Management of chronic obstructive pulmonary disease patients in the emergency department setting

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ABBREVIATIONS:

- AAT: Alpha-1-antitrypsin
- ABG: Arterial Blood Gas
- AE: Acute Exacerbation
- ARDS: Acute Respiratory Distress Syndrome
- BNP: Brain Natriuretic Peptide
- CBC: Complete blood count
- CHF: Congestive Heart Failure
- COPD: Chronic Obstructive Pulmonary Disease
- CO2: Carbon Dioxide
- CRP: C-reactive protein
- CT: Computed Tomography
- CXR: Chest X-ray
- ED: Emergency Department
- EPO: Erythropoietin
- FEV1: Forced Expiratory Volume in the first second
- FVC: Forced Vital Capacity
- GERD: Gastroesophageal reflux disease
- ICU: Intensive care unit
- JVP: Jugular Venous Pressure
- V/Q: Ventilation/Perfusion ratio
- 6MWD: Six-minute walk distance

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SUMMARY

Title: Management of chronic obstructive pulmonary disease patients in the Emergency Department setting

Key words: COPD, dyspnea, comorbidities, acute exacerbation

Author: Filip Pajnic

Chronic obstructive pulmonary disease is a progressive but preventable and treatable lung disease affecting at least 32 million people in the USA and predicted to be the 4th leading cause of death in the USA. People with a history of dyspnea, increased sputum production, chronic cough with a longstanding past of risk factors should raise the suspicion of the disease.

An abnormal chronic inflammatory response leading to persisting airflow limitation concomitant with signs of chronic bronchitis and emphysema are the hallmarks of the disease. Except for its pulmonary components, the disease systemically affects many systems of our bodies as the cardiovascular system, skeletal muscles, and metabolic cycles making it a multifaceted disease heavily affecting the quality of life in patients. Other comorbidities that are often seen are lung cancer and depression.

The disease is strongly associated with lifestyle and environmental living conditions. Tobacco smoke, air pollution, occupational exposures to toxic gases and genetic factors are the most common causes of developing the disease.

Early recognition, diagnosis, lifestyle changes, and treatment are crucial for improving mortality and decreasing complications and hospitalizations. Because of the complexity of the diseases and many comorbid factors these patients can acutely worsen. The challenge facing emergency departments are acute exacerbations of COPD which are common and usually triggered by bacterial infections rapidly deteriorating lung function and consciousness leading to respiratory failure and death. This is the reason why categorization of COPD patients, a combined assessment of the disease, acute exacerbation risk calculations, treatment guidelines, and accurate investigative studies are of immense importance. Proper triage of the patient at the ED is imperative to decide if hospitalization of the patient is necessary or if out-patient treatment and management is sufficient.

A multidisciplinary approach to the disease is vital and early interventions lower the risk of exacerbations and comorbidities that strongly contributes to the overall severity of the disease.

SAŽETAK

Naslov: Obrada i liječenje bolesnika s kroničnom opstruktivnom plućnom bolesti u odjelu hitne medicine

Ključne riječi: KOPB, zaduha, komorbiditeti, akutna egzacerbacija

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Kronična opstruktivna plućna bolest je progresivna, ali predvidljiva i potencijalno zaliječiva plućna bolest od koje boluje oko 32 milijuna ljudi u SAD-u i po učestalosti predstavlja četvrti uzrok smrtnosti u općoj populaciji u toj zemlji. Bolesnici sa simptomima zaduhe, povećanom produkcijom sputuma, kroničnim kašljem i s dugotrajnom izloženošću rizičnim faktorima pobuđuju sumnju na ovu bolest i zahtjevaju obradu i liječenje.

Abnormalan kronični upalni odgovor uzrokuje postojanu opstrukciju protoka zraka koja je praćena sa znakovima kroničnog bronhitisa i emfizema i čini glavna obilježja ove bolesti.
Osim plućna, bolest sustavno zahvaća i ostale organske sustave u tijelu: kardiovaskularni sustav, skeletne mišiće i metaboličke cikluse što ju čini višesustavnom bolesti koja ozbiljno narušava kvalitetu života u bolesnika koji boluju od nje. Drugi komorbiditeti koji se često javljaju u bolesnika koji boluju od KOPB-a su karcinom pluća i bronha i depresija.

Bolest je snažno povezana sa životnim stilom i okolišnim čimbenicima. Duhanski dim, zagađenje zraka, izlaganje otrovnim plinovima i genetski čimbenici su najčešći uzroci u razvitka ove bolesti.

Rano prepoznavanje, dijagnoza, promjene životnih navika i liječenje su ključni čimbenici u smanjenju mortaliteta, komplikacija i hospitalizacija. S obzirom na kompleksnost same bolesti i prisutnosti komorbiditeta, ovim bolesnicima stanje se često može akutno pogoršati. Najčešći izazovi koji se susreću u zavodima za hitnu medicinu su akutna egzacerbacija KOPB-a koja je često potaknuta bakterijskom infekcijom koja brzo pogoršava plućnu funkciju i svijest vodeći do zatajenja disanja i smrti. Gore spomenute činjenice su razlozi zbog kojeg kategorizacija bolesnika s KOPB-om, kombinirana s procjenom stanja bolesti, izračunom rizika od akutne egzacerbacije, terapijskim smjernicama i točnim istraživačkim studijama su od iznimne važnosti. Pravilna trijaža bolesnika u zavodima za hitnu medicinu je imperativ prilikom odluke o hospitalizaciji ili eventualnom izvanbolničkom zbrinjavanju.

Multidisciplinarni pristup bolesti je vitalan kao i rane intervencije koje smanjuju rizik od egzacerbacija te komorbiditeti koji snažno doprinose ukupnoj težini ove bolesti.

1. Introduction

By presenting the pathophysiology, aetiology and clinical presentation of COPD together with acute exacerbations of COPD and life threating comorbidities the aim of this review is to constructively present the work through needed for proper management and decision making regarding mild to severely ill COPD patients, focusing on the diagnostic and management challenges faced in the emergency department. The review will describe and discuss

- Clinical evaluation of COPD patients
- Conclusions made by making appropriate investigative studies and using correct diagnostic modalities
- Common differential diagnoses met by ED physicians
- Staging and assessing COPD
- Indications for hospitalization during exacerbations
- A stepwise approach to management and treatment of patients

2. Definition and pathophysiology

The pathophysiology of COPD is quite complex in its nature as it is commonly seen as an overlapping of three diseases; emphysema, chronic bronchitis, and asthma even if the latter is a reversible and more uncommon part of the long-lasting process of the disease. By different triggering factors a chronic pathologic inflammatory process occurs mainly in the central airways, peripheral bronchioles and the parenchyma of the lungs. The advancement of COPD showcases thickening of the walls in the smaller airways as well as a substantial mucus accumulation and ultimately their destruction into nonfunctional tissue (1).

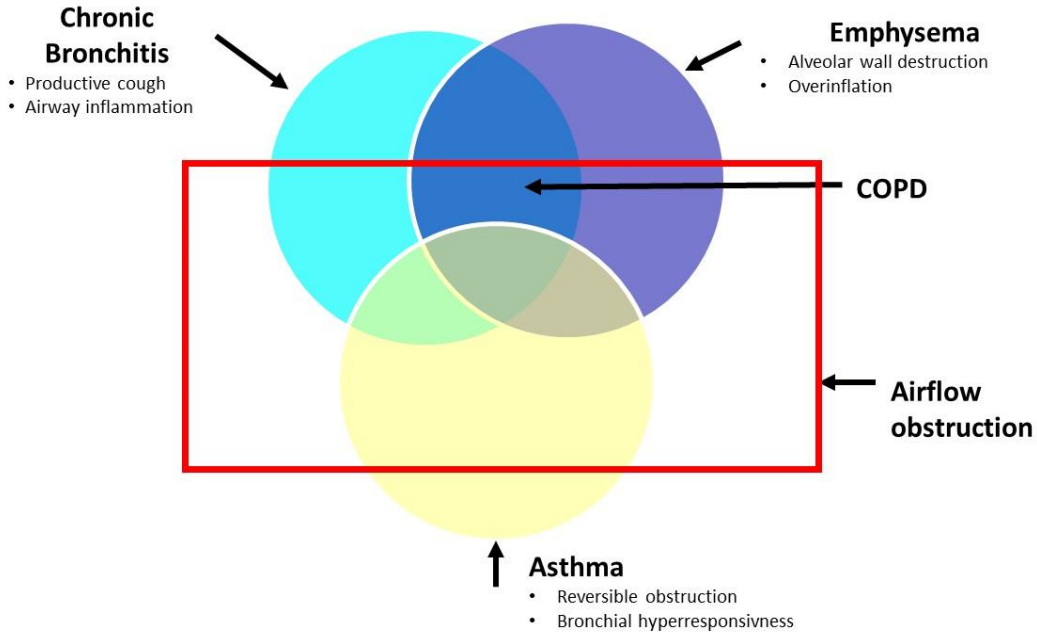


Figure 1: Schematic representation of overlap between chronic obstructive lung diseases. Modified according to Kumar. 2012 (2)

The most broadly accepted pathogenesis of the disease is the inflammatory hypothesis. Ultimately the conclusion is that the lung destruction occurs due to increased elastases release from inflammatory cells as macrophages and polymorphonuclear white blood cells (2,3). Because this is an overwhelming response to stress and noxious substances antiprotease activity gets overwhelmed and can't counteract properly, resulting in chronic destruction to lung parenchyma (apoptosis and necrosis of cells) due to the increased oxidative stress from free radicals (4). Research has suggested that the key element leading to the destruction of tissue is human leukocyte elastase acting in a synergistic fashion with metalloproteinases, cysteine proteinases and plasminogen activators (5).

To be able to understand the clinical picture, the comorbidities and the causes for acute exacerbations of COPD patients we have to understand the pathophysiology of chronic

bronchitis and emphysema as they usually are present concomitantly with a predominance of one to a higher degree. Commonly they both produce a state of airflow limitation.

Chronic bronchitis is histopathologically hyperplasia of mucous glands with inflammatory cell infiltration of airway walls (6). Chronic bronchitis is well-defined as airway obstruction and excessive mucus production (7,8). The structural changes that occur in the airway walls by the obstruction and inflammation are atrophy, smooth muscle hyperplasia with wall thickening (fibrosis) and focal squamous metaplasia. Consequences of ciliary impairment due to endothelial damage are a nonfunctioning clearance of mucus and bacteria resulting in mucous plugs. Combining these changes, narrowing of the airway lumen and airflow limitation is the inevitable outcome. Patients suffering from chronic bronchitis are often described as “blue bloaters”. Compensatory mechanism occurring because of CO2 retention and hypoxemia due to poor ventilation is an increased cardiac output. Finally, these patients develop right side heart failure (cor pulmonale) due to pulmonary arterial vasoconstriction as a consequence of hypercapnia, respiratory acidosis and polycythemia (9) (increased EPO production by kidneys).

The pathological process of emphysema is different from that occurring in chronic bronchitis. Emphysema is defined by destruction of alveolar walls and abnormal permanent enlargement of airspaces distal to the terminal bronchioles. As the alveolar walls and the supporting structure is destroyed airway narrowing (10) and elastic recoil reduction occurs. The alveolar surface area exchanging gas is decreased as the pulmonary capillary bed and alveolar septae are damaged and the V/Q mismatch occurs as blood oxygenation declines. In comparison to chronic bronchitis, the body lowers cardiac output and the lungs start hyperventilating since the V/Q mismatch is present due to limited blood flow through lungs with fairly normal pressures and blood gases. These patients are instead recognized as “pink puffers”. The natural consequence of low cardiac output is general tissue hypoxia with weight loss, muscle wasting, and pulmonary cachexia**.**

In emphysema lung elasticity (elastic recoil) decrease and airways get blocked; entrapment of air and hyperinflation of lungs develops gradually. Hyper-inflated states, except for creating dyspnea greatly add to comorbid states as muscles weakness and exercise intolerance. Hyperinflation can be both static during rest and dynamic during exercise (11).

Morphologically we can distinguish 3 patterns of emphysema with different aetiologies and locations according to the anatomical distribution within the lobule of the lung (12).

- Centriacinar (centrilobular) is usually seen in the upper lobes of the lungs with the destruction of the proximal respiratory bronchioles and central portions of the acini with none to slight destruction of surrounding lung parenchyma sparing distal alveoli. It's the most common form of emphysema as evidently it's strongly connected to the harms of cigarette smoking (1).
- Panacinar (panlobular) affects the lower part of the lungs with destruction distally to the terminal bronchioles disturbing the alveolus in its entirety, uniformly enlarging the acini. Persons with this form of emphysema are usually homozygously alpha1-antitrypsin deficient (7)**.**
- Distal acinar (paraseptal) involves the formation of space-occupying bullae (1) in the distal part of the airway and the alveolar structures (as the ducts and sacs) extending from the lung septae to the lung pleura. Bullae can both compress nearby lung structures and cause spontaneous pneumothorax. The etiology is unclear although it's usually seen in young adults with spontaneous pneumothorax (7).

3. Epidemiology and aetiology

The widespread presence of COPD is connected to the prevalence of tobacco smoking in the world. It's estimated that over 80 million people suffer from the disease in the world (8). As the general population is living longer and increasing in size obstructive lung diseases as asthma and COPD are increasing according to the Global Burden of Disease study (13). Some believe that these numbers are underestimated because numerous patients are undiagnosed until late stages of the disease. Even if asthma is more common, COPD has been much more deadly accounting for 3.2 million deaths versus 0.40 million for asthma (13). If the trend continues it's anticipated that COPD will be the 3rd most significant cause of death in the world (8)**.** The projected increase in mortality and morbidity will strike heavily in African and Asian countries (8) foremost connected to these countries smoking habits. In the BOLD study (Burden of Obstructive Lung Disease) it was established that the global prevalence of the disease was (10,1%) (14) being more common in men (11,8%) than in woman (8,5%). The prevalence was highest in Cape Town, South Africa impacting over 22% of the men while countries and regions with low smoking rates as Hannover, Germany had the lowest prevalence (15).

In the US according to The National Health Interview Survey, the prevalence of chronic bronchitis was 34 cases respectively 18 of emphysema per 1000 persons (16)**.**

Even if COPD is more common in males it's steadily increasing in the woman population as more woman are becoming chronic smokers. Smoking and especially having many pack years is the most common risk factor, but some longstanding smokers never develop COPD. Other risk factors increasing the individual susceptibility to the disease are listed in table 1.

Table 1: COPD risk factors.
Modified according to Davidson S. 2014 (8)

Risk factors for development of COPD
Environmental
• Tobacco smoke (accounts for 95% of cases in the UK) • Indoor air pollution • Occupational exposures, such as coal dust, silica and cadmium • Low birth weight may reduce maximally attained lung function in young adult life • Lung growth: childhood infections or maternal smoking may affect growth of lung during childhood, resulting in a lower maximally attained lung function in adult life • Infections: recurrent infections may accelerate decline in FEV1 • Low socioeconomic status • Cannabis smoking
Host factors
• Genetic factors: α_1-Antitrypsin deficiency; other COPD susceptibility genes are likely to be identified • Airway hyper-reactivity

4. Clinical evaluation

To be able to diagnose COPD, follow up the disease as well as suspecting acute or chronic exacerbations, the physician should be familiar with the clinical evaluation of these patients; being able to recognize important indications to manage the patient properly.

4.1 History

COPD usually presents gradually and patients often don't seek professional help until the disease has progressed. In-depth history taking is crucial to understand how long the patient has been suffering from COPD symptoms. Seeking emergency care for exacerbations of COPD can be the first encounter of the disease by the clinician. It's also important to keep in mind that as the disease progresses exacerbations become more common and more severe.

The patient usually presents with and describes a spectrum of symptoms in accordance with the characteristic overlapping of chronic bronchitis, emphysema, and asthma; cough, breathlessness, sputum production, intolerance to exercise, and in the case of exacerbations signs of acute pulmonary infection, wheezing and deterioration of the mental status. Most commonly productive cough and dyspnea (depending on how much the FEV1 value has declined) are the presenting symptoms. Other systemic manifestations will be discussed under comorbidities.

According to ACP/ACCP/ATS/ERS guidelines from 2011, the single best predictor of airflow obstruction is a history of more than 40 pack-years of smoking especially if patient describe wheezing and the physician confirms wheezing upon auscultating the lungs (17).

In conclusion, a patient with a history of chronic cough, sputum production, and dyspnea especially with risk factors for developing COPD as smoking should be further clinically evaluated as shown in table 2.

4.2 Physical examination

Physical examination findings can vary depending on the severity and type of COPD that is present. In severe COPD some typical thoracic findings are wheezing on expiration, hyper-resonance on percussion, decreased breath sounds and barrel chest due to hyperinflation. Frequently in severely ill patients peripheral edema, elevated JVP, central cyanosis and use of accessory respiratory muscles are present. Hoover sign (intercostal in-drawing during inspiration) could also be present (8). Crackles on lung auscultation may also point towards an underlying pulmonary infection and exacerbation of the COPD.

In milder forms of COPD the physical exam, its characteristics and patient phenotype can point towards the disease that predominates in the patient.

The phenotypically “blue bloater” suffering from chronic bronchitis can present as if the patient has congestive heart failure. Frequent coughing, use of accessory muscles during respiration and wheezing and rhonchi upon auscultation are normally present. These patients are usually obese and have a varying degree of cor pulmonale presenting with peripheral edema, cyanosis, and secondary polycythemia (8). A patient suffering from emphysema the “pink puffer” instead is usually thin with a barrel chest being breathless, hyper-resonant on auscultation with the absence of cough.

4.3 Differential diagnosis

Physicians, especially at the ED should keep in mind the most common diseases that can present as any of the diseases in the COPD spectrum. Some of the most common differential diagnosis to keep in mind are as follow:

- CHF (8) has some common features with emphysema and is very important to distinguish from AE at the ED. CHF can present with wheezing, crackles on the base of the lungs as well as paroxysmal nocturnal dyspnea and worsening of dyspnea. Peak expiratory flow is an easy test to distinguish the likelihood of CHF versus COPD exacerbation. Higher flows suggest CHF while blowing less than 150-200 ml suggests airflow limitation (18).
- Chronic asthma (8)**,** also an obstructive small airway disease that can precipitate in acute attacks (as status asthmaticus) leading to emergency care service. The disease is reversible and reacts better to bronchodilator therapy.
- Bronchiectasis (8)**,** can present with persistent chronic cough and purulent sputum production. CT imaging can distinguish the disease from emphysema.
- Infections as bacterial and viral pneumonia, empyema, abscesses, and tuberculosis
- Myocardial infarction
- Pleural effusion
- Pneumothorax
- Pulmonary embolism
- ARDS
- Bronchiolitis obliterans

4.4 Comorbidities

Systemic manifestations such as osteoporosis, impaired muscle function, anemia, cardiac disease, cerebrovascular disease, hypertension, diabetes mellitus, dyslipidemia, and depression are widely seen in COPD patients (8,19). As smoking tobacco is the most common risk factor; lung carcinoma is a common comorbidity and a noteworthy cause of mortality. It's important to know about non-pulmonary disease components of patients with COPD to understand the complexities and burden of the disease to be able to manage the patients correctly both long term and acutely. Comorbidities are also a common cause of hospitalization in COPD patients; cardiac disease being the most common one (20). Lack of treating these comorbidities, a wide range of pharmaceutical use and interactions of these medications all worsen the outcome in these patients. Use of systemic corticosteroids in COPD patients can contribute to patients impaired muscle function, osteoporosis, and hypertension to name one common medication problem patients can suffer from (21).
Reducing the polypharmacy and try to avoid unnecessary drugs or drug interactions will benefit the patients.

Both musculoskeletal dysfunction, altered fat metabolism with weight loss (malnutrition) greatly increase the exercise limitation and further escalate the inactivity, disability, and osteoporosis of these patients.
GERD has been reported to have a higher prevalence in COPD patients (22,23). It's been suggested that GERD and aspiration of Helicobacter pylori with the subsequent airway inflammation increases the frequency of COPD exacerbations and hospital admission (24).
Pulmonary hypertension usually develops as a complication of the hypoxic nature of COPD. Pathophysiologically hypoxia leads to pulmonary vasoconstriction, remodeling of the arterial walls (most prominent is intimal changes of the vessel) (25,26) and therefore leading to raised mean pulmonary artery pressure usually above 25 mmHg. In conclusion, pulmonary hypertension leads to right-sided heart failure which in turn leads to systemic congestion with peripheral edema. Cardiac findings are typically right ventricular hypertrophy and dilation secondary to pulmonary hypertension; cor pulmonale. Patients with pulmonary hypertension have an increased risk of exacerbations and decreased survival. Long term treatment with supplemental oxygen is the approved treatment option for secondary pulmonary hypertension (27).
A strategic approach should be taken to treat the comorbidities regardless of the treatment plan of the COPD since comorbidities contribute rigorously to the overall state of the COPD.

5. Investigative studies

The definite outcome suffering from COPD is irreversible airflow limitation that can be proven by pulmonary function tests. Spirometry will confirm and establish the diagnosis of COPD. Other investigative studies are important regarding the state of the patient, comorbidities, effectiveness and side effects of drug therapy and AE presenting in the ED. Presented beneath are these different studies and their purpose.

5.1 Spirometry

By using spirometry demonstration of airflow obstruction is made. The diagnosis requires a post-bronchodilator FEV1/FVC value that is < 0.70 (< 70%). Spirometric classification of COPD severity is then based on post-bronchodilator FEV1 according to table 3. Measuring lung volumes to asses hyperinflation can also be made with spirometry using the helium dilution technique (8). Body plethysmography can likewise be used especially in patients with large bullae (8).

5.2 Laboratory studies

- ABG (28) is crucial in evaluating the severity of the disease. As the disease progresses mild hypoxemia can turn into severe hypoxemia and hypercapnia. In acute respiratory failure and AE, the test can clearly confirm the severity of the disease as well as provide pH values that in acute life threating settings can go below 7.3.
- Serum electrolytes are important to follow in COPD patients due to various reasons. Pharmaceuticals as beta-adrenergic agonists, diuretics, and theophylline lower potassium level and increase renal excretion of calcium and phosphate which can have an impact on potential hypokalemic states. COPD patients also retain sodium to some degree. Lastly, measuring bicarbonate levels can help following the kidneys compensatory mechanism of chronic respiratory acidosis as patients instead develop metabolic alkalosis.
- CBC and hematocrit is a standard test that can exclude secondary polycythemia from chronic hypoxemia and anemia in the patient.
- BNP, even if not conclusive in its measurement can guide the physician and differentiate the similar and confusing clinical picture regarding CHF and

COPD exacerbations (29). An increased BNP value suggests myocytes stretching potentially due to CHF (30).

5.3 Imaging modalities

- CXR can be helpful both for diagnosing manifestations of COPD but also to exclude and rule out the differential diagnoses like lung cancer and cardiac failure. Frontal and lateral chest radiographs should be obtained. With chronic bronchitis, cardiomegaly and increased bronchovascular markings can be seen. As pulmonary hypertension develops right ventricular enlargement also becomes more prominent. In emphysema cardiomegaly doesn't develop instead narrow heart shadows, flattening of hemidiaphragm, hyperinflation, increased retrosternal air space is seen. Increased anteroposterior diameter and bullous formation is also a typical manifestation.
- CT can support the diagnosis of COPD but also evaluate the state of the disease. High-resolution CT is superior to X-ray when evaluating the type, location, and progression of emphysema and accompanied bullae.

5.4 Other tests

- Pulse oximetry is used for fast assessment of oxygen saturation status in the patient. ABG test is superior but for instant feedback at the ED, pulse oximetry is a non-invasive, inexpensive and easily accessible tool.
- Sputum evaluation particularly sputum culturing can be helpful to find the most common bacteria in an exacerbation. Those bacteria are usually Haemophilus influenza, Moraxella catarrhalis, Streptococcus pneumoniae and Pseudomonas aeruginosa (31). In exacerbations, sputum becomes more purulent and the quantity also increases.
- ECG is a key device to exclude any cardiac origin for seeking medical care at the ED. Many COPD patients have some coexisting cardiac pathology and the respiratory issue can be due to heart decompensation. Abnormal potassium levels that COPD patients are often experiencing can also raise red flags on the ECG-readings.
- 6MWD test measures exercise tolerance and capacity in patients with cardiopulmonary diseases. It estimates the status of the patient and can be a great tool in following patients' response and improvement after therapy, surgery and pulmonary rehabilitation. According to some studies, the 6MWD

test is a good predictor of respiratory mortality in patients suffering from COPD (32).

- AAT – In certain patients, especially non-smokers, younger than 40 years who develop emphysema, AAT levels should be measured to diagnose potential AAT-deficiency (33). Positive family history should also raise a warning for testing individuals.
- 2-dimensional echocardiography and right-sided heart catheterization are reserved for patients that have developed secondary pulmonary hypertension and cor pulmonale. These interventions can evaluate systolic pulmonary arterial pressure and right ventricular function.

6. Workflow and Assessment

Beneath are some key indicators that should raise suspicion of the disease and further investigations should be initiated. When the disease has been diagnosed assessment of the disease should be made.

Table 2: Key indicators for COPD diagnosis

Dyspnea	**Consider and investigate for COPD if any of these key indicators are present, particulary in individuals above age 40**
Chronic cough	
Chronic sputum production	
History of smoking **Number of pack-years =** (Number of cigarettes smoked per day / 20) * number of years smoked	
Reccurent respiratory tract infections	
Family history of COPD or other risk factors	
Spirometry = FEV1/FVC value that is < 0.70	

As the disease has been diagnosed the next step is to assess the degree of airflow limitation according to the GOLD classification presented in the table, to grade the severity of the COPD.

Table 3: Assessment of COPD**.** Modified according to GOLD. 2018 (34)

Assessment of COPD – Assess Degree of Airflow Limitation Using Spirometry		
Spirometric classification of COPD severity based on post-bronchodilator FEV1		
STAGE	**SEVERITY**	**FEV1**
GOLD 1	**Mild**	**FEV1/FVC < 0.70** **FEV1 ≥ 80% predicted**
GOLD 2	**Moderate**	**FEV1/FVC < 0.70** **FEV1 50-79% predicted**
GOLD 3	**Severe**	**FEV1/FVC < 0.70** **FEV1 30-49 % predicted**
GOLD 4	**Very Severe**	**FEV1/FVC < 0.70** **FEV1 < 30% predicted or FEV1 50% predicted if respiratory failure present**

The next step after assessing the degree of airflow limitation is to assess the impact of the symptoms on the patient's everyday life. This can be made with the COPD assessment test (CAT) which measures the impact the disease has on the patient's wellbeing and daily activities. The other test that can be used is the Modified British Medical Research (mMRC) breathlessness scale that assesses the degree of breathlessness in the patient.

Table 4: Modified Medical Research Council dyspnea scale. Adapted from Davidson S. 2014 (8)

Modified MRC dyspnea scale	
Grade	**Degree of breathlessness related to activities**
0	**No dyspnea** No breathlessness, except with strenuous exercise
1	**Slight dyspnea** Breathlessness when hurrying on the level or walking up a slight hill
2	**Moderate dyspnea** Walks slower than contemporaries on level ground because of breathlessness or has to stop for breath when walking at own pace
3	**Severe dyspnea** Stops for breath after walking about 100 meters or after a few minutes on level ground
4	**Very severe dyspnea** Too breathless to leave the house, or breathless when dressing or undressing

At the end of the combined assessment, both assessments of comorbidities and acute exacerbations should be made. After obtaining a clear picture concerning the state of the patient, decisions regarding non-pharmacological and pharmacological management can be decided with better care and outcome. Beneath is the refined ABCD assessment tool of the GOLD guidelines that summarize these steps.

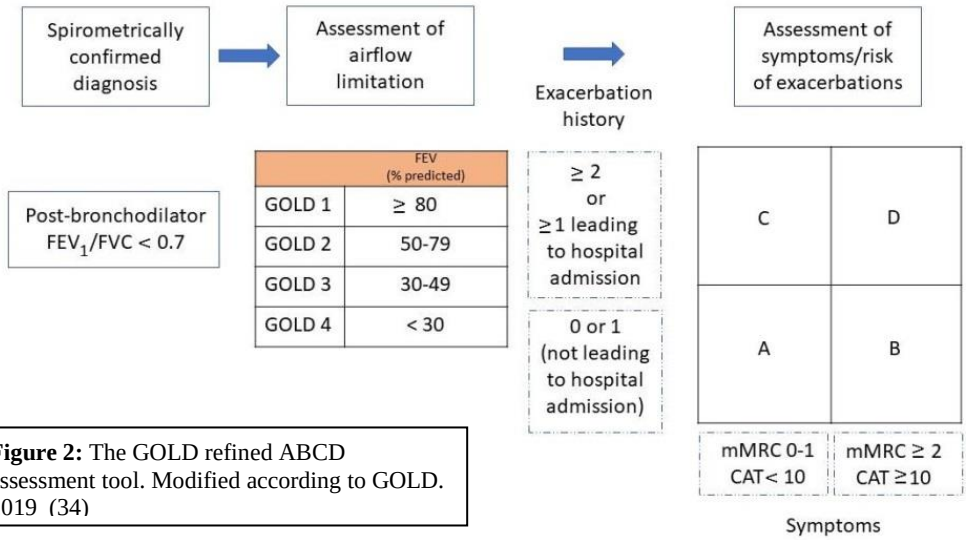


Figure 2: The GOLD refined ABCD assessment tool. Modified according to GOLD. 2019 (34)

7. Acute exacerbations

In the ED it's critical to be familiar with AE of COPD and its management. AE are important contributing factors of respiratory failure and death in patients suffering from COPD as well as the primary cause of decompensation and hospital admission of COPD patients (35). Most hospitalizations due to this cause occur during the winter months (36). AE of COPD usually presents as a decline in lung function, patients' health and mental status. These exacerbations usually come with an increased mucus and sputum production (with or without purulence), coughing, worsening of dyspnea, wheezing (34) and even fluid retention and concomitant pneumonia. To overcome exacerbations additional therapy not included in the general management plan is needed to stabilize and improve the status of the patient.
Frequency of AE increase as the disease progresses with time. Factors increasing the likelihood of developing AE include growing age, duration, and severity of COPD, history of antibiotic use, insufficient chronic management of COPD, comorbidities as chronic heart failure, increased blood eosinophil count (37) and having experienced AE in the past. Pulmonary hypertension also increases the risk of AE; decreased survival is noted in these patients.

Most common triggering factors are infections with bacteria, less commonly viruses. As mentioned before Haemophilus influenza, Moraxella catarrhalis, Streptococcus pneumoniae and Pseudomonas aeruginosa (31) are the most common bacteria causing AE. If the sputum is purulent and higher in amount, a bacterial cause should be the preliminary suspected aetiology.

ED decision making is based on the presenting symptoms and the clinical evaluation of the patient; deciding if home care with an increased bronchodilator, corticosteroid, and antibiotic therapy is enough (38) in the case of mild and moderate exacerbation or if hospital admission is more appropriate in the case of severely dyspneic patients with worsening of consciousness, cyanosis, low oxygen saturation, and peripheral edema. Patients with acute respiratory failure that are hemodynamically unstable should also be considered being admitted to the ICU.

Regular empirical treatment for inpatients includes bronchodilators as nebulized salbutamol (SABA) or ipratropium (SAMA), corticosteroids as IV methylprednisolone and IV antibiotics with non-pseudomonal coverage as ceftriaxone/moxifloxacin and with pseudomonal coverage as cefepime/ceftazidime/piperacillin-tazobactam and levofloxacin (34,39).

In patients that don’t improve after the initial treatment efforts or have decompensated breathing supplemental oxygen is needed. Oxygen saturation should be monitored by pulse oximetry or ABG and be titrated to 88-92% saturation using a high-flow nasal cannula (34) improving ventilation and decreasing the hypercarbia. Noninvasive positive pressure ventilation can also be used as an alternative. It’s immensely important not to give too much oxygen to inhibit the respiratory center and precipitate or worsen respiratory failure. Patients with accompanied peripheral edema and fluid overload should be treated with diuretics. As part of normal routines ABCs, CXR (excluding pneumonia) and sputum collection should also be made at the ED.

There are no biomarkers or definite sputum examinations that with high specificity and sensitivity can diagnose an exacerbation since the aetiology varies even tough bacterial origin is most common. Since viruses sometimes cause the exacerbation physician should administer antibiotics with care. CRP can indicate bacterial infection but is not optimal for guidance. According to recent research and the GOLD guidelines (34), procalcitonin levels in the serum can to some extent be used as a biomarker and guide the use of antibiotics (40,41). Initiating empirical antibiotic treatment for AE-COPD, Anthonisen criteria have been used by many physicians. It takes into consideration three important items; increased dyspnea, increased sputum volume and increased sputum purulence (34,42,43). If two or more items are met it's proposed that antibiotic treatment should be initiated. Patients experiencing four or more AE in a year or patients suffering from substantial cardiopulmonary comorbidities also meet the criteria for antibiotic treatment (43,44). In the end, the clinical picture should guide the physician's decision making and these guidelines together with CXR and laboratory values should serve as additional help in reaching a conclusion.

8. Management and treatment

Presented beneath are stepwise management and treatment options as the disease progresses and FEV1 declines and patients become more dyspneic, suffer from frequent AE and comorbidities.

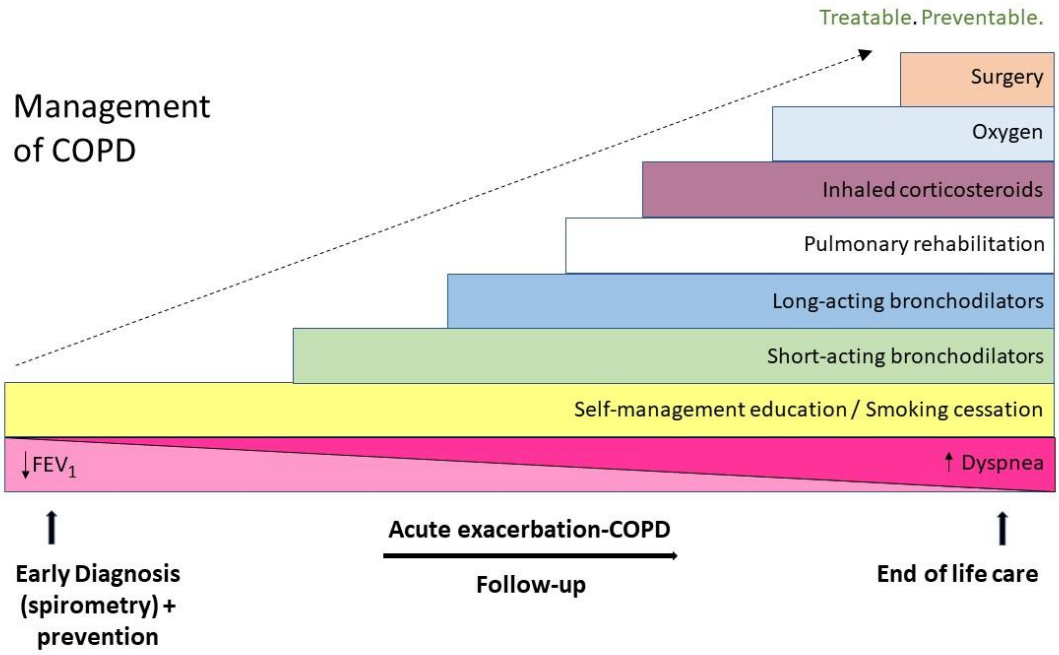


Figure 3: A comprehensive approach to the management of COPD. Modified according to O'Donnell et al. 2008 (45)

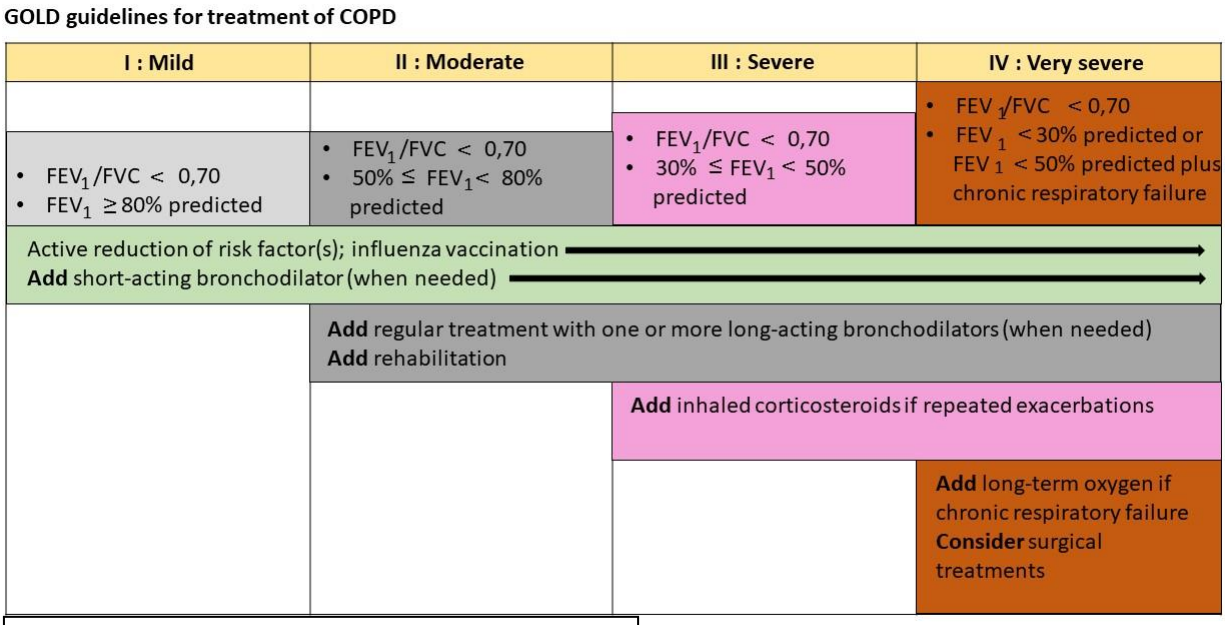
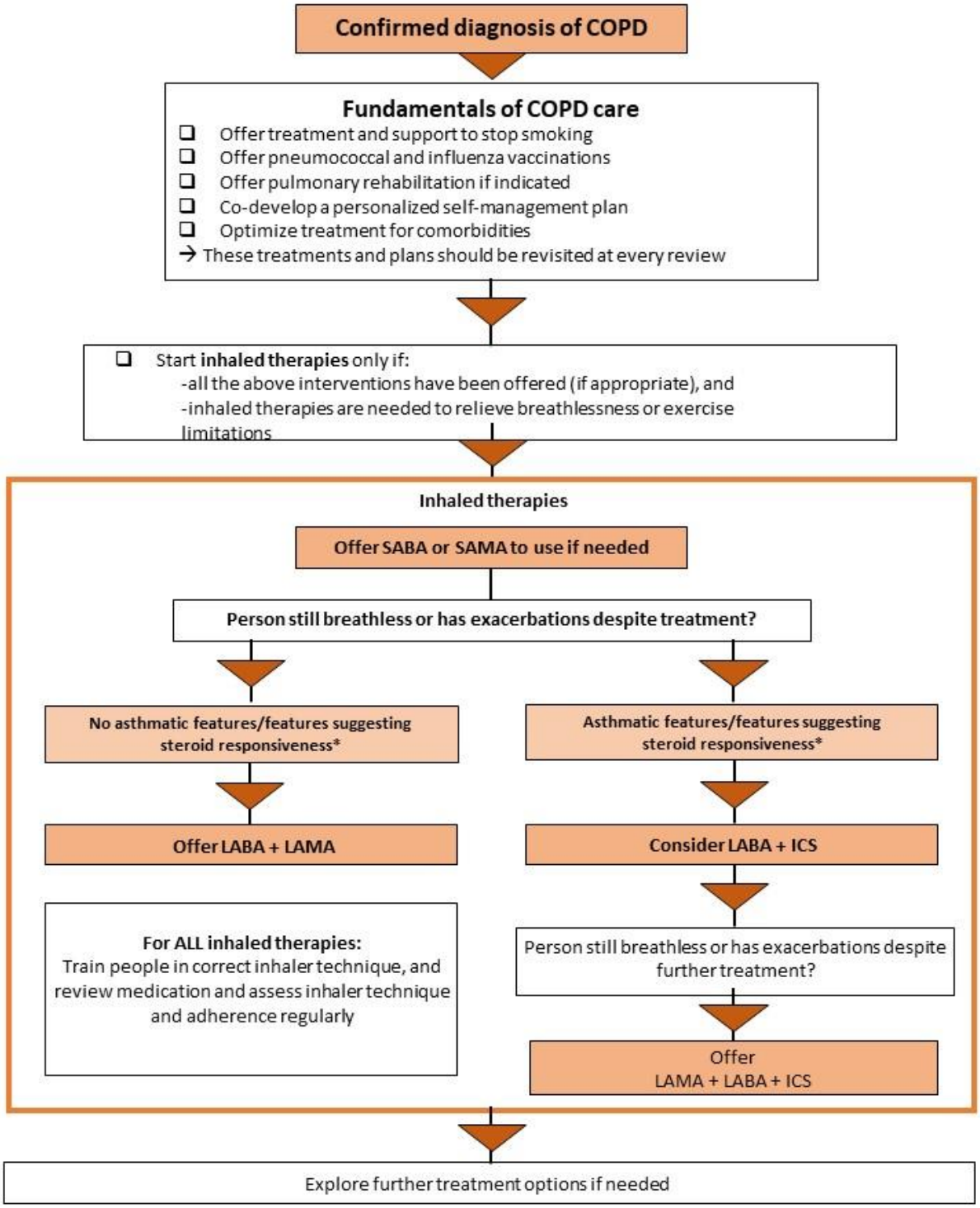


Figure 4: GOLD guidelines for treatment of COPD. Modified according to GOLD. 2018 (36)

General approach to inhalation-treatment after diagnosing COPD



SABA= short-acting beta2 agonist SAMA= short-acting muscarinic antagonists
LABA= long-acting beta2 agonists LAMA= long-acting muscarinic antagonists ICS= inhaled corticosteroids
* Asthmatic features/features suggesting steroid responsiveness in this context include any previous secure diagnosis of asthma or atopy, a higher blood eosinophil count, substantial variation in FEV1 over time or substantial diurnal variation in peak expiratory flow.

Figure 5: Summary of the recommendations on non-pharmacological management of COPD and use of inhaled therapies. Modified according to National Institute for Health and Care Excellence. 2018 (46)

9. Discussion and conclusion

COPD exacerbations and comorbid diseases represent treatment, diagnostic and decision making challenges for the ED. For the best possible outcome, a multi-disciplinary approach is indispensable starting from the anamneses, to choosing the right laboratory studies and imaging modalities.

Early diagnoses combined with proper assessment using different evaluation modalities greatly improves patient care, minimalize errors and improves management options as the disease progresses. Starting non-pharmacological and pharmacological treatment in combination with lifestyle changes and prophylactic immunization with pneumococcal and influenza vaccinations will decrease the burden of the disease and reduce episodes of AE and comorbid diseases.

The ED physician can use algorithms, diagnostic tools and assess risk factors and past history of AE in predicting if there is a potential bacterial cause of the AE, making antibiotics the necessary treatment option. Furthermore, clinical knowledge, experience, and judgment should guide the physician when deciding if hospitalization and oxygen treatment is required to treat severe COPD and save the patient's life in contrast to choosing home-care in the case of mild to moderate COPD.

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12. Biography

I was born in Lund, Sweden on December 22th 1992 alongside my twin sister Iva. I have Serbo-Croatian origins; my father Goran Pajnic a civil engineer from Zagreb, Croatia, and mother Dragana Severin who as a small child came to Sweden from Subotica, Serbia. I grew up in the south of Sweden in the university town Lund where I finished both primary school and high school (Spyken, natural science as a field of study).

In my free time, I started training and competing in tennis throughout my youth, later playing in and representing the Zagreb's Medical School tennis team. The affection for the sport made me become licensed tennis-coach teaching kids and adolescent players for many years.

Shortly after finishing high school my love for skiing made me move to Sankt Anton am Arlberg an alpine village in Austria. There I lived for 6 months combining work at a hotel with skiing. After returning to Sweden I started working with mentally challenged students at a high school in my home town. As I decided to study medicine I moved to Stockholm where I completed a pre-medical course and the entrance exam for Zagreb Medical Studies in English.

During my studies in Zagreb between 2013-2019, apart from studying and enjoying my time in Croatia, I served as a board member in the Swedish Medical Association for Students abroad. As a board member, I was helping, connecting and promoting Swedish medical students that are studying in the medical field outside of Sweden to integrate students to the Swedish medical system. Our board also arranged a congress for students that was held in Riga, Latvia 2017 offering lectures, seminars, workshops and meetings with Swedish hospital representatives enabling to give Swedish students studying abroad the first contact to future employers offering summer-jobs and clinical rotations. In 2019 I finished my medical school by doing my clinical rotations in Sweden and in Zagreb at the Department of Emergency Medicine, Sisters of Charity University Hospital Centre and Department of Surgery at Zagreb University Hospital Centre (Rebro).