Chapter 19
Chronic Obstructive Pulmonary Disease (COPD)

Seema O. Brij, Sumit Chatterji, and Malcolm Marquette

Key Points

- COPD is a major global health problem and is predicted to be the third commonest cause of death worldwide by 2030.
- COPD is characterised by airflow obstruction that is slowly progressive and persistent. This is easily measurable with spirometry, and the rate of decline in FEV1 predicts morbidity and mortality.
- Severity of COPD is based upon a combination of factors including symptoms, functional disability, rate of decline of FEV1, presence of respiratory failure, the number of exacerbations and whether they require hospital admission.
- Stopping smoking continues to be the most cost-effective way of preventing COPD.

Introduction

COPD is characterised by airflow obstruction that is not fully reversible and is persistent and usually progressive. COPD is underdiagnosed, especially in the early stages, because symptoms may not be apparent until the development of significant airflow obstruction.

COPD produces symptoms, disability and impaired quality of life which may respond to pharmacological and other therapies that have limited or no impact on

S.O. Brij, DM, FRCP (Lond), BM, BS (✉) • S. Chatterji, FRCP, FCCP, MB BChir, AHEA • M. Marquette, MBCHB, MRCP, MD
Department of Respiratory Medicine, Peterborough City Hospital, Peterborough PE3 9GZ, UK
e-mail: seema.brij@pbh-tr.nhs.uk

S.S. David (ed.), *Clinical Pathways in Emergency Medicine: Volume I*,
DOI 10.1007/978-81-322-2710-6_19

Table 19.1 Definitions of conditions associated with airflow obstruction

Condition	Definition
Chronic obstructive pulmonary disease (COPD)	Airflow obstruction that is usually progressive, not fully reversible and does not change markedly over several months. It is usually caused by smoking
Chronic bronchitis (CB)	Presence of chronic cough productive of sputum on most days for 3 months in each of 2 consecutive years, and other causes of productive cough have been excluded
Emphysema	Abnormal, permanently enlarged distal airspaces distal to the terminal bronchiole, accompanied by destruction of alveolar walls and without obvious fibrosis
Asthma	Airflow obstruction that is usually nonprogressive, fully reversible and changes in its severity over short periods of time either spontaneously or after treatment

the extent of airflow obstruction. COPD is now the preferred term that encompasses conditions previously known as chronic bronchitis and/or emphysema (Table 19.1).

Epidemiology

COPD is a common respiratory disorder affecting over 65 million people worldwide [2]. The prevalence of COPD increases with age, with a fivefold increased risk for those aged over 65 years compared with patients aged less than 40 years.

Mortality

According to the World Health Organization, COPD is the fourth leading cause of death in the world, with approximately 2.75 million deaths per annum, or 4.8 % of deaths [2].

Mortality from COPD is higher in males and increases with age in those over 45 yrs old.

Factors predictive of mortality:

- Severity of airflow obstruction (e.g. using GOLD [3] criteria)
- Nutritional status (body mass index)
- Exercise capacity using the 6-min walk test
- Severity of dyspnoea (using a dyspnoea functional scale such as the modified MRC scale (Table 19.2)), social status and poverty

Composite indices such as the commonly used BODE index [4] (*B*MI, severity of airflow *O*bstruction, severity of *D*yspnoea, 6-min walk *E*xercise distance) try to prognosticate using these factors and are often utilised by transplant teams to determine the timing of lung transplantation.

Table 19.2 The modified MRC Dyspnoea Scale

Grade	Degree of breathlessness related to activity
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground, *or*
	I get short of breath when walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, *or*
	I have to stop for breath when walking at my own pace on the level
3	I stop for breath after walking about 100 yards, *or*
	I stop for breath after a few minutes on level ground
4	I am too breathless to leave the house, *or*
	I am breathless when dressing

Risk Factors

The development of COPD is dependent upon the inhalation of noxious agents in a susceptible host.

Host Factors

- Genetic mutations (e.g. α_1 anti-trypsin deficiency)
- Airway hyperresponsiveness
- Reduced lung growth

Exposures

- Smoking (cigarettes, cigars, shisha, marijuana, heroin)
- Indoor and outdoor pollution
- Occupational dusts and chemicals
- Infections

Pathological Findings

The chronic inhalation of noxious particles incites inflammation in the lungs. This becomes exaggerated and uncontrolled, resulting in mucus hypersecretion (chronic bronchitis), progressive tissue destruction (emphysema) and a disordered repair mechanism (bronchiolitis). The result is the clinical syndrome of COPD: small airways become narrowed increasing resistance to airflow; the lungs are less elastic

with increased compliance; there is air-trapping (hyperinflation); and the changes are dose dependent and persistent, even following smoking cessation.

Pathological changes are predominantly seen in the airways but can also be seen in the lung parenchyma and also in the pulmonary vasculature.

Pathogenesis of COPD

Pulmonary injury involves stages of *initiation* (through exposure to injurious agents), *progression* and *consolidation*. The underlying pathology in COPD can be summarised as mucus hypersecretion, alveolar damage caused by proteolysis and apoptosis and subepithelial airway fibrosis.

Symptoms of COPD

Common

- Exertional breathlessness
- Chronic cough
- Sputum production
- Frequent chest infections or winter bronchitis
- Wheeze

Associated Symptoms

Weight loss and tiredness

Uncommon Symptoms

Haemoptysis, chest pain and significant weight loss and other disorders such as lung cancer, bronchiectasis and TB may need to be excluded.

Unfortunately, the presence of symptoms is not a reliable indicator of COPD, and diagnosis is often missed until more severe airflow obstruction is present.

Signs of COPD

Physical examination of persons with COPD, especially early in the disease process, is often normal.

Inspection may reveal tar-stained fingers in a heavy smoker who may also smell of cigarette smoke. Other signs such as cyanosis (peripheral and central), pursed-lipped breathing (which increases expiratory airway pressure preventing premature airways collapse), use of accessory muscles of respiration (scalene and sternocleidomastoid) and barrel-shaped chest (increased anterior posterior diameter indicating hyperinflation) with reduced expansion may be present. Auscultation may reveal vesicular breath sounds. Reduced breath sounds with or without wheeze are also a feature.

Signs of advanced COPD are usually related to the presence of cor pulmonale, defined as right ventricular hypertrophy caused by any chronic lung disease and is therefore not specific to COPD. Signs of right heart failure include raised jugular venous pressure, right ventricular heave, palpable thrill or loud P_2 heart sound, tricuspid regurgitation (pulsatile liver and mild jaundice) and pitting oedema.

Investigation of COPD

Spirometry

In order to confirm the diagnosis, a post-bronchodilator FEV1/FVC ratio of less than 0.7 must be present. The severity of airflow obstruction can be assessed according to the reduction in FEV1 (Table 19.3). Thus, by performing spirometry over a long period of time, it is possible to monitor lung function decline. The rate of decline in FEV1 is a good marker of disease progression and mortality.

Spirometry should be performed in patients who are over 35, are current or ex-smokers and have a chronic cough.

Further Investigations

- A plain chest radiograph (Fig. 19.1) – hyperexpansion (greater than eight posterior or six anterior ribs clearly visible), flattened diaphragms, long thin heart, prominent hilar vessels and barrel-shaped thorax.

Table 19.3 Severity of airflow obstruction

FEV1/FVC	FEV1 % predicted	Severity
<0.7	≥80	Mild[a]
<0.7	50–79	Moderate
<0.7	30–49	Severe
<0.7	<30	Very severe[b]

[a]Symptoms should be present to diagnose COPD with mild airflow obstruction [1]

[b]Or FEV1 <50 % with respiratory failure

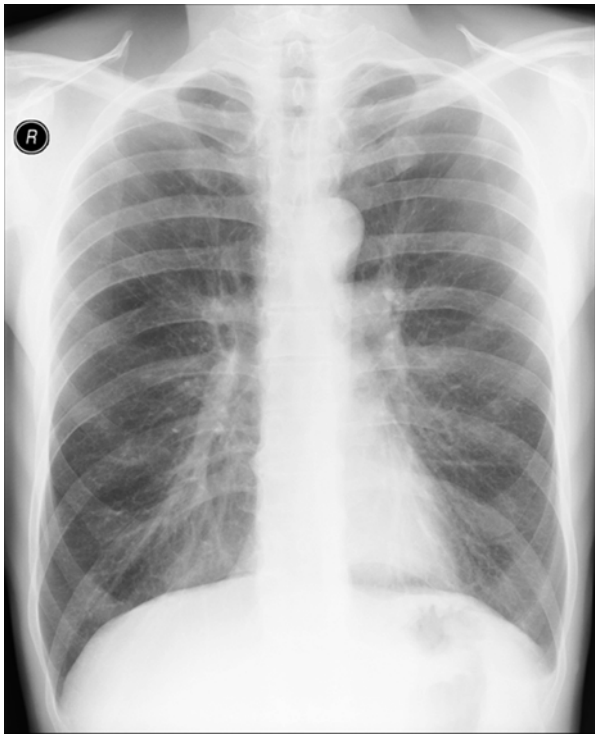

Fig. 19.1 CXR–COPD changes

- Full blood count is useful to ensure that there is not anaemia contributing to breathlessness symptoms nor polycythaemia related to hypoxaemia. A raised eosinophil count should always raise the possibility of asthma.
- Other useful investigations and their rationale are enumerated in Table 19.4.

Stable COPD Management

The management of stable COPD is a holistic approach to disease and symptom modification. The principles are outlined as four tenets of COPD management (Table 19.5).

Pharmacological Therapies for COPD

1. *Inhaled bronchodilators*
   - *Short-acting β_2-agonists* (*SABA*) such as salbutamol act on airway smooth muscle through β_2-adrenergic receptor agonism resulting in bronchial smooth muscle relaxation and therefore airway dilatation. The onset of airway dilatation is minutes with a duration of action up to 6 h. Short-acting

Table 19.4 Other useful investigations

Investigation	Rationale for testing
Peak flow diary exercise	Variable airflow obstruction is more likely to be asthma
α_1 anti-trypsin levels	Early onset COPD, minimal smoking history or family history
Transfer factor (TLCO)	To investigate symptoms that seem disproportionate to the impairment in FEV1
Chest CT	To investigate
	(a) Symptoms that seem disproportionate to the impairment in FEV1
	(b) Abnormalities seen on a chest radiograph
	(c) Extent and distribution of structural parenchymal and airways disease
ECG	Exclude arrhythmia and look for evidence of cor pulmonale
ECHO	Exclude significant LVD, valvular abnormalities and look for evidence of cor pulmonale
Pulse oximetry	Screen for hypoxaemia (suggestive if SaO_2 <92 %)
Sputum culture	Identify resistant or unusual organisms if sputum is persistent and purulent

Table 19.5 The four tenets of COPD management

Tenet	Theory	Practice
1. Stop smoking	Smoking is the most important aetiology for the development of COPD	Tobacco legislation
	Smoking cessation is the only proven way of modifying the natural course of COPD	Smoking cessation
2. Keep fit	Regular exercise training conditions the muscles and reduces the ventilatory demand of exercise	Pulmonary rehabilitation [5] should be undertaken and repeated if necessary
		COPD patients should be encouraged to keep as active and fit as possible
		Smoking cessation
3. Multidisciplinary patient-focused care	Good understanding of disease process, collaborative approaches to pharmacotherapy and regular review by highly motivated COPD team ensure high-quality care and favourable patient satisfaction	Smoking cessation
		Inhaler technique assessment
		Assess response to pharmacotherapy and amend/discontinue as required
		Yearly spirometry, BMI, flu vaccination
4. Self-management of exacerbations	Early identification of symptoms such that COPD patients are empowered to initiate empirical therapy thereby reducing severity of exacerbations	Rescue medication (antibiotics and oral corticosteroid therapy)
		SOS access to COPD team
		End of life and advanced care plan

β_2-agontists are therefore used as rescue medication to treat symptomatic breathlessness and to improve exercise tolerance on an as required basis.
- *Long-acting β2-agonists* (*LABA*) such as salmeterol and formoterol also act on airway smooth muscle with a longer duration of action, about 12 h.

2. *Anticholinergics*

- Short-acting anticholinergics such as ipratropium antagonise muscarinic receptors and therefore block reflex cholinergic bronchoconstriction. The onset of action is slower, but the duration of action is more sustained.
- Ipratropium is given regularly three to four times a day and reduces the need for rescue medication as well as improving lung function and quality of life.
- Long-acting anticholinergics such as tiotropium antagonise muscarinic receptors and block reflex cholinergic bronchoconstriction.

3. *Combination bronchodilators*

- The first combination long-acting β_2-agonists and long-acting anticholinergic.
- LABA/LAMA for the treatment of COPD has become available. Ultibro, indacaterol (LABA) and glycopyrronium (LAMA), is administered once daily using a Breezhaler device and has been shown to be comparable to treatment with Seretide.

4. *Inhaled corticosteroids* (*ICS*)

- The combination of inhaled corticosteroid and long-acting β_2-agonist (ICS/LABA) is considered standard therapy for COPD patients (with moderate or more severe airflow obstruction) who frequently exacerbate.
- Compared to placebo, Seretide (fluticasone propionate and salmeterol) and Symbicort (budesonide and formoterol) reduce exacerbation rates and improve lung function and quality of life.
- Newer treatments such as Relvar (fluticasone furoate and vilanterol) have the added advantage of being administered once daily.

5. *Methylxanthines*

- Methylxanthines, such as caffeine, theophylline and aminophylline are bronchodilators that can be administered orally.
- Only the slow-release formulations have been shown to be of benefit in stable COPD patients.

6. *Mucolytic therapy*

- Despite mucolytic therapy having no effect on lung function, there are studies demonstrating that regular usage is associated with reduced exacerbations.

7. *Antibiotic prophylaxis*

- There is growing evidence that low-dose macrolide therapy in selected COPD patients appears to have an immunomodulatory effect with reduced exacerbation rates and improved quality of life scores.

8. *Oral corticosteroid therapy*

   - If at all possible, oral corticosteroid therapy in the management of stable COPD should be avoided. However, there are some patients in whom prolonged oral corticosteroid therapy cannot be avoided, generally following exacerbations, and current guidelines advise that the lowest dose of oral corticosteroid is used.

9. *Oxygen therapy*

   Many patients with COPD will develop respiratory failure. This can either be hypoxic or hypercapnic in nature:

   (a) Type 1 respiratory failure is characterised by hypoxaemia (PaO_2 <8 kPa) secondary to impaired gas exchange in the lungs.
   (b) Type 2 respiratory failure (or ventilatory failure) is hypoxaemia accompanied by hypercapnia ($PaCO_2$ >6 kPa) and occurs as a result of impaired ventilation.

   The treatment for hypoxaemia is controlled oxygen therapy. In contrast, the treatment for hypercapnic respiratory failure is ventilatory support.

10. *Long-term oxygen therapy* (*LTOT*)

    Long-term oxygen therapy is defined as oxygen therapy administered for greater than 15 h per day and should be considered in patients with COPD who satisfy the following criteria:

    (a) PaO_2 <7.3 kPa performed on two separate occasions at least 3 weeks apart during a period of clinical stability
    (b) PaO_2 <8.0 kPa if there is stress polycythaemia, pulmonary hypertension, peripheral oedema or nocturnal hypoxaemia

11. *Ambulatory oxygen therapy* (*AOT*)

    Ambulatory oxygen therapy should be considered in two groups of COPD patients:

    (a) Patients on LTOT and have oxygen requirements not met by their concentrator, for example, when they are out of their home and during exercise
    (b) Patients, whom there is documented symptomatic exercise desaturation without the requirement for LTOT

12. *Non-invasive ventilation for chronic hypercapnic respiratory failure*

    Non-invasive ventilation should be considered in either of the following:

    - Chronic hypercapnic respiratory (ventilatory) failure.
    - Patients requiring assisted ventilation (whether invasive or non-invasive) during an exacerbation.
    - Patients who are hypercapnic or acidotic on LTOT should be considered for long-term non-invasive ventilation.

13. *Immunisation*

    - Although clinical trial data are limited, there is evidence that influenza and to a lesser extent pneumococcal vaccination can prevent some of the infections that cause COPD exacerbations and therefore should be administered to all patients with COPD.

14. *Surgical therapy*

- Surgical intervention is normally only considered in non-smokers and ex-smokers when maximal medical therapy has failed.
- The aim of surgery is to restore quality of life and alleviate symptomatology.
- NICE recommend that patients below the age of 65 with severe COPD who remain breathless with marked restrictions of their activities of daily living despite maximal medical therapy should be considered for referral for assessment for lung transplantation.

Acute Exacerbations of COPD

COPD exacerbations are defined as an acute worsening of patient symptoms and respiratory function, which is not explained by normal day-to-day variation in symptoms and which requires alteration in the pharmacological treatment.

The most common pathogens causing COPD in United Kingdom are *Haemophilus influenzae* and Rhinovirus. Less common pathogens such as *Streptococcus*, *Moraxella catarrhalis*, parainfluenza virus, respiratory syncytial virus and *Pseudomonas aeruginosa* cause exacerbation of COPD.

Management of Acute Exacerbation

- Oxygenation – controlled oxygen therapy to maintain SaO_2 88–92 %
- Nebulised bronchodilators
- Intravenous aminophylline, although the evidence for additional benefit is lacking.
- Corticosteroid (prednisolone 30–40 mg per day) or if unable to swallow then intravenous hydrocortisone (100–200 mg).
- Antibiotic therapy is most likely to be useful if the sputum is purulent.
- Chest clearance may be facilitated with the use of mucolytic agents such as carbocysteine, nebulised saline and chest physiotherapy.
- Acute hypercapnic respiratory failure is an indication for non-invasive ventilation.
- Venous thromboembolism prophylaxis unless contraindicated.
- Adequate hydration and nutrition.

Hospitalisation Criteria

The majority of patients experiencing an exacerbation of COPD do not require hospitalisation (Table 19.6), but more than 50 % of the total cost of COPD is accounted for by services related to exacerbations.

Non-invasive Ventilation (NIV) for COPD in the Acute Setting

NIV used appropriately reduces mortality, escalation to invasive ventilation, days in hospital and nosocomial pneumonia [6–8].

Table 19.6 Factors that may determine where COPD exacerbations are treated

Factor	Treat at home	Treat in hospital
Social factors		
Social circumstances	Good	Living alone or not coping
Able to cope at home	Yes	No
Severity of stable COPD		
Breathlessness	Mild	Severe
LTOT	No	Yes
Level of physical activity	Good	Poor or confined to bed
General condition	Good	Poor or deteriorating
Significant co-morbidity (particularly cardiac disease and insulin-dependent diabetes)	No	Yes
Severity of the exacerbation		
Rapid rate of onset	No	Yes
Breathlessness	Mild	Severe
Worsening peripheral oedema	No	Yes
Acute confusion	No	Yes
Level of consciousness	Normal	Impaired
Cyanosis	No	Yes
SaO_2 <90 %	No	Yes
Arterial pO_2	≥7 kPa	<7 kPa
Arterial pH level	≥7.35	<7.35
Changes on CXR	No	Yes

Equipment

NIV machines are typically bilevel positive airway pressure (BIPAP) ventilators.

Patient Selection

- NIV should be considered in patients with an acute exacerbation of COPD who have a respiratory acidosis (pH <7.35) and hypercapnia ($PaCO_2$ >6 kPa) despite intensive medical management for a maximum of 1 h from admission.
- There are relative contraindications to NIV (Table 19.7).
- The decision to proceed with NIV should be made on an individual basis considering all these potential factors.

Treatment Success and Failure

Success of NIV in the acute setting is defined by improvement in clinical parameters, normalisation of blood pH and a progressive return of respiratory rate to normality.

Table 19.7 Relative contraindications to NIV

Facial trauma/burns
Recent facial, upper airway or upper gastrointestinal tract surgery[a]
Fixed obstruction of the upper airway
Inability to protect the airway[a]
Life-threatening hypoxaemia[a]
Haemodynamic instability[a]
Severe co-morbidity[a]
Glasgow coma score <10[a]
Confusion/agitation[a]
Vomiting
Bowel obstruction[a]
Copious respiratory secretions or pneumonia[a]
Pneumothorax[a]

[a]NIV can be used as a ceiling of treatment in these circumstances

References

1. National Institute for Health and Care Excellence. COPD guideline CG 101 (Published 2010 and revised 2014). www.nice.org.uk.
2. Halbert RJ, Natoli JL, Gano A, Badambarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. Eur Respir J. 2006;28:523–32.
3. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease (Revised 2011).
4. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, Pinto Plata V, Cabral HJ. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med. 2004;350(10):1005–12.
5. Lareau SC, ZuWallack R, et al. Pulmonary rehabilitation: official statement of the American Thoracic Society. Am J Respir Crit Care Med. 1999;159:1666–82.
6. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. Lancet. 2000;355:1931–5.
7. Confalonieri M, Parigi P, Scartabellati A, et al. Noninvasive mechanical ventilation improves the immediate and long-term outcome of COPD patients with acute respiratory failure. Eur Respir J. 1996;9:422–30.
8. Vitacca M, Clini E, Rubini F, et al. Non-invasive mechanical ventilation in severe chronic obstructive lung disease and acute respiratory failure: short-and long-term prognosis. Intensive Care Med. 1996;22:94–100.