ULTRASONOGRAPHIC ASSESSMENT OF DIAPHRAGM TO PREDICT INVASIVE VENTILATION IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

by

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Dissertation submitted to the

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VIJAYAPURA, KARNATAKA

In Partial fulfilment of requirements for the degree of

DOCTOR OF MEDICINE

In

ANAESTHESIOLOGY

Under the guidance of

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I, **DR. KOLA SAMATHA REDDY.,** hereby declare that this dissertation/thesis entitled "**ULTRASONOGRAPHIC ASSESSMENT OF DIAPHRAGM TO PREDICT INVASIVE VENTILATION IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE"** is a bonafide and genuine research work carried out by me under the guidance of **Dr RENUKA HOLYACHI,** Professor and Head, Department of Anaesthesiology, B.L.D.E (DU)'s Shri B.M Patil Medical College, Hospital and Research Centre, Vijayapura.

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ABBREVATIONS

COPD- chronic obstructive pulmonary disease

AECOPD- Acute exacerbation of chronic obstructive pulmonary disease

USG- Ultrasonography

NIV- Non-invasive ventilation

DUS- Diaphragm ultrasound

IMV- Invasive mechanical ventilation

DI- Diaphragmatic impairment

DTF- Diaphragm thickness fraction

FVC- Forced vital capacity

FEV1- forced expiratory volume in one second

GOLD- Global Initiative for Chronic Obstructive Lung Disease

LLN- lower limit of normal

GLI- Global Lung Initiative

PEF- Peak expiratory flow

TLC- total lung capacity

FRC- functional residual capacity

RV- residual volume

DLCO- diffusing capacity for carbon monoxide

ABG- arterial blood gases

CT- computed tomography

ICU- Intensive Care Unit

ABSTRACT

Background: To study the impact of ultrasound-assessed Diaphragmatic impairment on predicting the need for invasive mechanical ventilation in patients with Acute Exacerbations of Chronic Obstructive Pulmonary disease (AECOPD) and also, its impact on invasive mechanical ventilatory days, length of ICU stays and outcome.

Methodology: A total 95 patients with AECOPD requiring NIV support in the ICU were included in the study in our hospital from April 2023 to November 2024. This was a prospective observational study. Ultrasound-assessed Diaphragm Thickness Fraction (DTF) was done to assess the Diaphragmatic Impairment (DI). Either the patient was weaned off from NIV or put on IMV based on clinical condition and ABG analysis.

Results: ROC curve analysis of diaphragmatic thickness fraction on the Right & Left-side gives a cut off 31.88% and 28.2% with 100% sensitivity and 20.9% specificity for the need of IMV. It predicted that there is a requirement of IMV below this cut-off. Out of 43 patients that were put on IMV, 34 were below and 9 were above the cutoff. Mean Duration of IMV was significantly higher in expired patients compared to survived patients. (8.56+/-2.11 vs 2.78+/-0.83 days). Mean Duration of ICU stay was also significantly higher in expired patients compared to survived patients. (9.95+/-2.46 vs 5.37+/-1.17 days).

Conclusion: From this prospective observational study, we concluded that USG guided assessment of Diaphragmatic thickness fraction is a good indicator in determining the diaphragmatic impairment and predicting the need for invasive mechanical ventilation in AECOPD patients with 100% sensitivity and 20.9% specificity. DI as assessed by DTF can be used as a prognostic factor for determining Invasive Mechanical Ventilatory days, ICU stay and Outcome of the patient.

Key Words: DI- Diaphragmatic Impairment**,** DTF- Diaphragm Thickness Fraction**,** ICU- Intensive Care Unit**,** NIV- Non-Invasive Ventilation**,** IMV- Invasive Mechanical Ventilation**,** USG- Ultra sonography**,** AECOPD- Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Introduction

"Global initiative for chronic obstructive lung disease 2023 defines chronic obstructive pulmonary disease (COPD) as a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnoea, cough, expectoration, and exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction".[1,2] "Acute exacerbation of COPD (AECOPD) may lead to respiratory failure that increases morbidity and mortality. The key respiratory changes in COPD-related failure are intrinsic positive end-expiratory pressure and dynamic hyperinflation."[3,4] The respiratory mechanical issues become more severe during an acute exacerbation of COPD (AECOPD), which greatly heightens the demand for oxygen and respiratory effort.[5,6] This strain surpasses the compensatory capacity of the respiratory muscles, such as the diaphragm, resulting in low blood oxygen levels, elevated carbon dioxide levels, and type II respiratory failure.[7,8]

"Chronic obstructive pulmonary disease (COPD), a common chronic respiratory disease, has become the third leading cause of death and is one of the most serious public health problems worldwide."[9,10]

"Recent research indicates that dynamic pulmonary hyperinflation and intrinsic positive end-expiratory pressure are the most crucial mechanical respiratory alterations observed in COPD patients experiencing respiratory failure."[13,14] "In individuals with acute exacerbations of COPD (AECOPD), these two mechanical respiratory abnormalities become even more pronounced, leading to a notable increase in oxygen consumption and the respiratory workload on patients, surpassing the effective compensatory ability of respiratory muscles like the diaphragm. This situation can result in varying degrees of hypoxemia and hypercapnia, ultimately culminating in type II respiratory failure."[4,5] Therefore, evaluating diaphragm functionality is essential for the diagnosis and management of AECOPD. [8,9] If not addressed

promptly, respiratory failure poses a significant threat to the patient's life. Currently, beyond standard treatments such as infection control, antispasmodic medications, cough relief, and mucus clearance, adequate respiratory support is a critical component of AECOPD therapy. [6,15]

"Mechanical ventilation establishes a pressure difference between the airway opening and the alveoli to keep the airway open, thereby improving oxygenation and reversing hypoxia and carbon dioxide retention in the body."[16] Mechanical ventilation is two types: Invasive ventilation & non-invasive ventilation.[17] "Invasive ventilation involves the connection to the ventilator by invasive means such as tracheal intubation or tracheotomy, which is mostly used for critically ill patients. It can rapidly correct hypoxemia and hypercapnia, but it may also have unavoidable complications, such as ventilator-associated pneumonia and pneumatic injuries, and will bring a huge economic burden to the patient." [18]

"Non-invasive ventilation is a non-invasive way to connect a ventilator through a nasal mask or mask. It can provide patients with double-level pressure support and–reduce the work of breathing. Meanwhile, it can avoid lung injury and infection caused by invasive ventilation to the greatest extent. The value of non-invasive ventilation in the treatment of respiratory failure caused by AECOPD has been recognized, and the effective rate is more than 80% in patients with different degrees of carbon dioxide retention."[19] However, "in clinical application, due to the occurrence of adverse reactions such as man-machine incoordination, poor sputum drainage, suppressed fear, flatulence, and facial pressure sores, about 20% of patients cannot tolerate the treatment."[20]

"Ultrasonography (US) is a safe, non-invasive, and accurate technique widely used in intensive care for bedside assessment of diaphragmatic function. Studies have described its feasibility and high reproducibility in identifying diaphragm dysfunction in severely ill patients."[21]

Study by Boon et al[22] found that, "ultrasound has a sensitivity of 93% and a specificity of 100% for diagnosing neuromuscular diaphragm dysfunction."[22]

"Patients with severe hypoxia requiring non-invasive ventilation (NIV) are at risk of diaphragmatic impairment, which can negatively impact outcomes, potentially leading to the need for invasive mechanical ventilation. US has been widely used in various studies to assess the functionality of the diaphragm and assist in predicting outcomes for patients with NIV."[23]

"Ultrasonography can more directly observe the changes in the diaphragm and has the advantages of being safe, non-invasive, economical, accurate, and reproducible. Therefore, it is increasingly widely used in clinical assessment of diaphragm structure and function."[24]

"Research has indicated that utilizing DUS to assess the diaphragm-related rapid shallow breathing index for guiding the weaning process of ICU patients from ventilators has yielded significant findings."[25] It can serve as an early indicator for the necessity of discontinuing non-invasive ventilators in cases of AECOPD, as well as evaluate patient prognosis to help prevent or mitigate the advancement of the condition. However, there is a scarcity of literature discussing the predictive value of DUS indicators concerning mechanical ventilation therapy; thus, we undertook this study to investigate how ultrasound-assessed diaphragmatic impairment (DI) can predict the need for invasive mechanical ventilation (IMV) in patients undergoing treatment with non-invasive ventilation (NIV).

Aim and objectives

AIM:

Study the impact of ultrasound-assessed diaphragmatic impairment (DI) on predicting need for invasive mechanical ventilation (IMV) in patients treated by non-invasive ventilation (NIV).

OBJECTIVE:

Primary objective:

- The importance of diaphragmatic dysfunction in predicting the need for invasive mechanical ventilation following non-invasive ventilation failure.

Secondary objective:

- Effects of diaphragmatic impairment on the duration of IMV days, length of ICU stay, and outcome.

Review of literature

Marchioni A et al[53] in 2018 "conducted the study with the objective to investigate the impact of US-assessed DD on non-invasive ventilation (NIV) failure in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD) and its correlation with the transdiaphragmatic pressure assessed using the invasive sniff maneuver (Pdi sniff). ΔTdi highly correlated with Pdi sniff (Pearson's r =0.81; p=0.004). ΔTdi < 20% showed better accuracy in predicting NIV failure. Early and noninvasive US assessment of DD during severe AECOPD is reliable and accurate in identifying patients at major risk for NIV failure and worse prognosis."[53]

Sung Yoon Lim et al[54] in 2019 "conducted the study with the objective to investigate the changes in diaphragmatic function during acute exacerbation of COPD, by US. Diaphragmatic excursion and its thickening fraction (TF) were measured as markers of diaphragmatic function. The change in excursion between the stable and exacerbation periods was positively correlated with time to the next exacerbation and negatively correlated with the time taken to recover from the exacerbation. Conclusion: These data support the possibility that a defect in diaphragm thickening is related to acute exacerbation of COPD. "[54]

Amr Abdalla Elsayed et al[55] in 2020 "conducted the study with the objective to the impact of ultrasound-assessed diaphragmatic impairment (DI) on predicting need for invasive mechanical ventilation (IMV) in acute exacerbation of chronic obstructive pulmonary disease (AECOPD) patients treated by non-invasive ventilation (NIV). A prospective observational study. DTF was a good indicator of DI that could predict need for IMV after NIV failure in AECOPD patients with good sensitivity and moderate specificity. MV Days, ICU stay, and 28-day mortality were significantly higher in patients with DI who needed IMV. "[55]

Zhang X et al[56] in 2020 "conducted the study with the objective to explore the value of the right hemi-diaphragmatic excursion (DE) and its variation in predicting extubation outcome in mechanically ventilated patients with COPD. The cut off point of DTF was below 0.306 to predict failure of NIV with a P value 0.002. Assessment of DTF by diaphragm ultrasound in B-mode represents an easy to obtain new index for prediction of success or failure of NIV in AECOPD patients needing NIV. "[56]

Kheir M. et al[58] in 2023 "conducted the study with the objective to systematically review and compare ultrasonographic methods and their utility in predicting non-invasive ventilation (NIV) outcomes.This systematic review emphasizes the importance of using lung and diaphragm ultrasound, in particular the lung ultrasound score and diaphragm thickening fraction respectively, to accurately predict NIV failure, including the need for ICU-level of care, requiring invasive mechanical ventilation, and resulting in higher rates of mortality. "[58]

Patel NB et al[59] in 2023 "conducted the study with the objective to investigated the utility of DD detected 2 hours after NIV initiation in estimating NIV failure in acute exacerbation of chronic obstructive pulmonary disease (AECOPD) patients. The DD was assessed at baseline (T1 timepoint) and 2 hours after initiating NIV (T2 timepoint). We defined DD as ultrasound-assessed change in diaphragmatic thickness (ΔTDI) <20% (predefined criteria [PC]) or its cut-off that predicts NIV failure (calculated criteria [CC]) at both timepoints. The ΔTDI cut-off that predicted NIV failure (DD-CC) at T1 was ≤19.04% (area under the curve [AUC], 0.73; sensitivity, 50%; specificity, 85.71%; accuracy; 66.67%), while that at T2 was ≤35.3% (AUC, 0.75; sensitivity, 95.65%; specificity, 57.14%; accuracy, 74.51%; hazard ratio, 19.55). The NIV failure rate was 35.1% in those with normal diaphragmatic function by PC (T2) versus 5.9% by CC (T2). The odds ratio for NIV failure with DD criteria ≤35.3 and <20 at T2 was 29.33 and 4.61, while that for ≤19.04 and <20 at T1 was 6, respectively. The DD criterion of

≤35.3 (T2) had a better diagnostic profile compared to baseline and PC in prediction of NIV failure. ”[59]

Suttapanit K. et al[60] in 2023 “conducted the study with the objective to investigate the ability of right-sided diaphragmatic excursion (RDE) to predict the need for invasive mechanical ventilation (IMV). The ability of RDE to predict the need for IMV was assessed by multivariable logistic regression and analysis of the area under the receiver-operating characteristic curve (AUROC). An increase of RDE value per each 0.1 cm was identified to be an independent predictor of IMV (adjusted odds ratio 0.08, 95% confidence interval [CI] 0.04–0.17, p < 0.001; AUROC 0.850, 95% CI 0.807–0.894). The RDE cutoff value was 1.2 cm (sensitivity 82.3%, 95% CI 74.0–88.8; specificity 78.1%, 95% CI 71.7–83.6). Time on a ventilator was significantly longer when the RDE was ≤ 1.2 cm (13 days [interquartile range 5, 27] versus 5 days [interquartile range 3, 8], p = 0.006). In this study, RDE had a good ability to predict the need for IMV in critically ill patients. The optimal RDE cutoff value was 1.2 cm. Its benefit in patient management requires further investigation.”[60]

Banjade P et al[61] in 2024 “conducted the study that retrospectively analyzed ninety-four acute exacerbations of chronic obstructive pulmonary disease patients who received mechanical ventilation from January 2022 to December 2023. The study found that the diaphragm thickening fraction, an index from diaphragm ultrasound, can better predict the outcome of non-invasive ventilation in patients with AECOPD. The value of non-invasive ventilation in treating respiratory failure caused by AECOPD has been widely acknowledged. Diaphragmatic dysfunction diagnosed with ultrasound is associated with prolonged mechanical ventilation and weaning times and higher mortality. ”[61]

Qu LL et al[62] in 2024 “conducted the study with the objective to explore the predictive value of DUS indexes for non-invasive ventilation outcome in patients with AECOPD. The patients

with successful non-invasive ventilation had shorter hospital stays and lower partial pressure of carbon dioxide (PaCO2) than those with failed treatment, while potential of hydrogen (pH), diaphragm thickening fraction (DTF), diaphragm activity, and diaphragm movement time were significantly higher than those with failed treatment ($P < 0.05$). The DUS index DTF can better predict the outcome of non-invasive ventilation in AECOPD patients. ”[62]

Epidemiology of COPD:

Definitions:

Chronic Obstructive Pulmonary Disease (COPD): "It is defined as a preventable and treatable disease with pulmonary component characterized by airflow limitation that is of not fully reversible which is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases and some significant extrapulmonary effects that may contribute to the severity in individual patients."[26,27]

"According to Global Initiative for chronic obstructive lung disease (GOLD), it is also defined as a heterogenous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction."[28]

COPD includes Emphysema, Chronic Bronchitis, Small airway disease.

Emphysema: "It is defined as an abnormal, permanent enlargement of the distal airspaces, distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis."[29]

Chronic Bronchitis: "A clinically defined condition with presence of chronic productive cough on most days for 3 months in each of 2 consecutive years in a patient in whom other causes of chronic cough have been excluded."[29]

Small airway disease: It is a condition in which small bronchioles are narrowed.

Problem statement:

Burden of disease:

"COPD is a growing global epidemic and it is estimated to kill around 3 million people every year. It is currently the 4th largest killer disease in the world and expected to climb to 3rd position by the year 2030. WHO has estimated that 600 million people worldwide have COPD. It affects around 5-10% of population over the age of 40 years but still there is wide variations in the prevalence between countries."[30,31]

ECONOMIC BURDEN:

"The National Heart, lung and Blood Institute provides estimate of 38.8 billion US $ for US and 38.6 billion US $ for Europe. COPD accounts for 56% of total health care budget. According to National Commission on macroeconomics and health published in India that per capital expenditure on COPD is Rs.42664 in 2006 and expected to increase to Rs. 62630 by 2016. Upto 84% of the costs spent on COPD is due to inpatient hospitalization due to which the loss in productivity due to COPD account for between 40% and 67% of the overall costs across the world. Hence it is a severe economic burden for countries throughout the world."[32-36]

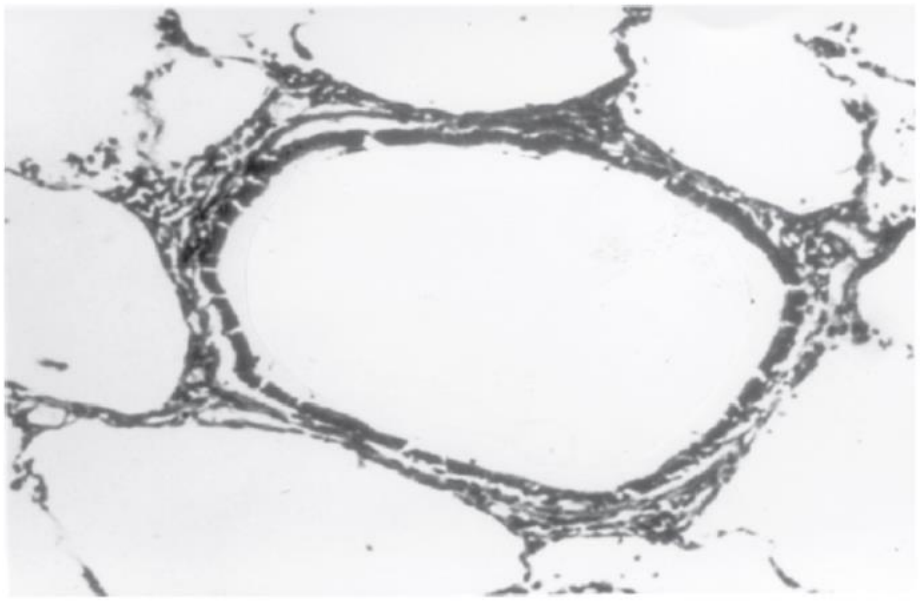


Image 1. Small respiratory bronchiole with surrounding alveolar attachments

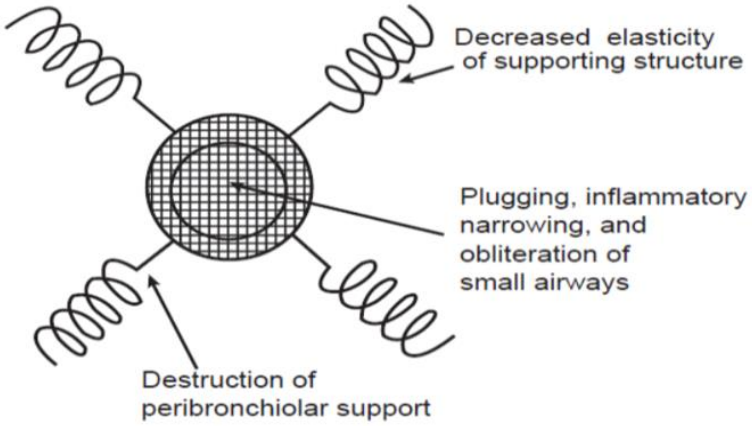


Image 2. Mechanism of Airflow obstruction due to loss of elastic recoil and airway Narrowing

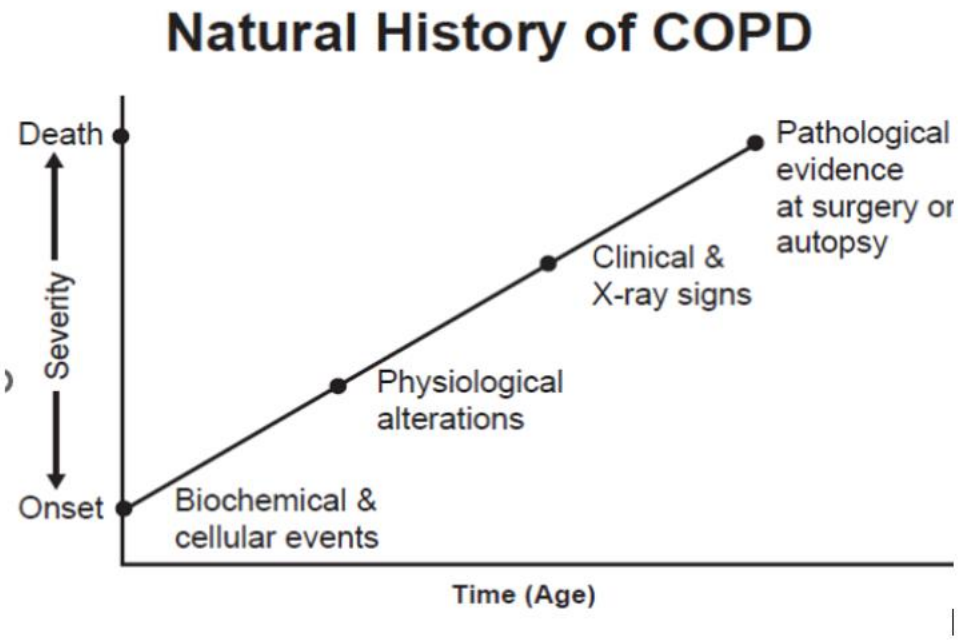


Image 3. Natural history of COPD

Pathogenesis and Pathophysiology of COPD:[37]

Pathogenesis:

"Inflammation is present in the lungs, particularly the small airways, of all people who smoke. This normal protective response to the inhaled toxins is amplified in COPD, leading to tissue destruction, impairment of the defence mechanisms that limit such destruction, and disruption of the repair mechanisms. In general, the inflammatory and structural changes in the airways increase with disease severity and persist even after smoking cessation. Besides inflammation, two other processes are involved in the pathogenesis of COPD—an imbalance

between proteases and antiproteases and an imbalance between oxidants and antioxidants (oxidative stress) in the lungs."[37]

- **Inflammatory cells**

"COPD is characterised by increased numbers of neutrophils, macrophages, and T lymphocytes (CD8 more than CD4) in the lungs. In general, the extent of the inflammation is related to the degree of the airflow obstruction. These inflammatory cells release a variety of cytokines and mediators that participate in the disease process. This inflammatory pattern is markedly different from that seen in patients with asthma. "[37]

- **Inflammatory mediators**

"Inflammatory mediators like Leukotriene-B4, a neutrophil and T cell chemoattractant which is produced by macrophages, neutrophils, and epithelial cells. Chemotactic factors such as the CXC chemokines, interleukin 8 and growth-related oncogene alpha, which are produced by macrophages and epithelial cells. These attract cells from the circulation and amplify pro-inflammatory responses. Pro-inflammatory cytokines such as tumour necrosis factor-alpha and interleukins 1& 6, Growth factors such as transforming growth factor-alpha, which may cause fibrosis in the airways either directly or through release of another cytokine, connective tissue growth factor. "[37]

- **Protease and antiprotease imbalance**

"Increased production (or activity) of proteases and inactivation (or reduced production) of antiproteases results in imbalance. Cigarette smoke, and inflammation itself, produce oxidative stress, which primes several inflammatory cells to release a combination of proteases and inactivates several antiproteases by oxidation. The main proteases involved are those produced by neutrophils (including the serine proteases elastase, cathepsin G, and protease 3) and macrophages (cysteine proteases and cathepsins E, A, L, and S. The main antiproteases involved in the pathogenesis of emphysema include alpha 1 antitrypsin, secretory leucoprotease inhibitor, and tissue inhibitors of metalloproteases. "[37]

- **Oxidative stress**

"The oxidative burden is increased in COPD. Sources of oxidants include cigarette smoke and reactive oxygen and nitrogen species released from inflammatory cells. This creates an imbalance in oxidants and antioxidants of oxidative stress. Many markers of oxidative stress are increased in stable COPD and are further increased in exacerbations. Oxidative stress can lead to inactivation of antiproteases or stimulation of mucous production. It can also amplify inflammation by enhancing transcription factor activation (such as nuclear factor alpha B) and hence gene expression of pro-inflammatory mediators. "[37]

Pathophysiology:

"The above pathogenic mechanisms result in the pathological changes found in COPD. These in turn result in physiological abnormalities—mucous hypersecretion and ciliary dysfunction, airflow obstruction and hyperinflation, gas exchange abnormalities, pulmonary hypertension, and systemic effects. "[37]

- **Mucous hypersecretion and ciliary dysfunction**

"Mucous hypersecretion results in a chronic productive cough. This is characteristic of chronic bronchitis but not necessarily associated with airflow obstruction. The hypersecretion is due to squamous metaplasia, increased numbers of goblet cells, and increased size of bronchial submucosal glands in response to chronic irritation by noxious particles and gases. Ciliary dysfunction is due to squamous metaplasia of epithelial cells and results in an abnormal mucociliary escalator and difficulty in expectorating. "[37]

- **Inflammatory cells and mediators in COPD**

"Neutrophils, which release proteases, are increased in the sputum and distal airspaces of smokers; a further increase occurs in COPD and is related to disease severity. Macrophages, which produce inflammatory mediators and proteases, are increased in number in airways, lung parenchyma, and in bronchoalveolar lavage fluid. T lymphocytes (CD4 and CD8 cells) are increased in the airways and lung parenchyma, with an increase in CD8:CD4 ratio. Numbers of Th1 and Tc1 cells, which produce interferon alpha, also increase. CD8 cells may be cytotoxic and cause alveolar wall destruction. "[37]

Proteases and antiproteases involved in COPD

Proteases	Antiproteases
Serine proteases	α_1 antitrypsin
Neutrophil elastase	
Cathepsin G	Secretory leucoprotease inhibitor
Protease 3	Elafin
Cysteine proteases	Cystatins
Cathepsins B, K, L, S	
Matrix metalloproteases (MMP-8, MMP-9, MMP-12)	Tissue inhibitors of MMP (TIMP1-4)

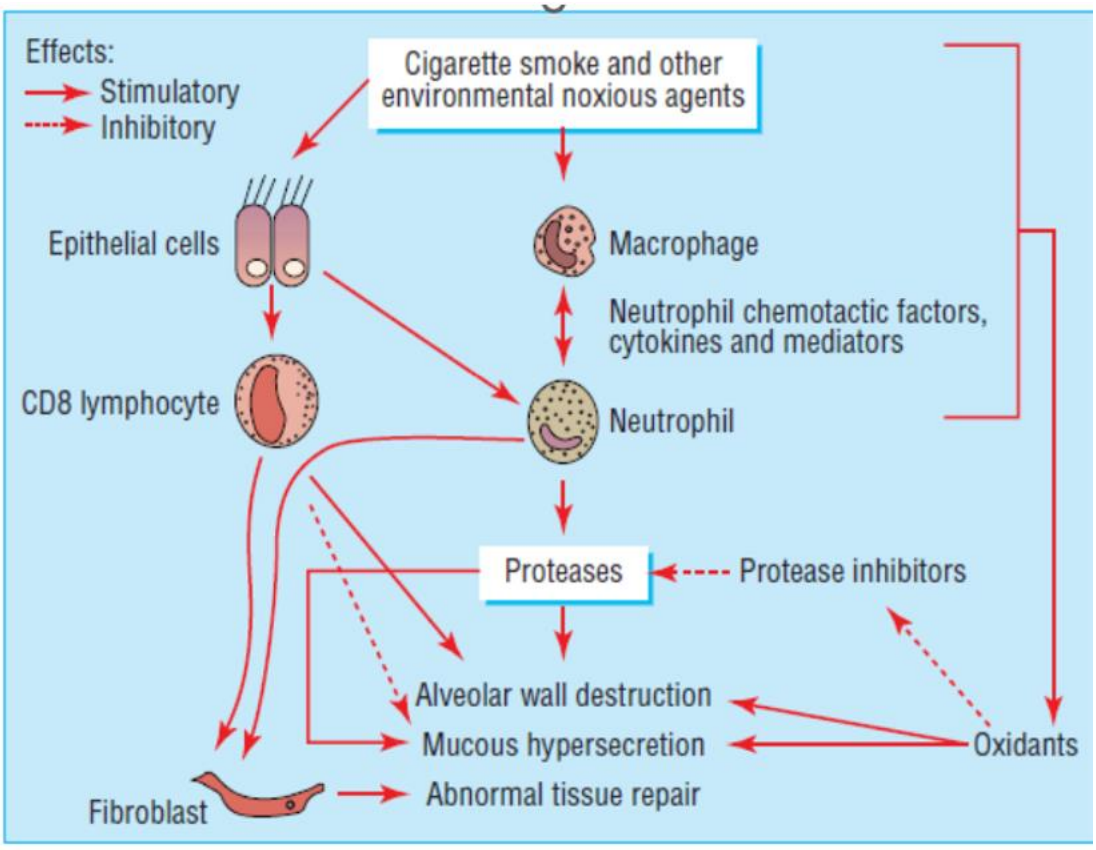


Image 4. Inflammatory Mechanism in COPD

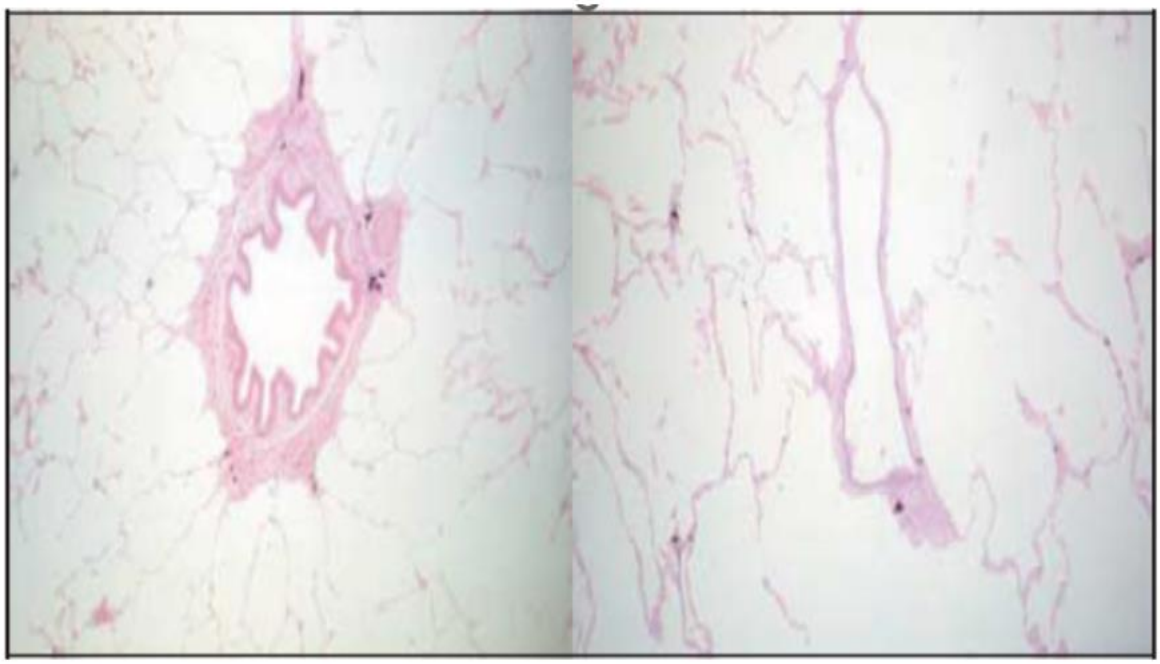


Image 5. Left: Normal small airway with alveolar attachments. Right: Emphysematous airway, with loss of alveolar walls, enlargement of alveolar spaces, and decreased alveolar attachment

- **Airflow obstruction and hyperinflation or air trapping**

"The main site of airflow obstruction occurs in the small conducting airways that are < 2 mm in diameter. This is because of inflammation and narrowing (airway remodelling) and inflammatory exudates in the small airways. Other factors contributing to airflow obstruction include loss of the lung elastic recoil (due to destruction of alveolar walls) and destruction of alveolar support (from alveolar attachments). The airway obstruction progressively traps air during expiration, resulting in hyperinflation at rest and dynamic hyperinflation during exercise. Hyperinflation reduces the inspiratory capacity and therefore the functional residual capacity during exercise. These features result in breathlessness and limited exercise capacity typical of COPD. The airflow obstruction in COPD is best measured by spirometry and is a prerequisite for its diagnosis. "[37]

- **Gas exchange abnormalities**

"These occur in advanced disease and are characterised by arterial hypoxaemia with or without hypercapnia. An abnormal distribution of ventilation: perfusion ratios-due to the anatomical changes found in COPD-is the main mechanism for abnormal gas exchange. The extent of impairment of diffusing capacity for carbon monoxide per litre of alveolar volume correlates well with the severity of emphysema. "[37]

- **Pulmonary hypertension**

"This develops late in COPD, at the time of severe gas exchange abnormalities. Contributing factors include pulmonary arterial constriction (as a result of hypoxia), endothelial dysfunction, remodelling of the pulmonary arteries (smooth muscle hypertrophy and hyperplasia), and destruction of the pulmonary capillary bed. Structural changes in the pulmonary arterioles result in persistent pulmonary hypertension and right ventricular hypertrophy or enlargement and dysfunction (cor pulmonale). "[37]

- **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. Patients also have an increased risk of cardiovascular disease, which is associated with an increase in C reactive protein. "[37]

Pathophysiology of exacerbations:

"Exacerbations are often associated with increased neutrophilic inflammation and, in some mild exacerbations, increased numbers of eosinophils. Exacerbations can be caused by infection (bacterial or viral), air pollution, and changes in ambient temperature. In mild exacerbations, airflow obstruction is unchanged or only slightly increased. Severe exacerbations are associated with worsening of pulmonary gas exchange due to increased inequality between ventilation and perfusion and subsequent respiratory muscle fatigue. The worsening ventilation-perfusion relation results from airway inflammation, oedema, mucous hypersecretion, and bronchoconstriction. These reduce ventilation and cause hypoxic vasoconstriction of pulmonary arterioles, which in turn impairs perfusion. "[37]

"Respiratory muscle fatigue and alveolar hypoventilation can contribute to hypoxaemia, hypercapnia, and respiratory acidosis, and lead to severe respiratory failure and death. Hypoxia and respiratory acidosis can induce pulmonary vasoconstriction, which increases the load on the right ventricle and, together with renal and hormonal changes, results in peripheral oedema. "[37]

Systemic features of COPD:

- Cachexia
- Skeletal muscle wasting and disuse atrophy
- Increased risk of cardiovascular disease (associated with increased concentrations of C reactive protein)
- Normochromic normocytic anaemia
- Secondary polycythaemia
- Osteoporosis
- Depression and anxiety

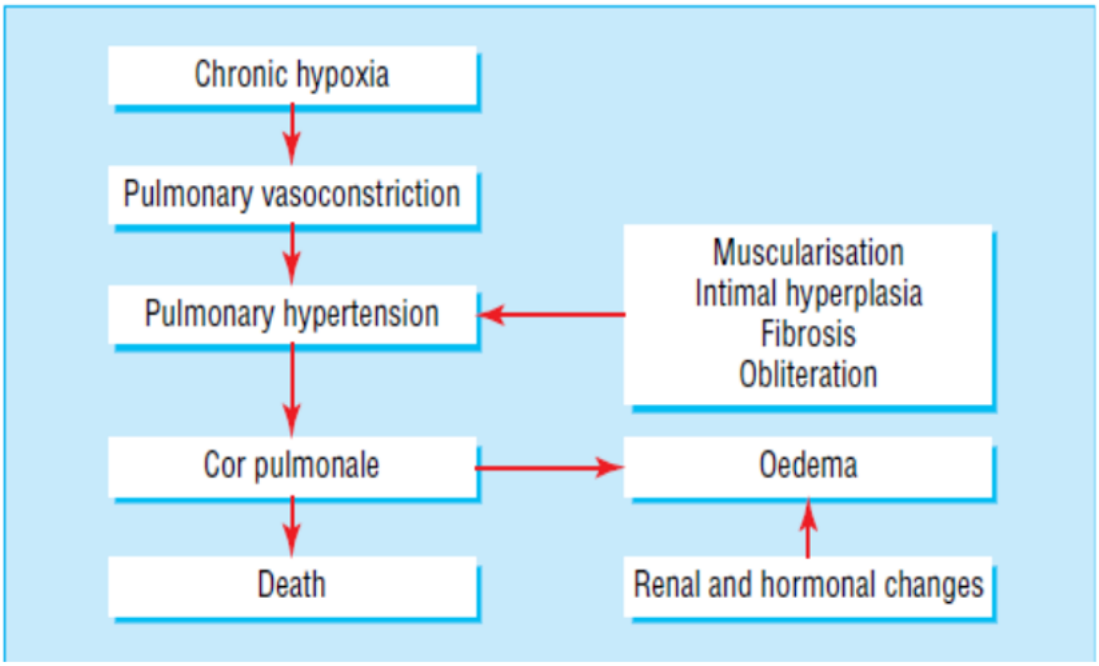


Image 6. Development of Pulmonary hypertension in COPD

Risk factors for COPD:[38,39]

1. "Smoking- cigarette or Bidi-50% of smokers develop COPD.73% of mortality in COPD is due to smoking among which 40% is from low and middle socioeconomic status. Smoking leads to ciliary destruction and hyper mucus secretion and decreased mucociliary clearance. "[37]
2. "Aging-As the lung function starts to decline by third and fourth decade of life"[37]
3. "Tuberculosis (this is very common in India) "[37]
4. "Respiratory infection in early life"[37]
5. "Passive or second-hand smoking"[37]
6. "Ambient air pollution-WHO estimates 1% of COPD cases in high income countries is due to urban air pollution where as it is 2% in nations of low and middle income. "[37]
7. "Occupational exposure-coal mining, cotton textile dust, mining"[37]
8. "House hold exposure-biomass fuels -Ninety percent of rural households and 32% of urban households cook their meals on a biomass stove.3 billion people are exposed to biomass all over the world and it carries the same amount of risk of developing COPD as tobacco smoke. WHO states that 35% of population in countries of low and middle income develop COPD due to its inhalation and 36% of mortality from lower respiratory disease is due to biomass inhalation. "[37]
9. Low Socioeconomic status
10. "Genetic factors-α1 antitrypsin deficiency leads to emphysema in 1-3% of patients"[37]

11. "Gender-In high income countries COPD prevalence is similar in both sexes due to smoking whereas condition is different in low- and middle-income countries as smoking in female is low. **"[37]**

Causes of acute exacerbation of COPD: **[39]**

Infectious agents:

"Virus, Gram positive and gram negative aerobic bacterial, atypical bacteria."[39]

Environmental conditions:

"Sudden change in temperature, humidity, air pollution exposure, tobacco smoke exposure, noxious gases or irritating chemicals**"[37]**

Host factors:

"Patients with poor general health, poor nutrition, immunocompromised state, lack of compliance to prescribed medicines, adoption of unhealthy life styles modes, poor level of personal hygiene, lack of compliance with long term oxygen therapy, failure to participate in pulmonary rehabilitation. Among all causes infection is the most common precipitating factor. Molecular diagnostics have given strong evidence that Microorganisms are involved in 80% of cases but the interaction between microorganisms and host is more important." [40,41]

Viral infections:

It accounts for 30% of infection.

"The common viruse are Rhinovirus, Coronavirus, Influenza virus, Parainfluenza virus, Adenovirus, Respiratory syncytial virus"[42]

Bacterial infections:

"It accounts for 60% of infection. Most common are Haemophilus influenzae, Moraxella Catarrhalis, Streptococcus pneumoniae. A number of studies have shown that virulent organisms are isolated in severe AECOPD patients like Staphylococcus aureus, Pseudomonas aeruginosa and members of Enterobactericeae family." [42]

Atypical bacteria:

"The role of Chlamydia, Legionella and Mycoplasma is conflicting in causing AECOPD as these microorganisms might also interact with airway bacteria and viruses. A study done by using real time PCR by Diederen et.al. found no role for these atypical bacteria in AECOPD." [42]

Clinical features and Management of COPD:

Smoking and inhalational exposure history — "The most important risk factor for chronic obstructive pulmonary disease (COPD) is cigarette smoking. Other exposures including passive smoke and biomass fuel use also play roles."[44]

"The amount and duration of smoking contribute to disease severity. Thus, a key step in the evaluation of patients with suspected COPD is to ascertain the number of pack years smoked (packs of cigarettes per day multiplied by the number of years), as the majority (about 80 percent) of patients with COPD in the United States have a history of cigarette smoking."[36,37] "A smoking history should include the age of starting and the age of quitting, as patients may underestimate the number of years they smoked. With enough smoking, almost all smokers will develop measurably reduced lung function. While studies have shown an overall "dose-response curve" for smoking and lung function, some individuals develop severe disease with fewer pack years and others have minimal to no symptoms despite many pack years."[44]

Symptoms and pattern of onset —

"The three cardinal symptoms of COPD are dyspnea, chronic cough, and sputum production and the most common early symptom is exertional dyspnea. Less common symptoms include wheezing and chest tightness. However, any of these symptoms may develop independently and with variable intensity."[45]

There are three typical ways in which patients with COPD present: [45]

"Patients who have an extremely sedentary lifestyle but few complaints require careful questioning to elicit a history that is suggestive of COPD. Some patients unknowingly avoid exertional dyspnoea by shifting their expectations and limiting their activity. They may be unaware of the extent of their limitations or that their limitations are due to respiratory symptoms, although they may complain of fatigue. "[45]

“Patients who present with respiratory symptoms generally complain of dyspnoea and chronic cough. The dyspnoea may initially be noticed only during exertion. However, it eventually becomes noticeable with progressively less exertion or even at rest. The chronic cough is characterized by the insidious onset of sputum production, which occurs in the morning initially, but may progress to occur throughout the day. The daily volume rarely exceeds 60 mL. The sputum is usually mucoid, but becomes purulent during exacerbations. ”[45]

“Patients who present with episodes of increased cough, purulent sputum, wheezing, fatigue, and dyspnoea that occur intermittently, with or without fever. Diagnosis can be problematic in such patients. The combination of wheezing plus dyspnoea may lead to an incorrect diagnosis of asthma. Conversely, other illnesses with similar manifestations are often incorrectly diagnosed as a COPD exacerbation (eg, heart failure, bronchiectasis, bronchiolitis). The interval between exacerbations decreases as the severity of the COPD increases. ”[45]

“Approximately 62 percent of patients with moderate to severe COPD report variability in symptoms (e.g. dyspnoea, cough, sputum, wheezing, or chest tightness) over the course of the day or week-to-week; morning is typically the worst time of day.”[45]

“Patients with COPD may experience weight gain (due to activity limitations), weight loss (possibly due to dyspnoea while eating), limitation of activity (including sexual), cough syncope, or feelings of depression or anxiety. Weight loss generally reflects more advanced disease and is associated with a worse prognosis. However, the majority of COPD patients are overweight or obese. Comorbid diseases that may accompany COPD include lung cancer, bronchiectasis, cardiovascular disease, osteoporosis, metabolic syndrome, skeletal muscle weakness, anxiety, depression, and cognitive dysfunction. Patients may also report a family history of COPD or other chronic respiratory illness.” [45]

“It is also important to note that current and former smokers without spirometric evidence of airflow obstruction can have a substantial respiratory symptom and radiographic burden of disease. While such individuals are being actively investigated, the natural history of such individuals has not been fully studied and there is currently no evidence base to guide treatment in such individuals. ”[45]

Physical examination — The findings on physical examination of the chest vary with the severity of the COPD.

“Early in the disease, the physical examination may be normal, or may show only prolonged expiration or wheezes on forced exhalation.”[45]

“As the severity of the airway obstruction increases, physical examination may reveal hyperinflation (eg, increased resonance to percussion), decreased breath sounds, wheezes, crackles at the lung bases, and/or distant heart sounds. Features of severe disease include an increased anteroposterior diameter of the chest ("barrel-shaped" chest) and a depressed diaphragm with limited movement based on chest percussion. ”[45]

“Patients with end-stage COPD may adopt positions that relieve dyspnoea, such as leaning forward with arms outstretched and weight supported on the palms or elbows. This posture may be evident during the examination or may be suggested by the presence of callouses or swollen bursae on the extensor surfaces of forearms. Other physical examination findings include use of the accessory respiratory muscles of the neck and shoulder girdle, expiration through pursed lips, paradoxical retraction of the lower interspaces during inspiration (ie, Hoover's sign), cyanosis, asterixis due to severe hypercapnia, and an enlarged, tender liver due to right heart failure. Neck vein distention may also be observed because of increased intrathoracic pressure, especially during expiration. ”[45]

"Yellow stains on the fingers due to nicotine and tar from burning tobacco are a clue to ongoing and heavy cigarette smoking. Clubbing of the digits is not typical in COPD (even with associated hypoxemia) and suggests comorbidities such as lung cancer, interstitial lung disease, or bronchiectasis. "[45]

Evaluation of COPD:

"Evaluation for COPD is appropriate in adults who report dyspnea, chronic cough, chronic sputum production or have had a gradual decline in level of peak activity, particularly if they have a history of exposure to risk factors for the disease (eg, cigarette smoking, indoor biomass smoke). All patients are evaluated with spirometry and selected patients have laboratory testing and imaging studies." [46]

"There is no evidence to support the benefit of population-based screening of asymptomatic adults for COPD but the Global Initiative for Chronic Obstructive Lung Disease (GOLD) does advocate active case finding among at risk individuals. The CAPTURE questionnaire (**C**hronic obstructive pulmonary disease **A**ssessment in **P**rimary care **T**o identify **U**ndiagnosed **R**espiratory disease and **E**xacerbation risk) can help identify patients who would likely benefit from therapy for COPD and would be candidates for diagnostic evaluation."[46]

Laboratory:

No laboratory test is diagnostic for COPD, but certain tests are sometimes obtained to exclude other causes of dyspnea and comorbid diseases.

Assessment for anemia is an important step in the evaluation of dyspnoea.

"Measurement of plasma brain natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP) concentrations is useful as a component of the evaluation of suspected heart failure (HF). Blood

glucose, urea nitrogen, creatinine, electrolytes, calcium, phosphorus, and thyroid stimulating hormone may be appropriate depending on the degree of clinical suspicion for an alternate diagnosis.**"**[46]

"Among stable COPD patients with normal kidney function, an elevated serum bicarbonate may indirectly identify chronic hypercapnia. In the presence of chronic hypercapnia, the serum bicarbonate is typically increased due to a compensatory metabolic alkalosis. Abnormal results must be confirmed with arterial blood gas measurement. **"**[46]

"Testing for alpha-1 antitrypsin (AAT) deficiency should be obtained in all symptomatic adults with persistent airflow obstruction on spirometry, possibly excepting those from geographic areas with a low prevalence of AAT deficiency. Features that are particularly suggestive of AAT deficiency include the emphysema in a young individual (eg, age ≤45 years), emphysema in a non-smoker or minimal smoker, emphysema characterized by predominantly basilar changes on the chest radiograph, or a family history of emphysema. However, AAT deficiency may be present in a patient with otherwise typical COPD." [46]

Pulmonary function tests:

"Pulmonary function tests (PFTs), particularly spirometry, are the cornerstone of the diagnostic evaluation of patients with suspected COPD. In addition, PFTs are used to determine the severity of the airflow limitation, assess the response to medications, and follow disease progression. "[46]

Spirometry:

"When evaluating a patient for possible COPD, spirometry is performed pre and post bronchodilator administration (eg, inhalation of albuterol 400 mcg) to determine whether airflow limitation is present and whether it is partially or fully reversible. Airflow limitation that is irreversible or only partially reversible with bronchodilator is the characteristic physiologic feature of COPD. Screening spirometry is not currently recommended. In contrast, spirometry should be performed in patients with suggestive symptoms.**"[46]**

"The most important values measured during spirometry are the forced expiratory volume in one second (FEV_1) and the forced vital capacity (FVC). The postbronchodilator ratio of FEV_1/FVC determines whether airflow limitation is present; the postbronchodilator percent predicted value for FEV_1 determines the severity of airflow limitation. **"[46]**

Lower limit of normal FEV1/FVC:

"GOLD guidelines support using the traditional postbronchodilator FEV_1/FVC ratio less than 0.7 as the threshold that indicates airflow limitation. However, the FEV_1/FVC ratio decreases with age, so use of the fifth percentile lower limit of normal (LLN) of the FEV_1/FVC ratio, rather than the absolute value of <0.7, has been advocated by some as a dividing point for the diagnosis of COPD.**[51-55]** However, the distinction between the LLN and the fixed ratio as dividing points is unlikely to lead to major clinical problems because current recommendations combine physiologic assessment with assessment of symptoms and exacerbations in staging

severity. Moreover, in a study of 13,847 subjects, an increased mortality was noted among those with an FEV_1/FVC <0.7, but >LLN FEV_1/FVC, when compared with those whose FEV_1/FVC was 0.7 or higher." [46]

Global Lung Initiative equations:

"As an alternative to using the LLN of FEV_1/FVC to define normal airflow on spirometry, a new approach may utilize equations developed by the Global Lung Initiative (GLI).[56] Using GLI equations, z scores (number of standard deviations above or below mean) were calculated for FEV_1, FVC, and FEV_1/FVC and compared with fixed ratio data. The findings suggest that among adults with GLI-defined normal spirometry, the use of a fixed ratio may misclassify individuals as having respiratory impairment. These findings await additional study in other cohorts."[46]

Forced expiratory volume in six seconds:

"The forced expiratory volume in six seconds (FEV_6), obtained by stopping the expiratory effort after 6 seconds rather than at cessation of airflow, is an acceptable surrogate for the FVC.[57] The advantages of the FEV_1/FEV_6 include less frustration by the patient and technician trying to achieve an end-of-test plateau, less chance of syncope, shorter testing time, and better repeatability, without loss of sensitivity or specificity. The appropriate LLN for FEV_1/FEV_6 from NHANES III should be used to diagnose airflow limitation." [46]

Peak expiratory flow:

"Peak expiratory flow (PEF) is often used as a measure of airflow limitation in asthma, but may underestimate the degree of airflow limitation in COPD. In addition, a low PEF is not specific for airflow limitation and requires corroboration with spirometry." [46]

Lung volumes:

"Lung volume measurement is not needed for all patients with suspected COPD. However, when a reduced FVC is noted on postbronchodilator spirometry, lung volume measurement by body plethysmography is used to determine whether the reduction in FVC is due to air trapping, hyperinflation, or a concomitant restrictive ventilatory defect. Decreased inspiratory capacity (IC) and vital capacity, accompanied by an increased total lung capacity (TLC), functional residual capacity (FRC), and residual volume (RV) are indicative of hyperinflation. An increased FRC or RV with a normal TLC is indicative of air trapping without hyperinflation."[46]

Diffusing capacity:

"The diffusing capacity for carbon monoxide (DLCO) is an excellent index of the degree of anatomic emphysema in smokers with airflow limitation, but is not needed for routine assessment of COPD. The indications for performing a DLCO measurement include hypoxemia by pulse oximetry (eg, arterial oxygen tension [PaO_2] <92 mmHg), breathlessness out of proportion to the degree of airflow limitation, and evaluation for lung resection or lung volume reduction surgery. The DLCO decreases in proportion to the severity of emphysema; however, it cannot be used to detect mild emphysema because it is neither a sensitive nor a specific test" [46]

Pulse oximetry and arterial blood gases:

"Pulse oximetry is a non-invasive, easily performed test that assesses blood oxygen saturation. It has reduced the number of patients who require arterial blood gases (ABGs), as supplemental oxygen is not needed when the pulse oxygen saturation (SpO_2) is >88 percent. However, pulse oximetry does not provide information about alveolar ventilation or hypercapnia

($PaCO_2$ >45mmHg), and assessment of oxygenation by pulse oximetry may be inaccurate in the setting of an acute exacerbation of COPD." [46]

The indications for measuring ABGs (eg, PaO_2, $PaCO_2$, and acidity [pH]), which must be considered in the clinical context, include the following:

- Low FEV_1 (eg, <50 percent predicted)
- Low oxygen saturation by pulse oximetry (eg, <92 percent)
- Depressed level of consciousness
- Acute exacerbation of COPD

"Assessment for hypercapnia in at risk patients 30 to 60 minutes after initiation of supplemental oxygen. In patients with mild to moderate COPD, arterial blood gases usually reveal mild or moderate hypoxemia without hypercapnia. As the disease progresses, the hypoxemia becomes more severe and hypercapnia may develop. Hypercapnia becomes progressively more likely when the FEV_1 approaches or falls below one litre. Blood gas abnormalities worsen during acute exacerbations and may also worsen during exercise and sleep. The compensatory responses to acute and chronic respiratory acidosis are shown in the figure and discussed separately." [46]

Imaging:

"Chest radiography and computed tomography (CT) are typically performed in patients with COPD when the cause of dyspnoea or sputum production is unclear and during acute exacerbations to exclude complicating processes (eg, pneumonia, pneumothorax, heart failure). Imaging is not required to diagnose COPD. However, in patients with severe COPD, CT scanning identifies individuals with predominantly upper lobe disease who may be candidates

for lung volume reduction surgery or medical lung volume reduction with endobronchial valves."[46]

Chest radiography:

"The main reasons to obtain a chest radiograph when evaluating a patient for COPD are to exclude alternative diagnoses, evaluate for comorbidities (eg, lung cancer with airway obstruction, bronchiectasis, pleural disease, interstitial lung disease, heart failure), or to look for complications of COPD (eg, pneumonia, pneumothorax) that might be suggested by a change in symptoms. "[46]

"Plain chest radiographs have a poor sensitivity for detecting COPD. As an example, only about half of patients with COPD of moderate severity are identified as having COPD by a plain chest radiograph (ie, sensitivity of 50 percent). "[46]

"Radiographic features suggestive of COPD (usually seen in advanced disease) include: Rapidly tapering vascular shadows, increased radiolucency of the lung, a flat diaphragm, and a long, narrow heart shadow on a frontal radiograph. A flat diaphragmatic contour and an increased retrosternal airspace on a lateral radiograph. These findings are due to hyperinflation. "[46]

"Bullae, defined as radiolucent areas larger than one centimeter in diameter and surrounded by arcuate hairline shadows. They are due to locally severe disease, and may or may not be accompanied by widespread emphysema. When advanced COPD leads to pulmonary hypertension and cor pulmonale, prominent hilar vascular shadows and encroachment of the heart shadow on the retrosternal space may be seen."[59,60] The cardiac enlargement may become evident only by comparison with previous chest radiographs.

Computed tomography:

"CT has greater sensitivity and specificity than standard chest radiography for the detection of emphysema. This is particularly true with high resolution CT (ie, collimation of 1 to 2 mm). The use of expiratory scans, particularly when used in conjunction with the inspiratory scans, can also be used to assess non-emphysematous air trapping as a surrogate measure for small airway abnormality. However, CT scanning is not needed for the routine diagnosis of COPD. Usually, it is performed when a change in symptoms suggests a complication of COPD (eg, pneumonia, pneumothorax, giant bullae), an alternate diagnosis (eg, thromboembolic disease) is suspected, lung cancer screening is indicated, or a patient is being considered for medical lung volume reduction with endobronchial valves, lung volume reduction surgery, or lung transplantation. "[46]

"Certain CT scan features can determine whether the emphysema is centriacinar (centrilobular), panacinar, or paraseptal, although this is usually not necessary for clinical management. "[46]

"Centriacinar emphysema occurs preferentially in the upper lobes and produces holes in the centre of secondary pulmonary lobules. The walls of emphysematous spaces are usually imperceptible, but central vessels may be visible. In contrast, the walls of cysts in pulmonary Langerhans histiocytosis, another cystic lung disease of cigarette smoker, are thicker. "[46]

"Panacinar emphysema more commonly involves the lung bases and involves the entire secondary pulmonary lobule. Panacinar emphysema can cause a generalized paucity of vascular structures. Among patients with alpha-1 antitrypsin deficiency, panacinar emphysema is the more common pattern. "[46]

“Paraseptal (distal acinar) emphysema produces small, subpleural collections of gas located in the periphery of the secondary pulmonary lobule. It is considered to be the precursor of bullae. **”46**

Diagnosis:

“The presence of symptoms compatible with COPD (eg, dyspnea at rest or on exertion, cough with or without sputum production, progressive limitation of activity) are suggestive of the diagnosis, especially if there is a history of exposure to triggers of COPD (eg, tobacco smoke, occupational dust, indoor biomass smoke), a family history of chronic lung disease, or presence of associated comorbidities. **”46**

The diagnosis of COPD is confirmed by the following:

“Spirometry demonstrating airflow limitation (i.e., a forced expiratory volume in one second/forced vital capacity [FEV_1/FVC] ratio less than 0.7 or less than the lower limit of normal [LLN]) that is incompletely reversible after the administration of an inhaled bronchodilator**”46**

“The Global Initiative for COPD (GOLD) guidelines suggest repeating spirometry on a separate occasion to demonstrate persistence of airflow limitation (FEV_1/FVC <0.7 or less than the LLN) for patients with an initial FEV_1/FVC between 0.6 and 0.8. After confirming the presence of COPD, the next step is to consider the cause. For the majority of patients, the etiology is long-term cigarette smoking. However, it is important to review with the patient whether underlying asthma, workplace exposures, indoor use of biomass fuel, a prior history of tuberculosis, or familial predisposition is contributory, because mitigation of ongoing exposures may reduce disease progression. It is appropriate to screen all patients with COPD

for alpha-1 antitrypsin (AAT) deficiency by obtaining an AAT serum level and AAT genotyping, possibly excepting areas with a low prevalence of AAT deficiency."[46]

Staging of COPD:

"The initial Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines used the forced expiratory volume in one second (FEV_1; expressed as a percentage of predicted) to stage disease severity. "[46]

"However, the FEV_1 only captures one component of COPD severity: two patients with the same percent predicted FEV_1 can have a substantially different exercise tolerance and prognosis. Other aspects of disease, such as the severity of symptoms, risk of exacerbations, and the presence of comorbidities, are important to the patient's experience of the disease and prognosis and are included in newer staging systems, such as the revised GOLD classification."[46]

GOLD system: [46]

"The therapeutic strategy of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy suggests using a combined assessment based on an individual's symptoms and exacerbation history to guide therapy. The multidimensional GOLD "ABCD" evaluation is discussed separately in the context of initial management of COPD. "[46]

"While not included in the GOLD "ABCD" symptom and risk assessments, spirometry is integral to the diagnosis of COPD and severity assessment which contributes to prognosis. Follow-up spirometric assessment may also be helpful in therapeutic decision making when, for instance, there is a discrepancy between spirometry and level of symptoms or in determining the need to consider alternative diagnoses if symptoms are disproportionate to the degree of airflow obstruction. GOLD also recommends annual spirometry to track decline in

FEV_1. Spirometry is also essential to decision-making for lung volume reduction and lung transplantation. "[46]

Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria[46]

- GOLD 1 - mild: $FEV_1 \geq 80\%$ predicted
- GOLD 2 - moderate: $50\% \leq FEV_1 < 80\%$ predicted
- GOLD 3 - severe: $30\% \leq FEV_1 < 50\%$ predicted
- GOLD 4 - very severe: $FEV_1 < 30\%$ predicted.

BODE index:[63-66]

"The BODE index, which is another system for assessment of COPD severity and prognosis, is calculated based on weight (BMI), airway obstruction (FEV_1), dyspnoea (mMRC dyspnoea score), and exercise capacity (six-minute walk distance), has been used to assess an individual's risk of death. This index provides better prognostic information than the FEV_1 alone and can be used to assess therapeutic response to medications, pulmonary rehabilitation therapy, and other interventions."[63]

COPD Foundation system: [47]

"The COPD Foundation has introduced a staging system that includes seven severity domains, each of which has therapeutic implications. These domains are based upon assessment of spirometry, regular symptoms, number of exacerbations in the past year, oxygenation, emphysema on computed tomography scan, presence of chronic bronchitis, and comorbidities. Within these domains, the COPD Foundation uses five spirometric grades: "[47]

SG 0: Normal spirometry

"SG 1: Mild, postbronchodilator FEV_1/FVC ratio <0.7, $FEV_1 \geq 60$ percent predicted"[47]

"SG 2: Moderate, postbronchodilator FEV_1/FVC ratio <0.7, 30 percent $\leq FEV_1 <60$ percent predicted. "[47]

"SG 3: Severe, postbronchodilator FEV_1/FVC ratio <0.7, FEV_1 <30 percent predicted"[47]

"SG U: Undefined, postbronchodilator FEV_1/FVC ratio >0.7, FEV_1 <80 percent predicted"[47]

"An advantage of this staging system is that it simplifies the interpretation of spirometry; any spirometric finding results in a classification, which is not the case in GOLD. "[47]

While FEV_1 is used to gauge severity, the FEV_1/FVC ratio is not used for this purpose because measurement of FVC becomes less reliable as the disease progresses (the long exhalations are difficult for the patients), thus making the ratio less accurate. **"[47]**

Anatomy of diaphragm

"The diaphragm in the thorax is called the thoracic diaphragm and serves as an important anatomical landmark that separates the thorax, or chest, from the abdomen. It functions during breathing when it contracts to enlarge the thoracic cavity and reduce the intrathoracic pressure so that lungs may expand and fill their alveoli with air. It is a dome-shaped muscle and tendon that functions as the main muscle of respiration and is essential to the breathing process. It is a fibromuscular sheet that has a convex upper surface that forms the floor of the thoracic cavity and a concave under surface to form the roof of the abdominal cavity. The esophagus, phrenic, and vagus nerves, descending aorta, and inferior vena cava pass through the diaphragm between the thoracic and abdominal cavities. The diaphragm is asymmetric with the left side slightly more inferior than the right, chiefly because of the presence of the liver located on the right. The left side may also be partially inferiorly located because of the push by the heart."[48]

Structure and Function[48]

Functions of the Diaphragm

Muscle of Inspiration

"The diaphragm pulls its central tendon down during contraction and then increases the vertical diameter of the thorax. This increases the negative pressure inside the thoracic cavity, which draws in air. Thus, the diaphragm is the most important muscle used in inspiration. During inhalation, the diaphragm contracts and is pushed inferiorly into the abdominal cavity where it appears flat. Simultaneously the external intercostal muscles located in between the ribs raise the anterior chest wall like the handles of a bucket. This results in the chest cavity becoming larger and wider, which allows air in from the outside. During exhalation, the rib cage and chest wall start to sag and revert to the original position. At the same time, there is relaxation and

elevation of the diaphragm. This motion forces the air within the lungs to push out of the body." [48]

Muscle of Abdominal Straining

"The contraction of the diaphragm will assist in the contraction of the muscles of the anterior abdominal wall in raising the intra-abdominal pressure will normal processes like micturition, defecation, and parturition." [48]

Weightlifting Muscle

"When a person takes and holds a deep breath, the diaphragm will assist the muscles of the anterior abdominal wall to raise the intra-abdominal pressure. This maneuver is also called as Valsalva maneuver and is used to augment heart murmurs and classify them whether they are clinically right-sided or left-sided." [48]

Thoracoabdominal Pump

"When people breathe in, the diaphragm descends, which decreases the intrathoracic pressure and improves the intra-abdominal pressure. This compresses the blood in the inferior vena cava (IVC) and forces it upward into the right atrium and helps to fill the heart. When abdominal lymph vessels are also compressed, its passage upward within the thoracic duct is aided by the negative intrathoracic pressure. Furthermore, valves in the thoracic duct prevent the backflow of the lymph in the thoracic duct." [48]

Embryology[48]

Diaphragm Formation

1. Septum transversum
2. Pleuro-peritoneal membrane
3. Mesentery of esophagus
4. Mesoderm of the body wall

Insertion

"The diaphragm inserts into a central tendon. The top surface of the tendon is partially connected to the lower surface of the fibrous pericardium. Muscle fibers arising from the right crus traverse up on the left side and encircle the orifice of the esophagus in a sling-like loop. These fibers act as a sphincter and likely assist in preventing the regurgitation of the stomach contents into the thoracic part of the esophagus." [48]

Origin of Diaphragm

Sternal

The sternal part originates as 2 fleshy slips from the back of the xiphoid process.

Costal

The costal part originates from inner surfaces of the cartilages, adjacent parts of the lower sixth ribs on each side. It interdigitates with transversus abdominis. [48]

Lumbar

"The medial lumbocostal arch is a tendinous arch in fascia covering psoas major. Medially, it attaches to the side of the body of vertebra L1. Laterally, it connects to the front of the transverse process of vertebra L1." [48]

"The lateral lumbocostal arch is a tendinous arch in fascia covering the upper part of quadratus lumborum. Medially, attach to the front of the transverse process of vertebra L1. Laterally, it connects to the lower border of the 12th rib." [48]

"The right crus arises from the anterolateral surface of the bodies of the upper three lumbar vertebrae and also the intervening intervertebral disc. "[48]

The left crus arises from the corresponding parts of the upper 2 lumbar vertebrae.

"Medial margin of two crura forms a tendinous arc across the front of the aorta called the median arcuate ligament."[48]

Blood Supply and Lymphatics[48]

Major Arteries Supplying the Diaphragm

1. Musculophrenic artery branch of the internal thoracic artery
2. Superior phrenic artery branch of the aorta
3. Lower five intercostal arteries and subcostal artery
4. Inferior phrenic artery

Nerves

Motor Nerve Supply

Right and left phrenic nerves (C3 through C5)

Sensory Nerve Supply[48]

"The phrenic nerve innervates the parietal pleura and peritoneum covering the central surfaces of the diaphragm. The lower 6 intercostal nerves supply the periphery of the diaphragm. When the diaphragm contracts, the large-sized myelinated phrenic afferents fire. On the other hand, the smaller diameter nerves continue to discharge throughout the respiratory cycle. It is now well established that activation of both non-myelinated and myelinated phrenic sensory nerves modulate respiratory output during each breathing cycle. However, the activation of the phrenic afferents does increase significantly as the diaphragm continues to work and develops fatigue. Once the phrenic afferents are activated, they also modulate the sympathetic motor outflow. Furthermore, the phrenic afferents also contribute to somatosensation of the diaphragm and make one aware of the sensation of breathing while awake. The exact influence of the spinal and supraspinal nerves and synapses between the non-myelinated and myelinated phrenic nerves is not known. The use of deep muscle training contributed to a significant change in the position of the body in the sagittal plane and the increase in the amplitude of breathing."[48]

Muscles

"One can find the origins of the diaphragm along the lumbar vertebrae of the spine and the inferior border of the ribs and sternum. The superior diaphragm origin is continuous from the xiphoid process anteriorly to lower 6 costal cartilages of the thorax laterally and first 2 lumbar vertebrae posteriorly. The musculoskeletal fibers radiate from all angles to the center of the body and converge into a central tendon which is the inferior attachment or muscular skeletal point. The diaphragm has a dome-like structure with the peripheral segment attached to the

chest wall and abdominal cavity. The muscle fibers from these attachments converge in a central tendon, which forms the crest of the dome. The periphery of the diaphragm is made of strong muscular fibers that have their origin from the surroundings of the inferior thoracic aperture. These muscle fibers than converge and insert into the central tendon." [48]

Ultrasonographic Assessment of the Diaphragm

"Although it is known that mechanical ventilation causes lung injury, it is less widely appreciated that ventilation also injures the diaphragm as well. Controlled ventilation for patients with acute respiratory failure leads to muscle atrophy in the diaphragm due to oxidative stress-mediated protein degradation." [49]

"Several technologies are currently available for this purpose; however, many have limitations, such as being invasive, less cost-effective, and difficult to use at the bedside. Diagnostic ultrasonographic devices are ideal in this regard, and they are becoming an important tool for visualizing and quantifying diaphragm morphology and function. Additionally, respiratory muscles like the diaphragm and abdominal muscles are relatively close to the body surface, making them easier to observe with ultrasonography. "[49]

Mechanisms of Diaphragm Muscle Injury Induced by Mechanical Ventilation

"To prevent diaphragm dysfunction, it is essential to understand the mechanisms of diaphragm muscle injury. Atrophy due to a suppression of inspiratory effort and injury owing to an excessive load are the two most important diaphragm injuries during mechanical ventilation." [49]

2.1. Disuse Atrophy

"Disuse atrophy due to a suppression of inspiratory effort and excessive respiratory support is the most important mechanism of diaphragm injury during mechanical ventilation. In animal

studies, controlled ventilation or high levels of pressure support ventilation caused acute muscle atrophy, damage of myofibers, and dysfunction." [49]

Levine et al reported that, "diaphragm inactivity for up to 18–69 h in brain-dead patients was associated with noticeable atrophy of the diaphragm; however, it did not cause atrophy in the pectoralis major. Furthermore, histological studies in humans have revealed that disuse of the diaphragm activated the proteolytic pathways, leading to both diaphragmatic atrophy and mitochondrial dysfunction, resulting in reduced contractility." [49]

2.2. Concentric Load-Induced Injury

"Insufficient ventilatory support against inspiratory effort overloads the diaphragm and causes muscle injury. In histological investigations in healthy subjects and patients with chronic obstructive pulmonary disease (COPD), contraction of the diaphragm against excessive load caused acute diaphragm injury, inflammation, and weakness. Importantly, in critically ill patients with systemic inflammation, mechanical stimuli can exacerbate sarcolemma and thus contribute to diaphragmatic dysfunction." [49]

2.3. Eccentric Load-Induced Injury

"It is known that muscle injury occurs when muscles eccentrically contract during lengthening and this also applies to the diaphragm. This muscle injury is supposed to occur in mechanically ventilated patients. One possible cause is patient–ventilator asynchrony. With asynchronies, such as premature cycling, ineffective effort, and reverse triggering, the diaphragm will be forced to contract during the expiratory phase of the machine cycle, which results in diaphragm injury." [49]

"Another cause is post-inspiratory diaphragm activity, or so-called "diaphragm braking". The diaphragm contracts even during the expiratory phase and suppresses the rate of decrease in lung volume to prevent acute alveolar collapse and following atelectasis. This physiological

contraction during the expiratory phase is potentially injurious to the diaphragm. Diaphragm braking is strong in situations where alveoli are predisposed to collapse such as when the positive end-expiratory pressure (PEEP) is set low. In addition, it has been suggested that the diaphragm may contract during expiration if the expiratory muscles are recruited, especially in patients with a small airway obstruction. However, the effects of eccentric contraction that occurs with expiratory muscle recruitment on diaphragmatic function remains unknown." [49]

2.4. Longitudinal Atrophy

"It is hypothesized in animal studies that if the diaphragm is maintained in a contracted state at a higher PEEP, the abrupt lowering of PEEP, such as during spontaneous breathing trials, can cause longitudinal atrophy. A higher PEEP shortens the length of sarcomeres (the basic contractile unit of muscle fibers composed of two main protein filaments, actin and myosin) in the longitudinal direction, and gradually, some sarcomeres drop out and others regain their original length (reconstruction). Here, the sudden lowering of the PEEP causes overstretching of the sarcomeres, leading to a change in the length–tension relationship of the diaphragm that may cause impaired contractility." [49]

Basics of Diaphragm Ultrasonography

"There are two approaches to diaphragm ultrasonography. One is the intercostal approach at the zone of apposition (the origin of the diaphragm in contact with the inner surface of the rib cage), and the other is the subcostal approach with the liver as the acoustic window. The former is primarily used to assess diaphragm thickness and contraction, while the latter is used to assess diaphragmatic exercise. Diaphragmatic exercise can be assessed under various conditions, such as during quiet breathing, maximum inspiration, and short diaphragm contractions during sniffing. Reference values for each parameter used in diaphragm ultrasonography are shown in Table 1. For intensive care unit (ICU) patients, cutoff values that

showed differences in clinical outcomes, such as success in spontaneous breathing trials (SBTs) or weaning from mechanical ventilation, are indicated. "[49]

Parameters and reference values for diaphragm ultrasonography. [49]

	Parameter	Reference Value	Abnormal Values *	Cutoff Value Related to Outcome
Healthy individual	End-expiratory thickness (mm)	male: 1.9 ± 0.4	male: <1.7	
		female: 1.4 ± 0.3	female: <1.3	
	TFdi	37 ± 9%	<20%	
		80 ± 50%	<20%	
		(maximal breathing)		
	Excursion (mm)	male: 18 ± 3	male: <10	
		female: 16 ± 3	female: <9	
ICU patient	End-expiratory thickness (mm)			<1.7
	TFdi			<30~36%
	Excursion (mm)			<10~14 <25 (maximal breathing)

*Lower limit of 95% confidence interval or minimum value. ICU, intensive care unit; TFdi, thickening fraction of the diaphragm.

3.1. Intercostal Approach

"The intercostal approach involves positioning a 10–15 MHz linear transducer vertically along the cephalocaudal axis at the right 8th–11th intercostal space on the anterior or mid axillary line in the zone of apposition. The diaphragm appears at a depth of 2–4 cm as a layered structure between the pleura and peritoneum, with a white linear structure in the center (Figure 1A, B). During measurements, the thickness of the pleura and peritoneum should not be included. The normal diaphragm thickness in healthy individuals is approximately 1.6 mm (1.9 mm in males and 1.4 mm in females). The diaphragm thickens upon contraction, and the thickening fraction of the diaphragm (TFdi) is the measure of diaphragmatic contraction activity." [49]

“The TFdi can be determined using B-mode (Figure 1A) or M-mode (Figure 1B) as the percentage increase in diaphragm thickness during inspiration: (end-inspiratory diaphragm thickness−end expiratory diaphragm thickness)/end-expiratory diaphragm thickness × 100. The TFdi is around 37% in healthy individuals at rest, but it shows considerable variability during maximum breathing efforts. Measuring diaphragm thickness is subject to technical and methodological limitations. The diaphragm is extremely thin, around 1.5–2.0 mm, so slight measurement errors can lead to an overestimation or underestimation of diaphragm thickness and the TFdi.” [49]

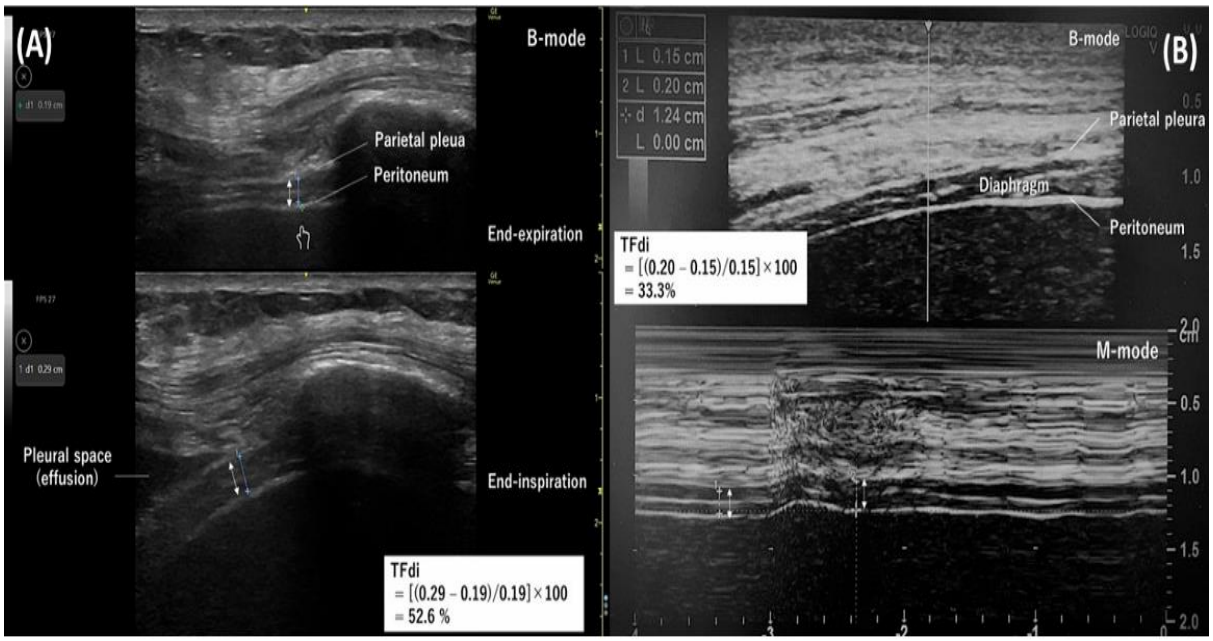


Image 7. Diaphragm ultrasonography with the intercostal approach. "The double arrow indicates the thickness of the diaphragm. (A) A B-mode diaphragm ultrasonographic image obtained with a linear transducer along the right mid-axillary line. Separate images measuring the diaphragm thickness at end-expiration (top) and end-inspiration (bottom) were used to determine the thickening fraction of Figure 1. Diaphragm ultrasonography with the intercostal approach. The double arrow indicates the thickness of the diaphragm. (A) A B-mode diaphragm ultrasonographic image obtained with a linear transducer along the right mid-axillary line. Separate images measuring the diaphragm thickness at end-expiration (top) and end-inspiration (bottom) were used to determine the thickening fraction of the diaphragm. (B) An M-mode ultrasonographic image (bottom) capturing temporal changes in one direction of the thickness of the diaphragm. The diaphragm thickness at end-expiration and end-inspiration were measured from this image to determine the thickening fraction of the diaphragm. the diaphragm. (B) An M-mode ultrasonographic image (bottom) capturing temporal changes in one direction of the thickness of the diaphragm. The diaphragm thickness at end-expiration and end inspiration were measured from this image to determine the thickening fraction of the diaphragm." [49]

3.2. Subcostal Approach

"To observe diaphragmatic movement using the subcostal approach, a low-frequency (2–5 MHz) transducer is placed just below the costal margin along the midclavicular line. The patient should be in a semi-recumbent position, and the ultrasound beam should be directed as cranially as possible, perpendicular to the diaphragm dome. In this view, the diaphragm appears as a bright line covering the liver or spleen. The right side is easier to image, since the liver is an acoustic window. Conversely, the spleen does not serve as an effective acoustic window, making it challenging to obtain clear images of the left diaphragm. This approach allows for the visualization of diaphragmatic exercise in over 95% of cases during quiet breathing but becomes difficult during maximum respiration, especially on the left side." [49]

Da Conceicao D et al. recently explored that, "a new approach to observe diaphragmatic movement using the subcostal approach, a low-frequency (2–5 MHz) transducer is placed just below the costal margin along the midclavicular line. The patient should be in a semi-recumbent position, and the ultrasound beam should be directed as cranially as possible, perpendicular to the diaphragm dome. In this view, the diaphragm appears as a bright line covering the liver or spleen. The right side is easier to image, since the liver is an acoustic window. Conversely, the spleen does not serve as an effective acoustic window, making it challenging to obtain clear images of the left diaphragm. This approach allows for the visualization of diaphragmatic exercise in over 95% of cases during quiet breathing but becomes difficult during maximum respiration, especially on the left side."[49]

Da Conceicao D et al. recently explored, "a new approach to assess diaphragmatic motion by measuring the excursion of the uppermost point of the zone of apposition at the mid-axillary line using a high-frequency linear transducer and reported that this new approach had a higher

success rate bilaterally (both 100%) than the subcostal approach (98.7% on the right side and 34.7% on the left side). Typically, the diaphragm moves toward the transducer during inspiration. To assess diaphragmatic motion by measuring the excursion of the uppermost point of the zone of apposition at the mid-axillary line using a high-frequency linear transducer and reported that this new approach had a higher success rate bilaterally (both 100%) than the subcostal approach (98.7% on the right side and 34.7% on the left side)." [49]

"Typically, the diaphragm moves toward the transducer during inspiration. To quantify this exercise, place the M-mode line perpendicular to the direction of the exercise and measure the excursion distance. Setting the sweep speed to about 10 mm/second allows for the visualization of approximately three respiratory cycles within a single image. However, excursion measurement is only feasible during unassisted spontaneous breathing (e.g., with a T-piece or low continuous positive airway pressure [CPAP]). This quantify this exercise, place the M-mode line perpendicular to the direction of the exercise and measure the excursion distance. Setting the sweep speed to about 10 mm/second allows for the visualization of approximately three respiratory cycles within a single image. limitation arises because it is impossible to distinguish between diaphragm exercise due to spontaneous contraction and that due to inspiratory pressure support from a mechanical ventilator, and because excursion is significantly influenced by the lung volume." [49]

4. Clinical Applications of Diaphragm Ultrasonography

4.1. Evaluation of Diaphragm Thickness

Diaphragm atrophy occurs early after the initiation of mechanical ventilation and is associated with diaphragm dysfunction. Zambon et al[50] "demonstrated a linear correlation between the duration of mechanical ventilation and the rate of diaphragm atrophy, with a decrease of 7.5%

per day under controlled ventilation and an increase of 2.3% per day during spontaneous breathing or CPAP. "[50]

Previous studies[51] reported that, "the end-expiratory diaphragm thickness decreased by >10% in 41% and 63% of patients and increased by >10% in 24% and 19% of patients, with both groups experiencing prolonged mechanical ventilation and higher mortality rates. In both studies, a decrease in the thickness of the diaphragm was observed until the third day of mechanical ventilation and during both controlled and partially assisted ventilation. These findings suggest the importance of monitoring changes in diaphragm thickness over time. "[51]

4.2. Evaluation of Diaphragm Function

"Diaphragm dysfunction is a common issue that can impact the outcomes of ICU patients. It is often indicated by an excursion of <10 mm during resting breathing or a TFdi of <20% during maximal breathing. In cases of unilateral diaphragmatic paralysis, both the excursion and TFdi of the paralyzed side decrease making diaphragm ultrasonography a suitable diagnostic tool. However, it is crucial to observe both sides, including the left diaphragm, which can be challenging to visualize. "[51]

"In emergency settings, non-invasive ventilation (NIV) is used for patients with acute exacerbations of COPD. An improvement in excursion 1 h after initiating NIV has been associated with successful NIV outcomes. Lung hyperinflation due to air trapping can restrict diaphragmatic movement; hence, evaluating diaphragm function can help assess NIV effectiveness and potentially prevent delays in intubation for patients with acute exacerbations of COPD. "[51]

4.3. Evaluation of Respiratory Effort

"The proper monitoring of respiratory effort in mechanically ventilated patients is crucial for optimizing diaphragm activity and ensuring lung and diaphragm protection. Although specific

indicators for diaphragm-protective respiratory efforts are not yet established, the levels observed in healthy individuals and patients who have been successfully weaned from mechanical ventilation serve as a reference value. The TFdi correlates with invasive measures like transdiaphragmatic pressure (Pdi) and the pressure–time product (PTP) of esophageal pressure, making it useful for noninvasive monitoring of the work of breathing. "[51]

4.4. Prediction of Weaning Outcomes

"There have been many attempts to predict weaning outcome by performing diaphragm ultrasonography during SBT.

DiNino et al[52] reported that, "a ΔTFdi ≥ 30% during SBT had a sensitivity of 88% and a specificity of 71% (area under the curve [AUC] 0.79) for predicting extubation failure (reintubation or NIV use within 48 h), which surpassed the predictive ability of the rapid shallow breathing index (RSBI). On the other hand, it has been reported that an excursion < 10 mm before the start of SBT did not predict extubation failure (AUC 0.61), whereas an excursion < 10 mm 30 min after the start of SBT predicted extubation failure at a high rate. "[52]

- There have been attempts to enhance the predictive ability by considering the time component of excursion.

Materials and Methods

Ethical committee clearance certificate (BLDE (DU)/IEC/949/2023-24) was taken.

Study setting: INTENSIVE CARE UNIT OF Department of Anaesthesiology, B.L.D.E. (Deemed to be University) Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura.

Study period: From April 2023 to November 2024

Study design: Prospective observational Study

Sample size:

With anticipated Proportion of successful cases of NIV 60%, the study would require a sample size of 95 patients with 95% level of confidence and 10% absolute precision.

Formula used

$$n=\frac{z^2 p*q}{d^2}$$

Where Z= Z statistic at α level of significance

d 2 = Absolute error

P= Proportion rate

q= 100-p

Sampling technique: Simple Random sampling method

Inclusion criteria:

- Patients of either sex admitted to the intensive care unit with acute exacerbation of chronic obstructive pulmonary disease.

Exclusion criteria:

- Contraindications of Non-invasive Ventilation (unconscious uncooperative patients, shock, severe hemodynamic instability)
- Neuromuscular disease
- Chest wall deformities
- Diaphragmatic palsy

Methods of data collection:

Patients admitted to ICU with suspected Acute exacerbation of COPD, were assessed for enrollment in the study. Informed consent for participation in the study were obtained. Clinical assessment and Arterial blood gases (ABGs) were performed on admission and then hourly or earlier until stabilization or worsening clinical parameters.

U/S assessment of the diaphragm were performed before starting NIV by an investigator who were blinded to the study. Motility of the diaphragm were assessed using a Sonosite with a 7-13MHz linear probe to assess the diaphragm at the zone of apposition, between the 8th and 10th intercostal space in the mid-axillary or anterior axillary line, 0.5–2 cm below the costophrenic sinus. Measurements were performed with the patient in supine position at an average inclination of 45 degrees. Two parallel echogenic layers identified at a depth of 1.5–3 cm, the superficial one being parietal pleura and the deeper layer being peritoneum.

"The diaphragm is the less echogenic structure in between these two lines. This approach was utilized to assess diaphragmatic thickness (DT) and thickening with inspiration, in B-mode. In the subcostal area, between the mid-clavicular and anterior axillary lines, using liver or spleen

as acoustic windows, diaphragm was identified as a hyperechoic line (produced by the pleura tightly adherent to the muscle) that approaches the probe during inspiration. The thickness of the diaphragm was measured bilaterally at end inspiration and end-expiration. Measurements were performed three times on both sides of the diaphragm, and the best value were recorded. **"[46]**

"The change in diaphragmatic thickness (ΔTdi) during spontaneous breathing from functional residual capacity (FRC) to tidal volume (Vt) is called diaphragmatic thickness fraction (DTF). It was calculated using the formula: (end-inspiratory DT – end expiratory DT)/end expiratory DT × 100). Non-invasive mechanical ventilation (NIV) was started and set by an ICU physician who were blinded to the study. NIV were delivered as long as needed over next days and then discontinued based on fulfilment of weaning criteria and clinical judgment. Patients were monitored and NIV gradually discontinued when there was a general improvement in the patient's condition with RR < 25/minute, pH > 7.35, SpO2 > 90%, and FiO2 < 0.3. Switching to IMV was performed at any time by the attending physician who was blinded to diaphragmatic assessment of these patients according to these indications: respiratory arrest, persistent or severe respiratory distress (respiratory pauses or gasping for air, massive aspiration, or life-threatening hypoxemia), deterioration of pH, persistent respiratory acidosis despite NIV, worsening neurologic status (deteriorating GCS or agitation), intolerance to NIV, and hemodynamic instability (without response to fluids and vasoactive drugs or severe ventricular arrhythmias). **"[46]**

Statistical analysis:

Data was collected by using a structure proforma. Data entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of proportions. Quantitative data was expressed in terms of Mean and Standard deviation. Association between two qualitative variables was seen by using Chi square/ Fischer's exact test. Comparison of mean and SD between two groups was done by using unpaired t test to assess whether the mean difference between groups is significant or not. ROC curve analysis was carried out for prediction of intact uterus with respect to different variables.

Validity of diagnostic test was seen with calculation of sensitivity and specificity, PPV, NPV and diagnostic accuracy. A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

Results

Table 1: Distribution according to age group

		Frequency	Percent
Age group in years	40-50	18	18.9
	51-60	17	17.9
	>60	60	63.2
	Total	95	100.0

We included total 95 patients admitted to ICU with suspected acute exacerbation of COPD, were assessed for enrolment in the study. Majority of the patients were from above 60 years age group i.e. 63.2% followed by 18.9% from 40-50 years and 17.9% from 51-60 years age group. Mean age of the study population was 63.09±9.44 years.

Figure 1: Bar diagram showing Distribution according to age group

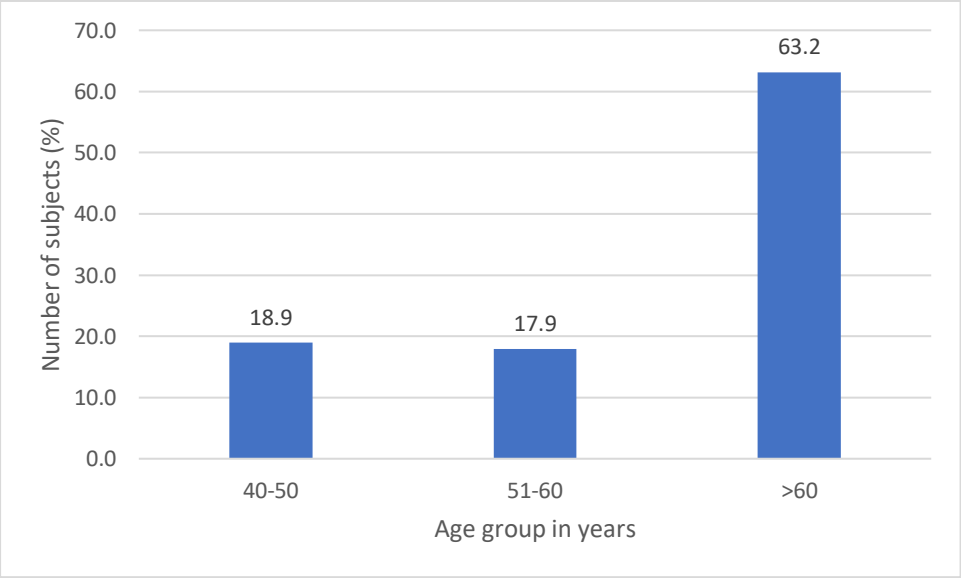


Table 2: Distribution according to gender

		Frequency	Percent
Gender	Male	60	63.2
	Female	35	36.8
	Total	95	100.0

63.2% were males and 36.8% were females in our study.

Figure 2: Pie diagram showing Distribution according to gender

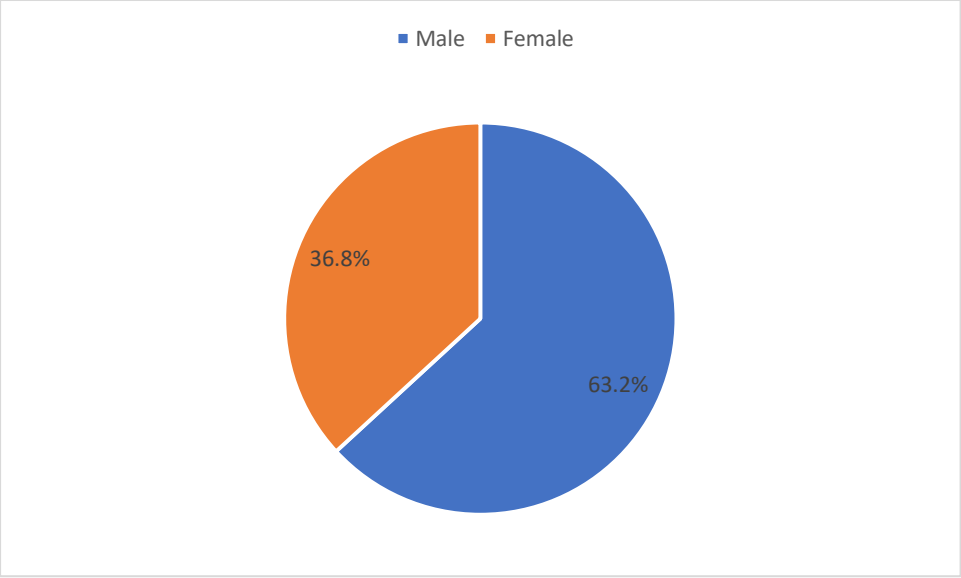


Table 3: Distribution according to comorbid conditions

		Frequency	Percent
Comorbid conditions	Hypertension	17	17.9
	Diabetes	17	17.9
	Asthma	26	27.4
	Stroke	0	0.0
	CKD	0	0.0

Distribution according to comorbid conditions showed that the prevalence of hypertension in our study was 17.9%, that of diabetes was 17.9% and asthma 27.4%.

Figure 3: Bar diagram showing Distribution according to comorbid conditions

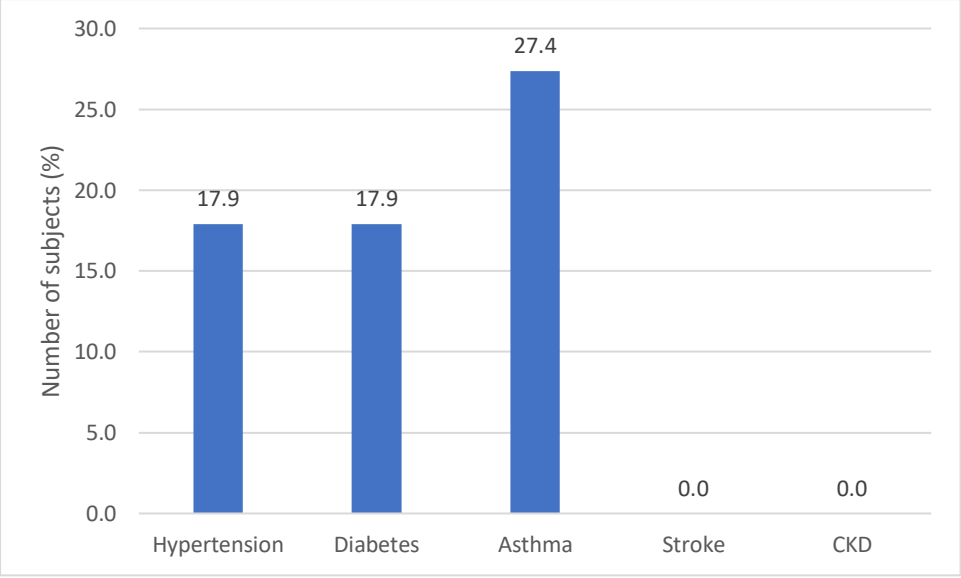


Table 4: Distribution according to use of invasive mechanical ventilation

		Frequency	Percent
Invasive mechanical ventilation	Yes	43	45.3
	No	52	54.7
	Total	95	100.0

Use of invasive mechanical ventilation was done in 43 patients accounting for 45.3%.

Figure 4: Pie diagram showing Distribution according to use of invasive mechanical ventilation

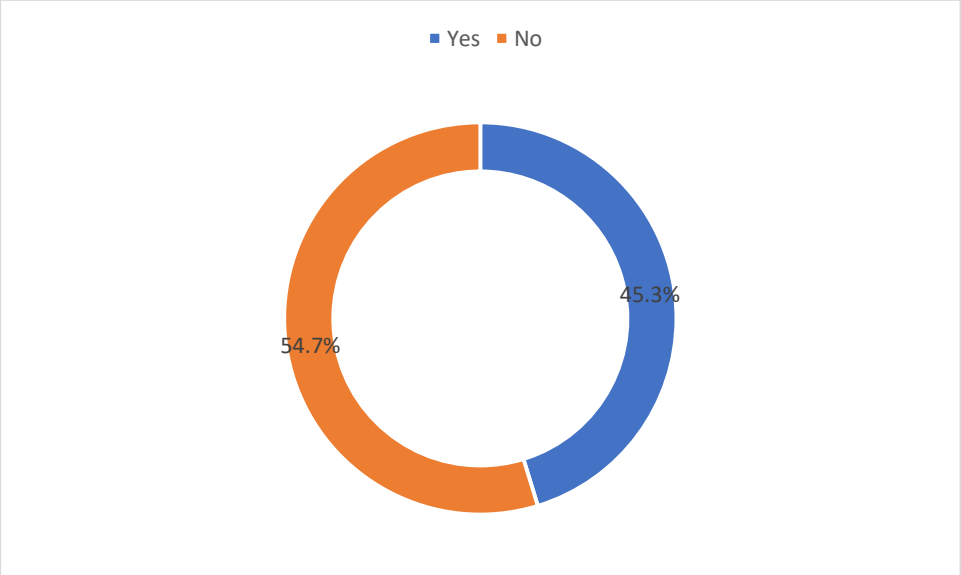


Table 5: Distribution according to age group and use of Invasive mechanical ventilation

		Invasive mechanical ventilation				Total	P
		Yes		No			
		Number	Percent	Number	Percent		
Age group in years	40-50	0	0.0	18	34.6	18	0.0001, Highly significant
	51-60	9	20.9	8	15.4	17	
	>60	34	79.1	26	50.0	60	
	Total	43	100.0	52	100.0	95	

Distribution according to age group and use of Invasive mechanical ventilation showed that out of 43 cases that were put on IMV, majority i.e. 79.1% were from above 60 years age group followed by 20.9% from 51-60 years. Out of 52 cases that were not put on IMV, majority i.e. 50% were from above 60 years age group followed by 34.6% from 40-50 years age group and 15.4% from 51-60 years. We observed statistically significant association between IMV and age group in our study ($p<0.05$).

Figure 5: Bar diagram showing Distribution according to age group and use of Invasive mechanical ventilation

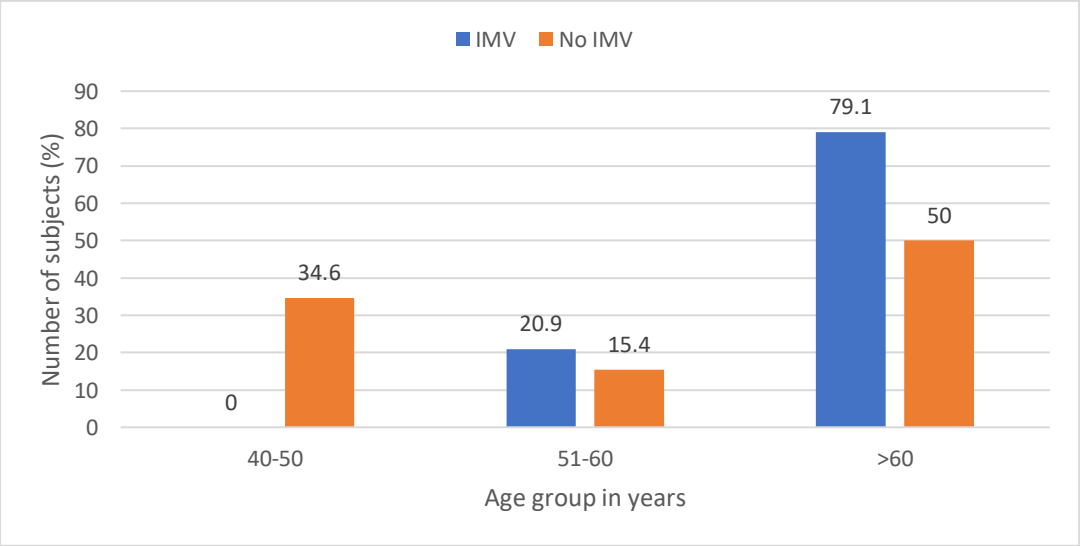


Table 6: Distribution according to gender and use of Invasive mechanical ventilation

		Invasive mechanical ventilation				Total	P
		Yes		No			
		Number	Percent	Number	Percent		
Gender	Male	34	79.1	26	50.0	60	0.003, Highly significant
	Female	9	20.9	26	50.0	35	
	Total	43	100.0	52	100.0	95	

Distribution according to gender and use of Invasive mechanical ventilation showed that out of 43 cases that were put on IMV, majority i.e. 79.1% were males and 20.9% were females. Out of 52 cases that were not put on IMV, 50% each were males and females. We observed statistically significant association between IMV and gender in our study ($p<0.05$).

Figure 6: Bar diagram showing Distribution according to gender and use of Invasive mechanical ventilation

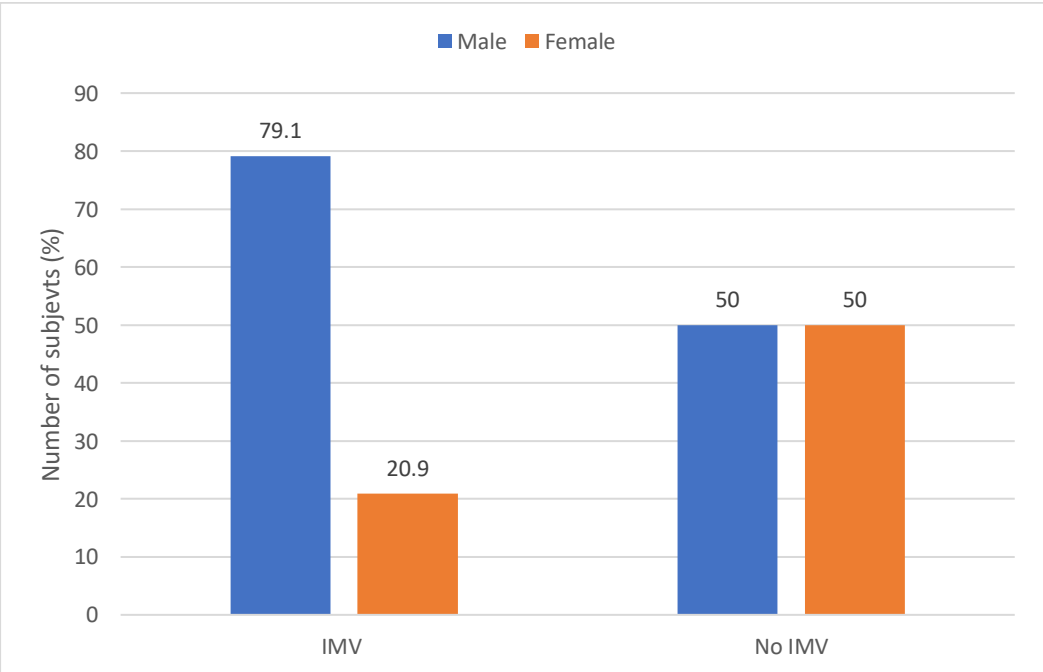


Table 7: Descriptive statistics of the variables

ABG analysis	Mean	Std. Deviation	Std. Error	Range	Minimum	Maximum
Age	63.09	9.44	0.97	33.0	45.0	78.0
PH On admission	7.26	0.16	0.02	0.5	7.0	7.5
PH During NIV	7.28	0.14	0.01	0.5	7.0	7.5
PaCO2 On admission (mmHg)	64.30	38.32	3.93	136.1	24.7	160.8
PaCO2 During NIV (mmHg)	57.16	38.73	3.97	142.0	23.0	165.0
PaO2 On admission(mmHg)	124.70	82.45	8.46	203.1	40.9	244.0
PaO2 During NIV (mmHg)	108.76	58.72	6.02	187.3	40.0	227.3
HCO3 On admission (mEq/L)	25.39	7.83	0.80	23.6	16.0	39.6
HCO3 During NIV (mEq/L)	23.94	7.06	0.72	23.0	16.3	39.3
SaO2 On admission(mmHg)	86.12	12.21	1.25	43.1	56.0	99.1
SaO2 During NIV (mmHg)	89.30	12.07	1.24	39.0	60.0	99.0

Mean Age was 63.09±9.44 years. Mean PH On admission was 7.26±0.16. Mean PH During NIV was 7.28±0.14 Mean PaCO2 On admission was 64.30±38.32 mmHg. Mean PaCO2 During NIV was 57.16±38.73 mmHg. Mean PaO2 On admission was 124.70±82.45 mmHg. Mean PaO2 During NIV was 108.76±58.72 mmHg. Mean HCO3 On admission was 25.39±7.83 mEq/L. Mean HCO3 During NIV was 23.94±7.06 mEq/L. Mean SaO2 On admission was 86.12±12.21 mmHg. Mean SaO2 During NIV was 89.30±12.07 mmHg.

Table 8: Descriptive statistics of the variables

	Mean	Std. Deviation	Std. Error	Range	Minimum	Maximum
On NIV, thickness of the diaphragm on the right-side during inspiration (mm)	3.95	2.21	0.23	6.9	1.9	8.8
On NIV, thickness of the diaphragm on the right-side during expiration(mm)	2.98	1.84	0.19	5.5	1.4	6.9
On NIV, thickness of the diaphragm on the left side during inspiration(mm)	4.52	1.97	0.20	5.8	2.4	8.2
On NIV, thickness of the diaphragm on the left side during expiration(mm)	3.37	1.43	0.15	4.7	1.8	6.5
On NIV, diaphragmatic thickness fraction right side(mm)	36.15	12.70	1.30	36.7	15.9	52.6
On NIV, diaphragmatic thickness fraction left side(mm)	33.60	14.39	1.48	43.9	13.8	57.7
Duration of NIV (days)	2.65	1.10	0.11	4	1	5
Duration of invasive ventilation (days)	3.33	4.20	0.43	14	0	14
Duration of ICU stay (days)	7.44	2.95	0.30	12	3	15
Duration of hospital stay (days)	8.36	2.63	0.27	11	5	16

Mean on NIV, thickness of the diaphragm on the right-side during inspiration was 3.95±2.21mm. Mean on NIV, thickness of the diaphragm on the right-side during expiration was 2.98±1.84mm. Mean on NIV, thickness of the diaphragm on the left side during inspiration was 4.52±1.97mm. Mean on NIV, thickness of the diaphragm on the left side during expiration was 3.37±1.43mm. Mean on NIV, diaphragmatic thickness fraction right side was 36.15±12.70 mm. Mean on NIV Diaphragmatic thickness fraction left side was 33.60±14.39 mm. Mean Duration of NIV was 2.65±1.10 days. Mean Duration of invasive ventilation was 3.33±4.20 days. Mean Duration of ICU stay was 7.44±2.95 days. Mean Duration of hospital stay was 8.36±2.63 days.

Figure 7: ROC curve analysis for prediction of need of invasive mechanical ventilation (IMV) based on diaphragm thickness fraction

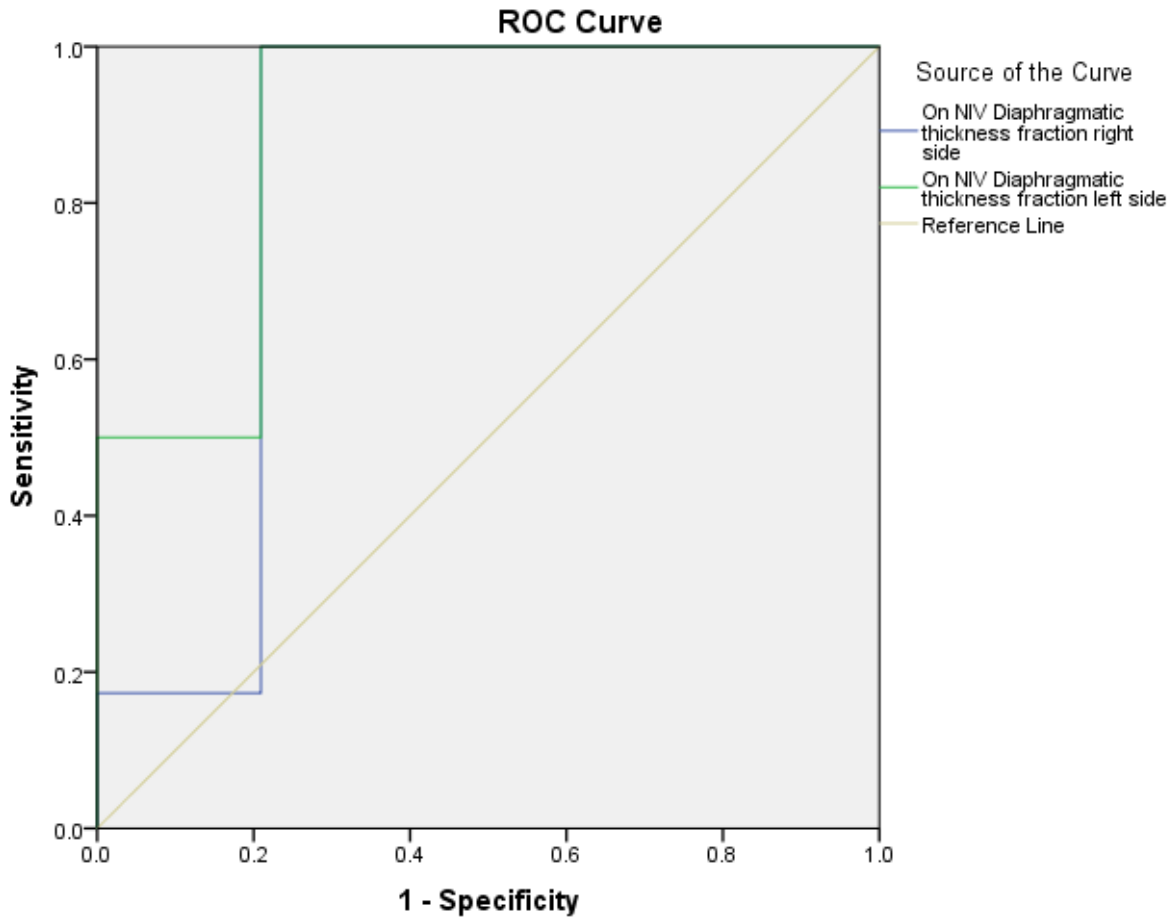


Table 9: Area Under the Curve for prediction of need of invasive mechanical ventilation (IMV) based on diaphragm thickness fraction

Area Under the Curve					
Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
On NIV, Diaphragmatic thickness fraction right side	0.827	0.053	.0001	0.724	0.930
On NIV, Diaphragmatic thickness fraction left side	0.895	0.035	.0001	0.828	0.963
a. Under the nonparametric assumption					
b. Null hypothesis: true area = 0.5					

ROC curve analysis for prediction of need of invasive mechanical ventilation (IMV) based on the diaphragm thickness fraction on the right-side showed the area under curve as 82.7% with 95% CI as 0.724 to 0.930 ($p<0.05$).

ROC curve analysis for prediction of need of invasive mechanical ventilation (IMV) based on the diaphragm thickness fraction on the left-side showed the area under curve as 89.5% with 95% CI as 0.828 to 0.963 ($p<0.05$).

Coordinates of the Curve			
Test Result Variable(s)	**Positive if Greater Than or Equal To[a]**	**Sensitivity**	**1 - Specificity**
On NIV, Diaphragmatic thickness fraction right side	14.9400	1.000	1.000
	17.9700	1.000	.791
	21.3600	1.000	.605
	25.9400	1.000	.419
	31.8850	**1.000**	**.209**
	34.9950	.827	.209
	35.5450	.654	.209
	41.5350	.500	.209
	48.6800	.327	.209
	51.1900	.173	.209
	52.5050	.173	.000
	53.6300	.000	.000
On NIV, Diaphragmatic thickness fraction left side	12.8400	1.000	1.000
	14.6100	1.000	.791
	16.6900	1.000	.605
	20.5350	1.000	.419
	28.2000	**1.000**	**.209**
	33.7700	.673	.209
	36.7450	.500	.209
	42.2550	.500	.000
	50.0300	.327	.000
	56.2600	.173	.000
	58.6900	.000	.000

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

On NIV, diaphragmatic thickness fraction on the right-side cut off 31.88% will give 100% sensitivity and 20.9% specificity for the need of IMV. On NIV, thickness of the diaphragm on the left-side cut off 28.2% will give 100% sensitivity and 20.9% specificity for the need of IMV.

It means below 31.88% of diaphragm thickness fraction there is requirement of IMV for right side. It means below 28.22% of diaphragm thickness fraction there is requirement of IMV for left side.

Table 10: Diaphragmatic thickness fraction and requirement of mechanical ventilation

		Invasive mechanical ventilation		Non-invasive ventilation		Total	P
		N	%	N	%		
Right side diaphragmatic thickness fraction	≤31.88	34	79.1	0	0.0	34	0.0001, Highly significant
	>31.88	9	20.9	52	100.0	61	
Total		43	100.0	52	100.0	95	
Left side diaphragmatic thickness fraction	≤28.2	34	79.1	0	0.0	34	0.0001, Highly significant
	>28.2	9	20.9	52	100.0	61	
Total		43	100.0	52	100.0	95	

With reference to ROC curve, we decided the right-side diaphragmatic thickness fraction cut-off as 31.88. We observed that 34 patients required IMV below the cutoff value whereas 9 patients also required IMV though they were above cut-off value. It showed that there was significant association between IMV and cut off value of diaphragmatic thickness fraction on right side ≤31.88 ($p<0.05$).

With reference to ROC curve, we decided the Left-side diaphragmatic thickness fraction cut-off as 28.2. We observed that 34 patients required IMV below the cutoff value whereas 9 patients also required IMV though they were above cut-off value. It showed that there was significant association between IMV and cut off value of diaphragmatic thickness fraction on Left side ≤28.2 ($p<0.05$).

Figure 8: Diaphragmatic thickness fraction and requirement of mechanical ventilation

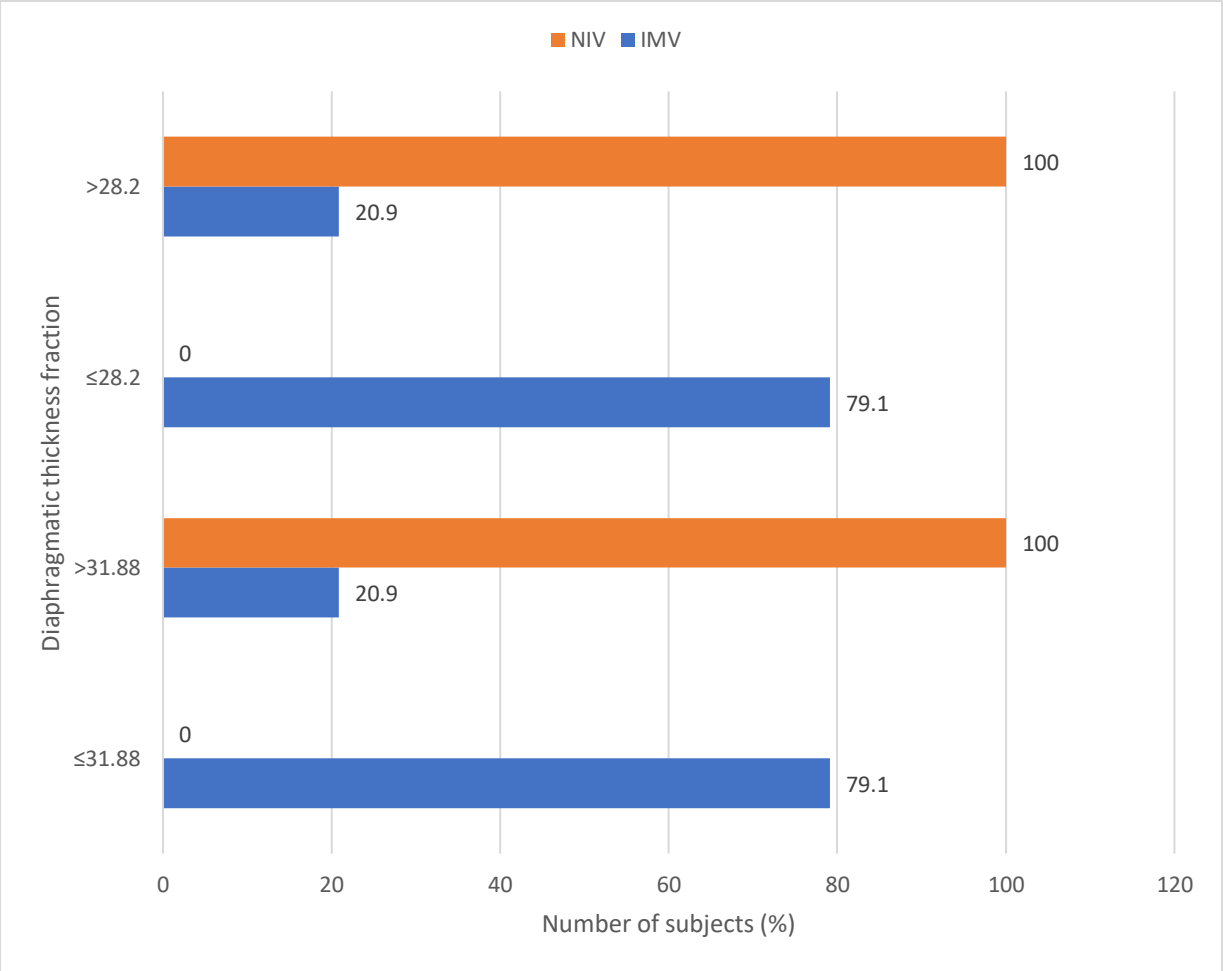


Table 11: Duration of invasive ventilation days in patients with respect to outcome

		N(43)	Mean	Std. Deviation	t	p	Inference
Duration of invasive ventilation (day)	Dead	34	8.56	2.11	8.01	0.0001	Highly significant
	Survived	9	2.78	0.83		(<0.01)	

Mean Duration of invasive ventilation is 3.33+/-4.2 in death and survived patients was 8.56±2.11 and 2.78±0.83 days respectively with statistically significant difference between two groups showing that duration of invasive ventilation days was significantly more in deaths in our study ($p<0.05$).

Figure 9: Bar diagram showing Duration of invasive ventilation days with respect to outcome

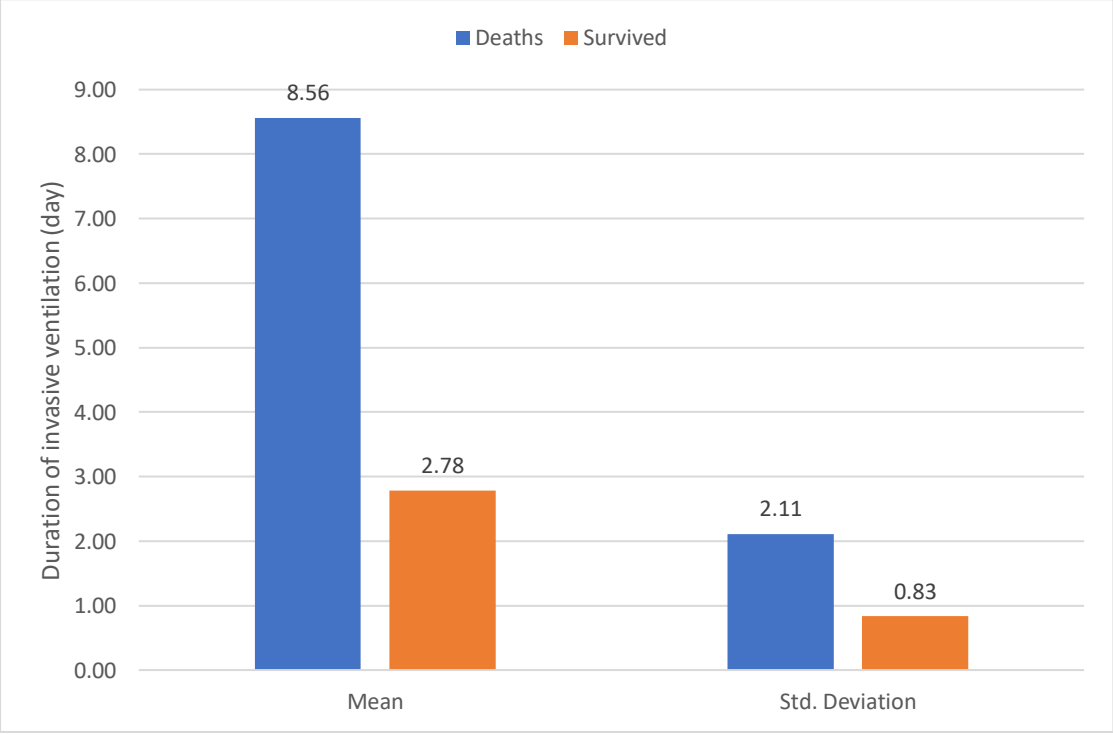


Table 12: Duration of ICU stay with respect to diaphragmatic impairment

		N	Mean	Std. Deviation	t	p	Inference
Duration of ICU stay	Diaphragmatic impairment	43	9.95	2.46	11.926	0.0001	Highly significant
	No Diaphragmatic impairment	52	5.37	1.17		(<0.01)	

Duration of ICU stay in patients with diaphragmatic impairment and in normal patients was 9.95±2.46 and 5.37±1.17 days respectively with statistically significant difference between two groups showing that duration of ICU stay was significantly more in diaphragmatic impairment patients in our study ($p<0.05$).

Figure 10: Bar diagram showing Duration of ICU stay with respect to diaphragmatic impairment

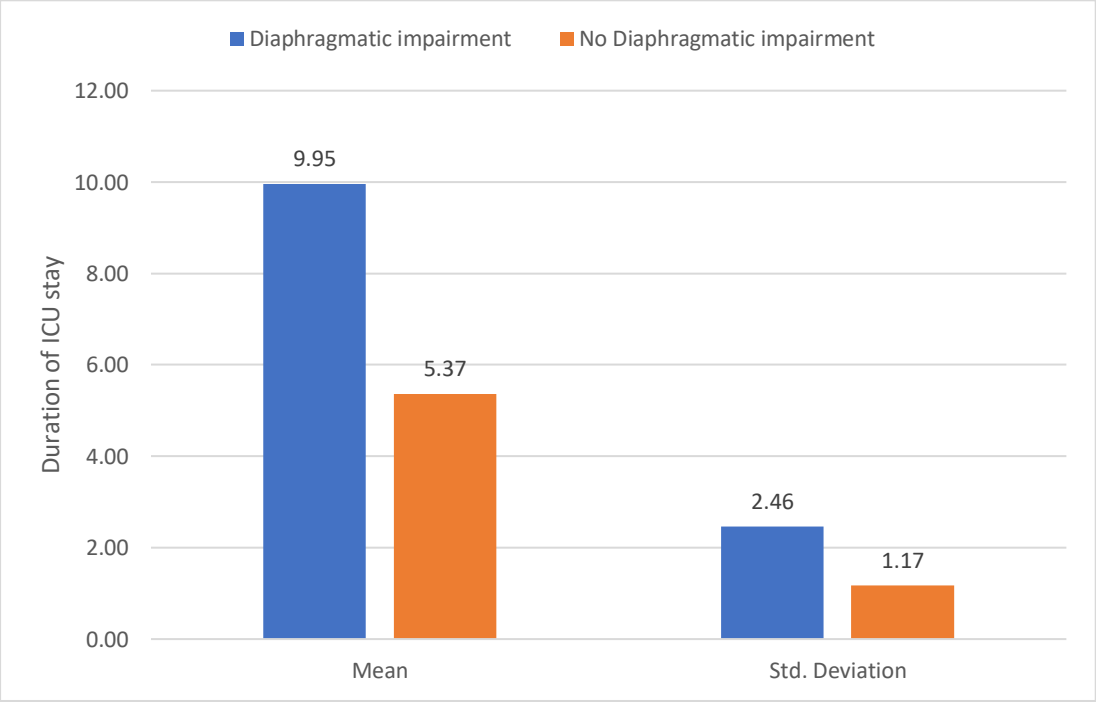
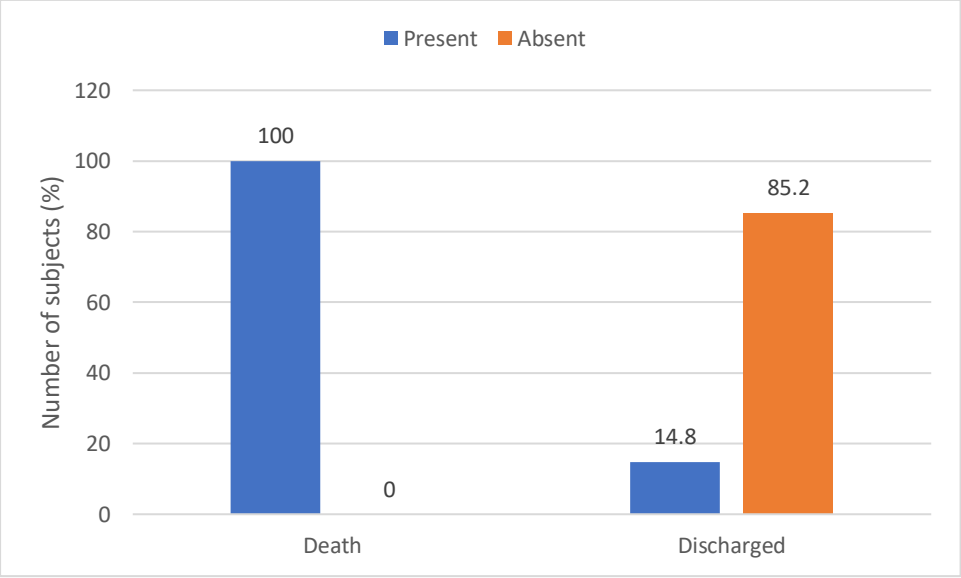


Table 13: Association of diaphragmatic impairment with outcome

		Death		Discharged		Total	P
		No	%	No	%		
Diaphragmatic impairment	Present	34	100.0	9	14.8	43	0.0001, Highly significant
	Absent	0	0.0	52	85.2	52	
Total		34	100.0	61	100.0	95	

Association of diaphragmatic impairment with outcome showed that all 34 deaths took place in patients with diaphragmatic impairment as against 9 cases of diaphragmatic impairment that were survived showing significant association between outcome and diaphragmatic impairment ($p<0.05$).

Figure 11: Bar diagram showing Association of diaphragmatic impairment with outcome



Discussion

In our study, the Diaphragm thickness fraction cut-off values of right and left side are 31.88% and 28.2% respectively (Tab10). Out of 43 patients that were put on IMV support, 34 patients were below and 9 patients were above the cut off values (Tab11). The majority of patients, who were below the cut off value are expired. It shows that the patients with severe diaphragmatic impairment are below the cut-off value.

In our study, the mean duration of IMV in expired (34) and survived patients (9) was 8.56+/-2.11 and 2.78+/-0.83 days respectively (Tab12). It shows that the people with severe diaphragmatic impairment required IMV for many days. The mean duration of ICU stay in patients with DI (43) and no DI (52) was 9.95+/-2.46 and 5.37+/-1.17 days respectively (Tab13). It shows that people with DI were in ICU for significantly more days compared to people with no DI. Out of the 43 patients who had DI and were put on IMV support, 34 patients were expired and 9 got discharged (Tab14).

Sociodemographic profile

We included total 95 patients admitted to ICU with suspected acute exacerbation of COPD, were assessed for enrolment in the study. Majority of the patients were from above 60 years age group i.e. 63.2% followed by 18.9% from 40-50 years and 17.9% from 51-60 years age group (Tab.1 &Fig.1). Mean age of the study population was 63.09±9.44 years. 63.2% were males and 36.8% were females in our study (Tab.2& Fig.2).

Sung Yoon Lim et al[54] included "14 patients with acute exacerbation of COPD were enrolled during the study period. Of these, 10 patients were included in this analysis; one patient was excluded because of the need for invasive mechanical ventilation after enrolment and three patients were excluded because of withdrawal of consent. All patients were male, and the mean age was 79.8 years.**"**[54]

Laz NI et al[57] in 2022 "conducted the study with the objective to evaluate the prevalence of diaphragmatic dysfunction (DD) during AECOPD, and its impact on NIV outcome. Mean age of the study population was 63.9 with the range of 45-85. Males were 73.2% and remaining 26.8% were females. **"**[57]

Suttapanit K. et al[60] "involved 60.2% males and remaining 39.8% females in their study. Mean age of the study population was 77 years with the range of 67 to 83 years. **"**[60]

Qu LL et al[62] in their study reported that "51.47% were males and 48.53% were females. The mean age of the study population was 64.74 ± 4.25 years. **"**[62]

The findings of the above-mentioned authors are approximately matching with our study findings.

Comorbid conditions

Distribution according to comorbid conditions showed that the prevalence of hypertension in our study was 17.9%, that of diabetes was 17.9% and asthma 27.4% (Tab.3 & Fig.3).

Qu LL et al[62] in their study reported that, "prevalence of hypertension was 57.35%, asthma-38.24% and diabetes was 32.35%. This prevalence was higher as compared to our study findings. **"**[62]

Invasive Mechanical Ventilation

Use of invasive mechanical ventilation was done in 43 patients accounting for 45.3% (Tab.4 & Fig.4).

Laz NI et al[57] reported that 36.6% required IMV.

Suttapanit K. et al[60] reported that, "two hundred and nineteen of the 314 patients received non-invasive respiratory support, 163 received NIV, 49 received HFNC, and seven received both NIV and HFNC. One hundred and thirteen patients (35.9%) required IMV; 67 (59.3%) required IMV within 6 h, and 88 (77.9%) within 24 h of ultrasound evaluation. "[60]

Age and gender wise Invasive mechanical ventilation

Distribution according to age group and use of Invasive mechanical ventilation showed that out of 43 cases that were put on IMV, majority i.e. 79.1% were from above 60 years age group followed by 20.9% from 51-60 years. Out of 52 cases that were not put on IMV, majority i.e. 50% were from above 60 years age group followed by 34.6% from 40-50 years age group and 15.4% from 51-60 years. We observed statistically significant association between IMV and age group in our study ($p<0.05$) (Tab.5 & Fig5). It shows that elderly patients are more prone for DI requiring invasive mechanical ventilation.

Distribution according to gender and use of Invasive mechanical ventilation showed that out of 43 cases that were put on IMV, majority i.e. 79.1% were males and 20.9% were females. Out of 52 cases that were not put on IMV, 50% each were males and females. We observed statistically significant association between IMV and gender in our study ($p<0.05$) (Tab.6 & Fig.6). It shows that majority of male patients are prone for DI compared to female patients.

Arterial Blood Gas analysis

Mean PH On admission was 7.26±0.16. Mean PH During NIV was 7.28±0.14 Mean PaCO2 On admission was 64.30±38.32 mmHg. Mean PaCO2 During NIV was 57.16±38.73 mmHg. Mean PaO2 On admission was 124.70±82.45 mmHg. Mean PaO2 During NIV was 108.76±58.72 mmHg. Mean HCO3 On admission was 25.39±7.83 mEq/L. Mean HCO3 During NIV was 23.94±7.06 mEq/L. Mean SaO2 On admission was 86.12±12.21 mmHg. Mean SaO2 During NIV was 89.30±12.07 mmHg (Tab.7).

Qu LL et al[62] "the mean values of pH 7.32 ± 0.16, PaO2 (mmHg) 47.69 ± 5.41, PaCO2 (mmHg) 62.21 ± 3.69 and PaO2/FiO2 98.35 ± 5.24. The findings of the above-mentioned authors are approximately matching with our study findings. **"**[62]

Prediction of need of invasive mechanical ventilation (IMV) based on the diaphragm thickness fraction

ROC curve analysis for prediction of need of invasive mechanical ventilation (IMV) based on the diaphragm thickness fraction on the right-side showed the area under curve as 82.7% with 95% CI as 0.724 to 0.930 ($p<0.05$). ROC curve analysis for prediction of need of invasive mechanical ventilation (IMV) based on the diaphragm thickness fraction on the left-side showed the area under curve as 89.5% with 95% CI as 0.828 to 0.963 ($p<0.05$) (Tab.9 & Fig.7).

On NIV, diaphragmatic thickness fraction on the right-side cut off 31.88% will give 100% sensitivity and 20.9% specificity for the need of IMV. On NIV, thickness of the diaphragm on the left-side cut off 28.2% will give 100% sensitivity and 20.9% specificity for the need of IMV (Tab.10).

It means diaphragm thickness fraction values of below 31.88% on right and 28.2% on left side there is requirement of IMV.

We observed that 43 patients required IMV. Out of 43patients, 34 patients were below the cut-off value and 9 patients were above the cut-off value. Majority of patients below the cut-off value were expired. Whereas, patients above the cut-off got weaned and survived. It showed that there was significant association between IMV and cut off values of diaphragmatic thickness fraction ($p<0.05$) (Tab.11 & Fig.8).

Amr Abdalla Elsayed et al[55] in their study showed "agreement (sensitivity and specificity) data after plotting receiver operating characteristics (ROC) curve for DTF to predict need for IMV after NIV failure in all patients. Cut-off value of DTF % (<29%) on the right side and <26% on the left side was associated with NIV failure with 96.67% sensitivity, 80- 82.22% specificity. **"**[55]

Qian et al[65] reviewed "ultrasound assessment of diaphragmatic dysfunction (DD) as a predictor of weaning outcome from MV. They concluded that both diaphragmatic excursion and DTF showed good diagnostic performance to predict weaning outcomes. They defined DD to be a predictor of weaning failure in critically ill patients. They showed DTF% cut-off values of successful and failed ventilation groups as 24.18+/-3.02 and 19.12+/-3.18. **"**[65]

Antenora et al[66] conducted "a study on the prevalence and clinical consequences of diaphragmatic dysfunction (DD) using USG in patients with AECOPD. They considered DTF < 20% as diaphragmatic impairment (DD). They reported that NIV failure was found to be strongly associated with DD ($p < 0.001$, $R2 = 0.27$). **"**[66]

In a similar study by **Kocyigit et al**[67] "on patients with AECOPD in the emergency department, DD (defined as DTF of <20% duri ng spontaneous breathing) had a high sensitivity of 84.6% (95% CI:54.6–98.1), specificity of 91.5% (95% CI:79.6–97.6), PPV 73.3% (95% CI:51.2–87.8), and NPV 95.6% (95% CI:85.7–98.7) in predicting NIV failure. **"**[67]

Marchioni et al[68] in their prospective observational study "investigated ultrasound-assessed diaphragmatic impairment as a predictor of outcome in AECOPD patients on NIV. Also, they investigated the correlation between US-assessed DD and the trans diaphragmatic pressure (Pdi) assessed using invasive sniff manoeuvre. They found that DTF < 20% demonstrated the same accuracy as Pdi sniff in identifying diaphragmatic dysfunction. They concluded that AECOPD patients admitted for NIV treatment have a high risk of NIV failure and mortality if they had DD as assessed by US. **"**[68]

Kheir M. et al[58] in 2023 "conducted the study with the objective to systematically review and compare ultrasonographic methods and their utility in predicting non-invasive ventilation (NIV) outcomes. Numerous studies have employed ultrasonography to assess functionality of

the diaphragm to assist in predicting outcomes for patients on NIV.[69-75] they reported that DTF of less than 20% was associated with NIV failure requiring invasive mechanical ventilation with a sensitivity of 80-84.6% and specificity 76.3-91.5%.**"**[58]

Barbariol et al[76] in "ICU patients admitted for acute respiratory failure. Diaphragmatic dysfunction was defined as a diaphragmatic excursion of less than 1.00 cm. Out of 47 patients, the patients without diaphragmatic dysfunction had about a 10% increase in NIV success than patients with diaphragmatic dysfunction, which was not statistically significant ($p = 0.54$). They also performed ROC analysis and noted that when using diaphragmatic excursion as a predictor of NIV response the area under the curve was 0.53; the best sensitivity (58.1%) and specificity (62.5%) was obtained with a diaphragmatic excursion cut-off of 1.37 cm. **"**[76]

The findings of the above-mentioned authors are approximately matching with our study findings.

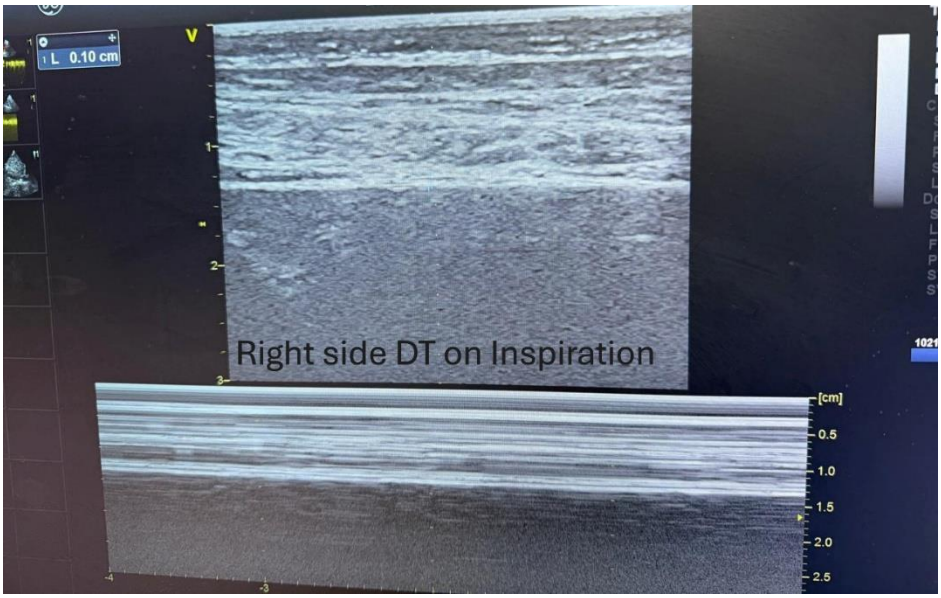


Image 8.Diaphragm thickness measurement during Inspiration on Right side

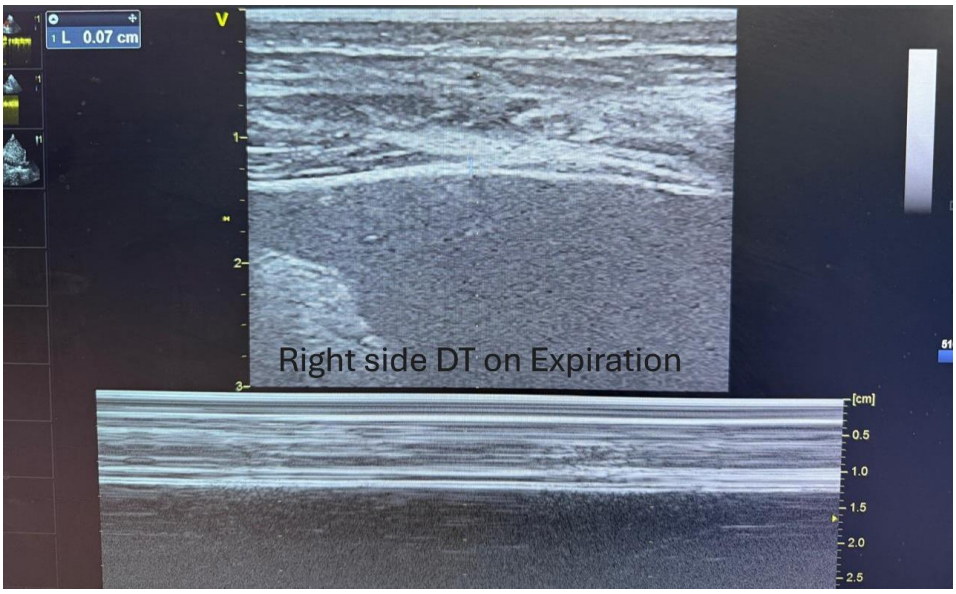


Image 9. Diaphragm thickness measurement during expiration on Right side

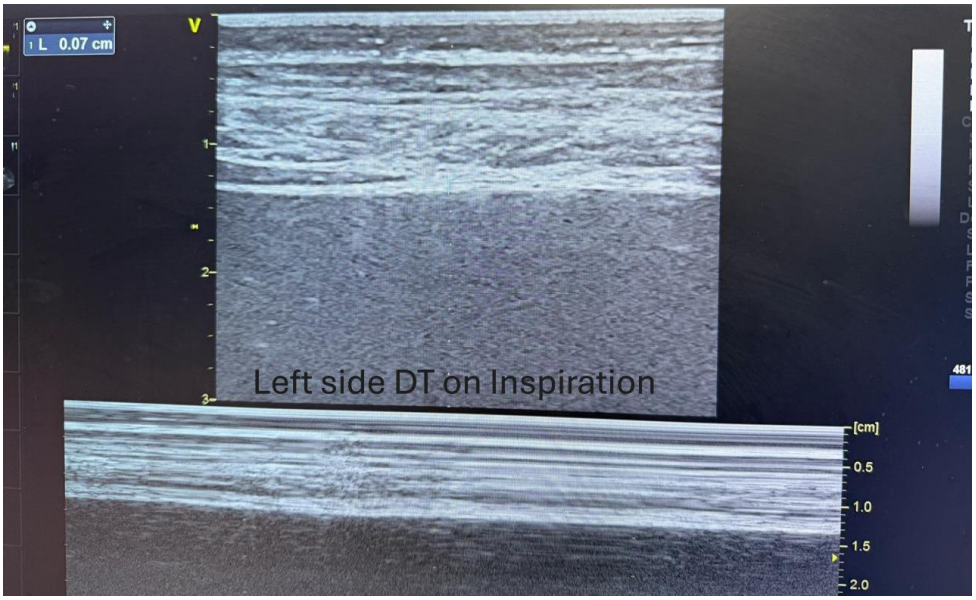


Image 10.Diaphragm thickness measurement during Inspiration on Left side

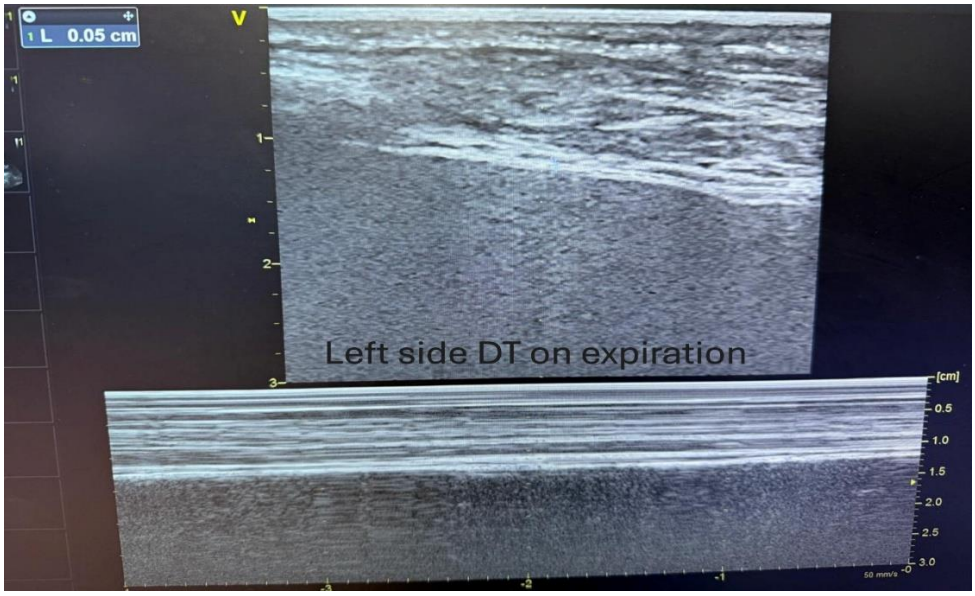


Image 11.Diaphragm thickness measurement during expiration on Left side

Impact of Diaphragmatic impairment on IMV days

We observed that, the mean duration for IMV days was 3.33+/-4.2. the mean duration of IMV in patients with DTF cut-off value below and above was 8.56+/-2.11 and 2.78+/-0.83 days (Tab.12 & Fig.9). It shows that patients with severe diaphragmatic impairment were put on IMV for more days compared to the patients with mild or moderate diaphragmatic impairment.

Amr Abdalla Elsayed et al[55] in his study showed that "patients with diaphragmatic impairement showed longer mechanical ventilatory days compared to patients with no diaphragmatic impairement. (14.25+/-2.8 vs 6.38+/-1.90 days). **"[55]**

Marchioni et al[68] in their prospective observational study showed that "patients with diaphragmatic dysfunction showed longer mechanical ventilatory days compared to patients with no diaphragmatic dysfunction. (16 vs 8 days)**. "[68]**

Antenora et al[66] "conducted a study on the prevalence and clinical consequences of diaphragmatic dysfunction (DD) using USG in patients with AECOPD. They found that patients with DD have prolonged mechanical ventilation (p = 0.023, R2 = 0.15). **"[66]**

The above-mentioned studies are approximately matching with our study.

Impact of Diaphragmatic impairement on ICU stay

We observed that, the mean duration of ICU stay in patients with DI and without DI were 9.95+/-2.46 and 5.37+/-1.17 days respectively. It shows that people with diaphragmatic impairement had significantly longer length of ICU stay ($p<0.05$) (Tab.13 & Fig.10).

Amr Abdalla Elsayed et al[55] in his study showed that, "patients with diaphragmatic impairement showed longer ICU stay compared to patients with no diaphragmatic impairement. (15.8+/-3.1 vs 10.98+/-2.67 days). **"[55]**

Marchioni et al[68] in their study showed that, "patients with diaphragmatic dysfunction showed longer ICU stay compared to patients with no diaphragmatic dysfunction. (17 vs 12 days). **"[68]**

Antenora et al[66] "conducted a study on the prevalence and clinical consequences of diaphragmatic dysfunction (DD) using USG in patients with AECOPD. They found that patients DD had longer ICU stay. ($p = 0.02$, $R2 = 0.13$). **"[66]**

The above-mentioned studies are approximately matching with our study.

Impact of Diaphragmatic impairement on the outcome

We observed that out of 43 patients that were put on IMV due to diaphragmatic impairement, 34 patients were expired and 9 patients got survived. We observed the death rate as 35.8% in our study. We observed statistically significant association between IMV and outcome in our study ($p<0.05$) (Tab.14 & Fig.11). It shows as the severity of DI increases; patients will have bad prognosis.

Amr Abdalla Elsayed et al[55] showed that, "patients with diaphragmatic impairment showed higher 28-day mortality rate compared to the patients with successful NIV. **"**[55]

Marchioni et al[68] showed that, "patients with diaphragmatic dysfunction showed higher mortality compared to patients with no diaphragmatic dysfunction. (10 vs 6). **"**[68]

The above-mentioned studies are approximately matching with our study.

Conclusion

From this prospective observational study, we concluded that USG guided assessment of Diaphragmatic thickness fraction is a good indicator in determining the diaphragmatic impairment and predicting the need for invasive mechanical ventilation in AECOPD patients with 100% sensitivity and 20.9% specificity. DI as assessed by DTF can be used as a prognostic factor for determining Invasive Mechanical Ventilatory days, ICU stay and Outcome of the patient.

Summary

The present prospective observational Study was conducted in INTENSIVE CARE UNIT OF Department of Anaesthesiology, B.L.D.E. (Deemed to be University) Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura. Patients admitted to ICU with suspected Acute exacerbation of COPD, were assessed for enrolment in the study. The objectives of our study is to assess the impact of ultrasound-assessed diaphragmatic impairment (DI) on predicting need for invasive mechanical ventilation (IMV) in patients treated by non-invasive ventilation (NIV) and to assess the impact of diaphragmatic impairement mechanical ventilatory days, ICU stay and outcome of the patients.

The results of our study are summarized as follows:

- We included total 95 patients admitted to ICU with suspected acute exacerbation of COPD, were assessed for enrolment in the study. Majority of the patients were from above 60 years age group i.e. 63.2% followed by 18.9% from 40-50 years and 17.9% from 51-60 years age group. Mean age of the study population was 63.09±9.44 years.
- 63.2% were males and 36.8% were females in our study.
- Distribution according to comorbid conditions showed that the prevalence of hypertension in our study was 17.9%, that of diabetes was 17.9% and asthma 27.4%.
- Use of invasive mechanical ventilation was done in 43 patients accounting for 45.3%.
- We observed the death rate as 35.8% in our study.
- Distribution according to age group and use of Invasive mechanical ventilation showed that out of 43 cases that were put on IMV, majority i.e. 79.1% were from above 60 years age group followed by 20.9% from 51-60 years. Out of 52 cases that were not put on IMV, majority i.e. 50% were from above 60 years age group followed by 34.6%

from 40-50 years age group and 15.4% from 51-60 years. We observed statistically significant association between IMV and age group in our study ($p<0.05$).

- Distribution according to gender and use of Invasive mechanical ventilation showed that out of 43 cases that were put on IMV, majority i.e. 79.1% were males and 20.9% were females. Out of 52 cases that were not put on IMV, 50% each were males and females. We observed statistically significant association between IMV and gender in our study ($p<0.05$).
- Distribution according to use of Invasive mechanical ventilation and outcome showed that out of 34 deaths, all 34 i.e. 100% were put on IMV whereas only 14.8% from the survived patients were put on IMV. We observed statistically significant association between IMV and outcome in our study ($p<0.05$).
- Mean Age was 63.09±9.44 years. Mean PH On admission was 7.26±0.16. Mean PH During NIV was 7.28±0.14 Mean PaCO2 On admission was 64.30±38.32. Mean PaCO2 During NIV was 57.16±38.73. Mean PaO2 On admission was 124.70±82.45. Mean PaO2 During NIV was 108.76±58.72. Mean HCO3 On admission was 25.39±7.83. Mean HCO3 During NIV was 23.94±7.06. Mean SaO2 On admission was 86.12±12.21. Mean SaO2 During NIV was 89.30±12.07.
- Mean on NIV thickness of the diaphragm on the right-side during inspiration and expiration was 3.95±2.21 mm and 2.98±1.84 mm respectively. Mean on NIV thickness of the diaphragm on the left side during inspiration and expiration was 4.52±1.97 mm and 3.37±1.43 mm respectively. Mean on NIV Diaphragmatic thickness fraction (%) on the right and left side was 36.15±12.70 and 33.60+/-14.39.
- ROC curve analysis of diaphragmatic thickness fraction on the right-side cut off 31.88% will give 100% sensitivity and 20.9% specificity for the need of IMV. On NIV,

thickness of the diaphragm on the left-side cut off 28.2% will give 100% sensitivity and 20.9% specificity for the need of IMV.

- It means below 31.88% of diaphragm thickness fraction there is requirement of IMV for right side. It means below 28.22% of diaphragm thickness fraction there is requirement of IMV for left side.
- Mean Duration of invasive ventilation was 3.33+/-4.2 days. Whereas, mean duration invasive ventilation in expired and survived patients was 8.56+/-2.11 and 2.78+/-0.83 days.
- Mean Duration of ICU stay was 7.44+/-2.95 days. Whereas, mean duration of ICU stay in patients with DI (43) and no DI (52) was 9.95+/-2.46 and 5.37+/-1.17 days.
- In patients with diaphragmatic impairement 34 patients expired and 9 patients got survived.

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ANNEXURE- 1
INFORMED CONSENT FORM

B.L.D.E(D.U) SHRI B.M PATIL MEDICAL COLLEGE HOSPITAL
AND RESEARCH CENTRE, VIJAYPURA- 586103, KARNATAKA

ULTRASONOGRAPHIC ASSESSMENT OF DIAPHRAGM TO PREDICT INVASIVE VENTILATION IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

I understand that I will be participating in the study. I understand that my ward's participation in this study will help in finding out. I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. If the data are used for publication in the medical literature or teaching purposes, no names will be used and other identifiers such as photographs and audio or videotapes. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission. I understand that I may ask more questions about the study at any time. **Dr. kola samatha reddy** is available to answer my questions or concerns. If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me and that a copy of this consent form will be given to me for careful reading. I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that **Dr. Kola Samatha Reddy** will terminate my participation in this study at any time after he/she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist if this is appropriate.

I understand that in the unlikely event of injury to me/my ward, resulting directly due to my participation in this study, such injury will be reported promptly, then medical treatment would be available to me, but no further compensation will be provided. I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to _____ the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

I confirm that **Dr. Kola Samatha Reddy** has explained to me the purpose of this research, the study procedure that I will undergo, and the possible discomforts and benefits that I may experience, in my own language. I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give consent to participate as subject in research project.

Date: **Dr. KOLA SAMATHA REDDY**

(Investigator)

Patient's signature

Witness to the above signature

PRINCIPAL INVESTIGATOR: DR. KOLA SAMATHA REDDY
Department of Anaesthesiology
BLDE (D.U)
Shri B.M Patil Medical College and Research Centre, Vijaypura-586103

PG GUIDE: DR. RENUKA HOLYACHI
Professor and HOD
Department of Anaesthesiology
BLDE (D.U)
Shri B.M Patil Medical College and Research Centre, Vijaypura-586103

ANNEXURE-2

B.L.D.E (DEEMED TO BE UNIVERSITY) ಶ್ರೀ ಬಿ.ಎಂ.ಪಟ್ಟೀಲ್ ಮೆಡಿಕಲ್ ಕಾಲೇಜು, ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ, ವಿಜಯಪುರ-586103

ಪ್ರಬಂಧ/ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಮಾಹಿತಿ ಪಡೆದ ಸಮ್ಮತಿ

ನಾನು, ಕೆಳಗಿನವರು_____ ಸಹಿಯಿಟ್ಟವರು, ಮಗ/ಮಗಳು/ಪತ್ನಿಯ _____ ವಯಸ್ಸು _____ವರ್ಷಗಳು, ಸಾಮಾನ್ಯವಾಗಿ ನಿವಾಸಿಸುವ ಸ್ಥಳದ ಹೆಸರು_____, ಇಲ್ಲಿ ಹೇಳಿದ್ದೇನೆ/ಘೋಷಿಸುತ್ತೇನೆ ಡಾಕ್ಟರ್ ಹೆಸರು_____ ಅವರು ಆಸ್ಪತ್ರೆ ಹೆಸರು_____ ಅವರು ನನ್ನನ್ನು ಪೂರ್ಣವಾಗಿ ಪರೀಕ್ಷಿಸಿದರು ದಿನಾಂಕದಲ್ಲಿ_____ ಸ್ಥಳ ಹೆಸರು_____ ಮತ್ತು ನನಗೆ ನನ್ನ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ ನಾನು ಒಂದು ರೋಗ (ಸ್ಥಿತಿ) ಅನುಭವಿಸುತ್ತಿದ್ದೇನೆ. ಮುಂದುವರಿದು ಡಾಕ್ಟರ್ ನನಗೆ ತಿಳಿಸಿದ್ದಾರೆ ಅವರು ಒಂದು ಪದ್ಧತಿ/ಸಂಶೋಧನೆ ನಡೆಸುತ್ತಿದ್ದಾರೆ ಶೀರ್ಷಿಕೆಯುಳ್ಳ_____ ಡಾಕ್ಟರ್_____ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ನನ್ನ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಯನ್ನು ಕೇಳಿದ್ದಾರೆ ಅಧ್ಯಯನದಲ್ಲಿ.

ಡಾಕ್ಟರ್ ನನಗೆ ಇದನ್ನು ಕೂಡಾ ತಿಳಿಸಿದ್ದಾರೆ ಈ ಕ್ರಮದ ನಡೆವಲ್ಲಿ ಪ್ರತಿಕೂಲ ಫಲಿತಾಂಶಗಳನ್ನು ಎದುರಿಸಬಹುದು. ಮೇಲೆ ಹೇಳಿದ ಪ್ರಕಟಣೆಗಳಲ್ಲಿ, ಅಧಿಕಾಂಶವು ಚಿಕಿತ್ಸಿಸಬಹುದಾದರೂ ಅದನ್ನು ನಿರೀಕ್ಷಿಸಲಾಗುತ್ತಿಲ್ಲ ಆದ್ದರಿಂದ ನನ್ನ ಸ್ಥಿತಿಯ ಹಿರಿದಾಗುವ ಅವಕಾಶವಿದೆ ಮತ್ತು ಅಪರೂಪದ ಸಂದರ್ಭಗಳಲ್ಲಿ ಅದು ಮರಣಕಾರಕವಾಗಿ ಪರಿಣಮಿಸಬಹುದು ಹೊಂದಿದ ರೋಗನಿರ್ಧಾರ ಮತ್ತು ಯಥಾಶಕ್ತಿ ಚಿಕಿತ್ಸೆ ಮಾಡಲು ಹೊಂದಿದರೂ. ಮುಂದುವರಿದು ಡಾಕ್ಟರ್ ನನಗೆ ತಿಳಿಸಿದ್ದಾರೆ ನನ್ನ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆ ಈ ಅಧ್ಯಯನದ ಫಲಿತಾಂಶಗಳ ಮೌಲ್ಯಮಾಪನದಲ್ಲಿ ಸಹಾಯಕವಾಗುತತ್ತದೆ ಇತರ ಸಮಾನ ಪ್ರಕರಣಗಳ ಚಿಕಿತ್ಸೆಗೆ ಉಪಯುಕ್ತ ಉಲ್ಲೇಖವಾಗಿದೆ, ಮತ್ತು ನಾನು ಅನುಭವಿಸುವ ರೋಗದಿಂದ ವಿಮುಕ್ತಿ ಅಥವಾ ಗುಣಮುಖಗೊಳ್ಳುವಲ್ಲಿ ನನಗೆ ಪ್ರಯೋಜನವಾಗಬಹುದು.

ಡಾಕ್ಟರ್ ನನಗೆ ಇದನ್ನು ಕೂಡಾ ತಿಳಿಸಿದ್ದಾರೆ ನನ್ನಿಂದ ನೀಡಿದ ಮಾಹಿತಿ, ಮಾಡಿದ ಪರಿಶೀಲನೆಗಳು / ಫೋಟೋಗ್ರಾಫ್‌ಗಳು / ವೀಡಿಯೋ ಗ್ರಾಫ್‌ಗಳು ನನ್ನ ಮೇಲೆ ತೆಗೆದುಕೊಳ್ಳಲಾಗುವ ಅನ್ವೇಷಕರು ರಹಸ್ಯವಾಗಿ ಇಡುವರು ಮತ್ತು ನಾನು ಅಥವಾ ನನಗೆ ಕಾನೂನು ದೃಷ್ಟಿಯಲ್ಲಿ ಸಂಬಂಧಿತrannu ಹೊರತುಪಡಿಸಿ ಇತರ ವ್ಯಕ್ತಿಯಿಂದ ಮೌಲ್ಯಮಾಪನ ಮಾಡಲಾಗುವುದಿಲ್ಲ. ಡಾಕ್ಟರ್ ನನಗೆ ತಿಳಿಸಿದ್ದಾರೆ ನನ್ನ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆ ಶುದ್ಧವಾಗಿ ಸ್ವೇಚ್ಛಾಯಿತ, ನನ್ನಿಂದ ನೀಡಿದ ಮಾಹಿತಿಯ ಆಧಾರದ ಮೇಲೆ, ಚಿಕಿತ್ಸೆ / ಅಧ್ಯಯನದ ಸಂಬಂಧದಲ್ಲಿ ರೋಗನಿರ್ಧಾರ, ಚಿಕಿತ್ಸೆಯ ವಿಧಾನ, ಚಿಕಿತ್ಸೆಯ ಫಲಿತಾಂಶ ಅಥವ ಆ ಭವಿಷ್ಯದ ಪ್ರವೃತ್ತಿಗಳು ಬಗ್ಗೆ ಯಾವುದೇ ಸ್ಪಷ್ಟತೆ ಕೇಳಬಹುದು. ಅದೇ ಸಮಯದಲ್ಲಿ ನನಗೆ ತಿಳಿಸಲಾಗಿದೆ ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಯನ್ನು ನಿಲ್ಲಿಸಬಹುದು ನಾನು

ಬಯಸಿದರೆ ಅಥವಾ ಅನ್ವೇಷಕರು ಅಧ್ಯಯನದಿಂದ ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನನ್ನನ್ನು ನಿಲ್ಲಿಸಬಹುದು.

ಪ್ರಬಂಧ ಅಥವಾ ಸಂಶೋಧನೆಯ ಸ್ವಭಾವ, ಮಾಡಿದ ರೋಗನಿರ್ಧಾರ ಮತ್ತು ಚಿಕಿತ್ಸೆಯ ವಿಧಾನವನ್ನು ಅರ್ಥಮಾಡಿಕೊಂಡು, ನಾನು ಕೆಳಗಿನ ಶ್ರೀ / ಶ್ರೀಮತಿ_____ ನನ್ನ ಪೂರ್ಣವಾದ ಪ್ರಜ್ಞೆಯ ಸ್ಥಿತಿಯಲ್ಲಿ ಹೇಳಿದ ಸಂಶೋಧನೆ / ಪ್ರಬಂಧದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಒಪ್ಪುತ್ತೇನೆ.

ರೋಗಿಯ ಸಹಿ ಡಾಕ್ಟರನ ಸಹಿ

ಸಾಕ್ಷಿಗಳು

1)

2)

ANNEXURE-3

SCHEME OF CASE TAKING

STUDY: ULTRASONOGRAPHIC ASSESSMENT OF DIAPHRAGM TO PREDICT INVASIVE VENTILATION IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

PROFORMA

Name: Age/ Sex:

I.P No: Date of admission :

Significant History:

Comorbidites:

Medication history:

Precipitating cause of acute exacerbation:

General Physical Examination:

Pallor Y/N Icterus Y/N Cyanosis Y/N Clubbing Y/N

Koilonychia Y/N Lymphadenopathy Y/N Edema Y/N Teeth Y/N

Dentures Y/N

Vital Parameters on admission:

Pulse (beats per minute): Blood Pressure:

Respiratory Rate: Temperature: spo2:

Requirement of supplemental oxygen (mask or nasal cannula):yes/no

Systemic Examination

1. CVS: 2.RS:

3. CNS 4. Per Abdomen:

INVESTIGATIONS:

Routine investigations:

Hemoglobin: TLC:

S. Urea: S. Creatinine:

RBS: Platelet count:

Urine Routine:

Chest Xray: ECG:

ECHO:

SL.NO.	STUDY PARAMETERS	
	DATE OF ADMISSION	
	DATE OF INITATION OF NIV	
	DATE OF INITATION OF INVASIVE VENTILATION	
	DATE OF DISCHARGE FROM ICU	
	OUTCOME OF PATIENT	

SL.NO	STUDY PARAMETERS	ON NIV	
		RIGHT	LEFT
	THICKNESS OF THE DIAPHRAGM AT END INSPIRATION(MM)		
	THICKNESS OF THE DIAPHRAGM AT END EXPIRATION(MM)		
	DIAPHRAGMATIC THICKNESS FRACTION		

ABG	ON THE DAY OF ADMISSION	DURING NIV
PH		
PaCO2(mmhg)		
PaO2(mmhg)		
HCO3(mEq/L)		
SaO2(%)		

ANNEXURE-4

BIO-DATA OF THE GUIDE

GUIDE NAME : DR RENUKA HOLYACHI
DATE OF BIRTH : 03/08/1980
EDUCATION : MBBS
KARNATAKA INSTITUTE OF MEDICAL SCIENCES
HUBLI, KARNATAKA
MD ANAESTHESIOLOGY
KARNATAKA INSTITUTE OF MEDICAL SCIENCES
HUBLI, KARNATAKA
DESIGNATION : PROFESSOR & HEAD, DEPARTMENT OF ANAESTHESIOLOGY
TEACHING EXPERIENCE : 14 YEARS
ADDRESS : PROFESSOR & HEAD
DEPARTMENT OF ANAESTHESIOLOGY

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INVESTIGATOR'S BIODATA

NAME : DR.KOLA SAMATHA REDDY
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ANNEXURE-5

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle-2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 949/2023-24 10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinized the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "ULTRASONOGRAPHIC ASSESSMENT OF DIAPHRAGM TO PREDICT INVASIVE VENTILATION IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.KOLA SAMATHA REDDY

NAME OF THE GUIDE: DR.RENUKA HOLYACHI., PROFESSOR,DEPT. OF ANAESTHESIOLOGY

Dr.Santoshkumar Jeevanagi
Chairperson
IEC-SBMPMC,
VIJAYAPURA

Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikawadi
Member Secretary
IEC-SBMPMC,
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

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ANNEXURE-6

MASTER CHART

Sr.No	Name of the patient	Age	aggrd	Gender (M/F)	Comorbid condition (P/A)	HTN	DM	Asthma	Stroke	CKD	IHD	PH On admission	PH During NTV	PaCO2 On admission	PaCO2 During NTV	PaO2 On admission	PaO2 During NTV	HCO3 On admission	HCO3 During NTV	SaO2 On admission	SaO2 During NTV	On NTV thickness of the diap...	On NTV thickness of the diap...	On NTV thickness of the diap...	On NTV thickness of the diap...	On NTV Diaphragmatic thickness	On NTV Diaphragmatic thickness	Duration of invasive ventilation (da...	IMV (yes/No)	Duration of ICU stay	Duration of hospital stay	Outcome /Death	Tracheostomy done 2
1	Dandappa	60	2	1		2	2	2	2	2	2	6.9804	7.428	160.8	24.7	208	104	37.4	26.9	98.7	97.6	3.1	2.4	3.2	2.6	23.16	23.07	3	1	12	12	1	1
2	mallikarju	65	3	1		2	2	2	2	2	2	7.27	7.067	42.1	83.2	222	40	18.9	23.4	99.1	60	3.2	2.1	3.9	2.8	52.38	39.28	3	4	1	10	13	2
3	mallappa	45	1	1		1	2	2	2	2	2	7.27	7.354	36.6	36.5	164.3	227.3	16	19.9	56	99	2.8	1.9	5.1	3.8	47.36	34.21	5	0	2	7	12	2
4	Bibi momin	78	3	2		2	1	2	2	2	2	7.032	7.277	65.9	48.3	64.1	90	22.3	24.3	94	96	8.8	6.5	8.2	5.2	35.38	57.69	4	0	2	7	10	2
5	avabai	50	1	2		2	2	1	2	2	2	7.139	6.994	93.1	165	65.1	92.7	30.9	39.3	89.5	94.5	2.9	1.9	2.4	1.8	52.63	33.33	4	0	2	7	9	2
6	parvati	65	3	2		2	2	2	2	2	2	7.377	7.318	77.2	69.3	43.2	64.3	39.6	34.7	84	90	8	6.9	7.4	6.5	16.94	13.84	2	12	1	14	14	1
7	subash	71	3	1		2	2	1	2	2	2	7.397	7.385	34	32	218	122	20	18	90	94	3.5	2.6	6.1	4.2	34.61	45.23	3	0	2	5	6	2
8	Dasarath singh	73	3	1		2	2	2	2	2	2	7.36	7.28	33.8	42.1	45.4	99	18.7	19.3	79	96.5	2.4	2	2.6	2.2	20	18	3	7	1	10	10	1
9	lavyava	57	2	2		1	1	1	2	2	2	7.154	7.35	84.5	36.1	244	60	29	20	97	70	3.6	2.4	4.8	3.1	50	54.83	2	0	2	3	5	2
10	revana siddappa	65	3	1		2	2	2	2	2	2	7.494	7.469	24.7	23	42.7	77.7	18.6	16.3	78.8	95	1.9	1.4	2.4	1.8	35.71	33.33	4	0	2	6	7	2
11	vittal	66	3	1		2	2	2	2	2	2	7.378	7.271	47.1	42.1	40.9	222	27	18.9	80.2	89	2.7	2.2	3	2.6	22.72	16.38	3	8	1	11	11	1
12	ravikumar	60	2	1		2	2	2	2	2	2	6.9804	7.428	160.8	41.7	208	104	37.4	26.9	98.7	97.6	3.1	2.4	3.2	2.6	23.16	23.07	2	10	1	14	16	1
13	durdappa	65	3	1		2	2	2	2	2	2	7.27	7.067	42.1	83.2	222	40	18.9	23.4	99.1	60	3.2	2.1	3.9	2.8	52.38	39.28	3	3	1	7	9	2
14	mahaveer	45	1	1		1	2	2	2	2	2	7.27	7.354	36.6	36.5	164.3	227.3	16	19.9	56	99	2.8	1.9	5.1	3.8	47.36	34.21	5	0	2	7	9	2
15	begamabi	78	3	2		2	1	2	2	2	2	7.032	7.277	65.9	48.3	64.1	90	22.3	24.3	94	96	8.8	6.5	8.2	5.2	35.38	57.69	2	0	2	4	6	2
16	shridevi	50	1	2		2	2	1	2	2	2	7.139	6.994	93.1	165	65.1	92.7	30.9	39.3	89.5	94.5	2.9	1.9	2.4	1.8	52.63	33.33	4	0	2	7	7	2
17	shantamma	65	3	2		2	2	2	2	2	2	7.377	7.318	77.2	69.3	43.2	64.3	39.6	34.7	84	90	8	6.9	7.4	6.5	16.94	13.84	1	10	1	13	13	1
18	shrimanth	71	3	1		2	2	1	2	2	2	7.397	7.385	34	32	218	122	20	18	90	94	3.5	2.6	6.1	4.2	34.61	45.23	3	0	2	5	6	2
19	komappa	73	3	1		2	2	2	2	2	2	7.36	7.28	33.8	42.1	45.4	99	18.7	19.3	79	96.5	2.4	2	2.6	2.2	20	18	2	8	1	10	10	1
20	chandravva	57	2	2		1	1	1	2	2	2	7.154	7.35	84.5	36.1	244	60	29	20	97	70	3.6	2.4	4.8	3.1	50	54.83	2	0	2	4	5	2
21	irappa	65	3	1		2	2	2	2	2	2	7.494	7.469	24.7	23	42.7	77.7	18.6	16.3	78.8	95	1.9	1.4	2.4	1.8	35.71	33.33	3	0	2	5	7	2
22	raju.kallur	66	3	1		2	2	2	2	2	2	7.378	7.271	47.1	42.1	40.9	222	27	18.9	80.2	89	2.7	2.2	3	2.6	22.72	16.38	1	7	1	8	8	1
23	chanbasappa	60	2	1		2	2	2	2	2	2	6.9804	7.428	160.8	41.7	208	104	37.4	26.9	98.7	97.6	3.1	2.4	3.2	2.6	23.16	23.07	2	9	1	12	12	1
24	nijappa	65	3	1		2	2	2	2	2	2	7.27	7.067	42.1	83.2	222	40	18.9	23.4	99.1	60	3.2	2.1	3.9	2.8	52.38	39.28	3	3	1	8	9	2
25	vinod	45	1	1		1	2	2	2	2	2	7.27	7.354	36.6	36.5	164.3	227.3	16	19.9	56	99	2.8	1.9	5.1	3.8	47.36	34.21	5	0	2	7	8	2
26	sushila bai	78	3	2		2	1	2	2	2	2	7.032	7.277	65.9	48.3	64.1	90	22.3	24.3	94	96	8.8	6.5	8.2	5.2	35.38	57.69	2	0	2	4	6	2
27	roopa	50	1	2		2	2	1	2	2	2	7.139	6.994	93.1	165	65.1	92.7	30.9	39.3	89.5	94.5	2.9	1.9	2.4	1.8	52.63	33.33	3	0	2	5	7	2
28	laxmi	65	3	2		2	2	2	2	2	2	7.377	7.318	77.2	69.3	43.2	64.3	39.6	34.7	84	90	8	6.9	7.4	6.5	16.94	13.84	1	9	1	10	10	1
29	hanamanth	71	3	1		2	2	1	2	2	2	7.397	7.385	34	32	218	122	20	18	90	94	3.5	2.6	6.1	4.2	34.61	45.23	3	0	2	5	7	2
30	darmu.umalu	73	3	1		2	2	2	2	2	2	7.36	7.28	33.8	42.1	45.4	99	18.7	19.3	79	96.5	2.4	2	2.6	2.2	20	18	2	8	1	11	11	1
31	lalita	57	2	2		1	1	1	2	2	2	7.154	7.35	84.5	36.1	244	60	29	20	97	70	3.6	2.4	4.8	3.1	50	54.83	3	0	2	5	6	2
32	shantappa	65	3	1		2	2	2	2	2	2	7.494	7.469	24.7	23	42.7	77.7	18.6	16.3	78.8	95	1.9	1.4	2.4	1.8	35.71	33.33	3	0	2	4	5	2

32	shamappa	65	3	1		2	2	2	2	2	2	7.494	7.469	24.7	23	42.7	77.7	18.6	16.3	78.8	95	1.9	1.4	2.4	1.8	35.71	33.33	3	0	2	4	5	2
33	namadeva	66	3	1		2	2	2	2	2	2	7.378	7.271	47.1	42.1	40.9	222	27	18.9	80.2	89	2.7	2.2	3	2.6	22.72	15.38	1	9	1	10	10	1
34	ambadas	60	2	1		2	2	2	2	2	2	6.984	7.428	160.8	41.7	208	104	37.4	26.9	98.7	97.6	3.1	2.4	3.2	2.6	29.16	23.07	2	7	1	9	9	1
35	rajuchavan	65	3	1		2	2	2	2	2	2	7.27	7.067	42.1	83.2	222	40	18.9	23.4	99.1	60	3.2	2.1	3.9	2.8	52.38	39.28	3	2	1	6	8	2
36	hanmanth	45	1	1		1	2	2	2	2	2	7.27	7.354	36.6	36.5	164.3	227.3	16	19.9	56	99	2.8	1.9	5.1	3.8	47.36	34.21	5	0	2	7	8	2
37	kashibai	78	3	2		2	1	2	2	2	2	7.032	7.217	65.9	48.3	64.1	90	22.3	24.3	94	96	8.8	6.5	8.2	5.2	35.38	57.69	2	0	2	4	5	2
38	kalavathi	50	1	2		2	2	1	2	2	2	7.139	6.994	93.1	165	65.1	92.7	30.9	39.3	89.5	94.5	2.9	1.9	2.4	1.8	52.63	33.33	3	0	2	6	7	2
39	indirabai	65	3	2		2	2	2	2	2	2	7.377	7.318	77.2	69.3	43.2	64.3	39.6	34.7	84	90	8	6.9	7.4	6.5	15.94	13.84	1	12	1	14	14	1
40	shivayogi	71	3	1		2	2	1	2	2	2	7.397	7.385	34	32	218	122	20	18	90	94	3.5	2.6	6.1	4.2	34.61	45.23	3	0	2	5	6	2
41	prashant	73	3	1		2	2	2	2	2	2	7.36	7.28	33.8	42.1	45.4	99	18.7	19.3	79	96.5	2.4	2	2.6	2.2	20	18	2	5	1	7	7	1
42	rajamma	57	2	2		1	1	1	2	2	2	7.154	7.35	84.5	36.1	244	60	29	20	97	70	3.6	2.4	4.8	3.1	50	54.83	2	0	2	5	6	2
43	sadashiv	65	3	1		2	2	2	2	2	2	7.494	7.469	24.7	23	42.7	77.7	18.6	16.3	78.8	95	1.9	1.4	2.4	1.8	35.71	33.33	3	0	2	6	7	2
44	gurupad	66	3	1		2	2	2	2	2	2	7.378	7.271	47.1	42.1	40.9	222	27	18.9	80.2	89	2.7	2.2	3	2.6	22.72	15.38	1	11	1	12	12	1
45	ramanagouda	60	2	1		2	2	2	2	2	2	6.984	7.428	160.8	41.7	208	104	37.4	26.9	98.7	97.6	3.1	2.4	3.2	2.6	29.16	23.07	2	7	1	9	9	1
46	sangappa	65	3	1		2	2	2	2	2	2	7.27	7.067	42.1	83.2	222	40	18.9	23.4	99.1	60	3.2	2.1	3.9	2.8	52.38	39.28	3	2	1	7	9	2
47	lalsab	45	1	1		1	2	2	2	2	2	7.27	7.354	36.6	36.5	164.3	227.3	16	19.9	56	99	2.8	1.9	5.1	3.8	47.36	34.21	5	0	2	7	8	2
48	mehboobi	78	3	2		2	1	2	2	2	2	7.032	7.217	65.9	48.3	64.1	90	22.3	24.3	94	96	8.8	6.5	8.2	5.2	35.38	57.69	2	0	2	4	5	2
49	laxmibai	50	1	2		2	2	1	2	2	2	7.139	6.994	93.1	165	65.1	92.7	30.9	39.3	89.5	94.5	2.9	1.9	2.4	1.8	52.63	33.33	3	0	2	5	6	2
50	gayatri	65	3	2		2	2	2	2	2	2	7.377	7.318	77.2	69.3	43.2	64.3	39.6	34.7	84	90	8	6.9	7.4	6.5	15.94	13.84	1	11	1	12	12	1
51	basavaraj	71	3	1		2	2	1	2	2	2	7.397	7.385	34	32	218	122	20	18	90	94	3.5	2.6	6.1	4.2	34.61	45.23	3	0	2	5	7	2
52	gurappa	73	3	1		2	2	2	2	2	2	7.36	7.28	33.8	42.1	45.4	99	18.7	19.3	79	96.5	2.4	2	2.6	2.2	20	18	2	9	1	12	12	1
53	lakavva	57	2	2		1	1	1	2	2	2	7.154	7.35	84.5	36.1	244	60	29	20	97	70	3.6	2.4	4.8	3.1	50	54.83	4	0	2	7	8	2
54	kasappa	65	3	1		2	2	2	2	2	2	7.494	7.469	24.7	23	42.7	77.7	18.6	16.3	78.8	95	1.9	1.4	2.4	1.8	35.71	33.33	3	0	2	5	6	2
55	sidappa	66	3	1		2	2	2	2	2	2	7.378	7.271	47.1	42.1	40.9	222	27	18.9	80.2	89	2.7	2.2	3	2.6	22.72	15.38	3	9	1	12	12	1
56	bhimray	60	2	1		2	2	2	2	2	2	6.984	7.428	160.8	41.7	208	104	37.4	26.9	98.7	97.6	3.1	2.4	3.2	2.6	29.16	23.07	2	7	1	9	9	1
57	bhimappa	65	3	1		2	2	2	2	2	2	7.27	7.067	42.1	83.2	222	40	18.9	23.4	99.1	60	3.2	2.1	3.9	2.8	52.38	39.28	3	2	1	7	9	2
58	irappa	45	1	1		1	2	2	2	2	2	7.27	7.354	36.6	36.5	164.3	227.3	16	19.9	56	99	2.8	1.9	5.1	3.8	47.36	34.21	5	0	2	7	8	2
59	devamma	78	3	2		2	1	2	2	2	2	7.032	7.217	65.9	48.3	64.1	90	22.3	24.3	94	96	8.8	6.5	8.2	5.2	35.38	57.69	2	0	2	4	6	2
60	shalubai	50	1	2		2	2	1	2	2	2	7.139	6.994	93.1	165	65.1	92.7	30.9	39.3	89.5	94.5	2.9	1.9	2.4	1.8	52.63	33.33	3	0	2	4	6	2
61	madina	65	3	2		2	2	2	2	2	2	7.377	7.318	77.2	69.3	43.2	64.3	39.6	34.7	84	90	8	6.9	7.4	6.5	15.94	13.84	4	8	1	12	12	1
62	sidappa	71	3	1		2	2	1	2	2	2	7.397	7.385	34	32	218	122	20	18	90	94	3.5	2.6	6.1	4.2	34.61	45.23	3	0	2	6	6	2
63	shrishail	73	3	1		2	2	2	2	2	2	7.36	7.28	33.8	42.1	45.4	99	18.7	19.3	79	96.5	2.4	2	2.6	2.2	20	18	2	11	1	13	13	1
64	madina	57	2	2		1	1	1	2	2	2	7.154	7.35	84.5	36.1	244	60	29	20	97	70	3.6	2.4	4.8	3.1	50	54.83	2	0	2	4	5	2

66	basavarakj	66	3	1		2	2	2	2	2	2	7.378	7.271	47.1	42.1	40.9	222	27	18.9	80.2	89	2.7	2.2	3	2.6	22.72	15.38	1	4	1	5	5	1
67	shivanand	60	2	1		2	2	2	2	2	2	6.984	7.428	160.8	41.7	208	104	37.4	26.9	98.7	97.6	3.1	2.4	3.2	2.6	29.16	23.07	2	7	1	9	9	1
68	basanna	65	3	1		2	2	2	2	2	2	7.27	7.067	42.1	83.2	222	40	18.9	23.4	99.1	60	3.2	2.1	3.9	2.8	52.38	39.28	2	3	1	7	8	2
69	yallappa	45	1	1		1	2	2	2	2	2	7.27	7.354	36.6	36.5	164.3	227.3	16	19.9	56	99	2.8	1.9	5.1	3.8	47.36	34.21	5	0	2	7	8	2
70	gouravva	78	3	2		2	1	2	2	2	2	7.032	7.217	65.9	48.3	64.1	90	22.3	24.3	94	96	8.8	6.5	8.2	5.2	35.38	57.69	2	0	2	4	5	2
71	nagawwa	50	1	2		2	2	1	2	2	2	7.139	6.994	93.1	165	65.1	92.7	30.9	39.3	89.5	94.5	2.9	1.9	2.4	1.8	52.63	33.33	3	0	2	5	6	2
72	mahaboobi	65	3	2		2	2	2	2	2	2	7.377	7.318	77.2	69.3	43.2	64.3	39.6	34.7	84	90	8	6.9	7.4	6.5	15.94	13.84	1	14	1	15	15	1
73	bhirappa	71	3	1		2	2	1	2	2	2	7.397	7.385	34	32	218	122	20	18	90	94	3.5	2.6	6.1	4.2	34.61	45.23	3	0	2	5	6	2
74	rangnath	73	3	1		2	2	2	2	2	2	7.36	7.28	33.8	42.1	45.4	99	18.7	19.3	79	96.5	2.4	2	2.6	2.2	20	18	2	8	1	10	10	1
75	kamalbai	57	2	2		1	1	1	2	2	2	7.154	7.35	84.5	36.1	244	60	29	20	97	70	3.6	2.4	4.8	3.1	50	54.83	2	0	2	5	6	2
76	laxman	65	3	1		2	2	2	2	2	2	7.494	7.469	24.7	23	42.7	77.7	18.6	16.3	78.8	95	1.9	1.4	2.4	1.8	35.71	33.33	3	0	2	6	7	2
77	lalsab	66	3	1		2	2	2	2	2	2	7.378	7.271	47.1	42.1	40.9	222	27	18.9	80.2	89	2.7	2.2	3	2.6	22.72	15.38	1	9	1	10	10	1
78	hanmanthu	60	2	1		2	2	2	2	2	2	6.984	7.428	160.8	41.7	208	104	37.4	26.9	98.7	97.6	3.1	2.4	3.2	2.6	29.16	23.07	2	7	1	9	9	1
79	dundappa	65	3	1		2	2	2	2	2	2	7.27	7.067	42.1	83.2	222	40	18.9	23.4	99.1	60	3.2	2.1	3.9	2.8	52.38	39.28	3	4	1	9	10	2
80	babu rathod	45	1	1		1	2	2	2	2	2	7.27	7.354	36.6	36.5	164.3	227.3	16	19.9	56	99	2.8	1.9	5.1	3.8	47.36	34.21	5	0	2	7	8	2
81	raziya	78	3	2		2	1	2	2	2	2	7.032	7.217	65.9	48.3	64.1	90	22.3	24.3	94	96	8.8	6.5	8.2	5.2	35.38	57.69	2	0	2	4	5	2
82	shivalingamma	50	1	2		2	2	1	2	2	2	7.139	6.994	93.1	165	65.1	92.7	30.9	39.3	89.5	94.5	2.9	1.9	2.4	1.8	52.63	33.33	3	0	2	5	6	2
83	dundamma	65	3	2		2	2	2	2	2	2	7.377	7.318	77.2	69.3	43.2	64.3	39.6	34.7	84	90	8	6.9	7.4	6.5	15.94	13.84	1	8	1	9	9	1
84	mallappa	71	3	1		2	2	1	2	2	2	7.397	7.385	34	32	218	122	20	18	90	94	3.5	2.6	6.1	4.2	34.61	45.23	3	0	2	4	5	2
85	rukmanna	73	3	1		2	2	2	2	2	2	7.36	7.28	33.8	42.1	45.4	99	18.7	19.3	79	96.5	2.4	2	2.6	2.2	20	18	2	11	1	13	13	1
86	itabai	57	2	2		1	1	1	2	2	2	7.154	7.35	84.5	36.1	244	60	29	20	97	70	3.6	2.4	4.8	3.1	50	54.83	2	0	2	5	6	2
87	ramu	65	3	1		2	2	2	2	2	2	7.494	7.469	24.7	23	42.7	77.7	18.6	16.3	78.8	95	1.9	1.4	2.4	1.8	35.71	33.33	3	0	2	5	6	2
88	basanna	66	3	1		2	2	2	2	2	2	7.378	7.271	47.1	42.1	40.9	222	27	18.9	80.2	89	2.7	2.2	3	2.6	22.72	15.38	1	7	1	8	8	1
89	laxman	60	2	1		2	2	2	2	2	2	6.984	7.428	160.8	41.7	208	104	37.4	26.9	98.7	97.6	3.1	2.4	3.2	2.6	29.16	23.07	2	7	1	9	9	1
90	appasab	65	3	1		2	2	2	2	2	2	7.27	7.067	42.1	83.2	222	40	18.9	23.4	99.1	60	3.2	2.1	3.9	2.8	52.38	39.28	3	2	1	7	8	2
91	bhimray	45	1	1		1	2	2	2	2	2	7.27	7.354	36.6	36.5	164.3	227.3	16	19.9	56	99	2.8	1.9	5.1	3.8	47.36	34.21	5	0	2	8	10	2
92	bhagirathi	78	3	2		2	1	2	2	2	2	7.032	7.217	65.9	48.3	64.1	90	22.3	24.3	94	96	8.8	6.5	8.2	5.2	35.38	57.69	2	0	2	5	6	2
93	jainabi	50	1	2		2	2	1	2	2	2	7.139	6.994	93.1	165	65.1	92.7	30.9	39.3	89.5	94.5	2.9	1.9	2.4	1.8	52.63	33.33	3	0	2	6	7	2
94	sushilabai	65	3	2		2	2	2	2	2	2	7.377	7.318	77.2	69.3	43.2	64.3	39.6	34.7	84	90	8	6.9	7.4	6.5	15.94	13.84	1	6	1	7	7	1
95	ayyapagouda	71	3	1		2	2	1	2	2	2	7.397	7.385	34	32	218	122	20	18	90	94	3.5	2.6	6.1	4.2	34.61	45.23	3	0	2	6	7	2

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