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Airflow Limitation and Spirometry

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http://dx.doi.org/10.5772/57549

1. Introduction

A patient with chronic obstructive pulmonary disease (COPD) may present with symptoms (dyspnea, cough, sputum production, chest tightness, wheezing, etc.) and appropriate history (cigarette smoking or occupational exposures). However, based on current accepted criteria established by professional societies, the diagnosis of COPD needs to be confirmed by the presence of airflow limitation as measured by spirometry testing. Unfortunately, as will be discussed in this report, the interpretation of spirometry testing that reveals airflow obstruction (a reduction in the FEV_1/FVC ratio) is an arbitrary metric for the presence of COPD.

As it is used, spirometry is one type of pulmonary function test that can measure the total amount of air that an individual can inhale and exhale and the speed or velocity with which the air moves. The test requires full cooperation of the individual performing the test, the supervision of a technician trained in this testing, and appropriate testing equipment (spirometer). The results of the testing session performed by the individual are reviewed to determine acceptable quality and repeatability before interpretation of the results can take place. Then the interpretation of airflow limitation can be made based upon the actual values of testing when compared to reference values for that individual.

2. Factors that contribute to maximal expiratory flow limitation

Expiratory flow rates from the lung have maximal values that cannot be exceeded in spite of increasing effort generated by the respiratory muscles of exhalation. The maximal flow that is achieved occurs close to total lung capacity and then decreases as lung volume (and in turn airway diameter) decreases until the lungs reach residual volume. This expiratory flow rate is affected by the elastic recoil of the lung and airway diameter. Expiratory flow limitation can

be explained in its simplest terms by a gas flowing through a collapsible tube. In the examples below, the lungs and conducting airways can be represented by a balloon for the alveolar spaces with a single tube as the conducting airways.

At rest (Figure 1), there is a balance between the negative pleural pressure (caused in turn by the outward elastic recoil of the chest wall) that is exerting a force to distend the lungs and alveolar spaces and the elastic forces of the lung parenchymal structures that are causing the alveolar spaces to collapse. As a result of the equal forces, the alveolar pressure is zero and there is no pressure gradient to cause air to be exhaled. In terms of lung volume status, this balance between the outward chest wall force and the inward pulmonary parenchymal forces is the functional residual capacity (FRC).
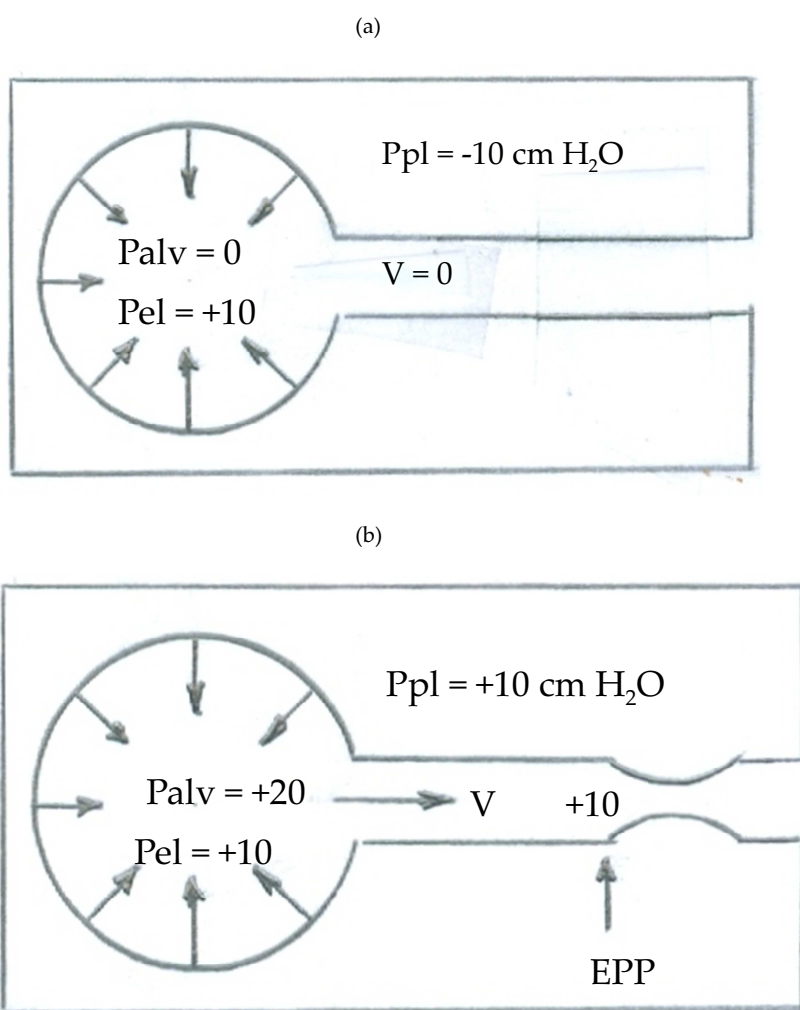
(a)

Ppl = -10 cm H$_2$O

Palv = 0

V = 0

Pel = +10

(b)

Ppl = +10 cm H$_2$O

Palv = +20

V   +10

Pel = +10

EPP

Figure 1. (a) Ppl=pleural pressure, Pel is the elastic recoil pressure of the lung, Palv is the resulting alveolar pressure which is a combination or balance between the elastic force which is attempting to collapse the alveolar space and the pleural pressure that is attempting to expand the alveolar space. Under these conditions, there is no flow rate of air since there is no pressure gradient from the alveolar space to the outside. (b) Force applied by respiratory muscles results in positive intrapleural pressure which when added to elastic recoil pressure of the parenchyma leads to positive intra-alveolar pressure which in turn creates a positive pressure gradient so that expiratory flow of air can occur.

When the expiratory respiratory muscles are activated, there is in an increase in the pleural pressure from -10 cmH$_2$O to +10 cmH$_2$O (Figure 2). This external pressure on the alveolar spaces is then in addition to the elastic force of the parenchymal structures to create a positive alveolar pressure of +20 cmH$_2$O. There is now a pressure gradient from the alveolar space to the outside of the lungs and as a result, air flow occurs. Because of the resistive forces in the airways, there will be a decrease in this driving pressure along the airway until a point is reached where the pressure within the airway is matched by the surrounding pleural pressure. This is referred to as the equal pressure point. The equal pressure point is defined physiologically and not anatomically and, for any individual, the anatomic location of the EPP may change with time based upon airway tone and other factors.

If the airway at this equal pressure point is in the larger airways/bronchi where cartilaginous support exists there would not be collapse of the airways. However, if this equal pressure point occurs closer to the alveolar spaces in smaller non-cartilaginous airways, then compression and collapse of the airway may occur. In either case, the expiratory flow rate is determined primarily by the elastic recoil pressure which in part determines the pressure gradient from the alveolar spaces to the outside and by the resistive elements of the airways which determine the pressure drop as flow occurs along the airways. Increasing the respiratory force generated by the expiratory respiratory muscles has little direct effect on most of the airflow during exhalation from total lung capacity to residual volume. In that regard, the expiratory flow is limited.

3. Anatomic location of airway resistance

As stated, the pressure drop when flow occurs during exhalation is determined by the presence of resistive forces within the airways. Airway resistance in turn depends on the flow pattern of the exhaled air (laminar vs turbulent flow), as well as the number and diameter of the airways which in turn determines the total cross-sectional area of the airways from the smallest airways to the major airways (bronchi and trachea). Because the airways divide again and again from the major airways, the number of smaller airways at the terminus of the conducting airways (0.6 mm) is over 40-60,000 in a normal individual so that the cross-sectional area is increased from 2.5 cm^2 at the trachea to 180 cm^2 at the level of these smaller airways.

Studies have shown that the airways < 2mm only contribute < 20% of the total airways resistance during expiratory flow. However, in the presence of COPD, that value has been shown to increase by 4-40 fold [1]. The question has been whether in COPD, the increase in resistance is due to a loss or destruction of these smaller airways or to a narrowing of these airways by disease. More recent studies using multidetector computed tomography (MDCT) and micro-CT imaging have shown that there is a combination of both a decrease in the number of the smaller airways due to destruction and also a reduction the airway diameter of these airways due to disease [1].

In summary, the factors that result in expiratory flow are 1) the elastic recoil of the lungs which is greater at higher lung volumes (highest at total lung capacity and decreases as exhalation

occurs) and 2) resistive elements of the airways (lowest at total lung capacity and increases as exhalation occurs) that determine the pressure drop as airflow occurs along the airway. In COPD, both of these factors can be affected. The elastic recoil of the lungs can be reduced in COPD if there is evidence of emphysema that results in destruction of parenchymal tissue and the elastic forces that cause the lungs to collapse. Also, in COPD with loss of the number of airways and reduction in airway diameter due to disease, the resistive elements are increased with a greater pressure drop for any given flow rate along the airways. Also, the loss of supporting forces with emphysematous changes will also reduce the stiffness of the airways resulting in airway collapse with movement of the equal pressure point closer to the alveolar spaces.

The hallmark of airflow limitation is reduced maximal expiratory flow rates as measured by spirometry. The pathological changes in the lungs that result in the reduced expiratory flow rates are 1) increased flow resistive properties of the airways (as in chronic bronchitis) and 2) reduced elastic recoil of the lung (as in emphysema). In COPD, the airways can be narrowed as a result of inflammatory changes and smooth muscle hypertrophy in the airway wall and increased amount of mucous and inflammatory material within the airway lumen. There is increased resistance to airflow as a result of the narrowed airway leading to reduced flow rates for the same driving pressure that is generated to cause expiratory flow. In addition, loss of parenchymal tissue with emphyematous changes can reduce the support of airway walls contributing to airway narrowing and increased airway resistance. Also, the emphysematous changes reduce the elastic recoil and in turn the pressure gradient that is in part responsible for the generation of the expiratory flow rates. The contribution of these separate pathological changes has been studied extensively to determine the location of the greatest effect on reduced expiratory flow rates. The specific mechanisms involved are complex and have been the subject of extensive physiological research. It is sufficient to say that the clinically relevant measurement of maximal expiratory flow rates by spirometry is thought to be an appropriate measurement used to evaluate the reduction in flow rates that is the hallmark of and confirms the diagnosis of COPD.

4. Role of spirometry in identifying the presence of airflow limitation or obstruction in COPD

Spirometry testing has been used to confirm the presence of airflow limitation or obstruction in COPD but the testing must be performed correctly. Spirometry testing must be done according to established guidelines [2,3] to ensure adequate quality of test results. This means that the equipment (spirometers) used must meet basic requirements [2] and the technicians performing the testing should have completed appropriate training that includes courses such as those that use the National Institute for Occupational Safety and Health (NIOSH) Spirometry Training Guide. Also, as part of the ongoing testing process, spirometry results will be reviewed with feedback to the technicians to ensure continued adequate quality of results. Testing is performed for the individual patient until three acceptable maneuvers are obtained

with the necessary evidence for repeatability. The testing is done both at baseline and after the administration of a bronchodilator (post-bronchodilator results).

Once testing is completed, the spirometry test results for that individual (specifically the forced expiratory volume in one-second (FEV_1), forced vital capacity (FVC) and the ratio of those two values FEV_1/FVC) are compared to predicted values based on established reference equations [4].

The results of spirometry testing can be shown both in graphical format and by numerical results in tabular format (Table 1). Airflow limitation or obstruction as identified by spirometry is shown in Figures 2a, 2b, 3a and 3b.
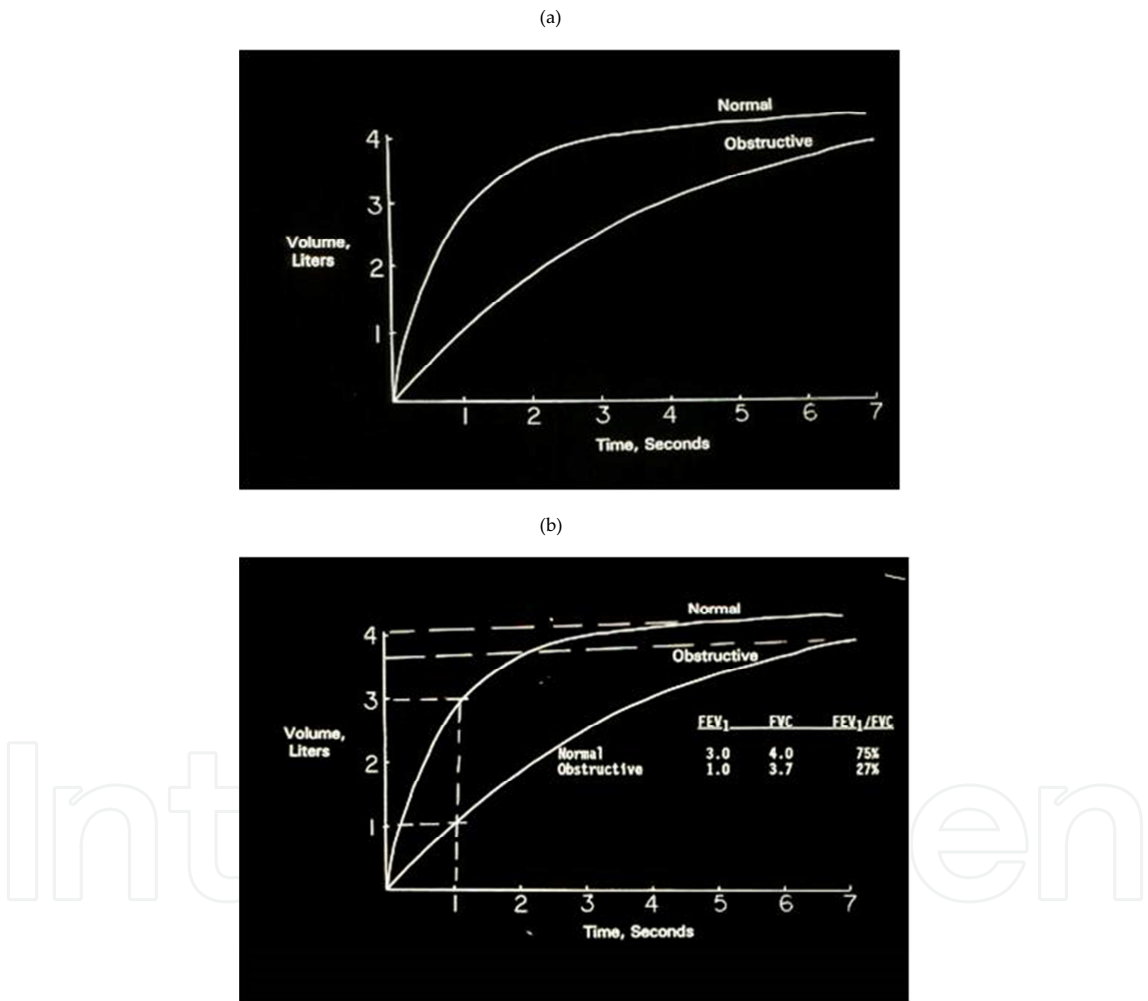

Figure 2. (a) Volume-time relationship from spiromtery testing for exhaled air in a normal individual and an individual with airflow obstruction (obstructive). Volume of exhaled air is in liters and time of exhalation in seconds. Note in airflow obstruction the volume of air exhaled at any time point is reduced compared to the exhaled air for the normal individual. (b) Calculation of the values of spirometry testing for a normal individual and an individual with airflow obstruction (obstructive). FEV_1 refers to the forced expiratory volume in one second and FVC refers to the forced vital capacity. The parameter that best describes the presence of airflow obstruction is a reduction in the ratio of FEV_1 to FVC as shown here: 27% for the ratio in the individual with airflow obstruction vs. 75% for the ratio for the normal individual.

4.1. Spirometry volume-time tracings

The results of a spirometry testing maneuver can be displayed as a volume-time tracing as shown in Figures 2a and 2b. After the individual has inhaled deeply to maximal inhaled volume (total lung capacity), he or she is asked to exhale forcefully and maximally without hesitation and told to keep exhaling until told to stop. The resulting tracing demonstrates the exhaled volume in liters against the time of exhalation in seconds. (Figures 2a and 2b) For a normal individual, the volume of air that is exhaled in the first second (Forced Expiratory Volume in 1 second or FEV_1) is usually about 70-80% of the total amount of air that can be exhaled (total amount of exhaled air is called the Forced Vital Capacity or FVC). It is that ratio of FEV_1/FVC when reduced that determines if airflow limitation is present. As shown in the example in Figures 2a and 2b, the normal individual has a ratio of FEV_1/FVC of 3.0 liters to 4.0 liters (3/4 or 75%) whereas the other individual with airflow obstruction or limitation has a ratio of FEV_1/FVC of 1.0 liters to 3.7 liters (1/3.7 or 27%). A reduced FEV_1/FVC ratio is the criterion for the intepretation of airflow obstruction.

4.2. Spirometry flow-volume tracings

In addition to displaying the results of spirometry as volume-time tracings, the same results can be expressed or displayed as flow-volume tracings or loops with both expiratory limbs and inspiratory limbs being displayed (Figures 3a and 3b). This additional information can be useful for evaluation of the actual expiratory flow rates achieved with spirometry and is also useful for the technician and the reviewer of spirometry testing to determine if the testing maneuvers are acceptable without errors. Errors that can occur with spirometry testing can be at the beginning of the maneuver (hesitancy, cough, sub-optimal effort, etc.) or at the end of the test (did not exhale completely).

Another example of spirometry test results is shown in Table 1 for a different individual with baseline testing and testing again after the administration of the one-time use of a bronchodilator.

Patient: BS2	Age: 72	Height: 69 inches		Weight: 231 pounds	Sex: Male Race: Caucasian		
		Baseline			Post-Bronchodilator		
	Actual	Predicted	%Pred	LLN	Actual	%Pred	%Change
FVC, L	2.05	4.18	49	3.27	2.23	53	8
FEV_1, L	1.11	3.05	36	2.27	1.19	39	7
FEV_1/FVC, %	54	73		63	53		
$FEF_{25-75\%}$, L/sec	0.48	2.28	21	0.73	0.61	27	26

FVC: Forced vital capacity; FEV_1: Forced Expiratory Volume in 1 second, $FEF_{25-75\%}$: Forced Expiratory Flow rates between 25 and 75% of vital capacity.

Table 1. The numerical results of spirometry testing for a patient with airflow obstruction
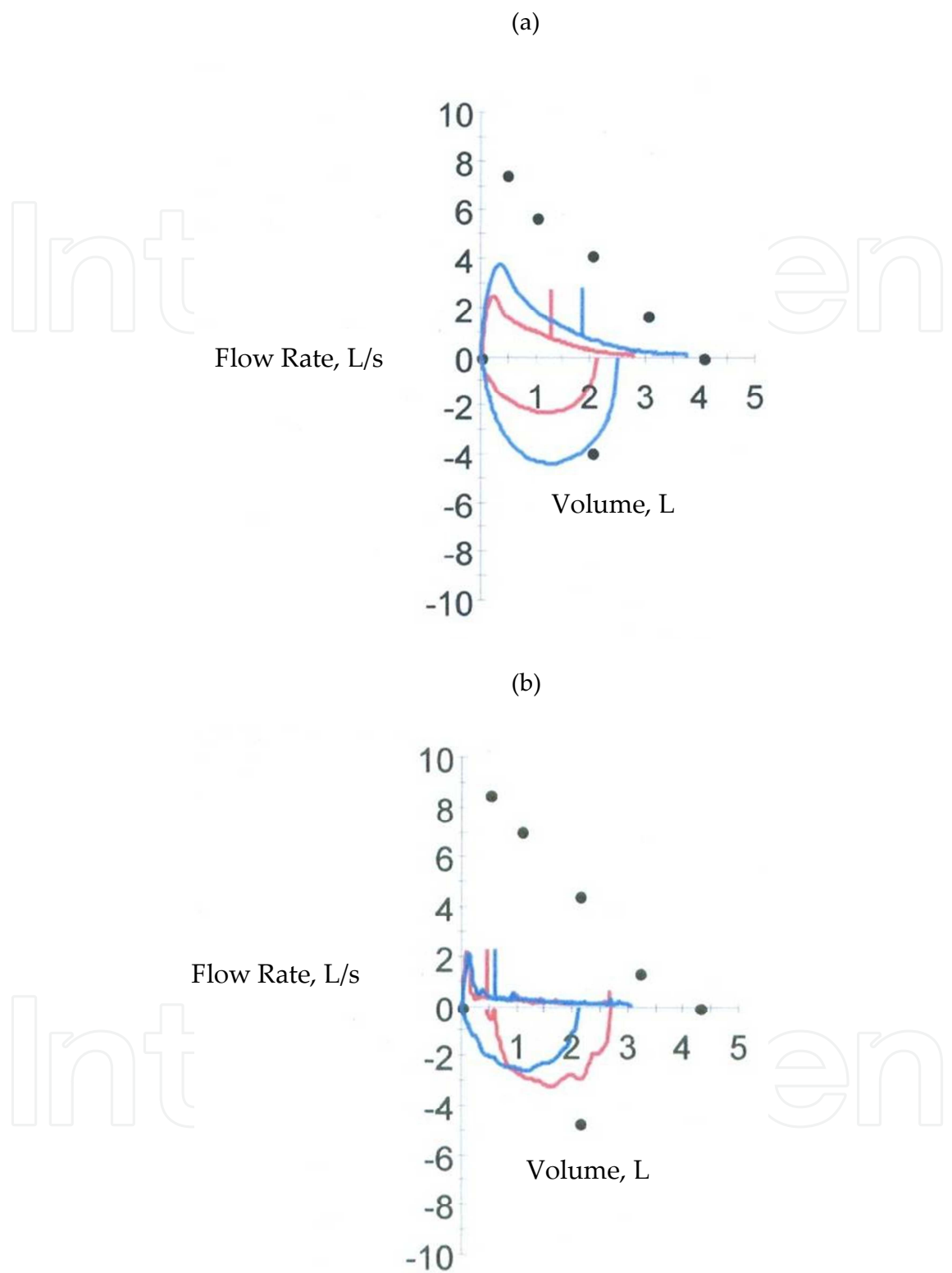
(a)

(b)

Figure 3. (a) and (b) Representations of airflow obstruction using flow vs. volume relationships. Flow of exhaled and inspired air in liters/second and volume of air exhaled and inhaled in liters. The red line refers to the baseline measurement of spirometry testing and the blue line represents the results after a bronchodilator has been given to the individual. The points refer to predicted values for the individual. (a) these figures shows an individual who has airflow obstruction of moderate severity. (b) these figures show an individual who has airflow obstruction that is very severe.

4.3. Definition of airflow limitation by spirometry

As mentioned, the determination of airflow limitation by spirometry depends on the criterion of a reduced FEV_1/FVC ratio. The specific definition of the actual criterion for airflow limitation or airflow obstruction has been a point of discussion based upon different statements from professional groups. Clinical guidelines for COPD disease management include the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [5], the VA/DoD Clinical Practice Guideline for Management of Outpatient Chronic Obstructive Pulmonary Disease [6], and the American Thoracic Society/European Respiratory Society Standards for the Diagnosis and Management of Patients with COPD [7]. These three guidance documents have recommended being more inclusive for identifying individuals who may have COPD and have proposed that the presence of airflow limitation exists when the post-bronchodilator FEV_1/FVC ratio is < 0.70. These guidelines acknowledge that this approach may be overly sensitive and include older individuals who are normal but who have an FEV_1/FVC ratio that is < 0.70. Other guidance documents are based on a statistical approach for the interpretation of airflow limitation using reference equations which in turn are based on population studies. The ATS/ERS document on Interpretative Strategies for Lung Function Tests [2] states that the presence of an obstructive ventilatory defect exists when the FEV_1/FVC ratio is below the 5th percentile of its predicted value, a value referred to as the lower limit of normal or LLN for that ratio based on the chosen reference values. The most recent revised GOLD guidance [5] does acknowledge that the LLN values are based on a normal distribution and that the use of a fixed ratio of 0.70 will result in more frequent diagnosis of COPD in the elderly. This problem of the difference between using a fixed cutoff of 70% for the ratio of FEV_1/FVC compared with using the LLN for this ratio is illustrated in Figure 4. Younger individuals with an FEV_1/FVC above 70% but below the LLN would be classified as no airflow obstruction by use of a 70% cutoff but would be interpreted as airflow obstruction by use of the LLN (false negatives). On the other hand, older individuals with FEV1/FVC ratios below 70% but above the LLN would be classified as having airflow obstruction by the use of a 70% cutoff but would have no airflow obstruction by use of the LLN (false positives).

Post-bronchodilator spirometry test results can be used for the determination of airflow limitation recognizing that as many as 50% of patients with COPD will have a significant response to the one-time use of a bronchodilator (at least a 12% increase and a 200ml absolute increase in FEV_1 or FVC). The use of post-bronchodilator results is consistent with the aforementioned clinical guidance documents [4,5,6].

Once airflow limitation is determined to be present, the severity of limitation is then assessed based on the FEV_1 % of predicted value. Using the ATS/ERS guidelines for Interpretative Strategies for Lung Function Tests [2], the following severity categories are used:

Mild obstruction: FEV_1% predicted > 70% (which means the actual value measured is greater than 70% of the predicted value which in turn is based on the patient's age, height and gender with correction for race as appropriate).

Moderate obstruction: FEV_1% predicted <69% but > 60%

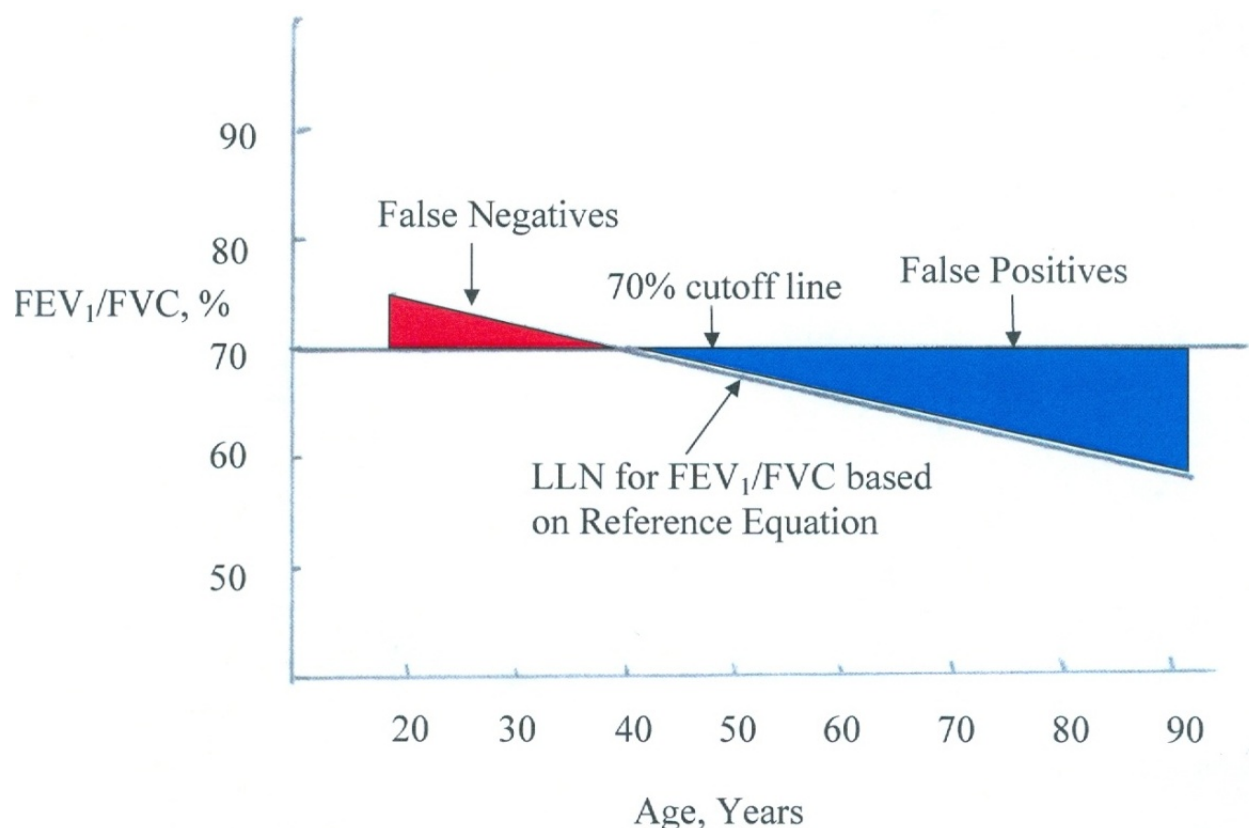Moderately Severe obstruction: FEV_1% predicted <59% but > 50%

Figure 4. The difference for the interpretation of the presence of airflow obstruction by using an absolute cutoff of 70% or less for the ratio of FEV_1/FVC as the criteria for airflow obstruction compared to using values for this ratio that are lower than the lower limit of normal (LLN) based on the NHANES III reference equation [4]. The LLN line decreases with age as does the predicted ratio of FEV_1/FVC. As a result, the red area would include younger individuals who would be considered to be normal if a value of 70% is used for the interpretation of airflow obstruction but actually by use of the LLN would be considered to have airflow obstruction (false negative). On the other hand, those individuals in the blue area would be considered to have airflow obstruction by ratios of FEV_1/FVC below 70% but would be above the LLN (false positives).

Severe obstruction: FEV_1% predicted <49% but > 35%

Very Severe obstruction: FEV_1% predicted <34%

There may be patients whose results from spirometry testing or from complete pulmonary function testing (if available) may be equivocal for the presence of airflow limitation or COPD. In those cases, it is recommended that the patient be referred to the pulmonary specialists for further evaluation. This may also include the presence of emphysema as noted on imaging studies such as CT scans of the chest.

4.4. Problem with using spirometry to diagnose COPD

Although it has been recommended by those professional societies that a reduction in FEV_1/FVC using either a 70% cutoff or the LLN should be used to establish a diagnosis of COPD, there has been some controversy over this recommendation. The choice of either 70% or a LLN is an arbitrary value given that there are problems with an absolute cutoff of 70%

knowing the decline in FEV_1/FVC that occurs with aging and the LLN which was determined by a statistical analysis of the results of spirometry testing in a population of non-smoking, "normal" individuals [4]. Thus, the clinical significance of a value for FEV_1/FVC below either 70% or LLN is of questionable relevance given the pathological changes that can occur with COPD involving the airways and parenchyma [8]. It is known that there is not one physiological parameter that can completely describe all the changes that occur in the disease that is COPD. Unfortunately, until we develop better means to characterize this disease, we are left with using spirometry to diagnose and characterize the severity of the disease.

5. Summary

Airflow limitation as determined by spirometry testing is the hallmark of COPD. The spirometry testing criterion for airflow limitation is a reduced FEV_1/FVC ratio when compared to the lower limit of normal for that measurement from a reference population. It is critical that the test be done in an acceptable manner under the supervision of a trained technician. The results of spirometry testing can be useful in characterizing the presence and severity of the obstructive lung disease for that individual.

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