 1-800-249-5770 or 1-678-366-7933
Fax: 1-770-500-1316
5550 Triangle Parkway, Suite 150
Norcross, GA 30092
E-mail: **ebm@ebmedicine.net**
Website: **www.ebmedicine.net**
To write a letter to the editor, please email:
jagodamd@ebmedicine.net

Subscription Information

Full annual subscription: $349 (includes 12 monthly evidence-based print issues; 48 *AMA PRA Category 1 Credits™*, 48 ACEP Category I credits, 48 AAFP Prescribed credits, and 48 AOA Category 2A or 2B CME credits. Call 1-800-249-5770 or go to www.ebmedicine.net/subscribe to subscribe.

Individual issues: $39 (includes 4 CME credits). Call 1-800-249-5770 or go to www.ebmedicine.net/EMPissues to order.

Group subscriptions at discounted rates are also available.
Contact groups@ebmedicine.net for more information.

Emergency Medicine Practice (ISSN Print: 1524-1971, ISSN Online: 1559-3908, ACID-FREE) is published monthly (12 times per year) by EB Medicine (5550 Triangle Parkway, Suite 150, Norcross, GA 30092).