AN ANALYSIS OF CARDIAC FUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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CERTIFICATE

This is to certify that this dissertation entitled "**AN ANALYSIS OF CARDIAC FUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE**" submitted by Dr. ANNU SUSAN GEORGE appearing for Part II M.D. Branch I General Medicine Degree examination in April 2012 is a bonafide record of work done by her under my direct guidance and supervision in partial fulfillment of regulations of The Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India.

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I solemnly declare that the Dissertation titled **"An Analysis of Cardiac Function in Chronic Obstructive Pulmonary Disease"** was done by me at Coimbatore Medical College & Hospital during the period from September 2010 to August 2011 under the guidance and supervision of **Prof. M. Raveendran M.D.,**. This dissertation is submitted to The Tamilnadu Dr. M.G.R Medical University towards the partial fulfillment of the requirement for the award of M.D. Degree (Branch I) in General Medicine.

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ABBREVIATIONS

COPD	Chronic Obstructive Pulmonary Disease
FEV_1	Forced Expiratory Volume at One Second
FVC	Forced Vital Capacity
BODE	Body-mass index (B), Airflow obstruction (O), Dyspnoea (D), and Exercise capacity
GOLD	Global initiative for Obstructive Lung Diseases
ATS	American Thoracic Society
BTS	British Thoracic Society
α 1 AT	Alpha 1 Antitrypsin
BMI	Body Mass Index
FVC	Forced Vital capacity
RA	Right Atrium
RV	Right Ventricle
LV	Left Ventricle
PH	Pulmonary Hypertension
6MWT	6 Minute Walk Test
6MWD	6 Minute Walk Distance
WHO	World Health Organisation
NHLBI	National Heart, Lung and Blood Institute
mPAP	Mean Pulmonary Artery Pressure
sPAP	Systolic Pulmonary Artery Pressure
IPAH	Idiopathic Pulmonary Artery Hypertension
pCO2	Partial Pressure Of Carbon Dioxide

pO2	Partial Pressure Of Oxygen
TAPSE	Tricuspid Annular Plane Systolic Excursion
RVSP	Right Ventricular Systolic Pressure
TR	Tricuspid Regurgitation
RVOT	Right Ventricular Outflow Tract
IVC	Inferior Vena Cava
LVEF	Left Ventricular Ejection Fraction
ECG	Electrocardiogram
RVH	Right Ventricular Hypertrophy
DLCO	Diffusion Lung Capacity For Carbon Monoxide
MMRC	Modified Medical Research Council
DALY	Disability Adjusted Life Years

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AN ANALYSIS OF CARDIAC FUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

"The disease which I designate by this title is very little known and has not hitherto been correctly described by any author. I , for a long time thought it very uncommon, because I had observed only a few cases of it, but since I have made use of the stethoscope, I have verified its existence as well on the living as the dead subject, and am led to consider it as by no means infrequent. I consider many cases of asthma, usually deemed nervous, as depending on this cause."

--- Rene Theophile Hyacinthe Laennec on Emphysema (1821)

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a collection of conditions characterized by expiratory airflow limitation that is not fully reversible. COPD includes emphysema, chronic bronchitis, and small airways disease.[1] Synonyms include chronic obstructive lung disease (COLD) and chronic obstructive airway disease (COAD). The British Thoracic Society (BTS) defines COPD as a slowly progressive disorder characterized by airways obstruction (reduced FEV_1 and FEV_1/FVC ratio),which does not change markedly over several months.[12]

COPD is the second most common lung disease in India after tuberculosis.[2] It is one of the leading causes of morbidity and mortality worldwide, putting a heavy economic and social burden especially on the developing countries of the world , like India. Increased life expectancy, has changed the structure of the world's population and more people now reach the age when COPD usually develops, so the prevalence and burden of COPD will continue to rise in the coming decades.

The Global Burden of Disease Study estimates that COPD, will rise to the third most common cause of death worldwide by 2020 from the current sixth place. But mortality offers only a restricted picture of the human burden of disease and so DALY or disability adjusted life years may be better suited to describe the disease burden. In 1990, COPD was the ninth leading cause of DALY's lost in the world, responsible for 2.1% of the total and is projected to rise to the fifth leading cause by 2020.[9]

COPD has many effects on cardiac function, including that of the right and left ventricles as well as the pulmonary blood vessels. The cardiovascular sequelae of COPD are known for decades .The spectrum of cardiovascular disease includes right ventricular (RV) dysfunction, pulmonary hypertension (PH), coronary artery disease (CAD), and arrhythmias .It is vital to know about them because they contribute greatly to the overall morbidity and mortality associated with COPD.[16]

Pulmonary artery hypertension (PH) is the main cardiovascular complication encountered in COPD[8] and cor pulmonale is the maladaptive response to pulmonary hypertension.[4] The prevalence of PH increases as COPD worsens, and the development of PH and cor pulmonale appears to affect survival of patients with COPD. Survival correlates negatively with pulmonary arterial pressure and pulmonary vascular resistance, and patients with COPD and PH have increased morbidity as well as risk for hospitalizations for acute COPD exacerbations.

Components of assessment to detect PH and cardiac dysfunction include physical examination, chest X ray, Electrocardiogram (ECG), and Doppler Echocardiogram.[6] Spirometry still remains the most valuable means of identification and estimation of the severity of COPD and responses to therapy, and is vastly underused for this purpose. Assessment of exercise capacity is a vital part of the appraisal of PH and the most commonly used exercise test is the 6 minute walk test(6MWT).

AIM OF STUDY

1. To study the clinical features and assess pulmonary function by spirometry in patients with Chronic Obstructive Pulmonary Disease.

2. To assess the radiological features with chest X ray.

3. To assess the cardiac function in COPD with Electrocardiography and Echocardiography.

4. To assess the functional exercise capacity with 6 minute walk test and correlate disease severity with BODE index.

5. To study the effect of smoking in COPD.

REVIEW OF LITERATURE

HISTORICAL BACKGROUND

Obstructive airway disorders have been known since ancient times. Ancient Indian texts describe similar disorders as ' kaphadosha'. Badham in 1808, first coined the term chronic bronchitis and used the word' catarrh 'to refer to the chronic cough and increased mucus secretion that are principal symptoms.[11]

In 1959 The Medical Research Council used the term "chronic bronchitis to define expectoration when other causes such as bronchiectasis or tuberculosis have been excluded, to patients who have coughed up sputum on most days, at least for 3 consecutive months in 2 successive years."[24]

Emphysema was described by Laennec (1821) in his 'Treatise of diseases of the chest'. Gough and his co-workers described centriacinar emphysema and distinguished it from panacinar emphysema in the 1950's.[8] William Briscoe is thought to be the first person to use the term COPD in a discussion at the 9th Aspen Emphysema Conference in 1965.[11]

The spirometer was invented in 1846 by John Hutchinson. Tiffeneau introduced the notion of timed vital capacity as a gauge of airflow (Tiffeneau and Pinelli 1947). Gaensler in 1951 introduced the concept of the air velocity index and later the forced vital capacity, based on which we get FEV_1 and FEV_1/FVC ratio, also called Tiffeneau index.[11]

Fletcher et al 1976 recognized accelerated rate of deterioration in FEV_1 in susceptible smokers and that quitting smoking would impede the rate of FEV_1 decline to that nearing the rates in age-related non-smokers (Peto et al 1983) which laid the foundation for smoking cessation in every stage of the disease (Anthonisen et al 1994).

Burrows in his study on prognosis of emphysema, in Tucson, Arizona, identified that patients with a low FEV_1/FVC percentage predicted the onset of rapid fall in FEV_1 over time. Patients with the most rapid rate of deterioration had the worst prognosis and he described this phenomenon as "The Horse Racing Effect" (Burrows et al 1987).

The landmark study by Hogg et al (1968) marshalled in ,the era of small airways disease.[11]In 2001, the Global Initiative of Obstructive Lung Disease (GOLD) was launched by the WHO and NHLBI. [11]

The term Cor Pulmonale was coined in 1931 by Dr. Paul D. White, prior to which it was generally known as emphysema heart, pulmonary heart disease, Ayerzas disease and 'Black Cardiacs'[32]. In 1934 Kountz and Alexander while studying emphysema stated that "it appears that heart is affected in majority of patients with emphysema".The WHO expert committee proposed a pathologic definition of cor pulmonale as "hypertrophy of the right ventricle resulting from diseases affecting the function and/or structure of the lungs, except when these pulmonary alterations are the result of diseases that primarily affect the left side of the heart, as in congenital heart diseases." Behnke and colleagues replaced the concept of hypertrophy with "an alteration in the structure and function of the right ventricle"in 1970.[5]

HYPOTHESES IN PATHOGENESIS OF COPD

There are several "hypotheses" to explain the pathogenesis of airflow obstruction. Orie et al espoused what is known as the "Dutch hypothesis", that asthma and airway hyperreactivity may eventually lead to fixed airflow limitation. This was in contrast with the idea that mucus hypersecretion led to airway remodeling and airflow limitation, termed the "British hypothesis." The association of homozygous alpha1 protease inhibitor deficiency with emphysema was discovered by Laurell and Eriksson leading to the concept of the "protease-antiprotease hypothesis" of emphysema, or the "Swedish hypothesis". Finally the concept that altered repair mechanisms play a role in the development of COPD has been termed the"American hypothesis."

The concept that altered airway anatomy would lead to heterogeneity of airflow distribution within the lung, resulting in ventilation-perfusion imbalance, hypoxemia, and right heart failure, is behind the "blue bloater" phenotype and that emphysema would not cause hypoxia, even though there is decreased airflow, resulting in a "pink puffer"phenotype.[8]

DEFINITIONS

According to April 2011 GOLD report COPD is now defined as

"A preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles and gases."[9]

The word emphysema originated from Greek and means “to blow into,” hence “air-containing” or “inflated”. Emphysema is defined “a condition of the lung characterized by irreversible enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls without obvious fibrosis”.[10]

Chronic bronchitis is defined as “the presence of a chronic productive cough on most days for 3 months, in each of 2 consecutive years, in patients in whom other causes of chronic cough have been excluded.” It has been classified into three forms:simple bronchitis ,defined as hypersecretion of mucus; chronic, recurrent or intermittent mucopurulent bronchitis in the presence of persistent or intermittent mucopururlent sputum; and chronic obstructive bronchitis when chronic sputum production is associated with airflow obstruction.[12]

With regard to COPD, small airways refer to airways with an internal diameter of 2 mm or less. In COPD, intraluminal mucus can be found in the small airways, and there seems to be a connection between the degree to which the airways are occluded by mucus and the FEV_1.

Pulmonary hypertension, an abnormal elevation in pulmonary artery pressure, may be due to left heart failure, pulmonary parenchymal or vascular disease, thromboembolism, or a combination of these factors.[1] Pulmonary hypertension in COPD is placed in group 3 of the 2003 WHO classification of PH, ie, PH associated with disorders of the respiratory system and/or hypoxemia. PH associated with lung disease is defined as resting mean PAP(mPAP) greater than 20 mm Hg, which is different from the definition of primary pulmonary hypertension (mPAP >25 mm Hg).[4]

Cor pulmonale, referred to as pulmonary heart disease, "is defined as dilation and hypertrophy of the right ventricle (RV) in response to diseases of the pulmonary vasculature and/or lung parenchyma. Historically, this definition has excluded congenital heart disease and those diseases in which the right heart fails secondary to dysfunction of the left side of the heart".[1]

EPIDEMIOLOGY AND PREVALENCE

COPD is a major public health problem, the prevalence and impact of which has been increasing for several decades, with the epidemic of cigarette smoking in the 20th century.[8] The number of patients with COPD is estimated at 600 million worldwide and is increasing.[13] It is the only disease in the top 10 that continues to rise in prevalence and mortality.[19]

COPD progresses with age and is more prevalent in elderly populations. In the United States, 15% of the total population aged 55 to 64 have at least moderate COPD (GOLD stage 2, FEV1 < 80% predicted) and this increases to over 25% for those older than 75yrs.[8] The rounded-off median prevalence rates were calculated as 5 %for males and 2.7 % for females over 30 years of age.[11] The prevalence of COPD reported from India are highly variable. Prevalence rates varying from about 2 to 22 per cent in men and from 1.2 to 19 per cent in women have been shown in different reports. Population prevalence from a multicentric study sponsored by the Indian Council of Medical Research (ICMR) showed prevalence of 5.0 % among men and3.2 % in women. The disease is clearly more common in males. The prevalence was found to increase with increasing age, in those with more than 20 pack–yrs of smoking and in low income

subjects. The male to female ratio varies from 1.32:1 to 2.6:1 in different studies with a median ratio of 1.6:1.[25]

Although the prevalence of pulmonary hypertension (PH) in individuals with COPD is not known precisely, the reported prevalence varies considerably from 20%–91% (Burrows et al 1972; Weitzenblum et al 1984; Oswald-Mammosser et al 1991; Scharf et al 2002; Thabut et al 2005) depending on the definition of pulmonary hypertension.[4]About 10%–30% of patients with moderate to severe COPD have elevated pulmonary pressures. PH associated with COPD is mostly mild to moderate, severe PH occurring in <5% of patients.[14]

ETIOLOGY AND RISK FACTORS

Exposure to Toxic Fumes and Gases

Cigarette Smoking.

Cigarette smoking is firmly established as the most important risk factor for COPD. Smokers lose lung function in a dose-dependent manner. 80% percent of individuals who have COPD and 80% who die from COPD in the United States are smokers. Similarly in India, tobacco smoking was reported to be responsible for over 82% of COPD.[82,83] It has been found that pipe and cigar smokers have higher mortality and morbidity rates for COPD than nonsmokers but lesser than cigarette smokers.[21] There is variable susceptibility to the effects of cigarette smoke. Patients with COPD usually have at least 20 pack years smoking history according to BTS guidelines.[23] An average cigarette smoker has a high annual rate of decline in FEV1, of approximately 50ml, which is almost twice the average value of 30ml in non smokers. In non smokers

the decline in FEV_1 begins at 30-35 years of age and it is earlier in smokers.[12] 15% of cigarette smokers develop clinically significant COPD.Mortality depends on age of initiation of smoking, total pack-years, and current smoking status.

The earliest demonstrable mechanical defect in a smoker is obstruction of small airways.[22] In people who stop smoking the rapid decline in FEV_1 stops, and have better survival.[15] In non-smokers, the most important form of air pollution is exposure to environmental tobacco smoke.

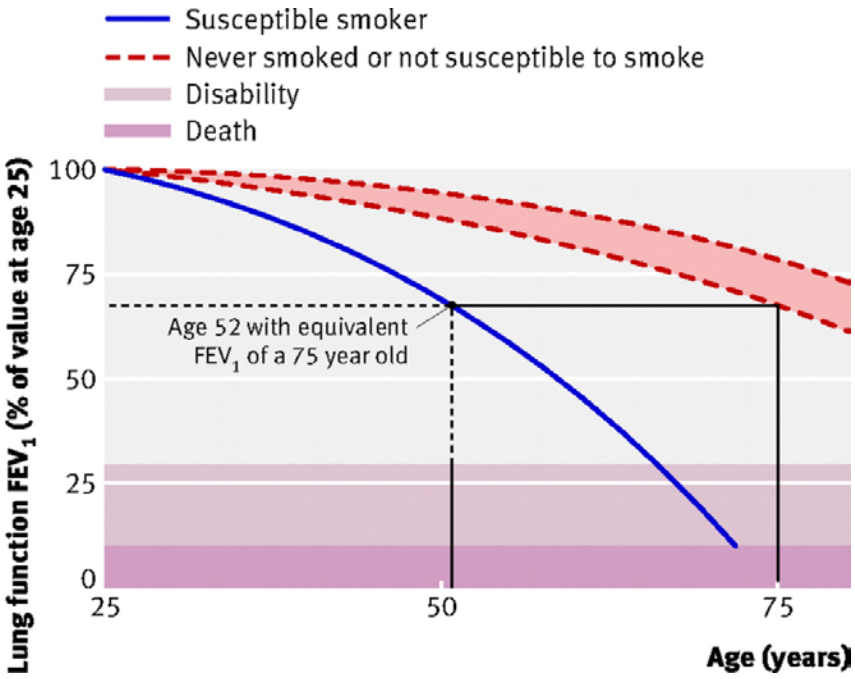

Fig 1.Peto Fletcher graph- Graph of lung function against age showing how smoking accelerates age related decline in lung function(*adapted from Fletcher and peto*)[97]

Other Exposures

Occupational exposures are also associated with increased risk for accelerated loss of lung function. Nearly 20% of COPD risk is due to occupational exposures among smokers and it is more than 30% among non smokers. Farming or work industry occupations increase the risk of developing chronic bronchitis 2- 3 fold. Indoor air pollution, especially from exposure to smoke generated from the use of biomass fuels, is a major cause of COPD in the developing world.[81]

Air pollution

In 1992, a World Health Organization (WHO) expert committee on air pollution concluded that high concentrations of sulphur dioxide ($150mg/m^3$) or similar concentrations of particulate air pollution, measured as black smoke, was associated with increased morbidity in adult patients with COPD.

Respiratory Infections and Tuberculosis

Though respiratory infections are important causes of exacerbations of COPD, the association of adult or childhood respiratory infections to the development of COPD remains to be proven.[1]HIV infection may accelerate onset of smoking related emphysema. Prior tuberculosis is an independent risk factor for airflow obstruction.[9]

Genetic Susceptibility

Mutations in the serine proteinase inhibitor, alpha1–protease inhibitor (A1PI) is the only proven genetic abnormality that predisposes to COPD .Though only 1–2% of COPD patients are found to have severe ά1AT deficiency as a contributing cause of COPD, these patients demonstrate that genetic factors have a significant influence on

the susceptibility for developing COPD. PiZ individuals often develop early-onset COPD.[1] Linkage analysis identified serpin E2 on chromosome 2 which may predispose to airway obstruction.[8] The hedgehog interacting protein (HHIP) on chromosome 4 may contain COPD susceptibility determinants.

Early Life Events

Maternal smoking may be a risk factor for the development of COPD. Studies have suggested that both low birth weight and childhood respiratory infections are risk factors for the development of COPD.[8]

Gender

The increased prevalence among men for COPD is related to the demographics of exposure to cigarettes or other inhaled toxins within a population,[8] however studies from developed countries show that the prevalence of the disease is now almost equal in men and women.[26] Some studies have suggested that women are more susceptible to the effects of tobacco smoke than men,[28-29] receiving a greater dose of smoke for a given number of pack years due to their smaller airway size. Women also have a higher prevalence of bronchial hyper reactivity than men, a suspected risk factor for COPD.[11]

Socioeconomic Status

Morbidity and mortality rates in COPD have been found to be inversely related to socioeconomic status.[8,30-32]

Asthma

In a report from a longitudinal cohort of the Tucson epidemiological study of airway obstructive disease, adults with asthma were found to have a 12- fold higher risk for acquiring COPD than those without asthma after adjusting for smoking.[9]

PATHOLOGY [8,12,15]

The pathologic changes of COPD involve large and small airways and the terminal respiratory unit i.e the respiratory bronchiole, alveolar ducts and alveoli. While changes in large airways are responsible for cough and sputum production, changes in small airways and alveoli lead to physiologic alterations. Small airways are also the main sites of airflow limitation.

Small airways exhibit a variety of lesions narrowing their lumina, including goblet cell metaplasia, mucosal and sub mucosal inflammatory cells infiltration, edema, peribronchial fibrosis, intraluminal mucus plugs and smooth muscle hypertrophy.

In large cartilaginous airways hypertrophy of sub mucosal mucus producing glands occurs which is the histological hallmark of chronic bronchitis. This is measured in anatomical terms by the Reid index, based on thickness of sub mucosal glands, to that of bronchial wall. In patients with chronic bronchitis it is 0.44+0.09, otherwise normally 0.52 + 0.08.Mucous gland size can also be assessed by measurement of the Absolute gland area, whereby the proportion of the wall volume occupied by glands is assessed. Sputum production and gland size do not have any relation to antemortem FEV_1.

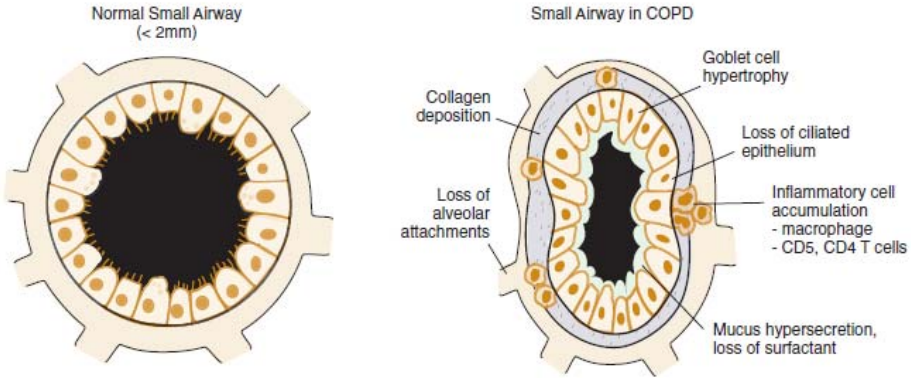

Fig 2.Small airway obstruction in COPD (*adapted from Shapiro SD, Reilly JJ Jr, Rennard SI.Chronic Bronchitis and Emphysema. Murray and Nadel's Textbook of Respiratory Medicine. 5th ed;3(I):919-967.* **)**

Emphysema

Emphysema begins as an increase in the number and sizes of alveolar fenestrate and results ultimately in destruction of alveolar septae and their attachments to terminal and respiratory bronchioles.

Emphysema has 3 morphologic patterns:

Centriacinar emphysema characterized by focal destruction limited to the respiratory bronchioles and the central portions of acinus. This form is associated with cigarette smoking and is most severe in the upper lobes and also superior segments of lower lobes.

Panacinar emphysema, involves the entire alveolus distal to the terminal bronchiole. It is most severe in the lower lung zones and usually develops in patients with homozygous ά1AT deficiency.

Distal acinar emphysema or paraseptal emphysema is the least common form and involves distal airway structures, alveolar ducts, and sacs. This form is localized to fibrous septa or to the pleura and leads to formation of bullae. It is not associated with airflow obstruction.

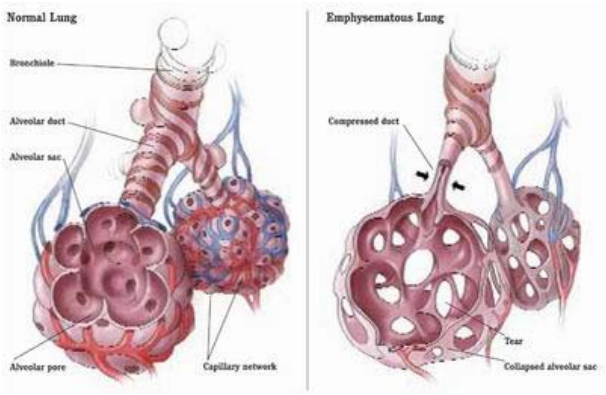

Fig 3. Comparison of normal and emphysematous lung

(*fromhttp://www.mesotheliomainfosearch.com/images*.)

PATHOPHYSIOLOGY

Air flow limitation

The expiratory limb of a flow-volume curve, shows persistent reduction in forced expiratory flow rates which is a distinguishing feature of COPD. In the initial stages of COPD, the airflow abnormality is only evident at lung volumes at or below the functional residual capacity, and appears as a scooped-out lower part of the descending limb of the flow-volume curve. The entire curve has decreased expiratory flow compared to normal, in more advanced disease.[1]

Hyperinflation

Hyperinflation, defined in several ways as increased functional residual capacity, increased total lung capacity, increased residual volume to total lung capacity or decreased inspiratory capacity to total lung capacity is common in COPD of moderate severity or worse. Hyperinflation, though compensates for airway obstruction can, however push the diaphragm into a flattened position with a number of adverse effects.[15]

Maldistribution of ventilation and ventilation-perfusion mismatching is characteristic of COPD and shows the heterogeneous nature of the disease as it affects the airways and lung parenchyma.[15]

PATHOGENESIS[1,8,15]

The pathogenesis of emphysema can be divided into four interrelated events (1) Exposure to cigarette smoke leads to inflammatory cell recruitment within the terminal airspaces of the lung. (2) Inflammatory cells release elastolytic proteinases which damage the extracellular matrix of the lung. (3) Loss of matrix-cell attachment leads to apoptosis of structural cells of the lung. (4) Airspace enlargement due to ineffective repair of elastin and other extracellular matrix components . Less is known about the pathogenesis of small airway obstruction.

Inflammation and oxidant- antioxidant imbalance

Inflammation occupies a central role in current knowledge about the pathogenesis of COPD. Smoking and other types of inhaled irritants lead to recruitment of inflammatory cells to the lungs and airways and products of these

recruited cells injure lung tissue and disrupt normal mechanisms of lung repair. On exposure to oxidants from cigarette smoke, histone deacetylase-2 is inactivated, shifting the balance toward acetylated or loose chromatin, exposing nuclear factor β sites and resulting in transcription of matrix metalloproteinase-9, proinflammatory cytokines interleukin 8 (IL-8), and tumor necrosis factor (TNF); which leads to neutrophil recruitment. Matrix metalloproteinases and serine proteinases, mainly neutrophil elastase, work together by degrading the inhibitor of the other, ultimately leading to lung destruction.

The Elastase - Antielastase Hypothesis

The elastase- antielastase hypothesis states that the balance of elastin-degrading enzymes and their inhibitors determines the susceptibility of the lung to destruction leading to airspace enlargement. Based on the clinical observation that patients with genetic deficiency in ά1AT, the inhibitor of the serine proteinase neutrophil elastase, were at increased risk of emphysema, and that instillation of elastases, particularly neutrophil elastase, to experimental animals resulted in emphysema, this hypothesis is a landmark in our understanding of the pathogenesis of emphysema.

Cell Death

Inflammation and cigarette smoking lead to increased oxidant stress and cell death.It has been suggested that inflammatory cell proteinases degrade the extracellular matrix of the lung as the initial event, and this leads to loss of cell anchoring, leading to apoptosis. Kasahara et al found that exposure to agents that initiate endothelial cell death (via VEGFR II inhibition) leads to non inflammatory airspace enlargement.[36]

Nagai and coworkers then found that epithelial cell death (via caspase 3 delivery) also causes emphysema.[37]

Ineffective Repair

Apart from restoring cellularity following injury, it is difficult for an adult to fully restore an appropriate extracellular matrix, especially functional elastic fibers and hence there is limited ability to repair damaged alveoli.[1]

PATHOGENESIS OF PULMONARY HYPERTENSION AND COR PULMONALE IN COPD[16,20,32-35]

Increased pulmonary vascular resistance and pulmonary hypertension are central mechanisms in all cases of cor pulmonale.

The pathogenesis can be dealt under 2 headings

1. Development of pulmonary hypertension and
2. Cardiac involvement following pulmonary hypertension.

1) Development of pulmonary hypertension:

The various factors responsible for the development of pulmonary hypertension are as follows -

1) Hypoxemia, Hypercapnia and Acidosis:

Hypoxia and the resultant hypoxemia (diminished pO2), hypercapnia (increased pCO2) and acidosis (increased H+ ion concentration) appear to be the main factors in the production of pulmonary vasoconstriction with the resultant pulmonary hypertension.[32] Hypoxic vasoconstriction appears to be the most common cause of

mild and moderate degrees of pulmonary hypertension. There is also a positive correlation between the pCo2 and PA pressure.

2). Anatomical changes in the pulmonary vascular bed

Both intimal and medial thickening have been described in the small pulmonary arteries of patients with COPD; however, intimal thickening with components of cellular hypertrophy and hyperplasia have been the most consistently demonstrated. Pulmonary artery endothelial dysfunction also occurs in PH.

3) Increased blood volume (hypervolemia)

Increased blood flow in the pulmonary vascular bed, particularly when its capacity is reduced due to diminished distensibility, vasoconstriction or anatomical changes in the vessels, also produces pulmonary hypertension.

4) Increased bronchomotor tone:

More the bronchoconstriction the greater will be the pressure in the alveoli. As a result, lesser will be the capillary blood flow and greater will be the pulmonary hypertension.[33]

The effect of airway resistance on pulmonary artery pressure may be particularly important when ventilation increases as in cases of acute exacerbation of COPD. Even small increases in flow that occur during mild exercise may increase pulmonary artery pressure significantly.

5) Development of bronchopulmonary shunts

In emphysema, there is a loss of tethering effect from reduced lung elastic recoil, partly responsible for the development of PH and subsequent RV dysfunction. Gas trapping during exercise may lead to dynamic compression of the pulmonary

arteries.[16] In COPD, the mean pulmonary arterial pressure is usually less than 30 mm Hg.

Since right ventricular failure occurs at this level of pulmonary hypertension, it is likely that the right ventricle in these patients is profoundly affected by hypoxemia and behaves like an ischemic right ventricle rather than a pressure-loaded right ventricle. A small subgroup of patients with COPD develop severe pulmonary arterial hypertension (mean PA pressure [PAP] > 45 mm Hg) and have a unique pattern of cardiopulmonary abnormalities with mild to moderate airway obstruction, severe hypoxemia, hypocapnia, and a low DLCO.

2. Cardiac involvement following pulmonary hypertension

The right ventricle dilates with even modest acute increases in afterload, that its effectiveness as a pump is compromised; resulting in failure of the right side of the heart - acute cor pulmonale. When the right ventricle hypertrophies in response to a chronic pressure load, many alterations occur like loss of cardiac myocytes and myocardial edema, followed by fibrosis and the hypertrophied ventricle becomes stiff, resulting in an increase in end-diastolic RV pressure that compromises endocardial perfusion .This creates a mismatch of myocardial oxygen demand and supply. As RV hypertrophy progresses, failure of its pump function with either persistence of increased pulmonary artery pressure or acute increases, due to the underlying lung disease is seen. The chronology of events is initial dilatation of the hypertrophied ventricle, an elevation in RV end-diastolic pressure causing an increased systemic venous pressure, and peripheral edema. Bouts of respiratory failure in COPD,cause acute worsening of RV function and peripheral edema which resolves if treatment of

the lung disease is effective. Systemic factors like generalized hypoxia, increased blood viscosity secondary to polycythemia, hypercapnia and the resulting acidemia adversely affect function either by directly affecting cardiac muscle or by exaggerating RV afterload .Once the basic heart failure starts, the other factors like diminished renal flow with sodium retention, secondary aldosteronism, excess of antidiuretic hormone, hypoproteinemia, increased capillary permeability etc, exaggerate the pre-existing heart failure .

The left atrial pressure is normal in cor pulmonale except when circulating blood volume is increased or if cor pulmonale is complicated by LV failure. Experimental observations have raised the prospect that hypertrophy and failure of the RV can lead to disorders in LV performance. One hypothesis has been that hypertrophy of the septal wall of the RV could be etiologically related. However there is no firm clinical evidence for this notion. The more usual cause of LV failure in cor pulmonale is independent disease of the LV.

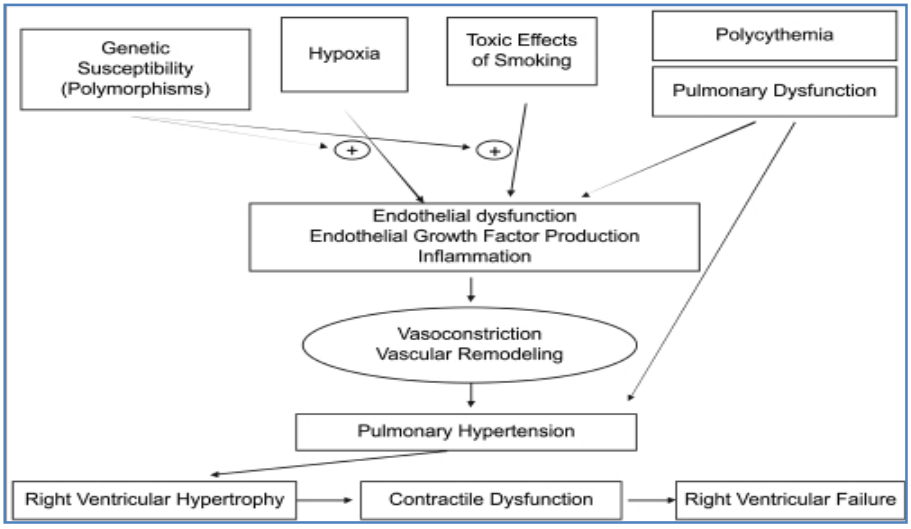

Fig4.Pathophysiology of PH and right ventricular dysfunction associated with COPD.[14]

CARDIOVASCULAR DISEASES AND COPD

COPD is an important risk factor for atherosclerosis.[41-43] The risk of ischemic heart diseases, strokes, and sudden cardiac deaths increases 2-to 3-fold, independent of other risk factors with even modest reductions in expiratory flow volumes.[41-45]Poor lung function has been shown to be a better predictor of all-cause and cardiac-specific mortality than established risk factors such as serum cholesterol.[5] Cardiovascular conditions are the leading cause of mortality among people with impaired lung function.[41,43,45] However mechanisms responsible for this association, remain unknown. Tobacco smoking is of course, a shared risk factor for both COPD and cardiovascular disease. Nevertheless, it is possible that others factors may increase the cardiovascular risk of patients with COPD even further.[46]

Sin DD et al showed that systemic inflammation is present in moderate and severe COPD and airflow obstruction is an important risk factor for cardiac injury. [47] They also showed that in the presence of elevated CRP, the risk increases almost 2-fold, which implies an important interplay of systemic inflammation with airflow obstruction in the development of ischemic heart disease. Sin DD et al also showed that in COPD patients, every 10% reduction in FEV_1 equates to an increase in cardiovascular mortality of 28%. Huiart et al using Saskatchewan Health databases showed that cardiovascular morbidity and mortality rates were higher in the COPD cohort than in the general population.[48] The epidemiologic evidence linking COPD and cardiovascular morbidity and mortality is strong. Patients with COPD, have a 2-3 fold increase in the risk of cardiovascular events including death even after adjustments for traditional cardiovascular risk factors such as serum total cholesterol, hypertension,

obesity and smoking.[49] The sympathetic nervous system is activated in COPD which in turn is a risk for cardiovascular disease. Endothelial dysfunction and arterial stiffness are contributors for both COPD and cardiovascular disease. COPD is also associated with increased risk for arrhythmias, especially multifocal atrial tachycardias.

SYSTEMIC EFFECTS OF COPD

Systemic inflammation and skeletal muscle wasting contribute to limiting the exercise capacity of patients and worsen the prognosis, irrespective of degree of airflow obstruction.[20] These may be mediated by increased concentrations of TNF ά, IL-6 and oxygen derived free radicals. Depression, fatigue, osteoporosis and chronic anemia are major comorbidities in COPD associated with poor functional performance and significant impairment in health status, causing a decline in daily functional activity.[9]

CLINICAL FEATURES

HISTORY

The three most common symptoms in COPD are cough, sputum production, and dyspnea.[1] Dyspnea is usually exertional until late in the course of the disease. Cough,may often be the presenting symptom.[8]

PHYSICAL FINDINGS

Patients usually have a normal physical examination in early stages of COPD. Smokers may have odour of smoke in their breath or nicotine staining of fingernails. Cyanosis may be seen while clubbing is not a sign of COPD.Patients may exhibit characteristic pursed lip breathing which slows expiratory flow and serves for better lung emptying. Coarse crackles occurring early in inspiration have been associated

with obstructive lung disease,while rhonchi are more prevalent in patients complaining of dyspnea. Wheezing is an inconsistent finding and does not relate to the severity of obstruction. Prolongation of the expiratory phase of respiration longer than the normal 4 seconds is indicative of significant obstruction and is the most consistent finding in symptomatic COPD. Signs of hyperinflation include a barrel chest, horizontal ribs and protruding abdomen .Use of accessory muscles of respiration, characteristic "tripod" sign posture, etc may be seen in patients with severe airflow obstruction. Although traditional teaching is that patients with predominant emphysema, termed "pink puffers," are thin and noncyanotic at rest and have prominent use of accessory muscles, and patients with chronic bronchitis are more likely to be heavy and cyanotic ("blue bloaters"), current evidence demonstrates that most patients have elements of both bronchitis and emphysema and that the physical examination does not reliably differentiate the two entities.[1,9]

Systemic wasting with weight loss and diffuse loss of adipose tissue may be seen in advanced disease and is a poor prognostic factor in COPD. Hoover's sign, the paradoxical inward movement of the rib cage may be seen in advanced disease.

There is no history that is specific for cor pulmonale. Episodes of leg edema ,atypical chest pain, dysnoea on exertion, exercise induced peripheral cyanosis, prior respiratory failure, excessive day time somnolence are all clues to the presence of cor pulmonale. Cough and easy fatigability are common, while shortness of breath is a universal symptom in cor pulmonale. Chest pain may occur due to right ventricular ischemia .Some patients with nocturnal hypoventilation and sleep apnoea may present with personality changes, mild systemic hypertension and headache.[34]

BODY MASS INDEX

Wasting is an important systemic manifestation as a loss of > 40% of actively metabolizing tissue is incompatible with life.[39-40] The body cell mass (BCM) represents the actively metabolizing (organs) and contracting (muscles) tissue. It cannot be measured directly. Changes in body cell mass can be clinically recognized by decrease in body mass index (BMI) in general and by loss in fat-free mass (FFM) in particular. Schols et al[40] demonstrated that low body mass index (BMI), age, and low pO2 were significant independent predictors of increased mortality rates in a retrospective study of 400 patients with COPD. After stratification of the group into BMI quintiles, a threshold value of 21 kg/m^2 was identified below which the mortality risk was clearly increased. Low body mass index (<19) is an independent risk factor for premature death.[68]

SPIROMETRY

GOLD international guidelines advice spirometry as the gold standard for accurate and repeatable measurement of lung function.

Table 1. GOLD criteria for COPD severity[9]

GOLD SPIROMETRIC CRITERIA FOR COPD SEVERITY	
I:MILD COPD	$FEV_1/FVC < 0.70$ $FEV_1 \geq 80\%$ predicted
II:MODERATE COPD	$FEV_1/FVC < 0.70$ $50\% \leq FEV_1 < 80\%$ predicted
III:SEVERE COPD	$FEV_1/FVC < 0.70$ $30\% \leq FEV_1 < 50\%$ predicted
IV:VERY SEVERE COPD	$FEV_1/FVC < 0.70$ $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Reversibility to bronchodilators

The GOLD guidelines recommend an increase in $FEV_{1,}$ that is both greater than 200 ml and 12% above the pre-bronchodilator FEV_1 as significant.[9]

LIMITATIONS OF SPIROMETRIC CLASSIFICATION

The FEV_1 is essential for diagnosing and quantifying the pulmonary impairment resulting from COPD.[51-53] The rate of decline in FEV1 is a good indicator of disease progression.[54,55] The FEV_1 is an independent predictor of cardiovascular mortality in COPD. The Lung Health Study reported that for every 10% decrease in FEV_1, there was an increase of approximately 28% in fatal coronary events, and 20% in nonfatal coronary events, among subjects with mild to moderate COPD.[76] But it does not reflect adequately all the systemic manifestations of COPD. FEV_1 correlates weakly with the degree of dyspnea[56] and the change in FEV_1 does not show the rate of decline in patient's health.[57] Prospective observational studies have found that the degree of dyspnea[66]and health-status scores[60] are more reliable predictors of the risk of death than FEV_1.Thus, although essential in the staging of disease in any patient with COPD, FEV_1 alone as the sole parameter of severity does not throw light on the systemic involvement in the disease.

6 MINUTE WALK TEST

Several modalities are available for the objective evaluation of functional exercise capacity.[69] A recent review of functional walking tests concluded that "the 6MWT is easy to administer, better tolerated, and more reflective of activities of daily living than the other walk tests".[60] It evaluates the integrated responses of all the systems involved during exercise, including the pulmonary and cardiovascular

systems, systemic circulation, peripheral circulation, blood, neuromuscular units, and muscle metabolism. The 6MWT may better reflect the functional exercise level for daily physical activities ,as the self- paced 6MWT assesses the submaximal level of functional capacity and most activities of daily living are performed at submaximal levels of exertion.[59] The reproducibility of the 6MWT (with a coefficient of variation of approximately 8%) appears to be better than the reproducibility of FEV_1 in patients with COPD.[61-65] The 6MWT was more responsive to deterioration than to improvement in heart failure symptoms.

BODE INDEX

Bode index was developed for the comprehensive evaluation of patients with COPD. This multisystem grading index has four variables.

1. Body mass index 2.Obstruction to airflow (FEV1) 3.Dyspnea (MMRC dyspnea scale) 4. Effort tolerance (6 minute walk test)

Each variable in the index correlates independently with the prognosis of COPD and is easily measurable. The body-mass index and distance walked in six minutes are the two descriptors of systemic involvement in the BODE index. Both are simply obtained and independently predict the risk of death.[67-69] The distance walked in six minutes is more sensitive than the body mass index.

GOLD and ATS recommend that a patient's perception of dyspnea be included in any new staging system for COPD. Dyspnea is the most disabling symptom of COPD and the degree of dyspnea gives information about the patient's perception of illness. The MMRC dyspnea scale is simple to administer and correlates with other dyspnea scales and scores of health status.[66] Also, in a large prospective study of

BODE index, the score on the MMRC dyspnea scale was a better predictor of the risk of death than was the FEV_1.

RADIOLOGY

CHEST X RAY

Chest radiography can help exclude other pathology in patients with COPD.COPD is a functional diagnosis and, chest radiographs can only suggest this diagnosis. Increased thickness of bronchial walls viewed on end and an increased prominence of lung markings, suggest the diagnosis of chronic bronchitis, though neither specific, nor sensitive.The triad of overinflation, oligemia, and bullae make up the arterial deficiency pattern due to hyperinflation in emphysema, while the increased markings pattern, resembles the "dirty chest" appearance seen in chronic bronchitis. The best evidence of overinflation is flattening of the diaphragms with a concavity of the superior surface of the diaphragm .Another sign is an increase in the width of the retrosternal air space, but this is less sensitive.[15]

COMPUTED TOMOGRAPHY.

Computed tomography (CT) has the resolution needed to delineate and quantify subtle findings in the chest and thus is more sensitive than conventional radiography,particularly in the diagnosis of emphysema. Because loss of density is a characteristic feature,CT density can be used to quantify emphysema, permiting estimation of both severity and extent of disease.[15]

ELECTROCARDIORAM

COPD influences the electrical events of the heart in the following ways.

i. The voluminous lungs have an insulating effect and diminishes the transmission of electrical potentials to the registering electrodes.

ii. The heart descends to a lower position within the thorax due to a lowering of the diaphragm which alters the position of the heart relative to the conventional precordial electrode positions.

iii. The right ventricle and atrium become compromised due to a reduction of the pulmonary vascular bed in chronic hypoxemia resulting in right ventricular hypertrophy and dilation as well as right atrial enlargement.

These will be manifested in electrocardiogram as

1. **Decreased magnitude of electrocardiographic deflections**

   The QRS and T deflections are markedly diminished in magnitude. The loss of R wave amplitude in precordial leads may also be due to low anatomic position of the heart.

2. **Right atrial enlargement**

   Right P wave axis deviation - The frontal plane P wave axis is deviatedto the right of +60º. It is commonly and characteristically directed to +90º.

   P pulmonale - reflected by P waves which are tall and peaked in standard leads II, III. P wave height in lead II will be > 2.5 mm with right axis deviation of the P wave.

3. **Abnormalities of QRS Complex**

   Right QRS axis deviation - The frontal plane of QRS axis is deviated to the right and commonly directed to +90º. QRS axis deviates clockwise to +120º or even +150º with worsening pulmonary hypertension.

Left QRS axis deviation - This occurs in about 10% of cases. The mechanism is still speculative.

The S1, S2 S3 syndrome -The prominent terminal S waves may appear in standard leads I, II and III giving rise to this syndrome. This indirectly reflects posterior displacement of the apex.

Abnormalities of the precordial QRS form - There is diminution of the QRS complexes in all the leads. The R waves are attenuated in the left precordial leads which consequently reflect rS or rs complexes. Right precordial leads may show QS or W shaped complexes which may indicate a downwardly displaced heart. In severe cases R/S in lead V4 to V6 may be less than 1 and R wave amplitude in lead V6 may be less than 5 mm.

Right Bundle Branch Block - There may be complete or incomplete right bundle branch block.

4. Abnormalities of the T wave

The frontal plane T wave axis - Frontal plane T wave axis is usually similar in direction to that of the QRS axis commonly directed to region of +80º to +90º.

The T wave form -It is diminished in amplitude in all leads.The T waves may be inverted in right precordial leads especially when pulmonary hypertension is marked. Q-T interval in cor pulmonale unlike in other forms of heart failure is not prolonged. The five most typical findings in emphysema have been grouped together into a pentology by Wasserburg and colleagues:

- Prominent P waves in II, III and aVF.

- Exaggerated Ta waves producing more than 1 mm depression of ST segment in II, III and aVF.
- Right ward shift of QRS axis.
- Marked clockwise rotation in the precordial leads.
- Low voltage of QRS complexes especially over left precordium.

Acute exacerbation of COPD can present with paroxysmal arrhythmias, mainly atrial at times, ventricular tachycardias. Increasing severity of COPD, is reflected electrocardiographically by the following manifestations:

- Progressive right QRS axis deviation.
- Progressive right axis deviation of the P wave.
- The R:S ratio becomes less than 1 in lead V6.
- The R wave amplitude becomes less than 5 mm in lead I.
- Increasing amplitude of the P wave in standard leads II , III and aVF.
- A Ta wave develops in standard leads II, III and aVF.

Some of the commonly used criteria for right ventricular hypertrophy include those of Mayor et al (1948) .Sokolow and Lyon(1949) Gold Berger (1953) Scott et al (1955) and Milnor (1957) .The criteria adopted by Sokolow and Lyon (1949) which gives highest number of positive results indicative of RVH in ECG also gives the highest number of false positives. Goldberger criteria have shown 68.7% reliability and 6.3% false positive, while Mayer et al criteria gave 50% reliability and only 3.1% false positive. It has been suggested that where classical RVH changes are absent, diagnosis be based on combination of rs in V5 V6, Righ axis deviation, QR in aVR,and P pulmonale.

In a study by Chabra and Agarwal[70], peaked P-wave was observed in 35.7% COPD patients, whereas duration of QRS complex was abnormal in only 8.1% of the patients. ECG changes were found less sensitive (35.7%) but highly specific (95.6%). Kok- Jensen[71] studied the ECG features of 228 patients with chronic bronchial obstructions. A decreased survival was seen in patients with a QRS axis of +90ºto 180º and a P-wave amplitude in lead II of 0.20 mV or greater; only 37% and 42%, respectively, of the patients with these features were alive at 4 years. In a small series of COPD patients, ECG signs of cor pulmonale were found to be the hallmark of pulmonary hypertension, but only 33% of patients with high pulmonary vascular resistances had ECG signs of cor pulmonale.[72]

ECHOCARDIOGRAPHY

Transthoracic echocardiography (TTE) is helpful both in detecting the presence of RV dysfunction and in excluding causation from left ventricle. The findings of cor pulmonale with two-dimensional echocardiography include, RV dilatation and/or hypertrophy, and diminished function. Whenever tricuspid regurgitation is present, Doppler studies can estimate RV, and therefore pulmonary artery systolic pressure in millimeters of mercury from the velocity (v) of the regurgitant jet by the formula

$$sPAP = (v^2 \times 4) + CVP$$

where sPAP is pulmonary artery systolic pressure and CVP is central venous pressure.[34]

RV dysfunction is difficult to measure echocardiographically, but the position and curvature of the intraventricular septum (D sign) provides an indication of right ventricular afterload.[35]

RV wall thickness is a useful measurement for RVH, usually the result of RVSP overload. Indexed RV end-diastolic diameter has been identified as a predictor of survival in patients with chronic pulmonary disease.

In the absence of a gradient of across the pulmonic valve or RVOT, sPAP is equal to RVSP .In general, TR velocity > 2.8 to 2.9 m/s, corresponding to sPAP of approximately 36 mmHg (assuming an RA pressure of 3 to 5 mmHg) indicates elevated RV systolic and PA pressure. sPAP is related to age ,obesity ,stroke volume and systemic blood pressure. Elevated sPAP may not always indicate increased pulmonary vascular resistance (PVR). In general, those who have elevated SPAP should be carefully evaluated.[18] Using RVSP, Doppler echocardiography is 79% to 100% sensitive and 60% to 98% specific for identifying pulmonary hypertension.[78.]Studies have reported that RSVP estimated by echocardiography closely correlates to RSVP measured by right heart catheterization.[79-81]

Regional Assessment of RV Systolic Function

TAPSE or TAM is a method to measure the distance of systolic excursion of the RV annular segment along its longitudinal plane, from a standard apical 4-chamber window. TAPSE is usually acquired by placing an M-mode cursor through the tricuspid annulus and measuring the amount of longitudinal motion of the annulus at peak systole.

In the initial validation study by Kaul et al, TAPSE correlated strongly with radionuclide angiography, with low inter observer variability. TAPSE of less than 1.8 cm was associated with greater RV systolic dysfunction, right heart remodeling and RV-LV disproportion, versus a TAPSE of 1.8 cm or greater. In patients with

pulmonary arterial hypertension, survival estimates at 1 and 2 yr were 94 and 88% respectively, in those with a TAPSE of 1.8 cm or greater versus, 60 and 50%, respectively, in subjects with a TAPSE less than 1.8 cm.[76] Prior studies indicates that a normal TAPSE is 2.4-2.7 cm, with lesser values indicating mild (2.0-2.3 cm), moderate (1.5-1.9 cm) and severe (<1.5 cm) RV dysfunction.[59]

TAPSE is not only determined by RV systolic function but also appears to depend on LV systolic function. TAPSE <2.0 cm is associated with some degree of either RV or LV dysfunction, whereas a value >2.0 cm suggests normal biventricular systolic function.[77]

MANAGEMENT[96]

TREATMENT OF STABLE COPD

The treatment of stable COPD is a three pronged strategy. It includes

1. **Minimization Of Risk Factors**

Smoking cessation is the most important way and the 5A strategy appears to be effective. It includes ASK (about tobacco use) ASSESS (the status and severity of use) ADVISE (to stop)ASSIST (in smoking cessation), ARRANGE (follow up programme).Other methods like avoidance of open burning of crop residue and wearing masks at work place are important. Specific measures like using smokeless 'chullahs' and substituting solid fuels with LPG or electricity are the best approaches.

2. Pharmacotherapy Appropriate To The Disease Severity

- Bronchodilators

Central to the symptomatic management of COPD are bronchodilators. Inhaled drugs are preferred over oral preparations. The long acting inhaled beta agonist salmeterol and inhaled tiotropium are found to be effective. Combination treatment produces greater and more sustained improvements in FEV_1.If inhaled treatments have failed to provide relief oral theophylline may be considered.

- Corticosteroids

Corticosteroids can increase post bronchodilator FEV_1 and decrease the number of exacerbations. Inhaled glucocorticosteroids should be used regularly in symptomatic patients with COPD with a established spirometric response to glucocorticosteroids or for those with FEV1<50% predicted with repeated exacerbations.

- Role of other drugs

Antibiotics should only be used to treat infectious exacerbations. Regular use of antitussives and respiratory stimulants is not recommended.

Nonpharmacological Measures

Pulmonary rehabilitation

Goals of pulmonary rehabilitation are (a) to reduce symptoms, disability and handicap, and (b) to improve functional independence. It should include a physical training programme, education about the disease, and nutritional, psychological, social and behavioural interventions.

MANAGEMENT OF ACUTE EXACERBATIONS

An exacerbation is defined as "an event in the natural course of the disease characterized by a change in the patient's baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD".[9]

Treatment of acute exacerbations

Bronchodilators form the mainstay of managing exacerbations of COPD. Short-acting bronchodilators should be administered using inhalers (preferably with spacers) and in severe cases with nebulizers. Antibiotics should be used when symptoms increase and sputum becomes purulent. Amoxycillin, flouroquinolones or a second generation cephalosporin are used as the first choice. Severe exacerbations may be treated with higher-grade antibiotics. Systemic glucocorticoids when used in acute exacerbations hasten recovery.

MATERIALS AND METHODS

In this study, 50 patients were selected from the wards and outpatient departments of Coimbatore Medical College Hospital by simple random sampling.

STUDY DESIGN – Cross sectional study to assess the cardiac function in COPD patients.

STUDY PERIOD – September 2010 to August 2011

INSTITUTIONAL ETHICS COMMITTEE APPROVAL – Obtained

INCLUSION CRITERIA

- Any patient attending the outpatient department or admitted in wards with symptoms suggestive of airway obstruction for a period of atleast 2 yrs and a clinical diagnosis of COPD.
- Spirometric criterion of FEV_1/ FVC ratio below 0.70 after bronchodilator.

EXCLUSION CRITERIA

- Spirometry proven bronchial asthma defined as post bronchodilator change of FEV_1 more than 12% and 200 ml.
- Pulmonary tuberculosis
- Bronchiectasis
- Known congenital or acquired valvular heart disease
- Known coronary heart disease
- Known case of Diabetes mellitus
- Known case of Hypertension

STUDY PROTOCOL

50 patients attending outpatient department or wards of Coimbatore Medical College were selected for the study.This study does not attempt to evaluate the outcome or assess the prognosis.

1.HISTORY AND PHYSICAL EXAMINATION

For each enrolled subject, detailed history including smoking history mentioned in pack years and previous medical history was obtained. History of dyspnoea was graded according to Modified Medical Research Council (MMRC) scale.

Modified Medical Research Council Dyspnoea Scale Grade

- "I only get breathless with strenuous exercise."
- "I get short of breath when hurrying on the level or walking up a slight hill."
- "I walk slower than people of the same age on the level."
- "I stop for breath after walking about 100 yards or after a few minutes on the level."
- "I am too breathless to leave the house" or "I am breathless when dressing."

Detailed physical examination was done including vitals, and signs of heart failure were looked for as indicated in proforma. Height was measured to the nearest millimeter and weight was measured bare foot to nearest 100 gm .Body Mass Index (BMI) was calculated by the formula

BMI -weight (kg)/ height ($m^{2)}$

INVESTIGATIONS

Sputum smear analysis for Acid fast bacilluwas done to rule out smear positive pulmonary tuberculosis.

Pulmonary function test

Spirometry was done using a standard spirometer and measurements obtained before and 20 minutes after inhalation of 200 microgram of salbutamol. FEV_1, FVC and FEV_1/FVC was obtained.

Radiographic examination

Chest X ray posteroanterior and lateral view was taken to look for evidence of emphysema, chronic bronchitis and/ or signs of cor pulmonale and pulmonary artery dilatation.

The presence of pulmonary hypertension can be assumed on a plain chest radiography if the right main pulmonary artery has a width of more than 16 mm or left main pulmonary artery more than 18mm.[14] Right ventricular hypertrophy is detected in lateral view by encroachment of retrosternal space.

Electrocardiogram

ECG was taken to look for signs of COPD and cor pulmonale .

QRS axis was determined by plotting the QRS potentials on a graph with lead I as X axis and aVF as Y axis. – 30 to + 90 was considered as normal axis, – 30º to – 90º as left axis , +90º to +180º as right axis and – 90º to + 180º was considered as north west axis.

Criteria of RVH

- Shift of the mean QRS axis to the right.
- An R : S ratio in lead V1 greater than 1.
- R : S ratio in lead V6 of less than 1 .
- R wave amplitude > 5mm in V_1.

P Pulmonale evidenced by P wave amplitude more than 2.5 mm in lead II with frontal plane P wave axis more than > + 60º.

Low voltage complexes evidenced by QRS amplitude of < 5mm in limb leads and 10 mm in chest leads.

Presence of conduction blocks. [17]

Echocardiogram

Echocardiogram using 2 D Echo, M Mode And Doppler to assess degree of cardiac involvement as evidenced by RA and RV enlargement, Left ventricular ejection fraction(LVEF), Tricuspid Annular Plane Systolic Excursion(TAPSE)in millimetres, Right ventricular systolic pressure(RVSP)in mmHg and presence of tricuspid regurgitation(TR) graded as mild, moderate and severe.

RV DIMENSION - On Apical 4 chamber view diameter > 42 mm at the base and > 35 mm at the mid level and longitudinal dimension > 86 mm indicates RV enlargement.

RA DIMENSION.

On apical 4-chamber view RA area > 18 cm^2, RA length > 53 mm, and RA diameter > 44 mm indicate at end-diastole RA enlargement.[18]

TRICUSPID REGURGITATION

The severity of tricuspid regurgitation was graded as absent (grade 0), mild (grade I, jet area< 20% of the right atrial area), moderate (grade II, jet area between 20% and 33% of the right atrial area), and severe (grade III, jet area > 33% of the right atrial area), according to established grading systems.[73]

TAPSE < 18mm indicates RV systolic dysfunction.

RVSP

TR velocity reliably permits estimation of RVSP with the addition of RA pressure, assuming no significant RVOT obstruction. RA Pressure was estimated to be 5 mm Hg when the IVC diameter was less than 20 mm and the collapsibility greater than 50%

$$RVSP = 4(V)^2 + RA\ pressure$$

where V is the peak velocity (in meters per second) of the tricuspid valve regurgitant jet, and RA pressure is estimated from IVC diameter. RVSP >40 mmHg is taken as suggestive of PH.

6MWT and BODE INDEX

6 Minute Walk Test was performed in accordance to ATS guidelines on a 30 metres walking course on level ground.

BODE index was calculated using body mass index (BMI), FEV1, distance covered in 6 6MWT and Modified Medical Research Council dyspnoea scale(MMRC). For BMI values were 0 for (>21) and 1 for (< 21).Scores for FEV1 were 0 for (≥ 65%),1 for (50-

64%),2 for (36-49%), and 3 for(<35%). MMRC dyspnoea was scored 0 points for grades 0 and I, 1 point for grade II , 2 for grade III and 3 for grade IV. 6MWD scores were 0 for (≥ 350 mts), 1 for (250- 349 mts), 2 for (150-249 mts) and 3 for (< 149 mts). Points for each variable was added so that BODE index scores ranged from 0- 10 points. BODE index score of 0-2 was taken as mild COPD, 3- 5 was moderate and ≥6 severe COPD.

Table 2.BODE INDEX

SCORE	0	1	2	3
FEV1 % PRED	≥65	50- 64	36-49	< 35
6 MWD (m)	≥350	250- 349	150- 249	<149
MMRC	0-1	2	3	4
BMI	≥ 21	<21		

TOTAL SCORE (0- 10)

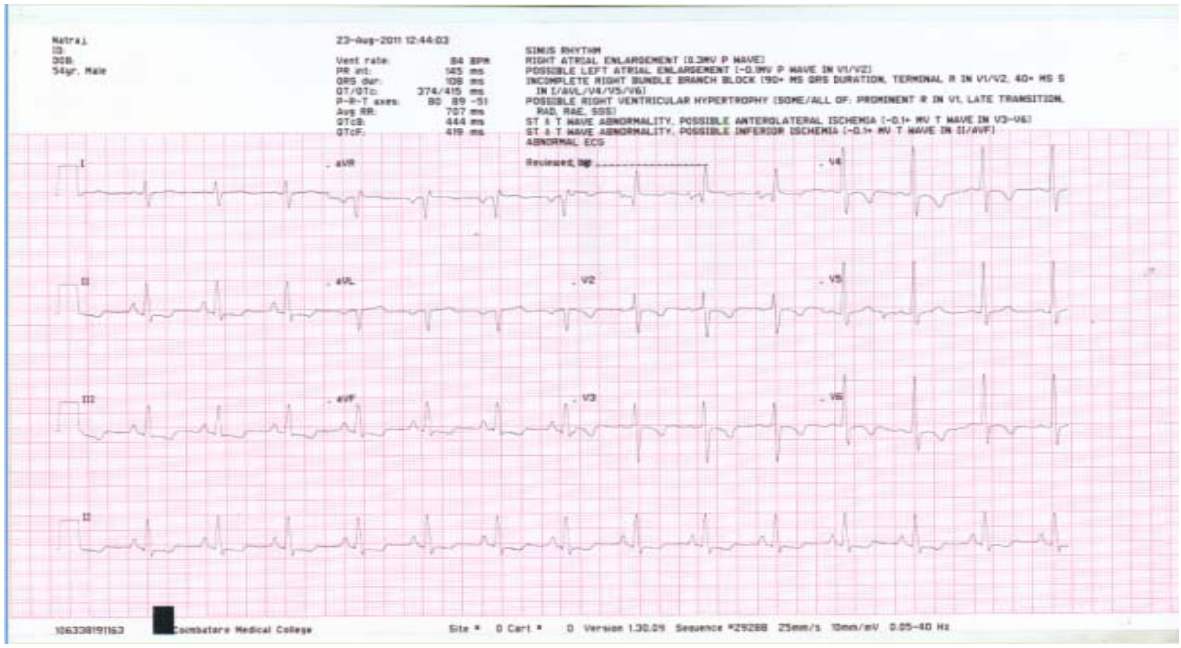

Fig 5. ECG Showing P Pulmonale, RVH, Incomplete RBBB and T inversion in precordial and inferior leads

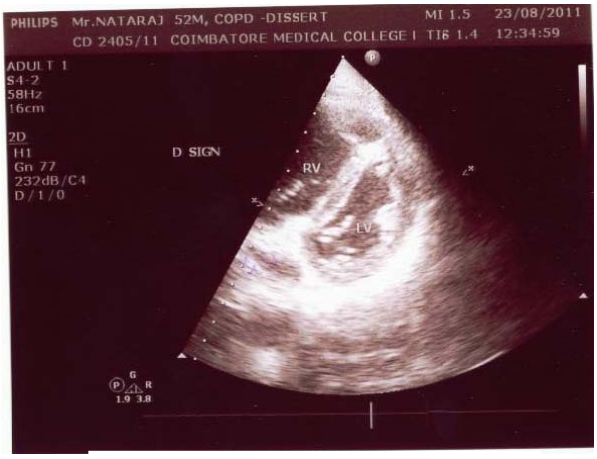

Fig 6 .Positive D SIGN

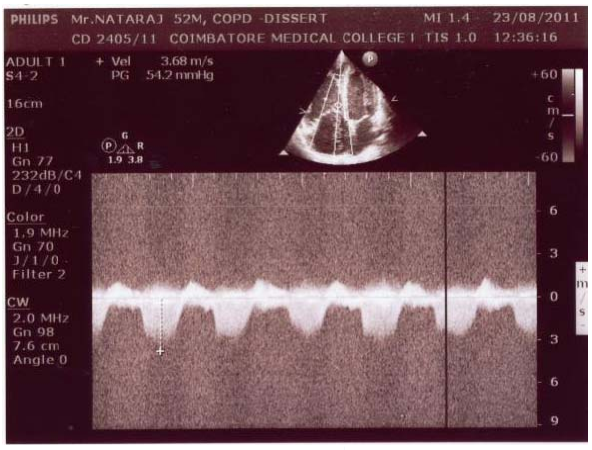

Fig 7.Echocardiogram showing severe TR and PH

OBSERVATIONS AND RESULTS

Statistical analysis was carried out in 50 subjects after categorizing the variable and significance was taken when the p value was less than 0.05. Statistical analysis was carried out using standard formulae. Microsoft excel 2007 and SPSS (statistical package for social sciences) version 13 software was used for data entry and analysis.

Table 3. AGE DISTRIBUTION

Age group (in years)	Number of cases	Percentage %
Less than 40	4	8
40 – 50	13	26
50- 60	17	34
60 – 70	12	24
➢ 70	4	8
Total	50	100

In this study 26% patients were in 40- 50 age group, 50- 60 in 34% age group and 24% in 60- 70 age group. Maximum number of patients are in 40-70 year age group.

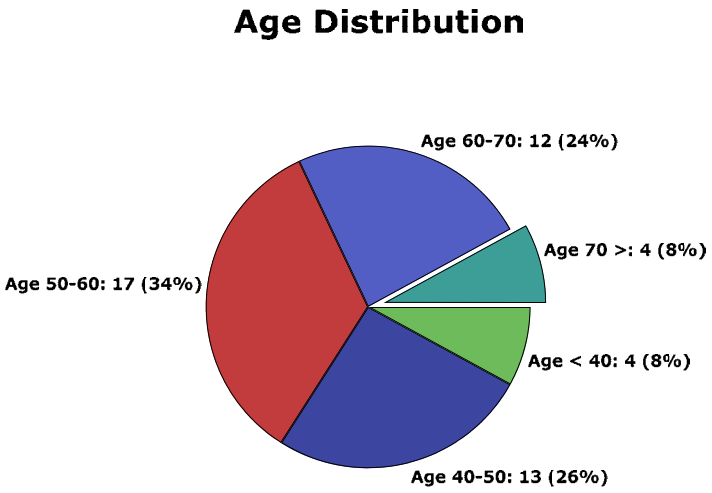

Fig 8. AGE DISTRIBUTION

Table 4: SEX DISTRIBUTION

Sex	Number of cases	Percentage %
Male	33	66
Female	17	34
Total	50	100

In my study 66% were males and 34% were females.

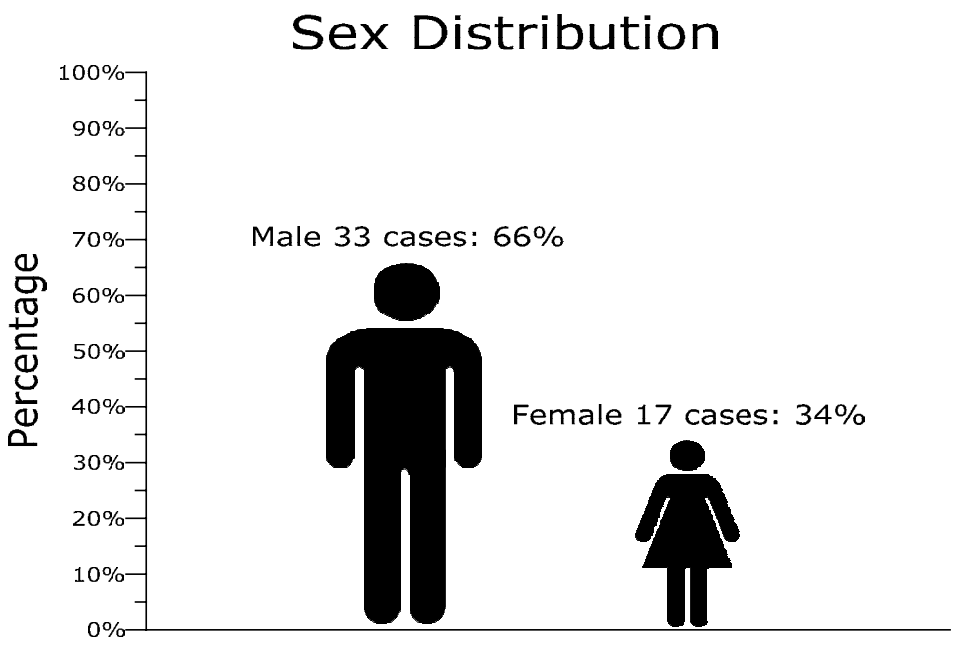

FIG 9. SEX DISTRIBUTION

Table 5.SMOKING DISTRIBUTION PATTERN

Smoking	Number of cases	Percentage %
Yes	29	58
No	21	42
Total	50	100

58% of patients in my study were smokers and 42% non smokers.

FIG 10. SMOKING DISTRIBUTION

Table 6. SMOKING IN PACK YEARS

Smoking In Pack Years	Frequency	Percentage %
0-10	23	46
10-20	2	4
20-30	9	18
30-40	10	20
➢ 40	6	12
total	50	100

46 % of smokers had a less than 10 year pack consumption.

Table 7.BODE INDEX

BODE Index	Frequency	Percentage %
0-2	11	22
3-5	10	20
≥ 6	29	58
total	50	100

58% of patients had a BODE score of more than 6 indicating severe COPD.

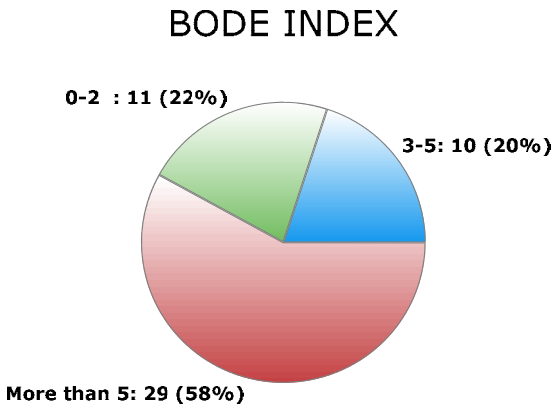

FIG 11. BODE INDEX DISTRIBUTION

Table 8. TAPSE DISTRIBUTION

TAPSE (mm)	Frequency	Percentage %
Less than 18	14	28
More than 18	36	72
total	50	100

Almost ¾ th of patients (72%) had TAPSE more than 18 mm.

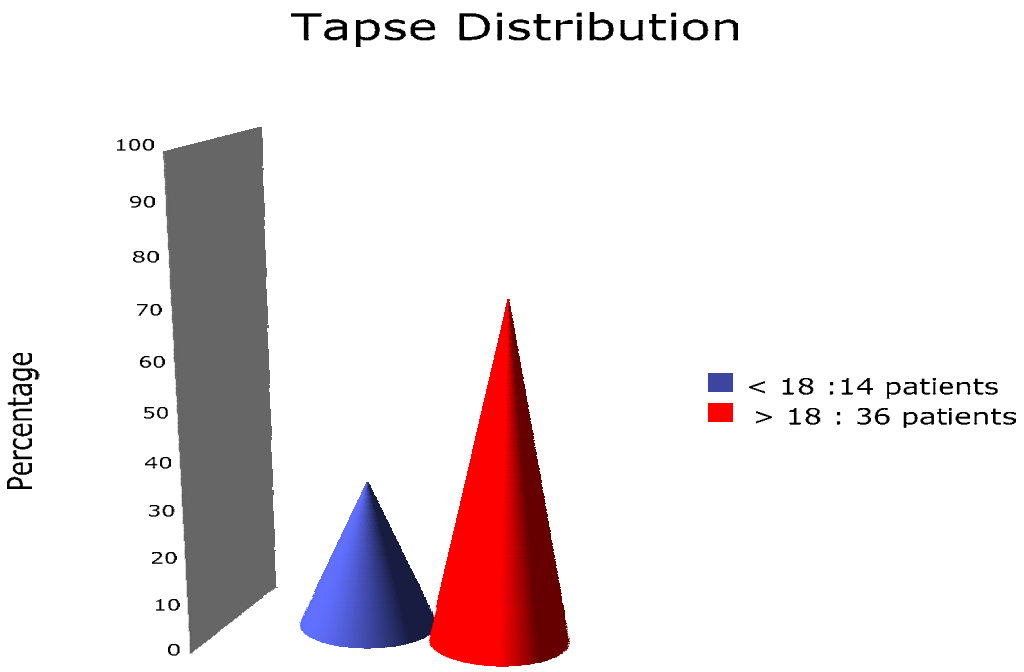

FIG 12. TAPSE DISTRIBUTION

Table 9.RVSP DISTRIBUTION

RVSP (mm Hg)	Frequency	Percentage %
Less than 40	24	48
40-50	13	26
50-60	4	8
More than 60	9	18
total	50	100

RVSP was less than 40 for almost half the patients (48%) while 26% had mild PH with RVSP between 40 – 50 mm Hg.

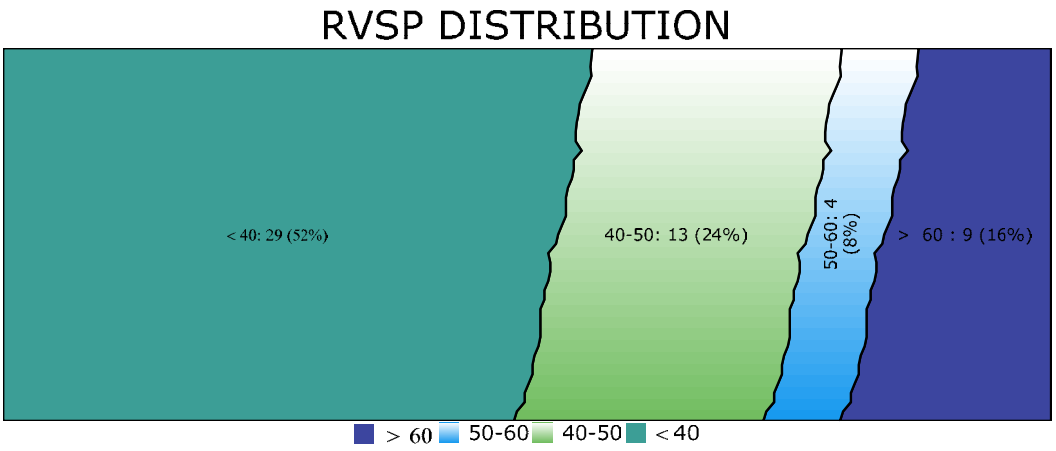

FIG 13. RVSP DISTRIBUTION

Table10. TR GRADIENT

Tricuspid regurgitation(TR)	Number of cases	Percentage%
Absent	14	28
1+	21	42
2+	4	8
3+	11	22
Total	50	100

42% of patients had mild TR while in 28% there was no evidence of TR .22% had severe grade 3 TR.

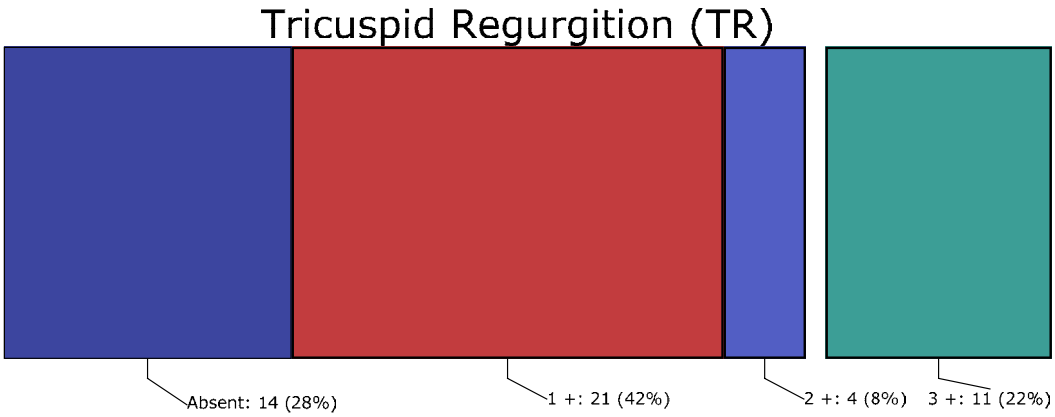

FIG 14. TR FREQUENCY DISTRIBUTION

Table 11. AGE AND BODE INDEX

Age	BODE Index Score			Total	Chi Square Test	Level Of Significance
Less than 40	3	1	0	4	9.86	0.275
40- 50	2	2	9	13		
50- 60	4	4	9	17		
60- 70	2	2	8	12		
> 70	0	1	3	4		
Total	11	10	29	50		

In the above tabular column the chi square test is 9.86 (p not < 0.05). So there is no significant association between age and BODE score.

Table 12. FEV_1 AND SEX

Sex	Number	Mean	Standard deviation	Z	Level of significance
Male	33	49.17	14.94	0.111	0.912
Female	17	49.68	15.8		

In the above table z value 0.111 for the mean difference in FEV_1 is not significant (p not < 0.05).The mean FEV_1 for males is 49.17 and for females 49.68 respectively. So it can be inferred that there is no significant difference in FEV_1 levels in relation to sex of the patient.

Table 13.SMOKING AND TAPSE

Smoking	Number	Mean	Standard deviation	Z	Level of significance
No	21	22.57	4.37	2.18	0.034
Yes	29	20.34	2.83		

Here z value 2.18 for the mean difference in TAPSE is significant ($p < 0.05$).The mean TAPSE for smokers is 20.34 and non smokers is 22.57 and it can be inferred that there is a significant correlation between smoking and TAPSE levels.

Table14.SMOKING AND ECG FEATURES OF PHT/COR PULMONALE

Smoking	ECG features of PHT/Cor pulmonale		Total	Chi square test	Level of significance
	Normal	Abnormal			
No	8	13	21	5.46	0.019
Yes	3	26	29		
Total	11	39	50		

The Chi square 5.46 for the association between smoking and ECG is significant ($p < 0.05$).So it can be inferred that there is an association between smoking and ECG abnormalities.

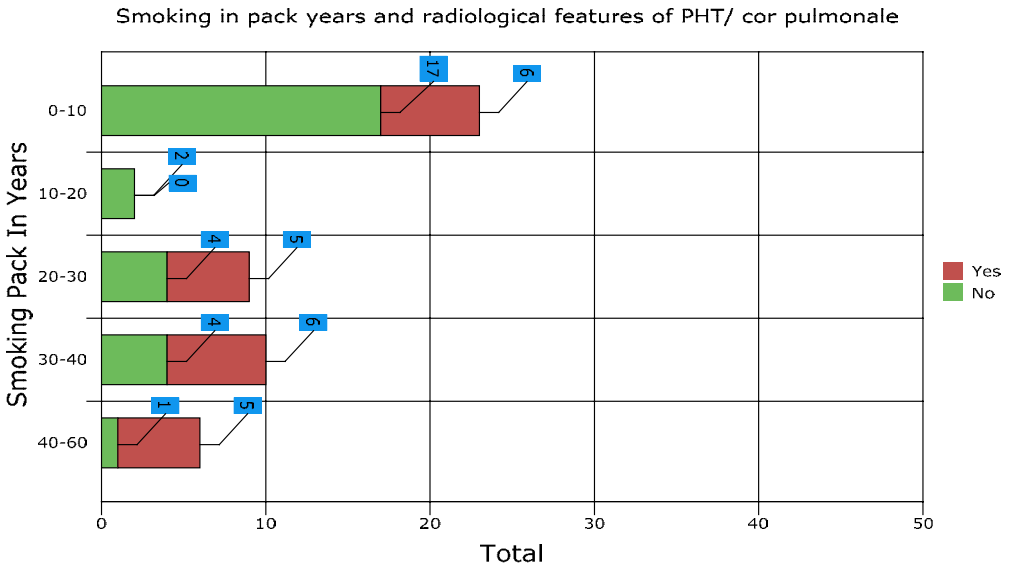

FIG 15. CORRELATION BETWEEN SMOKING IN PACK YEARS AND RADIOLOGICAL FEATURES OF PHT/COR PULMONALE

Table 15: BMI AND FEV_1

BMI	Number	Mean	Standard deviation	z	Level of significance
Above 21	27	56.71	14.43	4.37	0
Less than 21	23	40.7	10.77		

In the above table, the mean FEV_1 is 56.71 for those patients with BM1> 21 and 40.7 for those with BMI <21. For z value of 4.37 the mean difference in FEV_1 is significant ($p< 0.001$).So there is a strong correlation between BMI and FEV_1 values.

Table 16.BMI and 6MWD

BMI	Number	Mean	Standard deviation	z	Level of significance
Above 21	27	329.27	63.79		
Less than 21	23	245.08	70.84	4.424	0

For the table, correlating BMI and 6MWD, z value is 4.424 the mean difference in 6MWD is significant(P< 0.001).So there is strong correlation between the above parameters.

Table 17.BMI AND TAPSE

BMI	Number	Mean	Standard deviation	z	Level of significance
Above 21	27	23.44	2.92		
Less than 21	23	18.73	2.78	5.79	0

The z value , for the above table correlating BMI and TAPSE z is 5.79, the mean difference in TAPSE scores is significant(p< 0.001).So there is good correlation between BMI and TAPSE scores.

Table 18 .SIGNS OF RV DYSFUNCTION AND 6MWD

Signs of RV dysfunction	Number	Mean	Standard deviation	z	Level of significance
Negative	11	334.81	61.94	2.19	0.033
Positive	39	278.06	79.18		

z is 2.19 in the above tabular column for the mean difference in 6MWD ($p < 0.05$) showing a significant correlation between the above parameters.

Table19. RADIOLOGICAL FEATURES SUGGESTIVE OF COR PULMONALE AND RVSP (mm Hg)

Radiology	Number	Mean	Standard deviation	z	Level of significance
Negative	28	36.78	6.49	5.84	0
Positive	22	57.77	17.56		

In this table z is 5.84 for the mean difference of RVSP ($p<0.001$) suggesting a strong correlation between RVSP and radiological features of cor pulmonale.

Table 20.GOLD STAGING OF COPD (FEV_1) AND ECG FEATURES OF PHT/COR PULMONALE

GOLD Stage (By FEV_1) Of COPD	ECG Features Of PH/Cor Pulmonale		Total	Chi Square Test	Level Of Significance
	NO	YES			
Stage II Moderate COPD	10	11	21	13.9	0.001
Stage III Severe COPD	1	22	23		
Stage IV Very Severe COPD	0	6	6		
TOTAL	11	39	50		

The tabular column shows the correlation between severity staging of COPD by GOLD and ECG Changes suggestive of PH/ Cor Pulmonale. There were no subjects in stage I mild COPD in this study. Chi Square 13.90 for the association between GOLD severity staging of COPD and ECG changes of PH/Cor Pulmonale is significant ($p< 0.05$) It can be inferred that as the severity stage of COPD increases there is more likelihood of ECG changes of PH/Cor pulmonale.

Table 21.GOLD STAGING OF COPD (FEV_1) AND TAPSE

Group	N	Mean (mm)	Std. Deviation	Oneway ANOVA F test	Multiple comparison (LSD)
Stage II Moderate COPD	21	24.19	2.31	26.51	1 Vs 2,3
Stage III Severe COPD	23	19.82	2.93	P < 0.001	2 Vs 1,3
Stage IV Very Severe COPD	6	16.66	1.86		3 Vs 1,2
TOTAL	50	21.28	3.69		P< 0.05

TAPSE scores were found to decrease progressively with increasing severity of COPD.The mean TAPSE for the moderate COPD group was 24.199(Std deviation 2.31), that for those with severe COPD was 19.82(std deviation 2.93)and for those with very severe COPD mean TAPSE was 16.66(std deviation 1.86).There is a very significant difference in TAPSE between the moderate COPD and severe COPD ($p<0.001$) and a significant difference in TAPSE between those with severe and very severe COPD($p< 0.05$).

Table 22.GOLD STAGING OF COPD (FEV_1) AND RVSP (mmHg)

Group	N	Mean (mm)	Std. Deviation	Oneway ANOVA F test	Multiple comparison (LSD)
Stage II Moderate COPD	21	34.33	5.08	F=19.033	1 Vs 2,3
Stage III Severe COPD	23	51.65	15.67	P=0.00	2 Vs 1,3
Stage IV Very Severe COPD	6	65.33	16.02		3 Vs 1,2
TOTAL	50	46.02	16.31		P< 0.05

RVSP was found to increase with increasing severity of COPD. The mean RVSP is 34.33(std deviation 5.08) for those with moderate COPD, 51.65(std deviation 15.67) and 65.33(std deviation 16.02) for those with very severe COPD. The results were statistically significant with $p< 0.001$.

DISCUSSION

AGE

In this study, 50 cases of COPD proven by spirometry (GOLD criteria) were taken. The maximum number of patients were in the 50 – 60 year age group (34%). The mean age in this study is 56.2 (std deviation 10.59). Age is the most important determinant of survival independent of disease diagnosis but has limited value in the stratification of a specific disease process.[86]

Table 23. Comparative Studies with Mean Age

Higham M.A et al[94]	66.7
Migueres M et al	60
Mahesh et al[89]	43.09
Trivedi et al	59.5

SEX

The male to female ratio in this study is 1.94 which is similar to that in many Indian studies as shown in table.

SMOKING

The smoker to non smoker ratio in this study is 1.38. Of the 21 non smokers, 17 were females.

Table 24. Comparative Studies With Male:Female And Smoker : Non-Smoker Ratio.[22]

Author (yr)	Male: female ratio	Smoker: non-smoker ratio
Wig et al 1964	1.3	2
Sikand et al 1966	1.6	2.5
Vishwanathan 1966	1.6	
Joshi et al 1975		5.3
Radha et al 1977	1.8	1.8
Vishwananathan &Singh 1977	1.3	9.6
Thiruvengedham et al 1977	1.6	10.2
Nigam et al 1982		1.4
Malik &Kashyap1986	1.9	5.5
Jindal 1993	1.6	9.6
Ray et al 1995	1.6	1.6

As shown in table above there is a wide variation in the smoker: non-smoker ratio with some studies like Vishwanathan and Singh,Thiruvengedham et al having as high as 9.6 and 10.2 respectively. An estimated 25-45% of patients with COPD have never smoked. The burden of non-smoking COPD is therefore much higher than previously believed,[84] probably due to factors like aging, indoor air pollutants and use of biomass fuels.

BODY MASS INDEX

In my study, the mean FEV_1 for those with BMI more than 21 was 56.71 and for those with BMI less than 21 was 40.70 and there was a strong correlation between BMI and FEV_1 ($p< 0.001$).Schols et al[67] and Landbo et al[68] (COPENHAGEN CITY HEART STUDY) found low BMI predictive of poor prognosis and that the association was strongest in severe COPD. BMI is positively related to pulmonary function of COPD patients according to Qui Ting et al in a Chinese study.[92]

BODE INDEX

The BODE Index is a composite marker of disease taking into consideration the systemic nature of COPD.[85]Patients with higher BODE scores were at higher risk for death; the hazard ratio for death from any cause per one-point increase in the BODE score was 1.34 in one study. I have classified BODE index into 3 groups to assess severity of disease, i.e. 0-2, 3-5, and > 6 in keeping with studies by Celli et al and Kian- chung Ong et al.[88]

In my study 58% patients had BODE score ≥ 6 indicating severe disease. There was no significant correlation between age and BODE score (p not < 0.05) in agreement to studies by Domingo-salvany et al[90] and Burrows et al.[89] But other studies by Celli et al have shown BODE scores increase with age.There was a significant association between signs of RV dysfunction and BODE scores, ie patients with signs of RV dysfunction had higher BODE scores.

ECG

My study found a significant correlation between smoking and the development of ECG changes of PHT/cor pulmonale ($p < 0.05$). Ahn Von found that cigarette smoking during hypoxia increased the amplitude of the P waves, which was attributed to the development of right atrial enlargement and cor pulmonale.[91] A significant correlation ($p< 0.05$) was also seen between the GOLD stage of COPD and the development of ECG changes of Cor pulmonale, with all patients with GOLD stage IV, showing ECG changes of Cor pulmonale. Scott et al reported that right ventricular hypertrophy was present on the electrocardiogram in 29% with severe chronic obstructive pulmonary disease.[93]

6 MINUTE WALK DISTANCE (6MWD)

Initially developed in 1976 as a 12 Minute walk test, 6MWD is one of the components of BODE scoring. The mean 6MWD in my study is 290.55(std deviation 78.79).There was a significant association between 6MWD and signs of RV dysfunction ($p <0.05$). Those with signs of RV dysfunction had a mean 6MWD of 278.06 while those without signs of RV dysfunction had a mean of 334.8.A strong correlation between BMI and 6MWD was also observed in this study ($p< 0.001$). There are few studies correlating the above parameters previously. A poor correlation between FEV_1 and 6MWD was observed (p not< 0.05) in my study. Similar results were demonstrated by Pinto- Plata et al.[50]

ECHOCARDIOGRAPHY

Several Echocardiographic parameters were assessed in this study with more stress for RV function assessment. Mean LVEF was 60.94 %, mean TAPSE 21.28 mm and mean RVSP 46.02 mmHg.

TAPSE is an important tool in the assessment of RV function. 28% patients had TAPSE < 18 mm indicating right ventricular systolic dysfunction. RVSP which is equal to sPAP if there is no RVOT obstruction was taken for grading PH. In this study RVSP > 40 mmHg was taken as indicating PH. 48% had no PH(RVSP< 40 mmHg), 26% mild PH (RVSP 40- 50 mmHg), 8% had moderate PH(RVSP 50- 60 mmHg), 18% had severe PH (RVSP> 60 mmHg).There was no TR in 28%, grade 1 TR in 42% ,grade 2 in 8 %,and grade 3 in 22%. A study by Gupta et al[74] reflected similar results, where 50% cases had normal echocardiographic parameters. Measurable tricuspid regurgitation (TR) was observed in 27/40 cases (67.5%). Pulmonary hypertension (PH), (defined as systolic pulmonary arterial pressure (sPAP) > 30 mmHg in their study) was observed in 17/27 (63%) cases in which prevalence of mild, moderate, and severe PH were 10/17 (58.82%), 4/17 (23.53%), and 3/17 (17.65%), respectively. The frequencies of PH in mild, moderate, severe, and very severe COPD were 16.67%, 54.55%, 60.00%, and 83.33%.

SUMMARY

This study attempts a complete evaluation of patients with COPD, with particular emphasis on assessing the cardiac status of these patients. Salient findings include the following

1. Majority of patients were in the 50 -60 year age group with mean age of 56.2 and of male gender. The sex ratio was 1.94 (male:female).
2. Smoker: non smoker ratio was found to be 1.38 demonstrating the effect of factors like age, air pollutants, and biomass fuels.
3. The mean FEV_1 for those with BMI more than 21 was 56.71 and for those with BMI less than 21 was 40.70 showing positive correlation between BMI and pulmonary function.
4. 58% patients were found to have a BODE score ≥ 6 indicating severe disease and no significant correlation was observed between age and BODE score.
5. A significant correlation was observed between smoking and the development of ECG changes of PHT/cor pulmonale as well as between the GOLD stage of COPD and the development of ECG changes of Cor pulmonale.
6. The mean 6MWD was 290.55 and a significant association was observed between 6MWD and signs of RV dysfunction, as well as between BMI and 6MWD.
7. Echocardiographic evaluation showed that 28% patients had TAPSE < 18 mm indicating right ventricular systolic dysfunction. 48% had no PH (RVSP< 40 mmHg), 26% mild PH (RVSP 40- 50 mmHg), 8% had moderate PH(RVSP 50- 60 mmHg) and18% had severe PH (RVSP> 60 mmHg). Grade 3 tricuspid regurgitation was observed in 22%.

CONCLUSION

1. Chronic obstructive pulmonary disease has many cardiovascular effects which are the main contributors to the increased morbidity and mortality.
2. COPD is usually seen in patients more than 40 years of age and in males.
3. Smoking is the most important risk factor, but indoor air pollutants and use of biomass fuels may be responsible for disease in non smokers.
4. 6MWD is a simple tool to detect the exercise capacity of COPD patients and correlates well with signs of right ventricular dysfunction.
5. BODE Index is a reliable indicator of severity of COPD and also of cardiac involvement, particularly right ventricular dysfunction.
6. ECG is still a reliable tool in assessing the development of PH and cor pulmonale.
7. Echocardiography is an indispensable tool in assessing the cardiac status and, TAPSE and RVSP are excellent parameters for detection of PH in COPD.

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PROFORMA FOR ASSESSMENT OF CARDIAC FUNCTION IN COPD PATIENTS

1. NAME

2. AGE **3.SEX** **4.IP/OP NO**

5. CLINICAL HISTORY

Cough: Y/N

Sputum – nil / scanty / moderate / copious

Breathlessness – nil / exertional / orthopnea / PND

MMRC scale: 0 1 2 3 4

Wheezing

Chest pain

Hemoptysis

Fever

Swelling legs

Any other symptoms

EXCLUSION HISTORY

H/o Spirometry proven bronchial asthma: Y/N

H/o Coronary heart disease: Y/N

H/o Congenital or Acquired Valvular Heart Disease: Y/N

H/o Hypertension: Y/N

H/o Diabetes Mellitus:Y/N

H/o Pulmonary Tuberculosis:Y/N

H/o Bronchiectasis:Y/N

6. SMOKER -Y/N

7. PACK YEARS

8. PAST HISTORY - Similar Complaints / Tuberculosis / Asthma /Allergy / Cardiac Illness / Diabetes Mellitus.

9. HEIGHT **10.WEIGHT** **11. BMI**

12. Cyanosis: Clubbing: Oedema:

JVP: PR: BP: RR:

13. Respiratory system:

AP diameter: Transverse diameter:

Rhonchi : Y/N Crepitations : Y/N

14. Cardiovascular system: S1 S2 Murmur

INVESTIGATIONS

1. Hb TC DC

2. TOTAL CHOLESTEROL

3. ECG

AXIS P PULMONALE +/_ RVH (R/S in V1 > 1)

RBBB +/_ LOW VOLTAGE COMPLEXES +/_

OTHERS

4. CHEST XRAY

5. SPUTUM AFB

6. PULMONARY FUNCTION TEST

PARAMETER	PRE BD	POST BD	% CHANGE
FEV1			
FVC			
FEV1/FVC			

7. 6 MIN WALK TEST DISTANCE

8. BODE INDEX SCORE

SCORE	0	1	2	3
FEV1 %	≥65	50- 64	36-49	< 35
6 MWD (m)	≥350	250- 349	150- 249	<149
MMRC	0-1	2	3	4
BMI	≥ 21	<21		

TOTAL SCORE (0- 10)

9. ECHOCARDIOGRAPHY

CHAMBERS	
VALVES	
PERICARDIUM	
GREAT VESSELS	
LV SYSTOLIC FUNCTION (LVEF)	
LV DIASTLIC FUNCTION (MIV)	
RV SYSTOLIC FUNCTION (TAPSE) (RVSP)	

PROFORMA FOR 6 MINUTE WALK TEST

Lap counter: __ __ __ __ __ __ __ __ __ __

Patient name: _____

Patient ID _____

Walk No. _____ Date: _____

Gender: M F Age: ____ Height: _____ meters

Weight: _____kg

Blood pressure: _____ / _____

	Baseline	End of Test
Time	___:___	___:___
Heart Rate	_____	_____
Dyspnea	____	____ (MMRC scale)

Stopped or paused before 6 minutes? No /Yes, reason

Other symptoms at end of exercise: angina dizziness hip, leg, or calf pain

Number of laps: ____ (x60 meters) + final partial lap: _____ meters =

Total distance walked in 6 minutes: _____ meters

MASTER CHART

SL NO	AGE	SEX	SMOKING IN PACK YEARS	PR	BP(MM HG)	BMI	SIGNS OF RV DYSFUNCTION	CLUBBING	TOTAL CHOLESTEROL	RADIOLOGICAL FEATURES		FEV1 (%)	FVC (LITRES)	FEV1/FVC	6MWD	BODE INDEX SCORE	ECG	ECHOCARDIOGRAPHY					
										SUGGESTIVE OF COPD	SUGGESTIVE OF PHT/COR PULMONALE						ECG FEATURES OF PHT/COR PULMONALE	RA ENLARGEMENT	RV ENLARGEMENT	TR	LVEF (%)	TAPSE (mm)	RVSP (mmHg)
1	52	M	40	80	100/70	17.6	+	_	120	Y	Y	40	2.12	0.56	308	7	Y	+	+	+++	69	22	97
2	53	F	_	76	140/80	23.7	+	_	228	N	N	62	2.28	O.67	281.5	5	N	_	_	+	60	28	45
3	37	M	8	72	120/90	22.1	_	_	170	N	N	76	3.2	0.56	451	0	N	_	_	_	67	24	30
4	67	M	50	80	130/80	20.5	+	_	187	Y	N	26	2.06	0.37	240	9	Y	_	_	+	57	20	44
5	53	F	_	92	130/80	21.1	_	_	165	N	N	38	1.07	0.66	310	6	Y	_	_	_	70	26	42
6	80	F	_	80	110/80	18.7	_	_	173	N	N	44	1.21	0,56	372	6	N	+	+	_	72	25	40
7	60	F	_	70	120/70	22	_	_	196	Y	N	76	3.18	0.69	391	1	N	_	_	_	70	27	35
8	70	M	20	84	140/70	21.4	+	_	210	Y	Y	45	1.67	0.57	310	5	Y	_	_	+	48	24	42
9	68	M	30	80	110/70	20.7	+	_	210	Y	Y	37	1.12	0.68	215	7	Y	+	+	+	61	18	48
10	48	M	10	84	130/90	20	_	_	154	Y	N	44	2.56	0.68	292	6	Y	+	+	+++	62	18	46
11	60	M	25	92	128/70	18.6	_	+	214	Y	N	63	2.42	0.58	236	6	Y	+	+	++	54	18	42
12	74	F	_	78	140/90	19.9	_	_	320	Y	N	43	1.36	0.59	382	4	Y	+	+	+	70	20	40
13	53	M	30	98	138/90	19.4	+	_	400	Y	Y	37	1.47	0.64	210	7	Y	+	+	+++	50	17	66
14	60	M	40	76	120/80	22	_	_	204	Y	Y	34	2.46	0.55	258	4	Y	+	+	+	48	20	44
15	40	M	_	92	120/80	26.2	+	_	245	Y	N	53	2.46	0.59	318	3	Y	_	_	_	62	23	30
16	55	M	15	78	110/70	20.3	_	+	182	Y	N	56	2.25	0.59	292	4	N	_	_	+	58	24	46

17	52	M	_	88	130/80	28.2	_	+	230	N	N	78	3.05	0.65	405	1	N	_	_	_	80	26	30
18	63	M	40	106	110/70	26.5	_	_	175	N	N	66	2.65	0.69	348	2	Y	_	_	_	68	24	35
19	52	M	20	82	130/80	25.2	_	_	210	N	N	53	2.46	0.54	300	3	Y	_	_	+	56	20	38
20	48	F	_	80	136/76	18	+	_	165	Y	Y	29.8	1.03	0.68	158	8	Y	+	+	+++	52	16	76
21	56	F	_	92	120/90	22.8	_	+	194	Y	N	46.2	1.78	0.69	285	5	Y	_	_	+	65	24	32
22	65	M	40	84	110/80	23.6	+	_	281	Y	Y	42.2	3.04	0.32	278	5	Y	+	+	+	64	19	48
23	70	M	40	90	120/80	21.2	+	+	187	Y	Y	38	3.02	0.31	206	5	Y	+	+	+++	68	17	56
24	46	F	_	88	130/60	22.3	_	_	230	Y	N	56	2.25	0.59	315	3	Y	_	_	+	75	26	29
25	50	M	25	76	140/80	16	+	_	176	Y	Y	25.9	3.06	0.21	120	9	Y	+	+	+++	57	17	50
26	47	F	_	80	120/70	23.6	_	_	230	Y	N	62.5	1.83	0.64	378	1	N	_	_	_	60	27	30
27	39	M	15	68	110/70	22.8	_	_	270	N	N	77	2.63	0.69	420	0	Y	_	_	_	70	25	28
28	72	M	50	90	150/70	18	+	_	178	Y	Y	46.2	1.78	0.69	246	8	Y	+	+	++	48	20	56
29	56	M	_	80	130/70	25.2	_	_	260	Y	N	63.9	2.14	0.57	400	2	N	_	_	+	68	25	30
30	45	F	_	78	130/60	20.3	+	_	286	N	Y	47.2	2.48	0.38	178	8	Y	+	+	+++	54	16	78
31	67	M	50	94	118/78	21.1	_	_	173	Y	Y	56	2.25	0.59	275	3	Y	_	_	+	65	24	35
32	52	F	_	80	136/70	15.9	+	_	246	Y	Y	29.8	1.03	0.56	170	9	Y	+	+	+++	48	15	67
33	46	F	_	76	`120/70	21.6	_	_	158	Y	N	77	2.63	0.69	378	1	Y	_	_	_	68	26	32
34	39	F	_	84	130/70	23.4	_	_	214	Y	N	64.2	2.05	0.6	378	1	N	_	_	_	70	24	35
35	65	M	40	88	140/90	18	+	+	245	Y	Y	36	1.98	0.5	180	7	Y	+	+	+	47	18	58

36	50	M	25	78	120/70	21.7	+	_	178	Y	N	42.2	3.04	0.32	310	5	Y	+	+	+	60	20	45
37	48	M	30	66	110/70	24.6	_	_	286	Y	N	62	1.5	0.6	368	3	Y	_	_	_	55	23	34
38	56	M	20	80	136/70	20.4	+	_	160	N	Y	49.5	1.86	0.67	230	6	Y	+	_	+	65	19	47
39	58	M	40	96	150/90	23.8	_	+	336	Y	N	67	2.36	0.56	418	1	N	_	_	_	70	24	31
40	50	M	35	68	120/70	19.7	_	_	190	Y	Y	47.2	2.48	0.38	345	5	Y	_	_	+	60	19	40
41	67	F	_	58	100/70	15.8	+	_	346	N	Y	25.9	1.54	0.41	215	8	Y	+	+	+ + +	62	15	87
42	49	M	35	90	130/90	22.5	_	_	246	Y	N	43.6	2.66	0.39	267	5	Y	_	_	+	57	23	34
43	77	M	50	76	120/60	19.2	+	_	212	Y	Y	32.8	2.12	0.4	190	8	Y	+	+	+++	45	15	68
44	69	M	_	60	110/70	22.7	_	_	163	N	Y	57.8	2.65	0.52	332	3	Y	_	_	+	60	25	34
45	51	F	_	92	130/80	18.4	_	_	267	Y	N	62	2.65	0.57	278	4	N	_	_	_	56	23	38
46	41	F	_	82	114/76	16.8	+	_	198	Y	Y	34	2.25	0.37	175	7	Y	+	+	+ +	62	17	72
47	67	M	50	78	120/70	24.9	_	_	312	Y	Y	66.6	2.64	0.65	300	2	Y	_	_	+	67	22	34
48	55	M	40	68	130/80	17.6	+	_	343	Y	N	33	2.2	0.39	285	6	Y	+	+	++	54	19	52
49	47	F	_	70	110/90	16.8	_	+	297	Y	N	47	2.48	0.48	320	5	Y	+	+	+	65	20	37
50	65	M	50	88	100/70	21.3	+	_	187	Y	Y	28	2.61	0.27	210	7	Y	+	+	+++	48	17	68

KEY TO MASTER CHART

PR	-	Pulse Rate
BP	-	Blood Pressure
FEV_1	-	Forced Expiratory Volume at One Second
BODE	-	Body-mass index (B), Airflow obstruction (O), Dyspnoea (D), and Exercise capacity (E)
BMI	-	Body Mass Index
ECG	-	Electrocardiogram
RA	-	Right Atrium
RV	-	Right Ventricle
6MWD	-	6 Minute Walk Distance
TR	-	Tricuspid Regurgitation
LVEF	-	Left Ventricular Ejection Fraction
TAPSE	-	Tricuspid Annular Plane Systolic Excursion
RVSP	-	Right Ventricular Systolic Pressure