## LITERATURE REVIEW

## Lung Aging and Lung Function Assessment in Elderly

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#### INTRODUCTION

Aging populations will affect people everywhere. The World Health Organization (WHO) estimated that 400 million individuals will reach elderly age by 2050 and begin to lose cognitive function at 80 or older.<sup>1</sup> A difficulty associated with aging is multimorbidity, which includes chronic respiratory diseases.<sup>1</sup> One of the primary risk factors for mortality in adult patients with chronic illnesses is aging. The lungs are the largest organ in the body and have a special relationship with the external environment. Throughout a person's life, their cells change and are subject to oxidative, chemical, biological, immunological, and other stresses. Even in healthy individuals, lung function can gradually deteriorate with aging, beginning with anatomical changes that impact gas exchange and immune system modifications that increase susceptibility to infection.<sup>2</sup>

The lung is one of the organs that experiences the most frequent decline in function among the elderly. Reduced lung function associated with aging is a physiological condition. The lungs transform both their cellular composition and their functional capabilities. The lungs of an aging population may show structural changes to the respiratory muscles, chest wall, lung parenchyma, and upper and lower respiratory tracts. The elderly are more susceptible to reduced lung perfusion, respiratory mechanics, infection, and weaker respiratory muscles because of aging. The body plethysmograph, oscillometer, spirometry, and carbon monoxide (CO) diffusing lung capacity are techniques used to assess lung function in the elderly. For elderly people, lung function testing might be challenging due to frailty and cognitive decline. Consequently, choosing the best lung function test method for the elderly and offering an accurate and suitable interpretation of the test findings are crucial. Early detection of changes in lung function and accurate assessment of lung function can help identify lung function abnormalities in the elderly and give the appropriate treatment and intervention. This review focused on lung aging, the potential benefits and drawbacks of different lung function tests in the elderly, and the proper way to interpret specific lung function tests.

> Tests for lung function are crucial for clinical evaluation of respiratory illnesses, particularly in the elderly, as well as epidemiology and lung function assessment.<sup>3,4</sup> To get the best results possible when evaluating a person's lung function, pulmonary function tests depend on the operator's skill and the patient's willingness to comply with instructions. This should be taken seriously, particularly in cases where there are older individuals whose lung function has declined due to aging and who have problems adhering to instructions and appropriate lung function assessment techniques. The problem with lung function tests in the elderly is the difficulty in determining accurate lung function, caused by suboptimal testing due to comorbid, cognitive dysfunction, fragility, and inaccuracy in interpretation. Good instruction and the selection of lung function tests, interpretation methods, and criteria using ageappropriate reference values are needed.<sup>5</sup>

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ABSTRACT

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Lung function is one of the organs that decline most frequently in older people due to internal age, physical activity, and physical ability. Chronic obstructive pulmonary disease (COPD) is one of the many chronic illnesses that are linked to decreased lung function in aged persons.<sup>4,6</sup> Evaluations of adults and elderly patients are assessed differently. Senior patients, particularly those with disorders of the respiratory system, frequently exhibit unusual symptoms.<sup>3,6</sup> However, due to subpar lung function exam results and procedures, elderly patients are more likely to receive an diagnosis and insufficient therapy.7 incorrect Consequently, there is ongoing development of several criteria and scoring schemes for evaluating lung function in older people.

Monitoring frailty and cognitive impairment in older patients is particularly important since these conditions can impact their performance on pulmonary function tests. Elderly people still require evaluation, and the majority can have their pulmonary function tested, provided they receive clear instructions and evaluation.<sup>6</sup> Rapid diagnosis through precise and thorough assessment of lung function is essential for the comprehensive treatment of respiratory disorders, particularly in elderly patients.

## ANATOMY AND PHYSIOLOGIC CHANGES IN AGING LUNG

Even in individuals who do not have comorbidities, aging has an impact on the lungs' cellular composition and overall function. Peak lung function and lung maturation occur between the age of 18 years old and 25 years old, continue mostly unchanged until 35 years old, and then progressively deteriorate, beginning with alterations in lung elasticity, airway dilatation, mucociliary function, and alveolar surface. Aging brings about several mechanisms and alterations that have an impact on reduced lung function, including:<sup>2,8</sup>

# Changes in the chest wall and the respiratory muscles

Three factors cause the chest wall's compliance to decrease with age gradually: first, thinning of the bones and intervertebral discs causes changes in the chest wall that lower intrathoracic volume; second, osteoporosis can cause vertebral fractures that alter the shape of the chest wall; and third, changes in the stiffness of the chest wall that restricts its movement. Breathing patterns are affected due to a decline in chest wall muscular strength with age, especially the diaphragm, the primary respiratory muscle. Lung function metrics like forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) are influenced by anatomical alterations in the lungs. Older people are more vulnerable to ventilation failure due to diminished diaphragm strength and respiratory tract muscle function.<sup>8,9</sup>

## Changes in the lung parenchyma and alveoli

Human alveoli begin to expand in surface width at 50 years old because of compensatory airway widening and elastin fiber degeneration surrounding the alveolus. Alveolar wall breakdown and increased alveolar size without inflammation are examples of lung structural changes. Those who smoke will experience a more gradual growth in size. Senile emphysema is also caused by decreased flexibility of the lung parenchymasupporting structures. As people age, their alveolar surface tension falls due to increased alveolar diameter, which reduces lung elastic recoil. Changes in collagen and elastin in the lung parenchyma cause an increase in alveolar diameter. Vital capacity declines, but residual volume rises because of reduced elastic recoil and chest wall compliance. Interestingly, the overall lung capacity remains unchanged because the power also declines along with the chest wall's muscle strength and lung expansion capacity. The density of pulmonary capillaries and the lungs' ability to remove carbon monoxide (CO) decline with age, even though the distribution of alveolar ventilation and perfusion of the lungs is highly heterogeneous because of the alveoli's lower surface tension. These factors impact both physical activity and the development of breathing problems when you sleep.9

## Changes in the nervous system

The brain region responsible for controlling breathing starts to malfunction, leading to an inefficient process during inspiration and expiration. Because the neurological system that triggers the cough reflex becomes less sensitive, additional particles, including bacteria, can enter more easily and be harder to cough out.<sup>2</sup>

#### Changes in the immune system

The body becomes less capable of fighting infections and other illnesses as the immune system deteriorates. Older people are more vulnerable to respiratory illnesses because of the lungs' weakened ability to heal from exposure to cigarette smoke or other toxic particles that enter the airways, as well as the ensuing inflammatory response.<sup>2</sup>

## Changes in mucociliary clearance

The cilia in the airways start to lose their function as we age, which impairs their ability to clear debris. Elderly people are, therefore, more likely to choke and get illnesses. In addition to many other comorbidities, elderly individuals are more likely to experience shortness of breath, low oxygen levels, irregular breathing patterns during sleep, and lung infections, such as pneumonia and bronchitis.<sup>8</sup>

### LUNG FUNCTION IN THE ELDERLY

As people age, their lung function characteristics alter. These include a decrease in the ratio of FEV1/FVC and an increase in residual capacity. With aging, both FEV1 and FVC decline.<sup>2,6</sup> Reduced respiratory muscle strength, elastic recoil of the lungs, and decreased chest wall compliance are all major causes of diminished lung function. As one ages, FEV1 drops. In women, it drops to 1.514 L. In males, it drops to 2.128 L. Moreover, forced mid-expiratory flow (FEF<sub>25%-75%</sub>) declines in older people. Peak expiratory flow can also be used to evaluate the function of the major airways and the reduction in moderate-to-severe obstruction with aging.<sup>6</sup>

The physiology of the respiratory system declines with age. This includes decreased air transport between the capillaries and the mitochondria, a disruption in the appropriateness of oxygen demand with the oxygen supply, a decrease in the ability to carry oxygen and carbon dioxide, decreased cardiac output, decreased pulmonary vascular function, and decreased ventilation control. These can happen to healthy older people as well, and they can go down by as much as 40% by the time they turn 80 years old.<sup>4</sup> This will impact assessments and testing of lung function, particularly in the elderly. Determining appropriate limits is challenging in elderly people due to increased variability in lung function measures. It was discovered that lower educational attainment, a shorter 6-minute walk distance, and cognitive impairment were independent risk factors for a lower spirometry acceptance rate.9 According to several studies, these normal values can predict more or less than they should.<sup>8</sup> About 125 mL is the variability of this decline between individuals. Vital capacity reduces by 5 mL per year, and FEV1 drops by 25-30 mL per year, beginning at the age of 35-40 years old. It can reach 60 mL per year, beginning at 70 years old. One of the causes of this reduction is a drop in height. Older people typically see a decline in height because of structural changes to their spines.<sup>8</sup>

This decline does not imply that elderly individuals cannot function well on lung function tests. An assessment of lung function tests on elderly people and found no discernible difference in the quality of lung function tests conducted on adults between the ages of 40 years old and 50 years old and those over 80 years old.<sup>5</sup> Based on prospective cohort studies with follow-up periods of more than ten years, the average drop in FEV1 was found to be 17.7–46.<sup>4</sup> mL/year, with a

median of 22.4 mL/year. Men suffered a more significant decline (median 43.5 mL/year) than women (30.5 mL/year). It was revealed that the FEV1/FVC ratio decreased by 0.29%/year.<sup>2,8,10</sup>

## LUNG FUNCTION ASSESSMENT IN THE ELDERLY Spirometry

Spirometry is the most significant and widely utilized pulmonary function testing technique for assessing respiratory diseases, which uses forced expiratory motions to assess lung airflow. Age, sex, height, ethnic group, and other diagnostic factors affect predictive spirometry and other lung function tests.<sup>3,11</sup> Many older people have trouble completing a spirometry exam accurately. To get the best examination results, the patient, for instance, needs to be able to hear and obey the doctor's directions, close their mouth tightly on the mouthpiece, breathe normally, and exhale deeply and forcefully for a few seconds.<sup>12</sup> A previous study demonstrated that, when given instructions and followed, elderly people without significant cognitive problems, such as apraxia, can do spirometry exams well.<sup>7</sup> If the Mini-Mental State Examination (MMSE), used to evaluate the cognitive abilities of the elderly, yields negative findings, the spirometry results will be impacted. Individual cognitive impairment affects spirometry procedures and findings.<sup>13</sup>

Assessments of FEV1, FVC, and the ratio of FEV1/FVC are part of the spirometry examination. Although the FEV1/FVC ratio is a crucial diagnostic tool for obstructive lung disease, there is ongoing debate about what constitutes an obstruction in older patients.<sup>6</sup> According to the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) criteria, obstruction is defined as an FEV1/FVC ratio <0.70.1 However, this can potentially result in overdiagnosis in older patients, as many of them also have declining FEV1/FVC ratios. Assessment of lung function in the elderly needs appropriate criteria by using ageappropriate reference values such as the Global Lung Function Initiative (GLI) reference equation. Rather than just a percentage of the predicted value, GLI defines the lower limit of normal (LLN) as the 5<sup>th</sup> percentile based on the population distribution. By using this method, the possibility of overdiagnosing or underdiagnosing obstructive lung disease is decreased. Because the GLI considers the physiological deterioration of lung function with age, predicted values and LLN change dynamically as the patient ages.<sup>3</sup> Elderly patients typically require a minimum of three movements to obtain findings that match the requirements and the varying predictive values. Maneuvers must be repeated in elderly patients due to the FVC value. Advising

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patients to exhale maximally while exhaling is one way physicians can help reduce the number of repeated procedures that older patients do.<sup>12</sup>

## Oscillometry

Oscillometry is a non-invasive technique that can help with lung disease comprehension and management by evaluating the mechanical characteristics of the respiratory system during silent tidal breathing. It measures resistance and reactance by creating mild pressure or flow oscillations in the mouth. This information can be used to obtain insights into the upper and intrathoracic airways, lung tissue, and chest wall. When spirometry and other pulmonary function tests are impractical, oscillometry can be a helpful clinical tool. This is especially true for older patients. In older patients with or without concomitant conditions, oscillometry was found to be more accessible when spirometry and oscillometry were evaluated in multiple studies.<sup>14–16</sup>

Oscillometric exams are performed with the patient in a comfortable, relaxed seated, standing, or reclining position. The oscillometric device, typically attached to a computer or other equipment to capture and analyze data, requires the patient to close their mouth around it. The patient will be requested to breathe calmly and naturally for multiple breathing cycles throughout the examination, and they will not be allowed to speak during the measurement. Depending on the device being utilized, sensors, usually positioned around the patient's neck or chest, are employed to record impedance data from the respiratory system during pressure or flow oscillations produced by the device. In oscillometric analyses, the following primary parameters are frequently used:<sup>17,18</sup>

1. Respiratory system impedance (Zrs)

This is the overall force that must be overcome in relation to resistance, elasticity, and inertia to transport airflow into and out of the lungs. It is the total impedance of the respiratory system. Zrs delineates the mechanical characteristics of the respiratory system, encompassing the lungs, chest wall, and airways.

2. Respiratory system resistance (Rrs)

This is the resistance of the respiratory system, which reflects the fractional loss of gas passing through the airways and the deformation and stretching of the lung tissue and chest walls. Variations in airway resistance, susceptible to airway narrowing, are reflected in variations in Rrs at higher frequencies around 5 Hz.

3. Respiratory system reactance (Xrs)

This is the reactance of the respiratory system, which illustrates how flexible the chest wall and lungs are in reaction to volume variations. X-rays can reveal more details regarding the elastic characteristics of the respiratory system.

4. Respiratory system inertance (Irs)

The speeding gas in the airways causes this inertia. Inertance is also a crucial metric in assessing the mechanical characteristics of the respiratory system, even though it is not often utilized independently in clinical interpretation.

Evaluation of important metrics, such as reactance (X5), airway resistance at specific frequencies (such as R5, R20), and other factors representing airway elasticity and resistance, is necessary for analyzing oscillometry data. Reactance characterizes the suppleness of the airways, whereas airway resistance at various frequencies can indicate obstruction in the small airways. Additionally, early detection of peripheral airway disease can be achieved by alterations in oscillometric parameters, such as R5-R20. Diagnosing a respiratory condition like asthma or COPD may result from abnormal oscillometry results, such as an increase in Rrs suggesting higher airway resistance or a notable shift in Xrs showing alterations in lung elasticity. Monitoring a patient's response to treatment and the course of their illness, especially in the case of older patients, can be aided by analyzing oscillometry results.17,18

By using impulse oscillometry (IOS) to measure respiratory impedance (Z5), resonant frequency (Fres), respiratory resistance (R5, R20, R5–R20), and respiratory reactance (X5), it was demonstrated that the forced oscillation technique (FOT) was more relevant than spirometry for elderly patients. In assessing lung function in older subjects, IOS could be an alternative to spirometry.<sup>9</sup>

A well-known non-invasive lung function test that is simple to measure airway resistance and capacity is oscillometry.<sup>14,16</sup> Changes in oscillometry parameters were strongly correlated with changes in FEV1 and FEF<sub>25%-75%</sub>, but it was challenging to determine whether the patient had COPD or asthma. The resistance at 5–20 Hz analysis curve (R5–20) with the best cut-off changed by -15.4%. It was determined that oscillometry can be used to evaluate older patients' bronchodilator response but not to distinguish between COPD and asthma.<sup>16</sup>

#### Lung volume

In reaction to abnormal spirometry, body plethysmography and diffusing capacity of the lung for CO (DLCO) tests are performed to examine lung volume further. These tests include verifying the existence of restriction abnormalities, analyzing air trapping because of obstruction abnormalities, and evaluating for hyperinflation. Body plethysmography can assess lung volume, including residual volume (RV) and total lung capacity (TLC). Age-related alterations in the lung parenchyma's structure, such as modifications to the configuration and cross-linking of the elastic fiber network, resulting in a reduction in the lungs' elastic recoil. The surface area of the alveoli decreases from 75 m<sup>2</sup> at age 30 years old to 60 m<sup>2</sup> at age 70 years old due to these changes, which happen quickly after the age of 50 years old. Furthermore, it gives the impression that functional emphysema occurs. Total lung capacity, typically steady with age, in restricted illness, will drop.<sup>19</sup> Residual volume will rise with age due to a decrease in the chest wall's elastic recoil and compliance. This increase will be significantly greater if obstructive lung disease and a history of smoking are present.<sup>3,20</sup>

Lung volume, capacity, and resistance are measured using body plethysmography. Specialized tools, skilled workers, and the patient's consent are needed for this treatment. Boyle's rule is used in plethysmography to quantify residual volume, total lung volume, and intrathoracic gas volume, also known as functional residual capacity. Total lung capacity measurement is required to diagnose respiratory diseases. To quantify obstruction, one must first measure the total resistance, which consists of the lung tissue, chest wall, and airway resistance. Additionally, airway resistance is a more stable parameter that can be calculated by multiplying the measured value of airway resistance by functional residual capacity.<sup>21</sup>

A person may be unable to perform a body plethysmography examination for several reasons, including the patient's inability to enter the body plethysmograph room, their failure to follow instructions for the proper maneuver, their continuous use of oxygen that cannot be stopped, or their use of instruments like intravenous infusions that cannot be brought into the body, within the body plethysmography chamber.<sup>7,22</sup> The most common problem that results in suboptimal testing include inadequate instruction from the examiner, diminished hearing or vision impairment, and subpar test protocols. According to this problem, more thorough explanations and communication should be performed before pulmonary function tests. The Global Lung Function Initiative develops reference equations for static lung volumes using body plethysmography and gas dilution techniques.<sup>5</sup>

## Diffusion capacity of the lung

Evaluating and assessing gas exchange, focusing on blood gas analysis, DLCO technique, and measuring the lungs' diffusion capacity using CO is required. The lung's capacity for gas exchange is indicated by the rate at which gas moves from the alveoli to the capillaries, as measured by DLCO. Both DLCO and blood oxygen

pressure (PaO<sub>2</sub>) decline with age. Several factors determine age, but PaO<sub>2</sub> of 70 mmHg is considered the upper limit for the elderly. Disorders that disrupt the diffusion process, such as intestinal lung disease, pulmonary edema, vascular lung disease, and emphysema, will cause DLCO and PaO<sub>2</sub> levels to drop. Based on the pattern of results, the DLCO test can also assist in differentiating between different lung disorders, such as fibrosis, emphysema, and asthma. Most elderly patients can perform DLCO successfully.<sup>24</sup> An ageappropriate reference value is necessary for evaluating DLCO results because the diffusion capacity value decreases with age. The Global Lung Function Initiative has extended the references for transfer factor for CO (TLCO/DLCO), and additional information is also supplied to aid in the diagnosis of emphysema or pulmonary vascular diseases, such as CO transfer coefficient/KCO) (DLCO per liter of alveolar volume).5,23-25

Diffusing capacity of the lung for CO typically has a value of 20–30 ml/minute/mmHg. The amount of CO that is moved from the alveoli to the blood vessels per minute per millimeter of partial pressure of CO in the alveoli is shown by this value. The degree of DLCO severity can reveal further details on the substantial disturbance of lung gas exchange. Several age-related factors can make DLCO examination less accurate as people age. When performing DLCO exams on elderly patients, there are several factors to take into account, including:<sup>23,24</sup>

1. Decreased lung elasticity

Lung elasticity typically decreases with aging. This may affect the lung's capacity to exchange gases, affecting the DLCO value.

2. Decreased lung volume

As people age, their total lung volume likewise tends to decline. These modifications could impact the outcomes of the DLCO exam.

3. Changes in lung structure

The aging process can also cause changes in lung structure, including a decrease in the number and elasticity of alveoli. This can impact the lungs' ability to exchange gases.

4. Decreased respiratory muscle function

As people age, their respiratory muscles also lose some of their functionality, which can impact gas exchange and respiratory processes.

5. Comorbid factors

Comorbid medical disorders, such as diabetes, heart disease, or other illnesses, are common in old age and can have an impact on the DLCO examination results. How these factors interact with aging may make it more difficult to interpret DLCO data.

## INTERPRETATION OF LUNG FUNCTION TEST IN ELDERLY

Age, gender, and height all impact lung function evaluation. Various evaluations are used to forecast normal values on lung function tests, particularly in the elderly. They will be compared to the predicted values to determine if the measured findings are inappropriate. Many criteria involve age-based data constraints. For instance, the Third National Health and Nutrition Examination Survey (NHANES III) analysis cannot be performed on patients who are older than 80 years of age. Therefore, caution must be exercised while assessing and interpreting elderly people. An aging population's declining height will also impact the predictive value. To prevent misdiagnosis in patients with kyphosis, measuring the distance between the fingertips on one hand and the other while measuring body height is advised.<sup>3</sup>



Figure 1. Assessment of lung function in elderly patients<sup>1,17</sup>

Due to anomalies in the structure of the thoracic cavity and a decline in the capability of the respiratory muscles, the vital capacity of older people declines with age. As such, it is challenging to establish the normal ranges for the results of pulmonary function tests in the elderly due to their alterations. Several factors must be considered, including height, comorbidities, age, and medications often polypharmacy in older people. The most comprehensive and dependable spirometry prediction range is measured using the GLI. The age range defined for the GLI examination is 3-95 years old, considering factors like height and ethnicity. The spirometry parameters FEV1 and FVC are evaluated to see if they fall within the normal range by comparing them to the corresponding predicted values based on GLI data using LLN. For the elderly, GLI advises interpreting based on LLN to prevent misdiagnosis using a fixed ratio of 0.7. The GLI method interprets lung function tests by comparing observation values with references. When an observation value is transformed into a z-score, it indicates the degree to which it deviates from the reference population average. Z $\leq$ -1.645 (5<sup>th</sup> percentile) indicates an abnormal result, while Z=0 indicates an average value. Restrictive patterns are defined by a decline in FVC below the LLN with a normal FEV1/FVC ratio, while obstructive patterns are defined by a decrease in FEV1/FVC below the LLN.

Body plethysmography, or DLCO are additional tests for mixed obstructive and restrictive patterns.<sup>1</sup>

### SUMMARY

Aging causes a decline in lung function brought about by changes in the structure of the chest wall and lungs. Due to factors including multimorbidity, multipharmacy, and declining cognitive capacity, evaluating lung function in the elderly can be challenging. This makes it challenging to ascertain the best lung function test. Thus, an approach is needed to assess lung function and its interpretation in the elderly. The first point is education and instruction that is easy for the elderly to understand. The second point is choosing the proper lung function test for the elderly. The third point is the interpretation of lung function tests using age-appropriate reference values such as the GLI reference equation method. A method that uses GLI guidelines and covers the widest age range can help prevent overdiagnosis and give older adults an accurate assessment of their lung function. Accurate lung function test interpretation is necessary for the elderly experiencing respiratory symptoms receive to appropriate diagnosis and therapy.

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The author declares there is no conflict of interest.

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### **Authors' Contributions**

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