PAKISTAN CHEST SOCIETY
STRIVING FOR PULMONARY CARE

2020

GUIDELINES FOR THE MANAGEMENT OF COPD

National Clinical Guidelines: Pakistan Chest Society, 2020

GUIDELINES FOR THE MANAGEMENT OF

COPD

Chronic Obstructive Pulmonary Disease

Guidelines

2020

PAKISTAN CHEST SOCIETY
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COPD Guideline working group

Dr Maqbool A Langove (Chairman working group)

MBBS, FCPS (Pulmonology)
Assistant Professor
Fatima Jinnah General and Chest Hospital, Quetta

Prof Dr Nadeem Ahmed Rizvi

MBBS, FRCP (UK), MCPS (Chest)
Professor and Ex-HOD
Department of pulmonology,
Jinnah Postgraduate Medical Center, Karachi

Dr Kamran Khan Sumalani

MBBS, DTCD, MCPS (Chest), MD (Pulmonology)
Assistant Professor
Department of pulmonology,
Jinnah Postgraduate Medical Center, Karachi

Dr Nousheen Akhter

MBBS, FCPS (Pulmonology)
Consultant Pulmonologist
PNS Shifa Hospital, Karachi

Prof Dr Saadia Ashraf

MBBS, FCPS (medicine), MCPS (Chest),
FCPS (Pulmonology) Goldmedalist, MHPE
Professor and HOD Pulmonology Department
Khyber Medical College/ Khyber Teaching Hospital,
MTI, Peshawar

Dr Sanaullah Tareen

MBBS, MCPS, FCPS (Pulmonology), MMS
Assistant Professor
Bolan medical college, Quetta

PCS GUIDELINES COMMITTEE

Prof. Muhammad Irfan (Chairman)

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MESSAGE BY THE PRESIDENT Pakistan Chest Society (PCS)

It is a matter of great pleasure and satisfaction for me that PCS is successfully pursuing its agenda of formulating national guideline on COPD. This publication comprehensively but at the same time concisely sheds light on all the aspects of COPD.

COPD is a major cause of chronic morbidity and mortality throughout the world. It represents an important public health challenge that is both preventable and treatable. This risk is mainly associated with increase rate of smoking especially in Pakistan.

This guideline has covered every aspect related to COPD including pathogenesis, diagnosis and management. It has also covered management during exacerbation. Section on supportive treatment strategies also included like smoking cessation, vaccination, pulmonary rehabilitation etc.

PCS is fortunate that it has galaxy of intellectuals who are coherent to each other and ready to impart their part in the work assigned to them. I am thankful to the guideline working group for their hard work and devotion they paid in term of time without which it was not possible to bring this guideline in your hands.

I hope this guideline will be useful for postgraduate trainees, practicing physicians, pulmonologists, scientists and health workers with interest in COPD. It will become a powerful tool for them to enhance their knowledge, which in turn will positively impact the standard of medical care.

PROFESSOR NISAR AHMED RAO

President Pakistan Chest Society

MESSAGE BY THE Chairman Guidelines Committee, Pakistan Chest Society (PCS)

It is a matter of great pleasure, pride and satisfaction that guideline for the **Management of COPD** have been revised by the working group. Governing Council of PCS has mandated the Guideline committee to develop evidence based guidelines for important pulmonary diseases. Besides this document, guidelines on Asthma, Sleep apnea, Noninvasive ventilation, Pre-operative pulmonary risk assessment and guideline on smoking Cessation have already been developed and will distributed during the 14th Biennial Chest Con 2020 in Karachi. It is very encouraging to note that PCS has been consistently working on developing and updating guidelines. These guidelines provide a highly valuable resource for the trainees and practicing physicians.

COPD is a major global cause of chronic morbidity and mortality. This publication comprehensively covers all the aspects related to COPD diagnosis and management. I hope this guideline will be useful for trainees, practicing physicians and health care workers with interest in COPD.

Finally, I would like to acknowledge the hard work of Dr Maqbool and other members of the working group who revised this document and the members of PCS guideline committee for reviewing the document. PCS remain committed to always endeavor for the achievement of the best possible clinical practice.

Prof. Muhammad Irfan

Chairman Guidelines Committee, PCS

Acknowledgment

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We would like to extend gratitude to Pakistan Chest Society for their trust and giving us the opportunity to prepare this guideline.

Khalid Ahmed, Mr Imran Khan Sumalani

PREFACE OF REVISED EDITION

The first COPD guideline was issued in 2005 and revised in 2010; and as the new edition of the COPD guideline is in hand after 10 years, you will quickly recognize this edition differs significantly from its predecessor. There has been much change in the understanding and management of the disease over the past decade.

These changes are based on updated scientific literatures worldwide and locally, while at the same time maintaining simplicity for the practicing clinicians. PCS has been fortunate to have network of distinguished health professionals to bring COPD to the attention of Governments, public health officials, health care workers and the general public to raise awareness of the burden of COPD and to develop programs for early detection, prevention and approaches to management according to local needs based on the best scientific information available.

According to meta analysis prevalence of COPD in Pakistan is 13.8%, and it is more common in males than in females. In rural areas, it is commoner in females likely due to exposure to burning biomass fuel.

The most blamed and preventable risk to getting the disease is cigarette smoking. The overall prevalence of smoking in Pakistan is 14.5% (26.1% in males and 5.4% in females). Unfortunately, legislations against its use are not implemented in the country.

Although the disease is not curable, the attainable goals of management are to slow down deterioration, improves symptoms and lung function, thus improving the overall health status of the patient.

COPD patients might need hospitalization during exacerbations but most times it is the primary care physician who has to deal with managing the patients. This guideline will be of help to health care providers at all levels dealing with COPD patients.

Dr Maqbool A Langove

Chairman COPD guideline working group

ABBREVIATIONS

6MWT	Six minute walk test
ABGs	Arterial blood gases
AD	Alveolar duct
AECOPD	Acute exacerbation of chronic obstructive pulmonary disease
AFB	Acid fast bacillus
AS	Alveolar sac
BiPAP	Bilevel positive airway pressure
BLVR	Bronchoscopic lung volume reduction surgery
BMI	Body mass index
BODE	Body mass index, Obstruction, Dyspnea, Exercise
BOLD	Burden of Obstructive Lung Disease
cAMP	Cyclic adenosine monophosphate, or 3',5'-cyclic adenosine monophosphate
CAT	Combined assessment test
CI	Confidence interval
CO	Cardiac output
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
DALYs	Disability adjusted life years
DLCO	Diffusion capacity of lung for carbon monoxide
DPI	Dry powder inhaler
ECM	Extracellular matrix
EMRO	Eastern Mediterranean Regional Office
FEV1	Forced expiratory volume in one second
FVC	Forced vital capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HIV	Human immunodeficiency virus
HR	Hazard ratio; Heart rate
HrQOL	Health related quality of life
ICS	Inhaled corticosteroid
ICU	Intensive care unit
IV	Intravenous
JVP	Jugular venous pulse
LABA	Long acting beta agonist
LAMA	Long acting muscuranic antagonist
LLN	Lower limit of normal
LTOT	Long term oxygen therapy
LVRS	Lung volume reduction surgery
MDI	Metered dose inhaler
MMPs	Matrix metalloproteinases
mMRC	Modified medical research council
MV	Minute ventilation
NIV	Non invasive ventilation
O_2	Oxygen
OCS	Oral corticosteroids
OR	Odds ratio

P2	Pulmonic second heart sound
PAO_2	Partial pressure of oxygen in alveoli
$PaCO_2$	Partial pressure of carbon dioxide in arterial blood
PaO_2	Partial pressure of oxygen in arterial blood
PCS	Pakistan chest society
PCV	Pneumococcal conjugate vaccine
PDE-4	Phosphodiesterase 4 inhibitor
PEEP	Positive end expiratory pressure
PEFR	Peak expiratory flow rate
PHT	Pulmonary hypertension
PIO_2	Pressure of inspired oxygen
PPSV	Pneumococcal polysaccharide vaccine
RB	Respiratory bronchiole
RHF	Right heart failure
RSV	Respiratory syncitial virus
RV	Residual volume
SaO_2	Arterial oxygen saturation (measured by arterial blood gas analysis)
SARS	Severe acute respiratory syndrome
SERPIN	Serine protease inhibitor
SMI	Soft mist inhaler
SpO_2	Peripheral oxygen saturation (measured by pulse oximeter)
SR	Slow release
TB	Tuberculosis; Terminal bronchiole
TLC	Total lung capacity
V:Q	Ventilation: Perfusion
VC	Vital capacity
WHO	World health organization
WOB	Work of breathing

Contents

1: INTRODUCTION

The Pakistan Chest Society (PCS) guideline was developed by expertise in chronic obstructive pulmonary disease (COPD) and the aim of PCS is to provide evidence based recommendations, while maintaining simplicity for the assessment, diagnosis and management of COPD for graduates, post-graduates and general practitioners.

The Burden of COPD

Chronic obstructive pulmonary disease (COPD) is preventable and treatable disease. The available data suggest that the prevalence of physiologically defined COPD in adults aged ≥40 yrs is 9–10%.[1] Based on BOLD and other large epidemiologic studies the global prevalence of COPD in 2010 was 11.7%.[2] In addition to imparting a substantial economic burden on individuals and society, COPD imposes a significant burden in terms of disability and impaired quality of life. COPD was the 5th leading cause of mortality worldwide in 2002 and is projected to be 4th on the list till 2030.[3] It is projected to rank 8th among the top fifteen leading causes of disability adjusted life years (DALYs) by 2030.[3]

According to a metanalysis done in 2018, Pakistan has the highest prevalence of COPD (13.8%), in the EMRO region.[4] The prevalence of COPD increases with rising smoking trend and aging population. Table 1 shows the results of tobacco use prevalence from latest survey completed by end of December 2018.[5]

Table 1: Prevalence of tobacco use (latest survey completed by WHO, December 2018)

	Tobacco use		Tobacco smoking		Cigarette smoking		Smokeless tobacco use		E-cigarette use	
	Current	Daily	Current	Daily	Current	Daily	Current	Daily	Current	Daily
Survey: National Diabetes Survey of Pakistan, 2016-17; National, ages 20+#										
Male	26.1	..	..	..	..	..	11.4*	10.5*	..	..

Female	5.4	..	..	..	..	..	3.7*	3.5*	..	..
Both sexes	14.5	..	..	..	..	..	7.7*	7.1*	..	..
Survey: Global Youth Tobacco Survey, 2013; National, ages 13-15										
Male	13.3	..	9.2	..	4.8	..	6.4	..	..	..
Female	6.6	..	4.1	..	0.9	..	3.7	..	..	..
Both sexes	10.7	..	7.2	..	3.3	..	5.3	..	..	..

* Global Adult Tobacco Survey, 2014; National, ages 15+

4.4 % men, 1 % women and 2.7 % of the adult population are daily water pipe smokers

A systemic review published in 2011 reported the prevalence of waterpipe (Shisha) smoking to be 33% among university students and 6% among adult population of Pakistan.[6]

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2: DEFINITION OF COPD

"COPD is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development."[1]

In a developing country like Pakistan the impact of COPD on workplace and home productivity are equally important as the direct medical costs related to the disease. Hence COPD is a serious threat to a country's economy.

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3: RISK FACTORS OF COPD

Many factors contribute to the development of COPD.[1] The most important ones are discussed below.

Cigarette smoking is the most important risk factor for development of COPD.[2] But approximately 25 – 45% of patients with COPD are lifelong non-smokers.[3] On the other hand fewer than 50% of heavy smokers do not develop COPD.[4] Several mechanisms are proposed by which smoking may contribute to COPD.

Prenatal exposure
- Reduced lung development
- Low birth weight

Childhood
- Decreased lung growth

Adulthood
- Accelerated decline in lung function
- Lung destruction
- Impaired lung repair

The greater the total numbers of cigarette smoke, the greater the risk of development of COPD. It is good to quantify this exposure as under:[5]

$$\text{Pack year} = \frac{\text{Number of cigarettes smoked per day x Number of years of smoking}}{20}$$

Smokers suffer an irreversible loss of 4.4–10.4 ml in FEV1 per pack year smoked.[6,7] There is a strong dose–response relation between the smoking pack years and the risk,[8] severity,[9] and mortality[10] of COPD and the risk of lung cancer.[11]
Loose tobacco is quantified as tobacco smoked in "ounces per week", which can be converted into pack years:[12]

Pack years = Ounces of loose tobacco per week × 2/7 × number of years smoked

Indoor and outdoor air pollution like biomass fuel for cooking or heating in poorly ventilated dwellings, passive smoking and exposure to urban air pollution, organic and inorganic dusts, chemicals or fumes. In Pakistan, biomass fuel is used for cooking and heating by 52% of households overall, and 75% in rural area, figure 3.1.[13] The prevalence of COPD is two to three times higher in women exposed to biomass fuel as compared to urban women.[14,15] According to a meta-analysis, biomass-exposed individuals are 1.38 times more likely to be diagnosed with COPD than non-exposed (OR 1.38, 95% CI 1.28 to 1.57).[16]

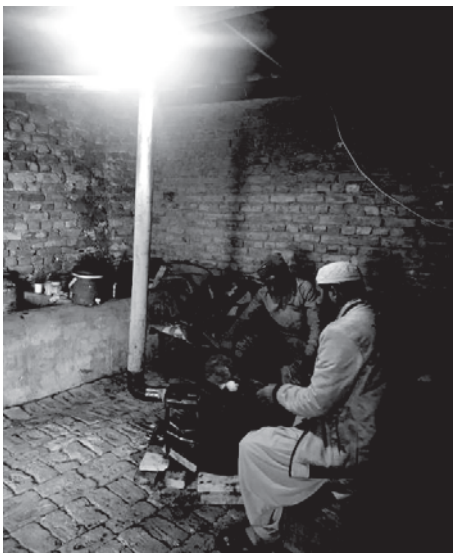

Figure 3.1: Indoor biomass exposure

Figure 3.2: Inside of the coal mine

Genetic predisposition[17] is possibly related to α1-proteinase inhibitor, α1-antichymotrypsin, α2-macroglobulin, matrix metalloproteinase 12, α-nicotinic acetylcholine receptor, hedgehog interacting protein and many others.

Most common is alpha-1 antitrypsin deficiency. Alph-1 antitrypsin is a serine protease inhibitor (SERPIN) secreted by the liver, which inhibits the enzyme neutrophil elastase from damaging the lung tissue. Deficiency of this alpha-1 antitrypsin leads to unopposed elasteolysis and development of emphysema (protease-antiprotease hypothesis). These patients usually present at an early age.

Infections during childhood may increase subsequent risk of COPD by affecting lung function, lung growth or pulmonary defense mechanisms.[18] HIV patients are an increased risk of COPD than HIV negative controls.[19] TB is an independent risk factor for COPD.[20] Psudomonas colonization increases the risk of exacerbations, hospitalizations and all-cause mortality of COPD.[21]

Socioeconomic status is a small risk factor and is difficult to separate from related factors such as smoking habit, industrial exposure, passive smoking and childhood infection. There is an increased risk of development of COPD in people of lower socioeconomic class.[22]

It is not clear whether increasing ***age*** itself causes changes similar to COPD or it is the cumulative effect of exposure throughout life that leads to COPD. In old literature it is proposed that males are more prone to get COPD, while today due to increasing trend of smoking among females this ***gender*** predisposition has become equal. Some studies have suggested that females get more severe disease than males for equal quantity of cigarettes consumed.

Poorly treated asthma and smoking may be a risk factor for development of chronic airflow limitation and COPD. Separating asthma from COPD in adults may be sometimes difficult.

Airway hyper-responsiveness may exist without a diagnosis of asthma and it is an independent predictor of COPD.

Chronic bronchitis has also been associated with increased likelihood of developing COPD and an increased frequency and severity of exacerbations.

Chronic intravenous drug abuse[23] especially cocaine methadone and heroin are linked to higher risk of developing COPD. This is attributed to the vascular damage induced by the insoluble filler (cornstarch, cellulose, talc, fiber etc) found in IV drugs. These patients are usually young at presentation.

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4: PATHOGENESIS

In health the lung shows an inflammatory response to noxious/irritant particles. In COPD this response is modified and pathological changes occur in airways, the lung parenchyma and the pulmonary vasculature. Several mechanisms have been proposed for the development of COPD.[1,2] ***Oxidative stress*** caused by excess of oxidants due to cigarette smoke may enhance the inflammatory response. Oxidants also inactivate the antiproteases and cause ***protease-antiprotease imbalance*** that leads to the breakdown of connective tissue components in the lung, resulting in emphysema.

Inflammatory cells like macrophages, activated neutrophils and lymphocytes are increased in COPD which release multiple inflammatory mediators. In some patients who have COPD asthma overlap there are increased eosinophils.

In healthy smokers and also in COPD there is ***peribronchiolar and interstitial fibrosis*** which may contribute to the development of small airway limitation and obliteration that precedes the development of emphysema.

Chronic bronchitis

Chronic bronchitis is defined as:

"Chronic cough and sputum for at least 3 months a year for 2 consecutive years."

It was once considered under the umbrella term of COPD. However it is now known that chronic bronchitis is a distinct entity that can exist with or without airflow limitation.[3]

	Air flow obstruction	**No airflow obstruction**
Chronic bronchitis symptoms	*COPD & Chronic bronchitis*	*Chronic bronchitis*
No chronic bronchitis symptoms	*COPD*	*None*

Small airway disease/ Bronchiolitis

Bronchiolitis, an important pathological change in COPD, can result in inflammation and scarring of the small airways. It is difficult to be assessed by respiratory function tests.

Pulmonary Emphysema

Pulmonary emphysema is defined as:

"Abnormal permanent enlargement of airspaces distal to the terminal bronchioles accompanied by destruction of their walls."

Figure 4.1 shows the pathogenesis of COPD.

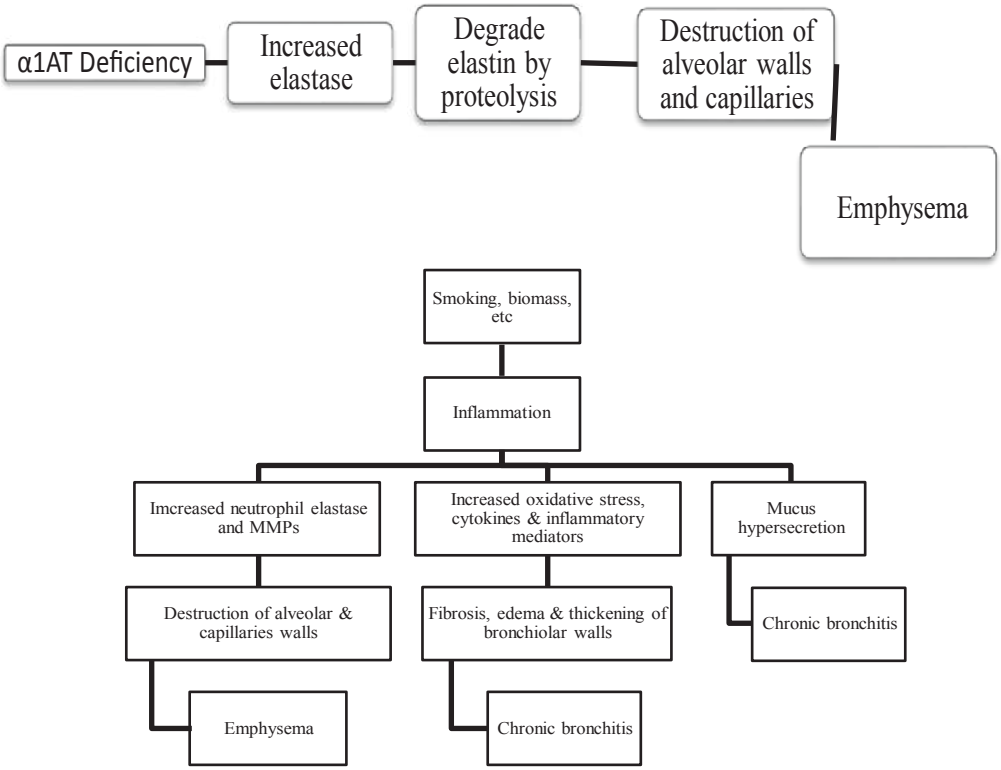

Figure 4.1: COPD pathogenesis
MMPs: Matrix metalloproteinases

Secondary lobule is the part of lung that contains several terminal bronchioles surrounded by connective tissue septa.

Acinus is that part of the lung parenchyma supplied by a single terminal bronchiole.

There are three main types of emphysema:[4]

- **Centriacinar emphysema**
  This is the most common type seen in smokers. It is focal enlargement of airspaces around the respiratory bronchiole. It is more prominent in upper zones of upper and lower lobes.
- **Panacinar emphysema**
  It is confluent even involvement of the acinar unit. It is more severe in lower lobe and is associated with α1-proteinase inhibitor deficiency.
- **Paraseptal emphysema**
  It is peripherally distributed enlarged airspaces where the acinar unit abuts a fixed structure, like pleura. It is the least common type.

Figure 4.2 shows the most common types emphysema.

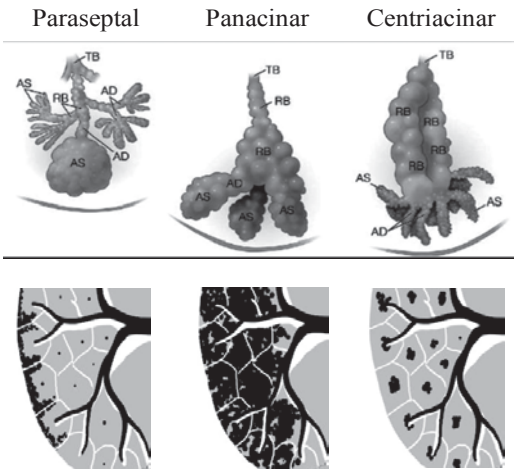

Figure 4.2: The common types of emphysema.

AD: alveolar duct, AS: alveolar sac, RB: respiratory bronchiole, TB: terminal bronchiole

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5: NATURAL HISTORY

Conclusions relating to life-long natural history of COPD resulted in the much reproduced diagram, frequently termed the "Fletcher-Peto curve"[1] (see figure 5.1). The focus on the FEV1 together with the compelling visual impact of the Fletcher-Peto curve has resulted in the FEV1 becoming the condicio sine qua non for COPD progression.

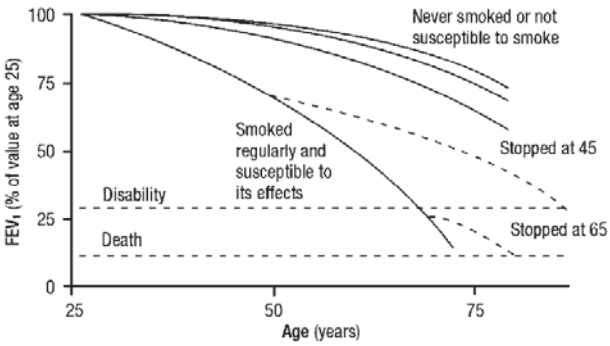

Figure 5.1: Natural history of COPD. The Fletcher-Peto curve. Fletcher C. Peto R. Br Med J 1977; 1: 1645-8

Lung function, after reaching a maximum in young adulthood, remains stable for a decade or so and then begins to decline at a slowly increasing rate. On average, FEV1 declines by about 20 mL/year after the age of 30, and by up to 30 mL/year by 70 years of age. Among individuals who smoke, expiratory airflow is lost at an increased rate. On average, this is approximately twice that associated with normal aging.[2]

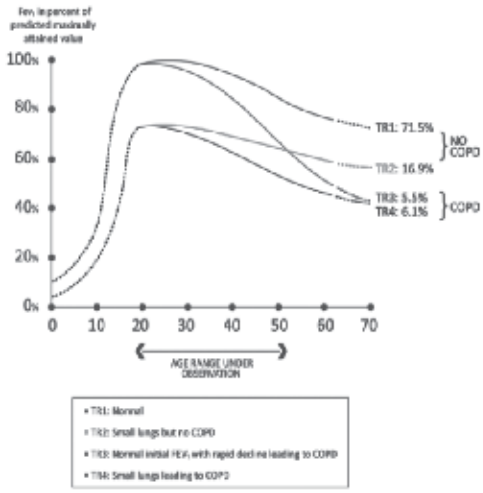

Figure 5.2: FEV1 decline over time

Lung function decline is not a constant process.[3] It is the accumulated result of mild losses during steady state and more severe losses in acute exacerbations that accelerate as exacerbations become more frequent and more severe over time (Figure 5.3).

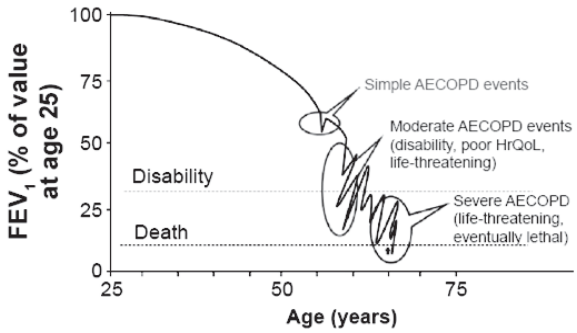

Figure 5.3: Lung function decline in COPD is not a constant process. AECOPD: Acute exacerbation of chronic obstructive pulmonary disease; HrQOL: Health related quality of life

It is important to view the natural history of COPD in terms of symptoms too (Figure 5.4). Some people will have symptoms at an early age while others will progress without being symptomatic. In addition dyspnea is not directly related to the decline in FEV1. Many people with COPD control dyspnea on exertion by decreasing their activities. As a result they forgo activities as their disease progresses, and they accept it as a normal aging process.

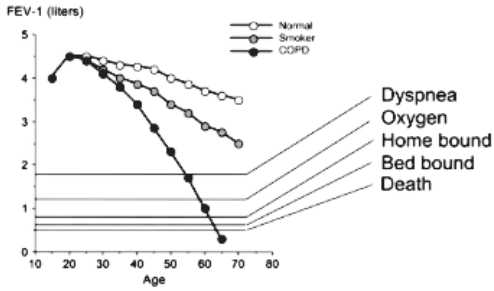

Figure 5.4: The clinical features of COPD are related to averages for FEV1. Data adapted from Fletcher et al. 1977.

The fact that people with COPD can have physiological and physical restriction at an early stage without getting symptomatic is the rationale behind the emphasis on early diagnosis and appropriate therapy by Global initiative for chronic obstructive pulmonary disease, the American thoracic society and the European respiratory society.

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6: SYMPTOMS & PHENOTYPES

Symptoms

The hallmark of COPD is chronic progressive ***dyspnea***.[1] It is the major cause of disability and anxiety associated with the disease. The breathlessness increases with exertion, and it is there all the time. The perception of dyspnea varies among individuals with the same level of activity. It can be assessed by using modified Medical Research Council (mMRC) Dyspnea Scale[2] (Table 4.1).

Table 4.1: Modified Medical Research Council (mMRC) Dyspnea Scale

Grade	Degree of breathlessness related to activity
0	Not troubled by breathlessness except on strenuous exercise
1	Short of breath when hurrying or walking up a slight hill (on climbing stairs)
2	Walks slower than contemporaries on the level because of breathlessness, or has to stop for breath when walking at own pace
3	Stops for breath after walking about 100m or after a few minutes on the level
4	Too breathless to leave the house, or breathless when dressing or undressing

Dyspnea is often affected by mood, temperature, exposure to dust or fumes and position, etc.

Cough and sputum production may be present in up to 50% of cigarette smokers. At times the cough of COPD may be non-productive. Cough is often worse in the morning. Out of exacerbation the sputum is usually small in quantity and often white or grey. Excessive sputum production raises the possibility of underlying bronchiectasis. The expectoration of persistent purulent sputum may be related to bacterial colonization of the airways.

In severe disease, the generation of high intra-thoracic pressures may produce syncope during bout of cough –the cough syncope and cough fractures of the ribs. Cough is also made worse by gastro-esophageal reflex.

Wheezing and chest tightness are common in COPD but are not universal. Their presence do not confirm the diagnosis, likewise their absence does not refute the diagnosis of COPD.

Other symptoms common in COPD is atypical ***chest pain, anorexia, fatigue, psychiatric morbidity*** especially depression, and ***poor sleep quality***. ***Weight loss*** is a feature of severe COPD. It is a bad prognostic sign, and survival is negatively correlated with body mass index[3] (Figure 6.1).

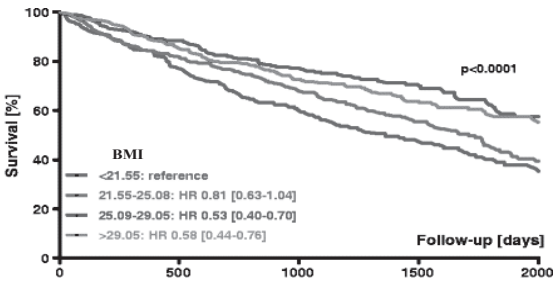


Figure 6.1: Survival is negatively correlated with body mass index. Data from Lainscak et al. Journal of cachexia, sarcopenia and muscle, 2011.HR hazard ratio; BMI: Body mass index

Signs

Physical signs are not specific to the disease. They include (Figure 6.2):

- Uniformly diminished breath sounds
- Prolonged expiratory phase of breathing
- Purse-lipped breathing
- Use of accessory muscles of breathing
- Barrel-shaped chest
- Horizontal ribs with prominent sterna angle and wide sub-costal angle
- Reduced distance between supra-sternal notch and the cricoids cartilage
- Inspiratory tracheal tug
- Hoover's sign – horizontal position of the diaphragm pulls in the lower ribs during inspiration
- Decreased hepatic and cardiac dullness on percussion
- Signs of pulmonary hypertension (RV heave, loud P2, gallop rhythm, pansystolic murmur, pitting pedal edema)
- Tender pulsatile liver
- Prominent *v* wave of jugular venous pulse

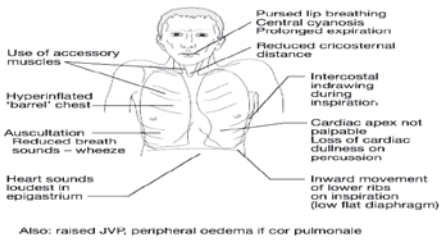


Figure 6.2: Physical signs of COPD JVP: Jugular venous pulse

Systemic effects of COPD

COPD is associated with a number of systemic effects and co-morbidities.[3]

- Skeletal muscle dysfunction
- Weight loss
- Ischemic heart disease
- Hypertension
- Heart failure
- Arrhythmia
- Stroke
- Deep venous thrombosis
- Pulmonary embolism
- Aortic aneurysm
- Osteoporosis
- Anxiety
- Depression
- Diabetes mellitus
- Lung cancer
- Bronchiectasis
- Skin wrinkling
- Peptic ulceration
- Gastro-esophageal reflux
- Polycythemia
- Anemia

Traditionally COPD is divided into 2 phenotypes: Emphysema and Chronic bronchitis (Figure 6.3)

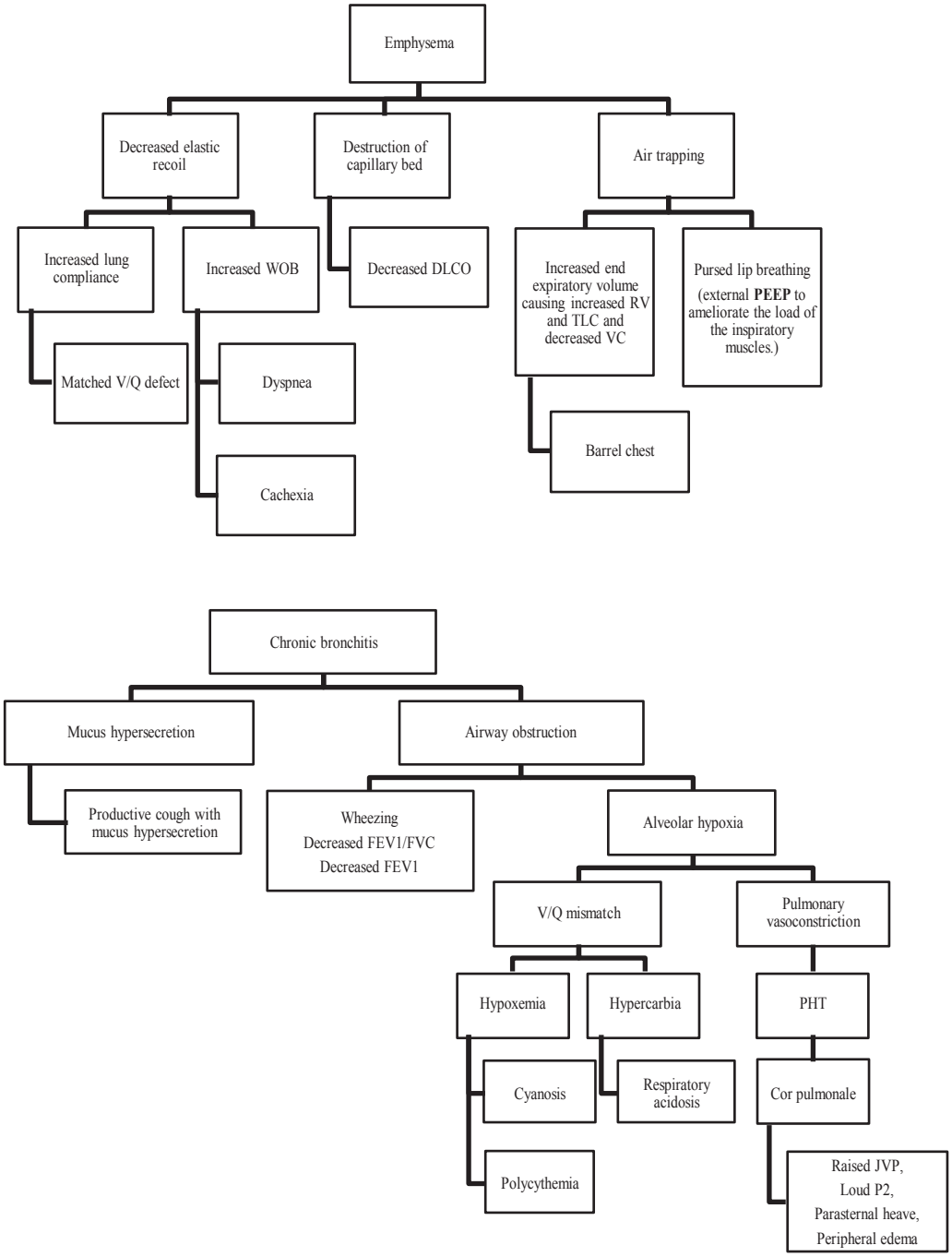


Figure 6.2: Two phenotypes of COPD: Emphysema and chronic bronchitis

DLCO: Diffusion capacity of lung for carbon monoxide; FEV1: Forced expiratory volume in one second ; FVC: Forced vital capacity; JVP: Jugular venous pulse; P2: Pulmonic second heart sound; PEEP: Positive end expiratory pressure; PHT: Pulmonary hypertension RV: Residual volume; TLC: Total lung capacity; VC: Vital capacity; WOB: Work of breathing

References

1. Kessler R, Partridge MR, Miravitlles M, et al. Symptom variability in patients with severe COPD: a pan-European cross-sectional study. ERJ. 2011, 37 (2) 264-272
2. Mahler, Donald A. et al. Evaluation of Clinical Methods for Rating Dyspnea. Chest. 1988;93(3):580-86.
3. MacNee W. Pathology, pathogenesis, and pathophysiology. BMJ. 2006;332(7551):1202–1204.

7: PATHWAY TO THE DIAGNOSIS OF COPD

COPD should be considered in any patient who has symptoms of the disease as discussed in chapter 6 and/or history of exposure to risk factors. Spirometry is required to diagnose the disease. (Figure 7.1)

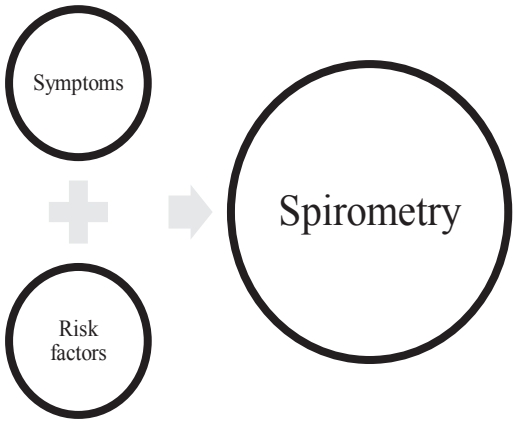


Figure 7.1: Pathway to the diagnosis of COPD

In patients with symptoms and exposure to risk factors,

post-bronchodilator FEV1/FVC < 0.70

confirms the diagnosis of COPD.

Post-bronchodilator forced expiratory volume in first second (FEV1)/forced vital capacity (FVC) below the LLN (lower fifth percentile of values from a reference population) should be preferably used as the criterion for diagnosis of airflow obstruction. However, in the absence of reference equations for LLN, FEV1/FVC < 0.7 may be used as the cutoff for defining airflow obstruction. Using fixed ratio of <0.7 is not inferior to LLN regarding prognosis.

Spirometry in COPD

In evaluation of COPD patient spirometry has following roles:

Diagnosis
Assessment of severity (prognosis)
Follow-up assessment
- Therapeutic decisions
- Identification of rapid decline

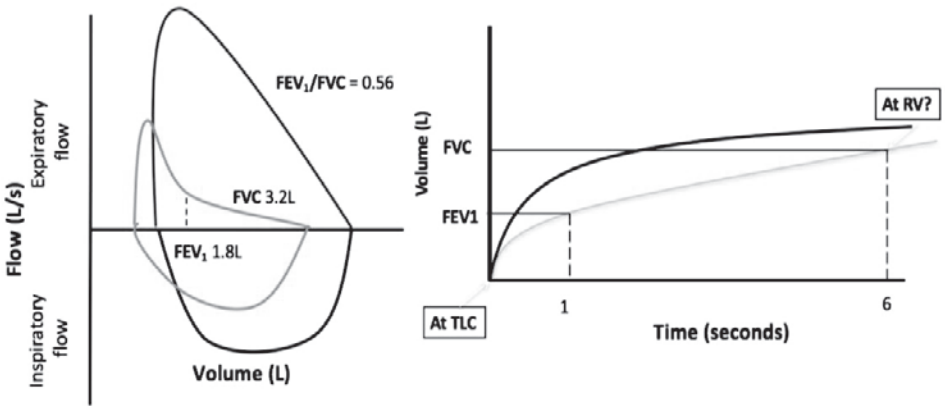


Figure 7.2: Typical spirometry trace of COPD patient

FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; TLC: Total lung capacity; RV: Residual volume

References

1. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2020.
2. Guidelines for diagnosis and management of chronic obstructive pulmonary disease: Joint ICS/NCCP (I) recommendations. Lung India. 2013;30(3).

8: SPIROMETRIC CLASSIFICATION OF SEVERITY OF COPD

Spirometry should be performed after the administration of short acting inhaled bronchodilator in order to minimize variability. The classification of airflow limitation severity in COPD based on spirometry is shown in table 8.1.

Table 8.1: Spirometric classification of severity of COPD, based on post-bronchodilator FEV1.

In patients with FEV1/FVC < 0.70

GOLD 1	Mild	FEV1 ≥ 80% predicted
GOLD 2	Moderate	50% ≤ FEV1< 80 % predicted
GOLD 3	Severe	30% ≤ FEV1< 50% predicted
GOLD 4	Very severe	FEV1 < 30% predicted

GOLD: Global Initiative for Chronic Obstructive Lung Disease

References

1. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2020.

9: ASSESSMENT OF COPD SEVERITY

COPD assessment is necessary to determine the level of airflow obstruction and its impact on health status of the patient and the risk of future exacerbations. This eventually guides therapy.

The following aspects of the disease must be assessed separately.

- The presence and severity of spirometric abnormality
- Current severity of symptoms
- History of exacerbations and future risk
- Presence of co-morbidities

The presence and severity of spirometric abnormality

It has been discussed in chapter 8.

Current severity of symptoms

Breathlessness being the cardinal symptom of the disease, one tool to assess severity of symptoms is mMRC dyspnea scale, discussed in chapter 6. But as a matter of fact COPD impacts patients beyond just dyspnea. So combined assessment test (CAT™) can be used to measure health status in COPD.[1] It has been translated and validated in Urdu. It is an 8-item Likert style questionnaire. Score ranges from 0 to 40, where 0 is asymptomatic patient and 40 is patient with severe symptoms. See Figure 9.1.

CAT
COPD Assessment Test

آپ کی پھیپھڑوں میں رکاوٹ کی پرانی بیماری (COPD) کیسی ہے؟ COPD کی تشخیصی جانچ (CAT)™ کروائیں

یہ سوالنامہ آپ کی تندرستی اور روز مرہ کی زندگی پر COPD (پھیپھڑوں میں رکاوٹ کی دیرینہ بیماری) کے اثر کی پیمائش کرنے میں آپ اور آپ کی نگہداشت صحت کے پیشہ ور فرد کی مدد کرے گا۔ آپ کے جوابات، اور جانچ کے اسکور کا استعمال آپ اور آپ کی نگہداشت صحت کے پیشہ ور فرد کے ذریعہ آپ کی COPD کے انتظام کو بہتر بنانے اور معالجے سے زیادہ سے زیادہ فائدہ حاصل کرنے میں مدد کے لیے کیا جاسکتا ہے۔

اگر آپ سوالنامہ کو کاغذ پر اپنے ہاتھ سے مکمل کرنا چاہتے ہیں تو براہ مہربانی یہاں پر کلک کریں اور پھر سوالنامہ کو پرنٹ کریں۔

درج ذیل ہر ایک آئٹم کے لیے، براہ کرم اس باکس میں(X) کا نشان لگائیں جو آپ کی موجودہ حالت کی بہترین وضاحت کرتا ہو۔ ہر سوال کے لیے صرف ایک ہی جواب کا انتخاب کرنے کو یقینی بنائیں۔

مثال: میں بہت خوش ہوں (0) (X) (2) (3) (4) (5) میں بہت غمگین ہوں

			اسکور
مجھے کبھی کھانسی نہیں ہوتی	0 1 2 3 4 5	میں ہر وقت کھانستا رہتا/کھانستی رہتی ہوں	
میرے سینے میں بلغم بالکل نہیں ہے	0 1 2 3 4 5	میرا سینہ بلغم سے پوری طرح بھرا ہوا ہے	
مجھے سینے میں بالکل بھی جکڑن محسوس نہیں ہوتی	0 1 2 3 4 5	مجھے سینے میں شدید جکڑن محسوس ہوتی ہے	
جب میں پہاڑی یا ایک زینے کی سیڑھیوں پر چڑھتا/چڑھتی ہوں تو میری سانس نہیں پھولتی ہے	0 1 2 3 4 5	جب میں پہاڑی یا ایک زینے کی سیڑھیوں پر چڑھتا/چڑھتی ہوں تو میری سانس بہت زیادہ پھول جاتی ہے	
مجھے اپنے گھر پر سرگرمیاں انجام دینے میں کوئی مجبوری نہیں ہے	0 1 2 3 4 5	میں اپنی گھر پر سرگرمیاں انجام دینے میں کافی محدود ہوں	
اپنے پھیپھڑے کی کیفیت کے باوجود میں اپنے گھر سے باہر جاتے ہوئے پراعتماد رہتا/رہتی ہوں	0 1 2 3 4 5	اپنے پھیپھڑے کی کیفیت کی وجہ سے میں اپنے گھر سے باہر جاتے ہوئے بالکل پراعتماد نہیں رہتا/رہتی ہوں	
میں گہری نیند سوتا/سوتی ہوں	0 1 2 3 4 5	اپنے پھیپھڑے کی کیفیت کی وجہ سے میں گہری نیند نہیں سوتا/سوتی ہوں	
میرے اندر بہت زیادہ توانائی ہے	0 1 2 3 4 5	میرے اندر بالکل توانائی نہیں ہے	
		مجموعی اسکور	

Figure 9.1: COPD assessment test. CAT™ score ≥ 10 indicates high level of symptoms.

Interpretation of CAT™

See table 9.1.

Table 9.1: Interpretation of CAT™

Score	Interpretation
< 10	Low
10 – 20	Medium
20 – 30	High
< 30	Very high

History of exacerbations and future risk

COPD exacerbation is defined as:

"An acute worsening of respiratory symptoms that require additional therapy."

Fletcher first described 'chest episodes' in 1976, since then the interest to develop criteria for these episodes increased steadily. In 1987 Anthonisen et al.[2] gave the classic definition describing three levels of exacerbation based on patient's symptomatology. This is the criteria recommended to be used in describing the exacerbations. It is used to decide the need of antibiotic therapy. See table 9.2.

Table 9.2: Anthonisen criteria for COPD exacerbation

Type I	Type II	Type III
Three of: Increased dyspnea, sputum volume, and sputum purulence	Two of: Increased dyspnea, sputum volume, or sputum purulence	One of: Increased dyspnea, sputum volume, or sputum purulence Plus one of the following: Upper respiratory infection within past 5 days, fever without other cause, increased wheezing, increased cough, increase in heart or respiratory rate by 20% compared with baseline.

* Type I requires escalation of treatment without addition of antibiotic.

Type II and III will benefit from antibiotic therapy

The predictors of future exacerbations risk are:

Two or more exacerbations in the past year

History of hospitalization due to COPD in the past year
Severe COPD, equivalent to GOLD 3 or 4
Increased blood eosinophil count
Use of LABA alone
Non compliance to treatment

Based on the management plan, COPD exacerbations are classified as shown in table 9.3:

Table 9.3: Severity of COPD exacerbation based on management plan

Mild	Need short acting bronchodilators only. Can be managed outside health care facility.
Moderate	Need short acting bronchodilator plus antibiotics and/or oral corticosteroids. Requires assistance of health care facility.
Severe	Need intravenous antibiotics and corticosteroids. Requires hospitalization.

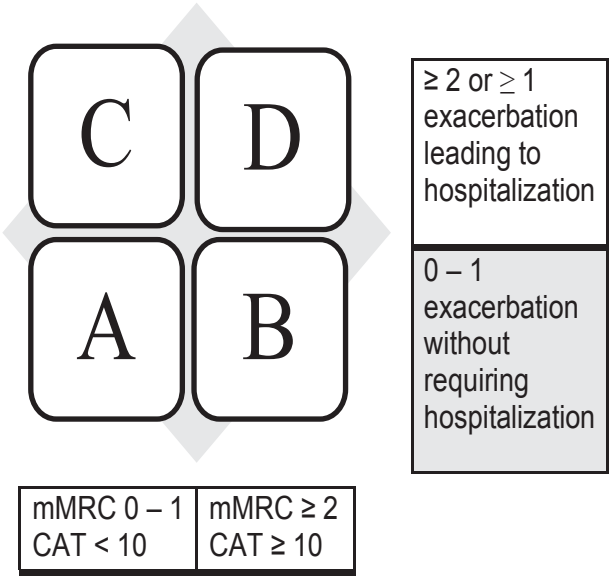
Co-morbidities should be taken into account when assessing severity of the exacerbation. Peak expiratory flow measurement is not useful in assessing the need for hospitalization in COPD exacerbation.

Assessment of co-morbidities

COPD is a systemic disease as discussed elsewhere. These conditions can increase the risk of hospitalizations and mortality in COPD. So co-morbid illnesses should be looked for and treated promptly.

The ABCD tool

A new version of the ABCD tool should be used which separates spirometric classification from patient's symptoms and history of exacerbations.[3] For symptom assessment CAT™ score is better.



References

1. Karloh M, Mayer AF, Maurici R, et al. The COPD Assessment Test: What Do We Know So Far?: A Systematic Review and Meta-Analysis About Clinical Outcomes Prediction and Classification of Patients Into GOLD Stages. Chest. 2016 Feb;149(2):413-425.
2. Anthonisen NR, Manfreda J, Warren CP, et al. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. Ann Intern Med. 1987 Feb;106(2):196-204.
3. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2020.

10: ADDITIONAL INVESTIGATIONS

α-1 antitrypsin deficiency

Although it is common in European whites, younger people (< 45 years) and with lower lobe emphysema should be screened for α-1 antitrypsin deficiency.

In Pakistan emphysema in young population is common in drug addicts.[1]

Six minute walk test

This test provides prognostic information and for monitoring of exercise capacity in COPD.[2]

Chest X-ray

It is useful in excluding other diagnosis. Radiological changes include (Figure 10.1):[3]

Increase lung volumes
Flattened diaphragm
Tubular heart (narrowed and more vertical cardiac silhouette)
Hyperlucency of lung fields
Bullae

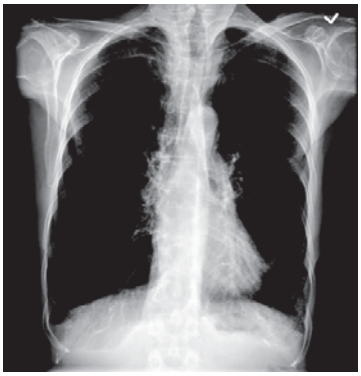


Figure 10.1: COPD X-ray

CT scan chest[3,4]

It is not routinely needed, but may be required if in doubt or to exclude bronchiectasis. It can also be requested for screening of lung cancer, before surgical treatment of COPD. A CT scan is also essential for patients being evaluated for lung transplantation.

Expiratory CT scan chest may show air trapping, it is not currently considered standard of care in the diagnosis and management of mild to moderate COPD.

Arterial blood gas analysis and pulse oximetry

Pulse oximetry should be used to screen for hypoxemia in stable disease with FEV1 < 50% and in the presence of clinical suspicion of hypoxemia.

ABGs can be requested in patients with SpO_2 <90%, having signs of hypercapnia, those with severe COPD or signs of cor pulmonale. These patients may benefit from long term oxygen therapy or non invasive ventilation.

Complete blood count

COPD may be related to anemia of chronic disease or polycythemia, requiring proper management.

Electrocardiogram

It can help in detecting underlying coronary artery disease, arrythmias or pulmonary hypertension.

References

1. Gotway MB, Marder SR, Hanks DK, et al. Thoracic Complications of Illicit Drug Use: An Organ System Approach. RadioGraphics 2002 22:suppl_1, S119-S135
2. Criner G. 6-minute walk testing in COPD: is it reproducible? ERJ. 2011;38 (2): 244-245.
3. Washko GR. Diagnostic imaging in COPD. Semin Respir Crit Care Med. 2010;31(3):276–285.
4. Labaki WW, Martinez CH, Martinez FJ, et al. The Role of Chest Computed Tomography in the Evaluation and Management of the Patient with Chronic Obstructive Pulmonary Disease. AJRCCM. 2017(196);11

11: DIFFERENTIAL DIAGNOSIS

The main differential diagnosis includes:

Asthma
Bronchiectasis
Tuberculosis and post-tuberculosis sequelae (Post TB obstructive airway disease is discussed elsewhere)
Heart failure
Interstitial lung diseases

A careful history, clinical examination, and investigations can help rule out these close mimics of COPD.

12: MANAGEMENT OF STABLE COPD

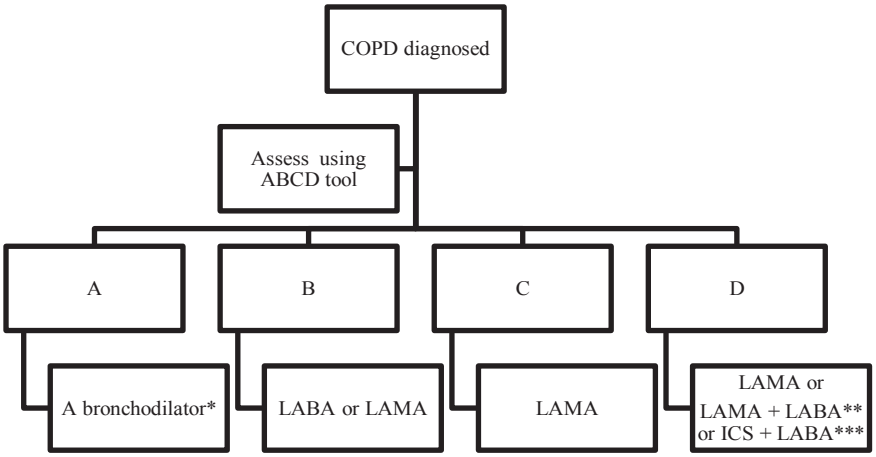
Bronchodilators are first line therapy for COPD. Pharmacologic management can reduce symptoms, improve exercise capacity, reduce the risk of exacerbations, improve overall health status and reduce mortality.

A previous version of management algorithms is given below for comparison. See figure 12.1.

<table>
<tr><td colspan="2">2005</td><td>2010</td><td>Characteristics</td><td rowspan="6">Avoidance of risk factor(s), Influenza vaccination</td><td rowspan="3"></td><td rowspan="3"></td><td rowspan="4"></td><td rowspan="5"></td></tr>
<tr><td colspan="2">0: At Risk</td><td>0: At Risk</td><td>Chronic symptoms
Exposure to risk factors
Normal spirometry</td></tr>
<tr><td colspan="2">I: Mild</td><td>I: Mild</td><td>FEV1/FVC <70%
FEV1 ≥80%
With or without symptoms</td><td rowspan="4">Add short acting bronchodilator when needed</td></tr>
<tr><td rowspan="2">II: Moderate</td><td>IIA</td><td>II: Moderate</td><td>FEV1/FVC <70%
50%<FEV1<80%
With or without symptoms</td><td rowspan="3">Add regular treatment with one or more long acting bronchodilators, Add rehabilitation</td></tr>
<tr><td>IIB</td><td>III: Severe</td><td>FEV1/FVC <70%
30%<FEV1<50%
With or without symptoms</td><td rowspan="2">Add inhaled glucocorticoids if repeated exacerbations</td></tr>
<tr><td colspan="2">III: Severe</td><td>IV: Very severe</td><td>FEV1/FVC <70%
FEV1 <30% or
FEV1 <50% predicted plus chronic respiratory failure</td><td>Add long term oxygen if chronic respiratory failure, Consider surgical treatment</td></tr>
</table>

Figure 12.1: COPD management algorithms used in past (for comparison)

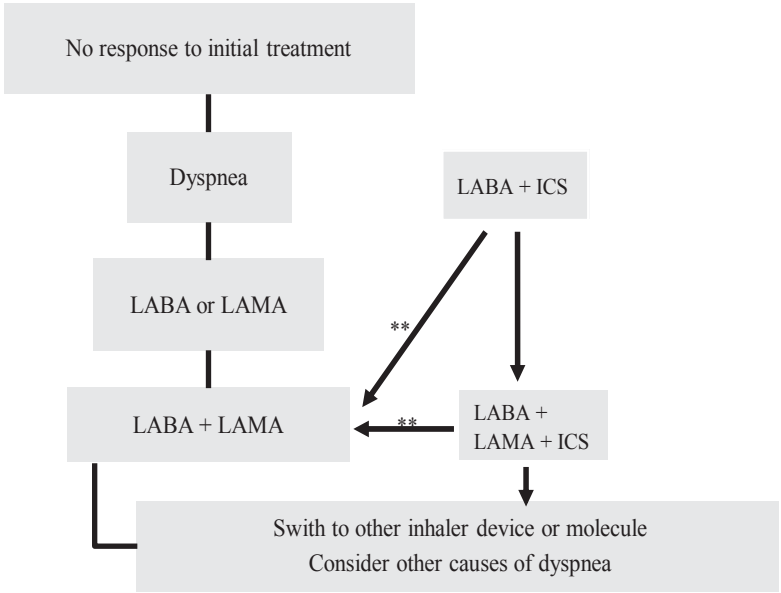
Currently adopted management plan for stable COPD population in Pakistan is given below, see figure 12.2.

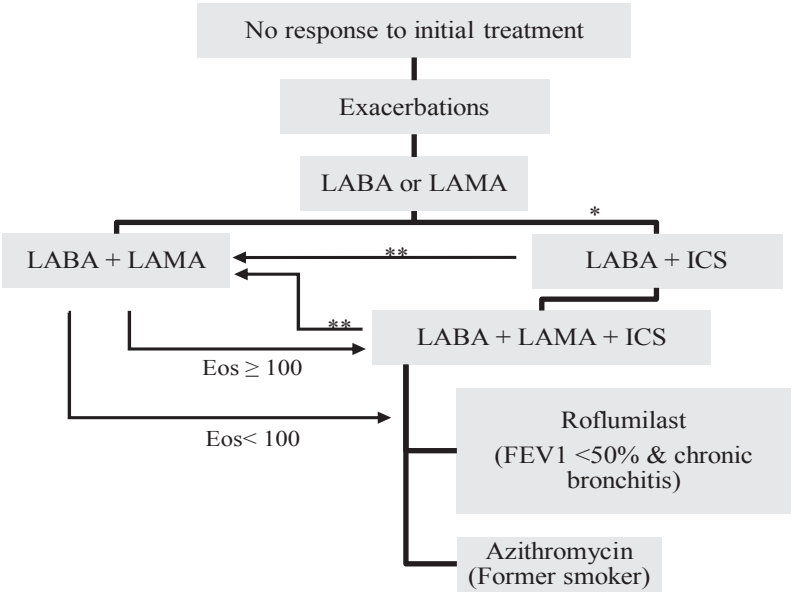


* Can be short acting or long acting.
** If highly symptomatic (CAT >20).
*** If eosinophils ≥300 cells/µL. First choice in COPD patients with asthma.

Figure 12.2: Management of stable COPD

If response to initial treatment is appropriate then maintain it. If not then consider the predominant treatable trait to target (Figure 12.3):





* Eosinophil ≥300 or eosinophil ≥100 And ≥2 exacerbations/ 1 hospitalization

** De-escalate ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS

Figure 12.3: Management of COPD if there is no response to initial treatment

Key points:

Choice of inhaler device should be tailored individually (depending on access, cost, prescriber, patient's preference and ability.
Teach inhaler technique technique and recheck on each visit.
Check inhaler technique and compliance before changing medicines.
Inhaled bronchodilators are preferred over oral.
Theophylline is not recommended unless other long acting treatment bronchodilators are not available or are unaffordable.
Long term monotherapy with ICS is not recommended.
Long term therapy with OCS is not recommended.

References

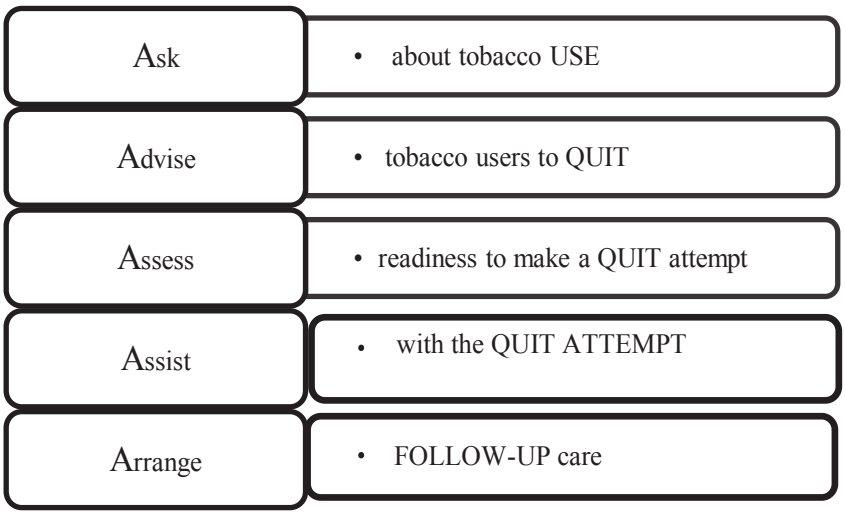
1. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2020.

13: NON-PHARMACOLOGIC MANAGEMENT OF COPD

Smoking prevention and cessation

Smoking cessation is the single most effective way to reduce the risk of developing COPD and stop its progression. Even a brief, three minute period of counseling to urge a smoker to quit can be effective. This should be done for every smoker at each visit. Figure 13.1 details the five As for counseling regarding smoking cessation.[1]

Figure 13.1: The five As: brief tobacco intervention.



The prevalence of tobacco smoking in Pakistan as per World Health Organization's report on the global tobacco epidemic, 2017 is shown below (Table 13.1):

Table 13.1: Tobacco use data from the latest survey as at 31 December 2016:

	Youth tobacco use		Adult tobacco smoking		Adult cigarette smoking	
Prevalence (%)	Current tobacco use	Current cigarette smoking	Current	Daily	Current	Daily
Male	13.3	4.8	22.2	20.6	19.4	17.9
Female	6.6	0.9	2.1	2.0	1.0	1.0
Total	10.7	3.3	12.4	11.5	10.5	9.6

Youth: Global Youth Tobacco Survey, 2013: National, ages 13-15
Adult: Global Adult Tobacco Survey (GATS), 2014: National, ages 115+

Comprehensive tobacco control policies and programs with clear, consistent, and repeated nonsmoking messages should be delivered through every feasible channel. Legislation should be implemented to establish smoke-free schools, public places and transport.

There is a misperception of using chewable tobacco (like snuff: naswar) or e-cigarettes to help in quit attempts. These are not recommended and should be discouraged.

Control of occupational and indoor pollution
Indoor pollution due to burning of wood and coal to keep houses warm in winter and use of biomass fuel in stoves should be minimized and measures should be taken to reduce exposure as by cooking in open air rather than a closed kitchen, having separate cooking area, making chimneys etc.

Exposure to irritant particles and gases should also be avoided at work place.

Pulmonary rehabilitation
The main goals of pulmonary rehabilitation are to increase over all resources of the patient, to reduce handicap caused by illness or disability and to allow integration of patient in society. This can be done by:

1. Exercise training[2]

   In patients with mild to moderate COPD, suitable exercises are walking, cycling and swimming. Daily exercise should be done for about 30 minutes, it may be divided into 2 – 3 phases or till the patient gets out of breath. In severe COPD, it should be done to improve strength and endurance of muscles. This should involve respiratory, abdominal, back, head, neck and limbs to improve quality of life.
2. Nutritional counseling[3]

   Low BMI is an independent risk factor for mortality in COPD patients. Increased calorie intake should be accompanied by regimens with anabolic action. On the other side obese individuals have greater levels of breathlessness and impairment of activity. Well-balanced diet is recommended.

3. Education

   Educate regarding disease, its progressive nature, smoking cessation, drug treatment and how to manage exacerbations.

Vaccination
Yearly influenza vaccination should be given to all patients with COPD.[4]

For adults age 65 or above give one dose of PPSV23; PCV 13 is to be given as per shared clinical decision. If PCV13 is given then give PPSV23 more than or equal to 1 year after PCV13 and more than or equal to 5 years after any PPSV23 at age less than 65 years. Pneumococcal vaccine (PPSV23) shall also be given to younger patients (<65 years) with concurrent heart or lung illnesses or FEV1 <40% predicted.[4]

Oxygen therapy
The algorithm given below (Figure 13.2) should be followed for prescribing supplemental oxygen to COPD patients.[5]

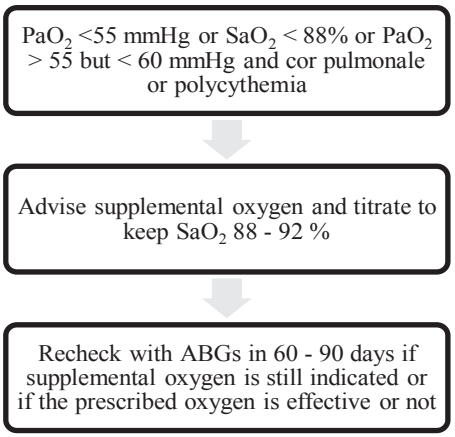


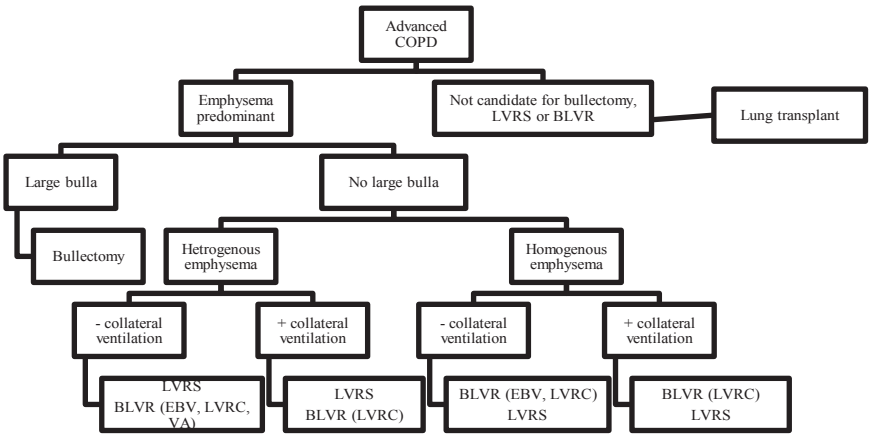
Figure 13.2: Algorithm for prescription of supplemental oxygen

Ventilatory support

Non invasive ventilation by using BiPAP can be helpful in some stable patients with severe COPD to decrease work of breathing or to reduce daytime hypercapnia.

Intervention bronchoscopy and surgery

The algorithm given below (Figure 13.3) is adapted from GOLD guidelines 2019. But most of these therapies are currently not being done in Pakistan.



LVRS: Lung volume reduction surgery
BLVR: Bronchoscopic lung volume reduction surgery
EBV: Endobronchial valve
LVRC: Lung volume reduction coil

VA: Vapor ablation

Figure 13.3: Algorithm for surgical management of advanced COPD. Adapted from GOLD COPD guidelines 2020

Lung transplant

Criteria for referral to lung transplant center include:[6]

COPD with progressive disease
Not candidate for BLVR or LVRS
BODE index 5 – 6
$PaCO_2 \geq 55$ mmHg and/or elevated pulmonary artery pressures with progressive deterioration, e.g cor pulmonale
$PaO_2 < 60$ mmHg
$FEV_1 < 25\%$ predicted without reversibility

Facilities for lung transplant are not available in Pakistan.

End of life care

End of life/ palliative care is an important consideration in patients with advanced COPD. Main goals are to reduce suffering and provide best quality of life for patients and their families. The discussion should focus disease course and prognosis, advanced healthcare directives, and strategies to relieve symptoms.

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14: MANAGEMENT OF COPD EXACERBATION

Acute exacerbation of COPD (AECOPD) is defined in chapter 9. The conditions that mimic COPD exacerbation are:

Pneumonia
Pneumothorax
Cor pulmonale
Pulmonary edema
Myocardial infarction
Arrhythmia
Pulmonary embolism
Upper airway obstruction
Pleural effusion

Exacerbation severity is assessed by using Anthonisen criteria, as detailed in chapter 7.

Investigations that are needed include:

Complete blood count
Sputum gram stain and culture
Sputum AFB smear and gene xpert
Serum urea, creatinine and electrolytes
Arterial blood gases
Chest X-ray
FEV_1
Peak expiratory flow rate
Electrocardiogram

The table below (Table 14.1) enlists the indications to treat AECOPD at home and for hospital admission.

Table 14.1: Indications for hospitalization versus treatment at home of COPD exacerbation.

	Treat at home	Treat in hospital
Ability to cope at home	Yes	No
Dyspnea	Mild	Severe
General condition	Good	Poor and worsening
Level of activity	Good	Poor
Cyanosis	No	Yes
Worsening peripheral edema	No	Yes
Level of consciousness	Normal	Impaired
On supplemental oxygen	No	Yes
Social support	Good	Not coping or alone
Acute confusion	No	Yes
Changes on Chest X-ray	No	Yes
Rapid rate of onset	No	Yes
Arterial Ph	≥ 7.35	< 7.35
PaO_2	≥ 52 mmHg	< 52 mmHg

Treatment for AECOPD treated at home

1. Add or increase dose of bronchodilator, metered dose inhalers are preferred with spacer device. Dose of salbutamol is 2 puff hourly (100 mg/puff) then 3 – 4 hourly. Ipratropium bromide 2 puff 4 hourly (20 – 40 mg) can be added.
2. If response is not adequate add 200 – 400 mg twice daily of sustained release theophylline.
3. Add antibiotic if any evidence of infection. Amoxicillin ± clavulanate can be a good first line option. Other antimicrobials that can be used are respiratory quinolones and macrolides.
4. Oral steroids are not recommended in mild exacerbations but can be prescribed for more severe symptoms and the dose is 30mg/day for one week.

Management of AECOPD at hospital

1. Give controlled oxygen. Use Venturi mask or nasal cannula. Target SpO2 level is 88 - 92%.
2. Get ABGs in first hour and within one hour of change in FIO_2.

3. Start bronchodilators. The dose of salbutamol is 5 mg (1ml) diluted in 2 – 3 ml normal saline ± ipratropium bromide 500 µg. Metered dose inhaler can be used as an alternate. Salbutamol up to 6 to 8 puff every half hour and/or ipratropium bromide 6 to 8 puffs every 3 to 4 hours can be used if nebulizer is not available. If PEFR is 200 L/min or FEV1 is 500 ml then compressor driven nebulizer is preferred.
4. Hydrocortisone 250 mg intravenous stat dose then 100 mg intravenous 8 hourly. Switch to oral 30 – 40 mg/day preferably as single morning dose when patient is able to take it by mouth. Therapy can be given for up to 14 days.
5. Start antibiotic. Respiratory quinolones, amoxicillin-clavulanate or 2nd or 3rd generation cephalosporin is preferred. Gam negative infection are more common in severe COPD so ciprofloxacin or 3rd gen cephalosporin are given.
6. Theophylline has a narrow therapeutic index and has major drug interactions with other drugs like erythromycin, so it should be used with caution. If patient has not taken it in last 24 hours give loading dose.

Loading dose = Required plasma concentration x volume of drug distribution

= 10 mg/L x body weight in kg x 0.5

It should be given over 30 minutes followed by a maintenance infusion at the rate of 0.5mg/kg/hour. Higher doses up to 0.9 mg/kg/hour can be used in children, young adults and smokers. Use small doses of 0.25 mg/kg/hour if status of prior theophylline use is doubtful.

7. Get ABGs after 1 hour of full medical management. Shift the patient to intensive care unit (ICU) if condition continues to deteriorate or ABGs worsened. Patients with hemodynamic instability or those planned for invasive mechanical ventilation should be managed in ICU.
   ICU admission may not be appropriate for patients with poor functional status or end stage lung disease.
8. Consider prophylaxis for venous thromboembolism.
9. Keep adequate fluid and nutritional balance.
10. Patients must be stratified into 5 treatment escalation groups on admission and managed accordingly particularly in resource constraint settings:
    a. Requiring immediate intubation and ventilation
    b. Suitable for NIV and suitable for escalation to intubation
    c. Suitable for NIV but not suitable for escalation to intubation
    d. Not suitable for NIV but for full active medical management
    e. Palliative care agreed as most appropriate management
11. Airway clearance by physiotherapy techniques, like manual percussion, the use of electrical percussor, cough assist machine, acapella device, vibration vest etc.

Ventilatory support

The main aim of ventilator support in patients with AECOPD is to reduce morbidity and mortality and to relieve symptoms. Both non invasive and invasive mechanical ventilation can be used. NIV should be the

preferred first line mode of ventilation for patients in acute respiratory failure. ***Indications for NIV*** in COPD exacerbation include:[1,2]

1. Severe dyspnea, use of accessory muscles
2. pH ≤ 7.35 and/or $PaCO_2$ > 45 mmHg
3. Respiratory rate > 25 breaths/minute

NIV with face mask ***should not*** be given in following conditions:

1. Respiratory arrest
2. Cardiovascular instability (arrhythmias, hypotension, myocardial infarction)
3. Altered level of consciousness – BiPAP can be used with caution
4. Uncooperative patient
5. Risk of aspiration
6. Copious secretion
7. Craniofacial trauma
8. Nasopharyngeal abnormality

Indications for invasive mechanical ventilation are as follows:[3]

1. Unable to tolerate or failure of NIV
2. Severe dyspnea or respiratory rate > 35/minute
3. Life-threatening hypoxemia
4. Severe acidosis (pH < 7.25) – NIV can be used with caution
5. Respiratory arrest
6. Impaired mental status
7. Cardiovascular instability (arrhythmia, hypotension, myocardial infarction)
8. Other complications like metabolic, sepsis, pneumonia, pulmonary embolism

The decision to use invasive ventilation in end stage COPD is influenced by patients' wishes and likelihood of reversing the acute event.

BiPAP through endotracheal tube can be used in patients not fit for invasive mechanical ventilation.[4] Many patients respond to this treatment as most of the time it is the lack to clear airways of copious viscous secretions, which can be easily handled by endotracheal tube.

Hospital discharge criteria are given below:

1. Patient is on inhaled bronchodilators and frequency of dosing is no more than 4 hours
2. Patient who was previously ambulatory is able to walk across room
3. Meals and sleeping is not disrupted by dyspnea
4. Clinically stable for 12 – 24 hours
5. Stable ABGs for 12 – 24 hours
6. Patient or caregiver fully understands correct use of medicines, inhalers, nebulizers, oxygen devices or NIV
7. Home care and follow up arrangements completed

Follow up assessment should be arranged 4 – 6 weeks after discharge from hospital. Assess for the following:

1. Ability to cope in usual environment
2. Review treatment regimen
3. Review inhaler technique
4. Status of co-morbidities
5. Document symptoms: CAT™, mMRC
6. FEV_1
7. Continued need for supplemental oxygen, NIV or nebulizer

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15: DRUGS USED IN COPD

Bronchodilators remain the mainstay of pharmacologic management of COPD. They increase FEV and/or change other spirometric variables. But their dose-response curve is flat so dosing is not based on spirometric response. Bronchodilators alter airway smooth muscle tone and tend to reduce dynamic hyperinflation, and improve exercise performance. Toxicity is dose dependent.

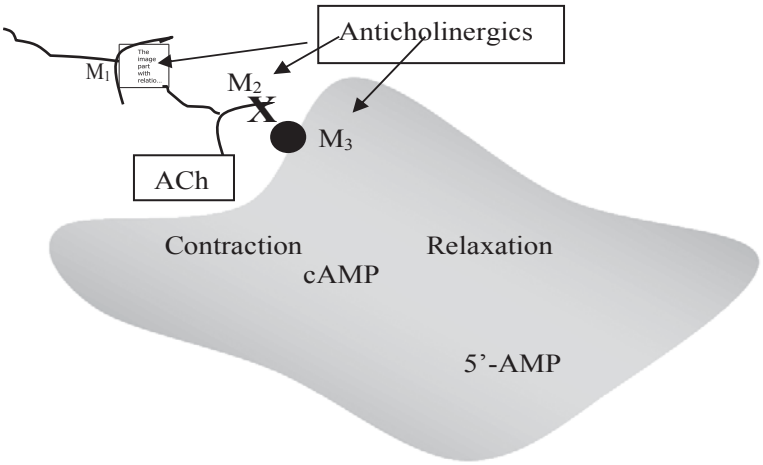
There are three main classes of bronchodilators:

β-agonists

Anticholinergics

Methylxanthines

Figure 15.1 is a pictorial representation of mechanism of action of bronchodilators.



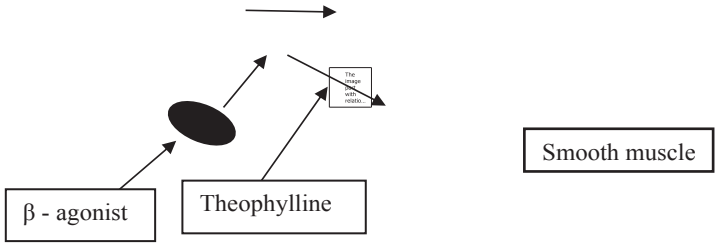


Table 15.1 shows formulations of commonly used β-agonists.

Table 15.2 shows formulations of commonly used anticholinergics.

Table 15.3 shows formulations of methylxanthines.

A number of fixed-dose combinations of β-agonists and anticholinergics are available. See table 15.4.

Table 15.1: Formulations of commonly used β-agonists.

Drug	Inhaler (mcg)	Solution for nebulizer (mg/ml)	Oral	Vials for injection	Duration of action (hours)
Short acting					
Fenoterol*	100 – 200 MDI	1	2.5 mg pill 0.05% syrup		4 – 6
Levalbuterol*	45 – 90 MDI	0.1, 0.21, 0.25, 0.42			6 – 8
Salbutamol	100, 200 MDI & DPI	1, 2, 2.5, 5	2, 4, 5 mg pill 8 mg extended release tablet 0.024%/0.4 mg syrup	0.1, 0.5 mg	4 – 6, 12 (extended release)
Terbutaline	500 DPI		2.5, 5 mg pill	0.2, 0.25, 1 mg	4 – 6
Long acting					
Arformoterol*		0.0075			12
Formoterol	4.5 – 9 DPI	0.01			12
Indacaterol	75 – 300 DPI				24
Olodaterol*	2.5, 5 SMI				24
Salmeterol	25 – 50 MDI & DPI				12

DPI: dry powder inhaler, MDI: metered dose inhaler, SMI: soft mist inhaler

Side effects of β - agonists: Sinus tachycardia, tremors, hypokalemia (shows tachyphylaxis)

Table 15.2: Formulations of commonly used anticholinergics.

Drug	Inhaler (mcg)	Solution for nebulizer (mg/ml)	Oral	Vials for injection	Duration of action (hours)

Short acting					
Ipratropium bromide	20, 40 MDI	0.2			6 – 8
Oxitropium bromide*	100 MDI				7 – 9
Long acting					
Aclidinium bromide*	400 MDI & DPI				12
Glycopyrronium bromide	15.6, 50 DPI		1 mg solution	0.2 mg	12 – 24
Tiotropium	18 DPI, 2.5 & 5 SMI				24
Umeclidinium*	62.5 DPI				24

DPI: dry powder inhaler, MDI: metered dose inhaler, SMI: soft mist inhaler

Side effects of anticholinergics: dry mouth, bitter taste.

Table 15.3: Formulations of methylxanthines.

Drug	Oral	Vials for injection	Duration of action (hours)
Aminophylline	105 mg/ml solution	250, 500 mg	Variable, up to 24
Theophylline (SR)	100 – 600 mg pill	250, 400, 500 mg	Variable, up to 24

Side effects of methylxanthines: Palpitations, atrial and ventricular arrhythmias, grand mal seizures. headache, nausea, insomnia, heartburn. Toxicity is dose related.

Table 15.4: Fixed-dose combinations of β-agonists and anticholinergics are available.

Drug	Inhaler (mcg)	Solution for nebulizer (mg/ml)	Duration of action (hours)
Fenoterol/ipratropium*	50/20 SMI	1.25, 0.5 mg in 4 ml	6 – 8
Salbutamol/ipratropium	100/20 SMI 75/15 MDI	0.5, 2.5 mg in 3 ml	6 – 8
Formoterol/aclidinium*	12/400 DPI		12
Formeterol/glycopyrronium*	9.6/14.4 MDI		12
Indacaterol/glycopyrronium*	27.5/15.6 & 110/50 DPI		12 – 24
Vilanterol/umeclidinium*	25/62.5 DPI		24
Olodaterol/tiotropium*	5/5 SMI		24

DPI: dry powder inhaler, MDI: metered dose inhaler, SMI: soft mist inhaler

Glucocorticosteroids

Oral steroids should be avoided if possible in stable COPD. Systemic steroids may be used for short-term treatment (7-14 days) during exacerbations.

Inhaled corticosteroids (ICS) have modest bronchodilator effect. They reduce exacerbation severity and frequency.

Drugs commonly used are:

Inhaled corticosteroids:

Beclomethasone ……. 500 µg twice a day

Triamcinolone …….. 400 µg twice a day

Budesonide…… 400 µg twice a day

Fluticasone…….. 100 – 500 µg twice a day

Oral corticosteroid:

Prednisolone …….. 30 mg/day

Combination of long acting β – agonist and inhaled corticosteroids are available:

Formoterol/ beclomethasone…….6/100 MDI & DPI

Formoterol/budesonide……..4.5/160, 4.5/80 MDI

9/320, 9/160 DPI

Formoterol/mometasone*……10/100, 10/400 MDI

Salmeterol/fluticasone…….5/100, 50/250, 5/500 DPI

21/45, 21/115, 21/230 MDI

Vilanterol/fluticasone furoate*…….25/100 DPI

Side effects of steroids: Increased risk of osteoporosis, cataract, adrenal suppression, hypertension, diabetes, obesity, skin thinning, muscle de-conditioning, reactivation of tuberculosis.

Phosphodiesterase 4 inhibitors

Roflumilast is the PDE-4 inhibitor currently in use. It is 500 µg pill, to be taken orally once a day. Its mechanism of action is shown in figure 15.2.

It has no direct bronchodilator activity; it reduces inflammation.

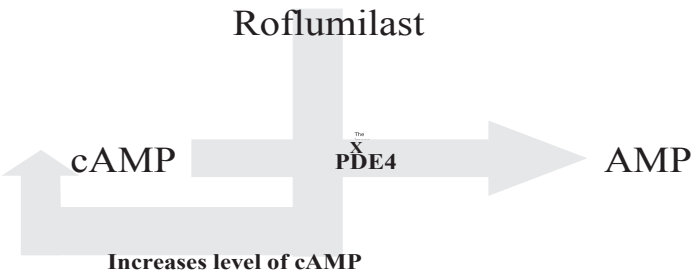


Figure 15.2: Mechanism of action of roflumilast.

Side effects of roflumilast: Diarrhea, nausea, decreased appetite, abdominal pain, weight loss, headache and sleep disturbance.

Vaccines

Discussed in chapter 13.

α1-antitrypsin augmentation therapy

It is not available in Pakistan. Intravenous therapy is indicated in patients with α1-antitrypsin deficiency who have progressive disease and $FEV_1 > 65\%$.

Antibiotics

Azithromycin 250 mg/day or 500 mg three times per week for 1 year may reduce exacerbation risk.

Clarithromycin 250mg /day in advanced copd having bronchiectasis.

Mucolytics

Carbocysteine and N-acetylcysteine can be used, they may reduce exacerbations.

Antitussives

No definite role is described for use of antitussives in COPD.

* Drugs not available in Pakistan

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16: AIR TRAVEL IN COPD

COPD patients should be informed about the "fitness to fly" concept and patients with moderate-to-severe disease need to be assessed for possible risk factors for in-flight hypoxaemia before flying.[1,2] Figure 16.1 shows pathophysiological changes during air travel in COPD patient.

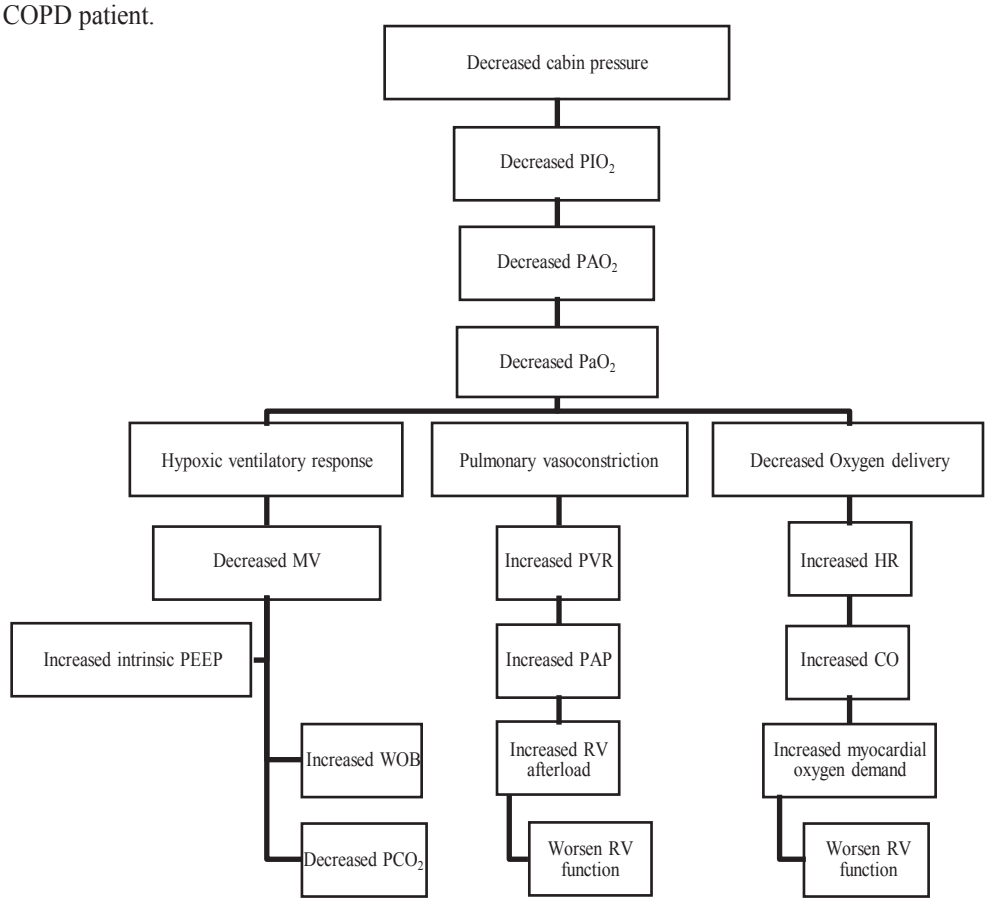

Figure: 16.1: Pathophysiologic changes in COPD patient during air travel

CO: Cardiac output; HR: Heart rate; MV: Minute ventilation; PAO_2: Partial pressure of oxygen in alveoli; PaO_2: Partial pressure of oxygen in arterial blood; PAP: Pulmonary artery pressure; PIO_2: Pressure of inspired oxygen; RV: Right ventricle; WOB: Work of breathing

Following algorithm can be used for assessment of fitness to fly in COPD patient (Figure 16.2).

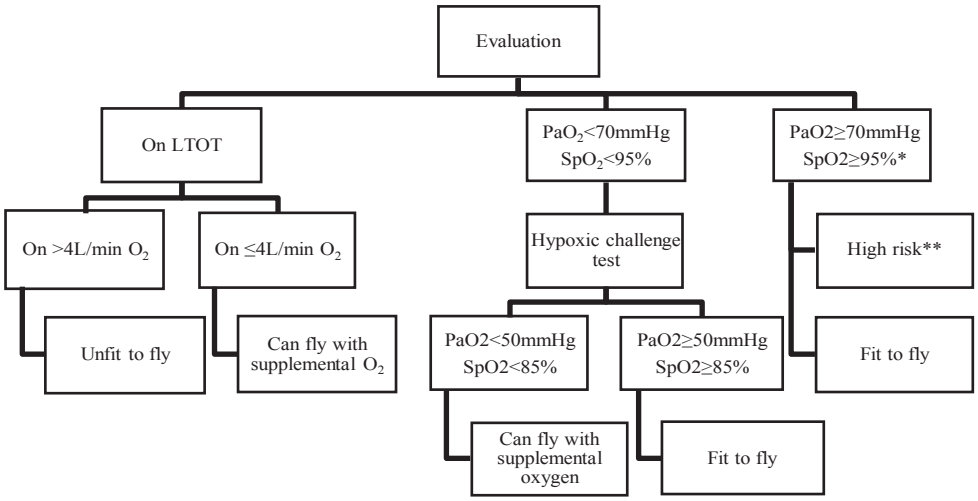

Figure 16.2: Algorithm for assessment of fitness to fly in COPD patient

**** Resting SpO2 >95% combined with a 6-min walk test SpO2 >84% has a sensitivity of 100% and specificity of 80% for fitness to fly***

***** Dyspnoea on exertion, forced expiratory volume in 1 second <1.5L or <30% predicted, a pre-existing requirement of oxygen or ventilator support, bullous lung disease, comorbid conditions that may worsen hypoxemia like cardiac disease and significant symptoms during previous air travel. For high risk patients do hypoxic challenge test and follow the algorithm.***

The safe threshold for oxygenation is to keep PaO2 >50 mmHg and SpO2 ≥85% during the flight.

Problems other than hypoxia

Jet lag: general advice and treatment options for jet lag (sleep hygiene, melatonin, etc.) are also valid for COPD patient.

Coagulation activation: the risk increases after 4 h and peaks at 8 h. Patients with low risk should be warned to avoid tight clothing below the waist and try to rehydrate during the flight. Moving along the aisle may be an option for patients without risk of desaturation. If the patient has a risk

of desaturation, below knee compression stockings and calf stretching exercises while sitting may be a safe alternative. Patients with high risk of thromboembolism (previous venous thromboembolism history, known active malignancy, known thrombophilia, and major surgery within 6 weeks) should ask for individual help for prophylactic low molecular weight heparin.

Risk of infection transmission: Patients should be warned, especially for outbreaks of RSV (SARS), and should be advised to postpone travel if necessary.

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17: POST-TB CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Pakistan is ranked fifth among high burden TB countries globally and it accounts for 61% of the TB burden in the WHO Eastern Mediterranean Region. TB is now recognized as a risk factor for developing chronic obstructive airway disease.[1]

Patients of pulmonary tuberculosis may develop airflow obstruction either during the active phase or post-treatment phase of the disease.

A study from Pakistan revealed that 55.3% of treated pulmonary TB patients with dyspnea had an obstructive ventilatory defect.[2] Patients with COPD secondary to TB have been shown to have significantly low forced expiratory volume in one second, higher airway resistance, and poor positive bronchodilator response (27% vs 82%) than only COPD patients.[3] These patients are also at risk for more frequent exacerbations of obstructive airway disease.[4]

The exact mechanism of airway obstruction in post-tuberculosis patients is not clear. Following mechanisms have been proposed:[5]

- Bronchiectasis
- Bronchiolar narrowing
- Bronchiolitis obliterans
- Accelerated emphysematous changes

Figure 17.1 shows the mechanism of airflow obstruction due tuberculosis.

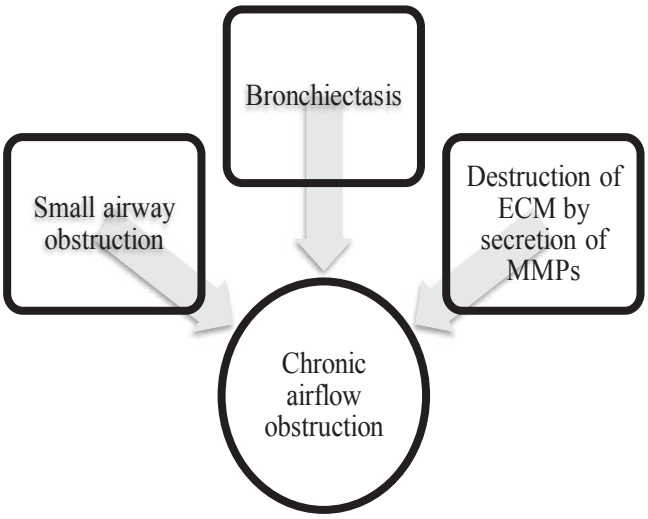

Figure 17.1: Mechanism of airflow obstruction due tuberculosis. ECM: extracellular matrix, MMPs: matrix metalloproteinases

Treatment for chronic airflow disease due to tuberculosis is the same as that of COPD.6

COPD and tuberculosis are major health problem in developing countries. Early diagnosis and appropriate treatment of tuberculosis is emphasized to reduce the future burden of COPD.

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