

**THE CORRELATION OF AIRWAY
OBSTRUCTION AND EMPHYSEMA ON HIGH
RESOLUTION COMPUTED TOMOGRAPHY
(HRCT) THORAX WITH SPIROMETRY IN
SEVERE CHRONIC OBSTRUCTIVE PULMONARY
DISEASE (COPD)**

DR. SYAHIDA BT SH OTHMAN

**DISSERTATION SUBMITTED IN PARTIAL
FULFILMENT OF THE REQUIREMENT FOR
MASTER OF MEDICINE (RADIOLOGY)**



UNIVERSITI SAINS MALAYSIA

2022

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LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

ATS	American Thoracic Society
BMI	Body Mass Index
CT	Computed Tomography
COPD	Chronic Obstructive Pulmonary Disease
DLCO	Diffusion Lung Capacity for Carbon Monoxide
ED	External Diameter
FEV1	Forced Expiratory Volume in one second
FVC	Forced Vital Capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
LA	Lumen Area
LD	Lumen diameter
LFT	Lung Function Test
LVRS	Lung Volume Reduction Surgery
mm	Millimetre
NETT	National Emphysema Treatment Trial
PACS	Picture Archiving and Communication System
PEFR	Peak Expiratory Flow Rate
RIS	Radiology Information System
RV	Residual Volume
TA	Total Airway Area
TLC	Total Lung Capacity
WA	Airway Wall Area
WT	Wall Thickness

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ABSTRAK

Latar belakang: Penyakit paru-paru obstruktif kronik (COPD) ialah penyakit yang kompleks melibatkan komponen paru-paru dan luar paru-paru. Komponen paru-paru adalah disebabkan oleh keterbatasan aliran udara kerana kerosakan pada parenkima paru-paru (emfisema) dan saluran udara yang hanya boleh diterbalikkan secara separa dan selalunya progresif. Walaupun spirometry adalah piawaian terbaik untuk mendiagnosis dan menilai COPD, tetapi masih belum menyeluruh dalam menilai kerumitan penyakit ini. Keupayaan tomografi berkomputer beresolusi tinggi (HRCT) dalam menentukan struktur paru-paru yang terlibat samada saluran udara ataupun parenkima dan juga mengukur tahap kerosakan. Oleh yang demikian, kajian ini dijalankan untuk menilai parameter dalam HRCT pesakit COPD yang serius dan menghubungkaitkan dengan parameter spirometri.

Metod: Kajian retrospektif keratan lintang dijalankan di Hospital Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia ke atas 34 pesakit yang telah didiagnosis dengan penyakit COPD yang serius dan menjalani ujian spirometry dan HRCT paru-paru. Keputusan imej HRCT telah dinilai untuk kelainan saluran udara and emfisema pada bahagian atas, tengah dan bawah paru-paru. “Pearson Correlation Coefficient” telah digunakan untuk menentukan korelasi di antara FEV_1 dengan saluran udara dan skor emfisema.

Keputusan: Kebanyakan pesakit mengalami kesukaran bernafas iaitu 25 (73.5%) pesakit dan majoriti pesakit adalah perokok, 31 (91.2%) pesakit. Keputusan spirometry menunjukkan purata FEV₁% yang diramalkan ialah 42.2 dengan sisihan piawai 6.84. Tiada korelasi antara parameter saluran pernafasan dan pegredan skor emfisema dengan FEV₁%. Lobus yang paling teruk dengan emfisema ialah lobus atas dan kebanyakannya adalah jenis Centriacinar. Kebanyakan pesakit mengalami kesukaran bernafas iaitu 25 (73.5%) pesakit dan majoriti pesakit adalah perokok, 31 (91.2%) pesakit. Keputusan spirometry menunjukkan purata FEV₁% yang diramalkan ialah 42.2 dengan sisihan piawai 6.84. Tiada korelasi antara parameter saluran pernafasan dan pengredan skor emfisema dengan FEV₁%. Lobus yang paling teruk emfisema ialah lobus atas dan kebanyakannya adalah jenis Centriacinar.

Kesimpulan: Kajian kami menunjukkan tiada korelasi di antara bacaan saluran udara dan FEV₁% ataupun skor emfisema dan FEV₁%. Perubahan tisu parenchymal seperti fibrosis dan bullae pada sesetengah pesakit juga menyumbang kepada tahap GOLD yang teruk selain daripada emfisema dan saluran udara tersumbat. Memandangkan pertambahan perokok di Malaysia, kemungkinan pertambahan pesakit COPD. Justeru itu, HRCT paru-paru membantu dalam menganalisa keadaan paru-paru sekiranya ada perubahan selain emfisema dan saluran udara tersumbat yang menyebabkan rawatan yang suboptimal.

Kata kunci: Ketebalan saluran udara, emfisema, HRCT paru-paru, COPD serius.

ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease which involves both pulmonary and extrapulmonary components. The pulmonary component is due to airflow limitation, due to parenchymal destruction (emphysema), and airway changes that is partially reversible and usually progressive. Although spirometry is the gold standard to diagnose and assess COPD, but it is unable to provide a comprehensive assessment of the complexity of the disease. On the other hand, high-resolution computed tomography (HRCT) is able to determine the structure involved either airway or parenchymal and extent of lung damage. Thus, this study was conducted to evaluate HRCT thorax parameters in severe COPD patients and correlate with spirometric parameters.

Methods: A retrospective cross-sectional study was conducted in Hospital Universiti Sains Malaysia (USM), Kota Bharu, Kelantan, Malaysia with 34 patients who were diagnosed with severe COPD and underwent spirometry and HRCT thorax. The HRCT images were evaluated for airway changes and emphysema at upper, middle and lower lung fields. Pearson Correlation Coefficient was used to determine correlation between FEV₁% predicted with airway parameters and emphysema scores.

Results: Majority of patients involved in this study comprise of smokers 91.2% (31 patients) and dyspnoea 73.5% (25 patients). Spirometry results showed the mean of FEV₁% predicted was 42.2 with standard deviation of 6.84. There was no correlation

between airway parameters and emphysema score grading with the FEV₁%. In our study, the worse affected area was the upper lobe and majority suffer from Centriacinar emphysema.

Conclusion: Our study showed no correlation between airway parameters with FEV₁% predicted or emphysema score grading. The other parenchymal changes such as fibrosis and bullae were also present in certain patients which was the likely cause of severe GOLD stage other than emphysema or airway obstruction. Thus, it is imperative that we should consider a combination of spirometry and HRCT Thorax, to diagnose as well as assess the extent of lung damage and provide timely and effective treatment for these patients.

Keywords: Airway wall thickness, emphysema, HRCT Thorax, severe COPD.

CHAPTER 1: BACKGROUND

1.1 Introduction

Chronic obstructive pulmonary disease (COPD) is a disease characterized by airflow limitation that is not fully reversible (Gerald and Bailey, 2002; COPD Global Initiative, 2020). The patients presented with chronic cough, breathlessness, and frequent exacerbation of bronchitis with history of exposure to risk factors especially tobacco smoke. The airflow limitation in COPD patients is caused by the airway obstruction (e.g: chronic bronchitis), parenchymal destruction (emphysema), or combination of both conditions. COPD is a major cause of chronic morbidity and mortality throughout the world, and is currently the fourth leading cause of death (Akinbami, Liu and American Lung Association, 2013). COPD is expected to increase and be the first non-oncologic cause of death by 2030 worldwide (Ministry of Health Malaysia, 2009).

Spirometry is a useful investigation tools in diagnosis and monitoring COPD patients as it can provide information in relation to the airway and parenchymal. It is used to stage the severity of COPD based on GOLD criteria or American Thoracic Society (ATS) criteria. However, there is limitation as the spirometry result can be influenced by several factors such as lack of patient's cooperation, declined n physiological lung function, especially in elderly and ill patients (He *et al.*, 2020). Thus, it unable to provide comprehensive assessment of the complexity of COPD itself.

High resolution computed tomography (HRCT) thorax is a radiological method in evaluating the lung parenchyma and airway changes in lung diseases. It is a well-established technique for assessing the presence, pattern and extend of emphysema

visually and quantitatively (Lynch *et al.*, 2015) as well as allow direct measurement of the luminal narrowing and airway wall thickening (Hackx, Bankier and Gevenois, 2012). HRCT is the best technique for diagnosing emphysema, with a sensitivity of 88%, a specificity of 90%, and an accuracy of 89% (Handa, 1996). Furthermore, the HRCT thorax is able to ascertain other abnormalities and detect both pulmonary (e.g., lung cancer, interstitial lung disease, pulmonary hypertension) and non-pulmonary (e.g., coronary artery calcification, heart failure, mediastinal disease).

The purpose of this study is to evaluate the HRCT thorax parameters in severe COPD patients and correlate them with spirometric parameters. In doing so, it will provide additional information to understand the disease heterogeneity and mechanism of COPD, which in turn, provide help for interventional pulmonologist in administering appropriate treatment for the patients.

1.2 Objective

1.2.1 General Objective

To correlate airway obstruction and emphysema on HRCT thorax with FEV₁ in severe COPD patients.

1.2.2 Specific Objectives

1. To correlate airway parameters on HRCT thorax with FEV₁ in severe COPD patients.
2. To correlate emphysema score on HRCT thorax with FEV₁ in severe COPD patients.
3. To describe the parenchymal changes in HRCT thorax other than emphysema among severe COPD patients.

1.3 Research Questions and Hypothesis

Question 1:

Does the morphology of the airway correlate with the severity of the FEV₁?

Hypothesis:

There is no correlation between morphology of the airway with FEV₁.

Question 2:

Is there a correlation between emphysematous changes in relation to the severity of FEV₁?

Hypothesis:

There is no correlation between emphysematous changes and severity of FEV₁.

Question 3:

What are other changes that are seen in lung parenchyma other than emphysema that causes severe airflow limitation and shortness of breath?

Alternative hypothesis:

Fibrosis, bullae, consolidation, pulmonary hypertension, mosaic attenuation, centrilobular nodules.

CHAPTER 2: LITERATURE REVIEW

2.1 Chronic Obstructive Pulmonary Disease (COPD)

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has defined COPD as a disease that is characterized by limitation of airflow that is not fully reversible (Gerald and Bailey, 2002; COPD Global Initiative, 2020). COPD patients are usually presented with chronic cough either productive or non-productive, breathlessness on exertion, and frequent exacerbation of bronchitis. There is also a history of exposure to risk factors, especially tobacco smoke, occupational dust, home cooking, and biomass fuel.

The chronic airflow limitation in COPD patients is caused by airway obstruction (e.g., chronic bronchitis), parenchymal destruction (emphysema), or a combination of both conditions. Different patients may experience different symptoms. Chronic bronchitis is a condition where there is an inflammation of the airway and remodelling. It is causing hyperplasia of the mucous glands with high secretion and inflammation of the bronchial wall. Thus, lead to worsening airflow obstruction by airway luminal narrowing, remodelling and alteration of the airway surface tension predispose to collapse. This cause increase risk of frequent exacerbation of the COPD. Obstructive bronchiolitis causes airflow limitation by narrowing and obliterating the airway lumen and actively constricting the airway. When COPD progresses, both large and small airways undergo reconfiguration, where the airway will thicken, , narrowing of the airway lumen and post-inflammatory airway fibrosis (Chen *et al.*, 2017).

Emphysema is described as an abnormal permanent enlargement of the airspaces distal to the terminal bronchioles, associated with destruction of the walls and without over fibrosis. Thus, causing reduction of the area available for the gas exchange. It also had concomitant loss of elastic recoil of the issue causing small airway collapsed and gas trapping. Emphysema is part of the spectrum of COPD which occur in the late stage of COPD. There are three main subtypes of emphysema based on the anatomical distribution of the destructive area. These subtypes are centrilobular emphysema, paraseptal emphysema and panlobular emphysema. Centrilobular emphysema affects respiratory bronchioles, with relative sparing of the distal alveoli. It is the most common encountered type and has strong association with smoking. Paraseptal emphysema occurs when the distal alveolar ducts and sacs are abnormal, while the entire proximal part of the acinus remains unaffected. It also associated with smoking and can cause subpleural bullae formation. Panlobular emphysema, occurs when enlarged acini are uniformly distributed from the respiratory bronchioles to the terminal alveoli. (Tuder and Petrache, 2012).

Chronic bronchitis vs. Emphysema

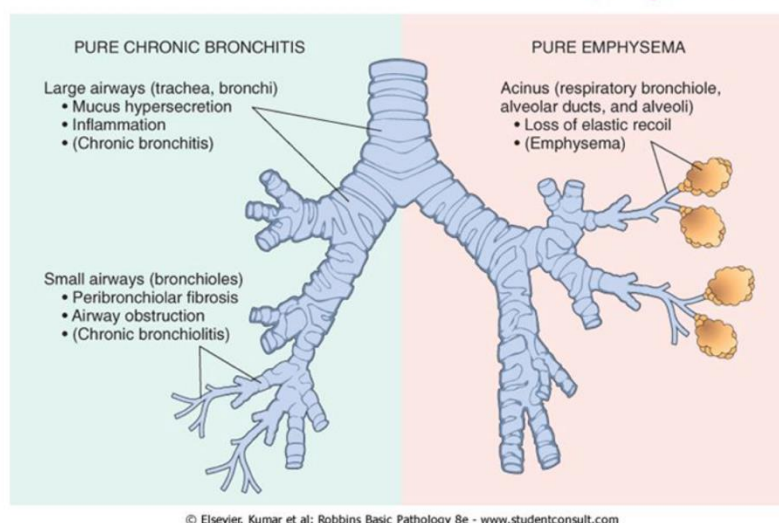


Figure 1: Chronic Bronchitis and Emphysema

2.2 Spirometry

Lung function tests (LFTs) are useful in the investigation and monitoring the patient with respiratory diseases. They give important information in relation to the large and small airways, pulmonary parenchyma as well as size and integrity of the pulmonary capillary bed. LFTs includes spirometry, lung volume measurements, and diffusion lung capacity assessment. The physiological indices to measure LFT are forced vital capacity (FVC), forced expiratory volume at one second (FEV_1), peak expiratory flow rate (PEFR), diffusion lung capacity for carbon monoxide (DLCO), residual volume (RV), and total lung capacity (TLC).

The spirometry is the part of the LFT and most frequently used as it is a non-invasive and easily available. It is done in a seated position, where patients would be asked to perform three consecutive violent full expiratory efforts, after a maximum inspiration. Their best effort was recorded (Figure 2). Spirometry indices are measured using the best out of three satisfactory performances. Although spirometry is widely used, it has certain limitations. Spirometry results can be influenced by several factors including lack of cooperation from patients, a decline in physiological lung function, especially in older adults, and inability to tolerate spirometry tests in certain critically ill patients (He *et al.*, 2020). In this study, spirometry was chosen because it is readily available in our center.

Spirometry measurements is used for diagnosis of COPD, including Forced Expiratory Volume in one second (FEV_1), Forced Vital Capacity (FVC), and FEV_1/FVC ratio. All these measurements will be evaluated with reference values based on patient's

age, height, sex, and race (Pellegrino *et al.*, 2005). Spirometry and calculation of FEV₁/FVC ratio allow for identification of obstructive or restrictive ventilatory defects.

FEV₁ is defined as the total volume of air a patient can exhale in one second during maximal effort. FEV₁ is decreased in both obstructive and restrictive lung diseases. The severity of most lung pathology is based on the percentage of predicted FEV₁ rather than the absolute value of FEV₁. FVC is a total volume of air, a patient can exhale for the total duration of the test during maximal effort. It indicates how quickly the lungs can be emptied. FEV₁/FVC ratio is the percentage of FVC expired in one second. The ratio FEV₁/FVC is between 70% and 80% in normal adults; a value of less than 70% indicates airflow limitation or obstructive ventilatory defect.

Reduction in FEV₁, FVC, and FEV₁ in relation to FVC ratio are characteristics of airway obstruction. The criteria for COPD diagnosis are, FEV₁/FVC ratio of less than 70%. There are four stages of classification based on severity of airflow limitation in COPD patients based on a decrease in FEV₁ using the GOLD criteria (Table 1), and five stages if it is based on the American Thoracic Society (ATS) criteria (Table 2). However, in our hospital, we employ the GOLD Criteria to assess and diagnose COPD patients.

For this study, we only included patients with severe and very severe COPD. For the mild to moderate stage of the disease, it is still under control with medication. However, for the severe and very severe cases, the disease has spiraled beyond control. As such, the use of HRCT will provide a better assessment of the lung condition and patient treatment and management.

GOLD Stage	COPD Severity	FEV ₁ /FVC Ratio	FEV ₁ Range
1	Mild	<0.70	≥ 80% of predicted
2	Moderate	<0.70	50% - 79% of predicted
3	Severe	<0.70	30% - 49% of predicted
4	Very severe	<0.70	<30% of predicted or <50% of normal with chronic respiratory failure present
COPD = chronic obstructive pulmonary disease; FEV ₁ = forced expiratory volume in 1 s; FVC = forced vital capacity; GOLD = Global initiative for Chronic Obstructive Lung Disease			

Table 1: Global Initiative for Chronic Obstructive Lung Disease (GOLD) Criteria

ATS Stage	COPD Severity	FEV ₁ /FVC Ratio	FEV ₁ Range
1	Mild	< 0.70	≥ 70% predicted
2	Moderate	< 0.70	60-69% predicted
3	Moderate to severe	< 0.70	50-59% predicted
4	Severe	< 0.70	35-49% predicted
5	Very severe	< 0.70	< 35% predicted
COPD = chronic obstructive pulmonary disease; FEV ₁ = forced expiratory volume in 1 s; FVC = forced vital capacity; ATS = American Thoracic Society			

Table 2: American Thoracic Society (ATS) Criteria.

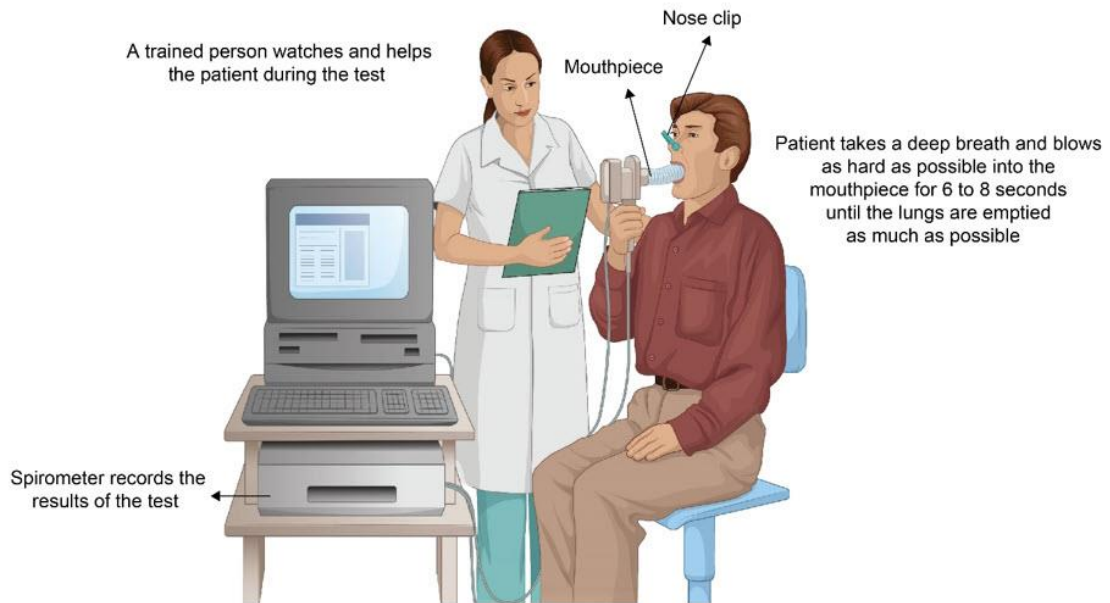


Figure 2: Spirometry procedure (Adapted from COPD foundation)

2.3 High Resolution Computed Tomography (HRCT)

HRCT is a radiological method which is particularly used in evaluating lung parenchyma changes. The use of HRCT allows clinicians to detect lung parenchyma changes. HRCT is a well-established technique for assessing the presence, pattern and extend of emphysema visually and quantitatively (Lynch *et al.*, 2015). HRCT is the best technique for diagnosing emphysema, with a sensitivity of 88%, a specificity of 90%, and an accuracy of 89% (Handa, 1996). HRCT also has the advantage to estimate the amount of air that is trapped and allow direct measurement of the luminal narrowing and wall thickening (Hackx, Bankier and Gevenois, 2012). Furthermore, the HRCT thorax is able to ascertain other abnormalities and detect both pulmonary (e.g.; lung cancer, interstitial lung disease, pulmonary hypertension) and non-pulmonary (e.g.; coronary artery

calcification, heart failure, mediastinal disease). Patients with similar GOLD stages may have different morphological appearances on CT (Lynch *et al.*, 2015).

Quantitative CT of the airways may be used independently or as a complement to emphysema quantification. Direct measurements of the large airways, including bronchial diameter and wall thickness. Measurements of the small airways are performed indirectly by quantifying air trapping on expiratory CT. Comparison of inspiratory and expiratory images in COPD patients allows the determination of the predominant pattern of abnormality: emphysema, airway obstruction, or mixed.

HRCT thorax can identify morphological features of COPD, including emphysema, bronchial wall thickening, expiratory air trapping, hyperinflation of the lung, and other associated features. Thus, HRCT has been used to differentiate between airway-predominant and emphysema-predominant. HRCT is able to provide vital insights into the underlying pathophysiological changes of COPD. According to the GOLD guidelines, CT is recommended when there is a need to look for differential diagnosis or when surgical options are being considered (COPD Global Initiative, 2020). The National Emphysema Treatment Trial (NETT) mentioned that, patients with advanced upper lobe emphysema and limited exercise ability improved after lung volume reduction surgery (LVRS) (Pizov, 2003). Currently, there is a minimally invasive technique using endobronchial therapeutic modalities for severe emphysema including coils, valves, sealant, and airway bypass. Thus, for a patient with severe heterogeneous emphysema, these treatments are beneficial in improving pulmonary physiology and functional capacity (Scirba *et al.*, 2010; Deslee *et al.*, 2014). CT can also identify bullous disease that is amenable to surgery and bullectomy to improve health status (Palla *et al.*, 2005).

Therefore, it is clear that patients with severe COPD require HRCT imaging to determine the appropriate candidate for these techniques.

Furthermore, HRCT is also able to identify the concomitant pulmonary pathology in COPD such as bronchiectasis, which is associated with worse airflow obstruction, increased exacerbations, higher airway, and systemic inflammation, and might lead to higher mortality (Patel *et al.*, 2004; Martínez-García *et al.*, 2011; Martínez-García *et al.*, 2013). Fibrosis is also commonly seen in COPD which leads to poor prognosis (Jankowich and Rounds, 2012). As we know, COPD is also an independent risk factor for lung cancer. Higher cancer rates are also associated with worsening airflow obstruction and emphysema (Kishi *et al.*, 2002; Zulueta *et al.*, 2012). Since these concomitant pathologies are common and frequently associated with poor outcomes, and require a change in management, it is important to use CT to detect them.

2.4 Conceptual framework

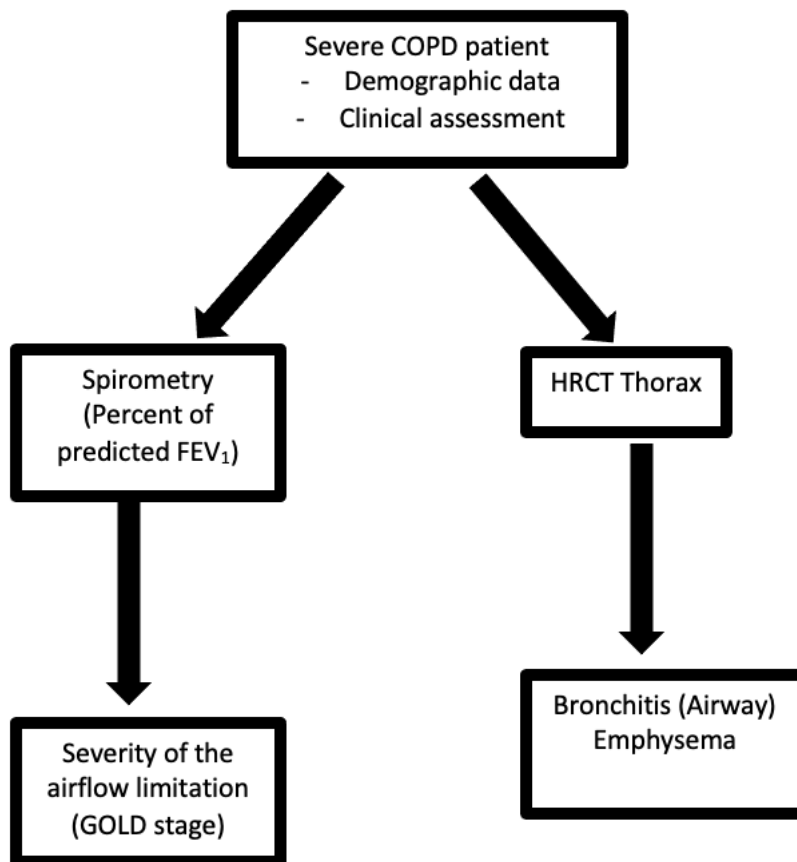


Figure 3: Conceptual framework

2.5 Problem Statement and Rationale of Study

Research and studies have shown that spirometry is the gold standard to diagnose and evaluate COPD because it is reproducible, systematic and objective in assessing airflow restriction. However, it does not reflect the complexity of the disease. Previous studies have shown that the degree of decline in spirometry parameters is inconsistent with pathological changes in certain patients. In addition, spirometry is dependent on factors such as patient's age, breathing effort, health status and etc. For further evaluation of the physiological sequence of COPD, other lung function test such as lung volumes and diffusion capacity should be performed as well. However, these tests are not available in our centre. In previous study by Muller mentioned that the emphysema involving the 30% of the lung parenchyma might not have airflow obstruction on conventional spirometry. Thus, HRCT Thorax is considered as a complementary tool to evaluate and describe the changes of the airways and lung parenchyma of COPD patients. Therefore, we are able to localize, quantify, ascertain the phenotypes and categorized patients for surgical or medical treatment.

CHAPTER 3: METHODOLOGY

3.1 Study Design

This was a retrospective, cross-sectional study which was conducted in HUSM, Kubang Kerian, Kelantan, Malaysia for patients who were diagnosed with COPD for a period of fourteen months from April 2021 to June 2022.

3.2 Sample Population

- i. Reference population – patients with confirmed COPD cases.
- ii. Source population – patients with confirmed COPD cases who underwent spirometry test in Hospital USM.
- iii. Target population – patients with confirmed COPD cases with severe COPD (GOLD 3 /4) who underwent HRCT thorax in Hospital USM.
- iv. Sampling frame – patients with confirmed COPD cases who underwent spirometry test and HRCT thorax in Hospital USM based on the inclusion and exclusion criteria.

3.3 Sample Size Calculation

Objective 1

The sample size is calculated using the Sample Size Calculator for Correlation Analysis v3.0 developed by Najib (2015). Using correlation coefficient (r) between airway parameters and FEV₁ (study by Hasegawa et al.2006) with 5% of type I error (α), 20% of type II error (β), the calculated sample size (n) is 30. By adding the anticipated dropout rate of 20%, the corrected sample size (n_c) is 34.

Sample Size Calculator for Correlation Analysis, (one sample)	
Instruction: enter data in green cells read output in gray cells	
Correlation coefficient, $r =$	0.5
Correlation H_0 , $r_0 =$	0
Type I error, $\alpha =$	5%
Type II error, $\beta =$	20%
Calculated sample size, $n =$	30
Anticipated dropout rate =	10%
Corrected sample size, $n_c =$	34

(NajibMY, 2015)

Objective 2

The sample size is calculated using the Size Calculator for Correlation Analysis v3.0 developed by Najib (2015). Using correlation coefficient (r) between emphysema scoring and FEV₁ (study by Vimala et al.2019) with 5% of type I error (α), 20% of type II error (β), the calculated sample size (n) is 21. By adding the anticipated dropout rate of 20%, the corrected sample size (n_c) is 24.

Sample Size Calculator for Correlation Analysis, (one sample)	
Instruction: enter data in green cells read output in gray cells	
Correlation coefficient, $r =$	0.589
Correlation H_0 , $r_0 =$	0
Type I error, $\alpha =$	5%
Type II error, $\beta =$	20%
Calculated sample size, $n =$	21
Anticipated dropout rate =	10%
Corrected sample size, $n_c =$	24

(NajibMY, 2015)

Based on sample size calculation for both objectives 1 and 2, the biggest number required for the sample size is 34.

Objective 3

This is a descriptive study, so no sample size calculation is needed.

3.4 Sampling Method

Convenient sampling method was used based on inclusion and exclusion criteria.

3.5 Inclusion Criteria

- i. All subjects are less than 80 years old.
- ii. Subjects with confirmed severe COPD on spirometry grade based on GOLD criteria.
- iii. Availability of the spirometry result within 6 months.

3.6 Exclusion Criteria

- i. Subjects with suboptimal images in PACS system.
- ii. Subjects with any current confirmed diagnosis of other respiratory conditions, including active pneumonia, thoracic deformity, interstitial lung disease, lung cancer, active tuberculosis, and history of thoracic surgery or other diseases that might affect pulmonary function.
- iii. Subjects with the co-existing cardiac disorder, e.g., congestive cardiac failure, cardiomyopathy, or coronary artery disease.

3.7 Research Tools

1. Image acquisition was obtained from Toshiba Aquilion Prime CT Scanner (160 slices, 80 detectors) and Siemen SOMATOM Definition AS + CT scanner (128 slices, 64 detectors). All scans were acquired after careful instruction, during a breath-hold after deep inspiration, and after deep expiration, while the patient lie in the supine position. No contrast media was used. Scan parameters were as follows: tube voltage, 140kVp; effective tube current, 100-110mAs; slice thickness, 1mm; pitch, 1.388 and 1.2 respectively. The acquired data were reconstructed using the B70f kernel for the lung window and B26f for the mediastinal window.
2. Radiology Information System (RIS) - Picture Archiving and Communication System (PACS) in Hospital USM (PACS Universal Viewer Version 6.0). All images are displayed on a monitor at the pulmonary window level setting (level, -550HU; width, 1600HU).
3. Socio-demographic data, clinical history, and spirometry results from the respiratory team and Viarad.
4. Data collection sheet.
5. IBM SPSS Statistics 27 (“IBM SPSS Statistics for Macintosh, “2020) was used for analysis.

3.8 Operational Definition

- i. Severe COPD is defined as FEV₁ of less than 50% of predicted.
- ii. Spirometry is a clinical tool used to diagnose or demonstrate airflow obstruction and assess COPD severity.
 - FEV₁ - the total volume of air a patient can exhale in the first second during maximal effort.

HRCT Thorax findings:

- i. Emphysema is characterized by permanent enlarged airspaces distal to the terminal bronchiole with the destruction of the alveolar wall. The CT appearance consists of focal areas or regions of low attenuation, usually without visible walls. It is further classified in terms of acinus areas that are predominantly affected; (Hall, 2008).
 - a. Centriacinar emphysema (proximal): Centrilobular area of decreased attenuation, without a visible wall, nonuniform distribution, and predominantly in upper zone (Figure 4).

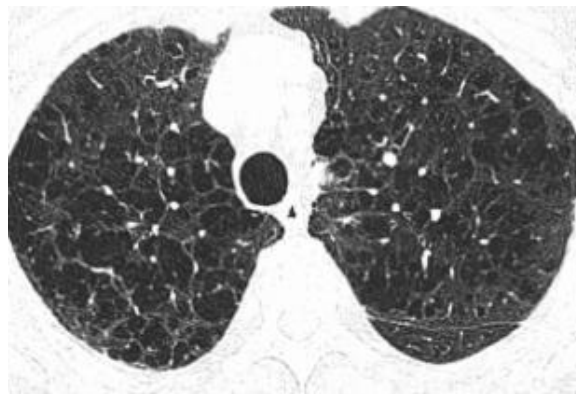


Figure 4: Centriacinar emphysema in axial view.

- b. Paraseptal emphysema (distal): Subpleural and peribronchovascular regions of low attenuation separated by intact interlobular septa (Figure 5).

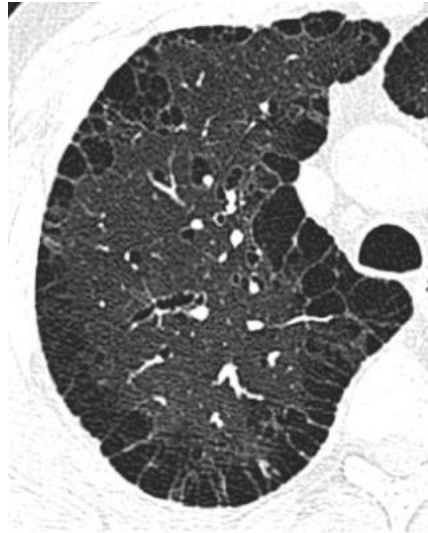


Figure 5: Paraseptal emphysema in axial view.

- c. Panacinar emphysema (whole): General decrease of the lung parenchyma with a decrease of blood vessels calibre in affected lungs (Figure 6).



Figure 6: Panacinar emphysema in axial view.

- ii. Bullae: A sharply demarcated area of emphysema measuring 1cm or larger in diameter and possessing a wall less than 1mm in thickness (Figure 7).

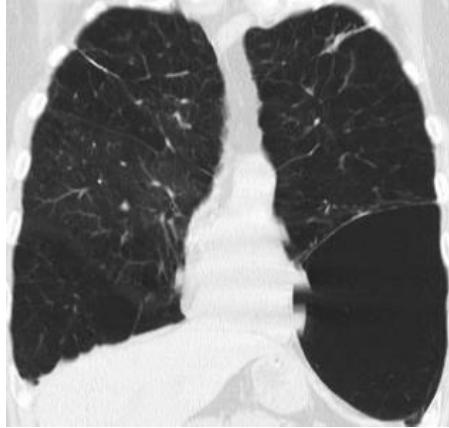


Figure 7: Large bullae at left lower lobe in coronal view.

- iii. Bronchial wall thickening: Thickening of the segmental and subsegmental airways (Figure 8).



Figure 8: Bronchial wall thickening in axial view (arrow).

- iv. Consolidation: Appears as a homogeneous increase in pulmonary parenchyma attenuation that obscures the margins of vessels and airway walls (Figure 9).

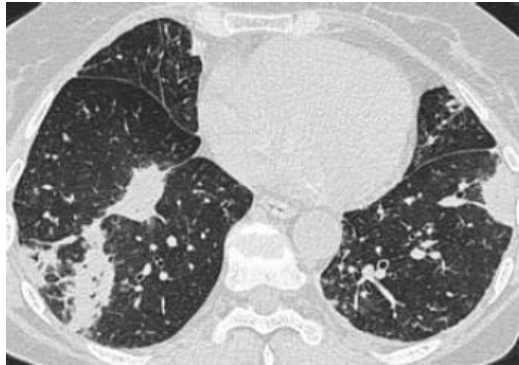


Figure 9: Consolidative changes at bilateral lower lobes in axial view.

- v. Mosaic attenuation: Appears as a patchwork of regions of differing attenuation that may represent patchy interstitial disease, obliterative small airways disease, or occlusive vascular disease (Figure 10).



Figure 10: Mosaic attenuation in axial view.

- vi. Centrilobular nodules: Small lung nodules, 5-10mm which are anatomically located centrally within secondary pulmonary lobules (Figure 11).

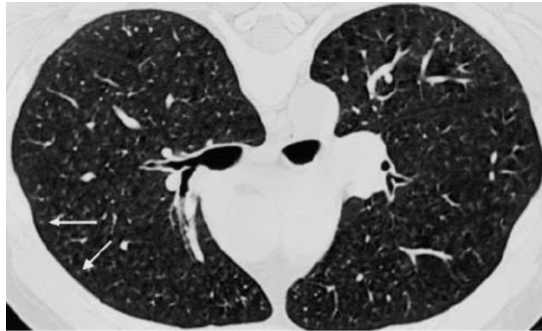


Figure 11: Centrilobular nodules (arrow) in axial view.

3.9 Data Collection

Data was collected from January 2020 till June 2022. This study had obtained approval from the Human Research Ethics Committee of USM (USM/JEPeM/20120694). We included 34 patients who were diagnosed with severe Chronic Obstructive Pulmonary Disease (COPD) and had done spirometry and HRCT Thorax with availability of CT images in Picture Archiving and Communication System (PACS) that fulfilled the exclusion criteria which are suboptimal images in PACS system. Any patients with current confirmed diagnosis of active pneumonia, active tuberculosis, interstitial lung disease, lung cancer, thoracic deformity or history of thoracic surgery as well as patients with co-existing cardiac disorder. The patients were identified through Radiology Information System (RIS). Data was compiled using a data entry sheet, calculated, and analysed using IBM SPSS Statistics 27 ('IBM SPSS Statistics for Macintosh,'2020). Results were written up together with tabulations and graphs.