Course Name: Pulmonary Function Test - Interpretation and Application in clinical practice
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W4_L4_Diffusion Capacity of Lungs for Carbon Monoxide DLCO

Good day, I am going to talk on the topic Diffusion Capacity of Lung for Carbon Monoxide DLCO. In this video, we are going to talk on the objectives understanding the basics of DLCO, DLCO testing methods and techniques, diseases associated with altered DLCO and interpretation of DLCO report. First let us see the basics of DLCO. Diffusing capacity is also referred to as the transfer factor is used to assess the gas exchange ability of the lungs. It measures the transfer of a diffusion limited gas like carbon monoxide across the alveolar capillary membrane. It is measured as volume of gas, ml that will diffuse through the membrane each minute at standard temperature, pressure and dry condition.

So, it is measured in terms of ml per minute per millimeters of mercury at standard temperature, pressure and dry conditions. Why carbon monoxide is chosen for diffusion studies? It is a diffusion limited gas. It combines avidly with hemoglobin approximately 210 times more than the oxygen. It has low solubility in membranes not normally present in the alveoli or blood.

So, carbon monoxide is in pulmonary capillary blood can be taken as 0. Let us take a closer look at the alveolar capillary membrane. So, in it is composed of on the alveolar part, it is composed of the alveolar fluid, alveolar epithelium, alveolar basement membrane, then comes the interstitial space. On the capillary side, it is composed of the capillary basement membrane, capillary endothelium, the RBC membrane and then the hemoglobin. So, for any gas to transfer across these layers, it has to cross two important barriers that is the alveolar capillary membrane barrier and blood plasma red blood cell barrier.

To understand the determinants of the diffusing capacity, we should understand this equation

$$1/DLCO = 1\ Dm + 1/\theta\ Vc$$

where dm is nothing but the membrane conductance that is the diffusion across the alveolar capillary membrane which again depends on the area and thickness of the alveolar capillary membrane. θ (Theta) is the reaction rate that is the uptake of carbon monoxide by the hemoglobin and Vc is the pulmonary capillary blood volume. So, from this equation what we have to understand that when the ventilatory function of lungs and the hemoglobin are

normal, then the diffusion capacity is solely dependent only on the characteristics of the alveolar capillary membrane. So, indications for performing diffusion study are to diagnose pulmonary cause of dyspnea, screening when the patient is symptomatic, but the imaging is normal like in early interstitial lung disease, early emphysema, pulmonary vascular disease, occupational lung disease, drug induced lung disease. It is also used to assess the severity of the disease like in chronic obstructive pulmonary disease, interstitial lung disease.

It is also used for the monitoring of disease progression as well as response to drug therapy in interstitial lung disease and sarcoidosis. What are the contraindications of doing a diffusion study? When there is a known exposure to carbon monoxide and the patient has carbon monoxide toxicity, then it is contraindicated. Patient is severely desaturating without oxygen supplementation, then this is again a contraindication. Mental confusion, muscular incoordination, preventing the subject from adequately performing the maneuver or inability to obtain or maintain an adequate lip seal on the instrument mouthpiece is again a contraindication. Other relative contraindications are large meal or vigorous exercise immediately before the test, smoking within 24 hours of the test administration.

Now let us see the DLCO testing and testing methods and techniques. There are various methods available which are single breath hold method, re-breathing method, steady state method and intra breath method. But the most commonly and widely used method is the single breath hold method as this method is widely accepted by various international societies. It is very standardized and has reference values in the literature and it is comparatively easy to perform. So henceforth we are going to see about single breath hold method.

Patient preparation, like spirometry the equipment has to be calibrated and kept ready before the test is performed. I am not going into details, but what I wanted to highlight is before doing test the DLCO machine has to be calibrated with a 3-litre syringe. Patient preparation, patient must be asked to refrain from smoking or other sources of carbon monoxide exposure on the day of the test. No alcohol ingestion on the day of the test. No exercise immediately before the test.

The patient should be made seated for 5 minutes before the test. Patient on supplemental oxygen should be switched to room air for 10 minutes before testing if it is clinically acceptable. So, what are the gases that we are going to use for single breath hold method? We are going to use a standardized gas mixture which is composed of carbon monoxide, a tracer gas, oxygen and nitrogen. Tracer gas is nothing but a chemically biologically inert and insoluble gas that is used to estimate the amount of alveolar volume. Commonly used tracer gases are helium, neon and methane.

This is the setup of the equipment in which we are going to perform the single breath hold method. So, it is composed of a spirometer and then it has a cylinder that has the standardized gas mixture in fixed combinations that is 0.3% of carbon monoxide, 10% helium, 21% oxygen and rest nitrogen. So, this gas is delivered by means of an automatic valve to the patient. Patient inhales this gas and then exhales it which is getting collected in the end tidal sampler and this collected sample will be analyzed by means of two analyzers, one helium analyzer and one carbon monoxide analyzer.

What are the steps of the test? So initially the patient is made to be seated comfortably with a nose clip and he is given the mouthpiece. The first part is asking the patient to take tidal breathing. As much as the patient becomes comfortable with the nose clip and the mouthpiece and there are no leaks, patient performs tidal breathing. After tidal breathing we ask the patient to exhale up to the residual volume. Then the patient has to quickly inhale the predefined mixture of gas to reach up to the total lung capacity.

Then the patient has to hold the breath for 10 seconds and then quickly exhale without non-forcefully the patient has to exhale through the valve that is the last part of the test. As the test is performed, we will be able to trace the volume time graph on the computer. Now let us take a look at the volume time graph. So, it starts with the patient exhaling up to the residual volume. Next part is when the patient inhales up to the level of TLC, then we give a breath hold of 10 seconds where the equilibrium is reached and then the patient exhales and the gases get collected.

In this the first part of the gas which consists of air from the dead space is let out and rest of the part is collected for the sampling analysis. So, what are the acceptability criteria and repeatability criteria? So inspired volume should be more than 85 percent of the largest we see in the same test session. Breath hold should be adequate that is at least 8 to 12 seconds. There should not be any evidence of leak Valsalva maneuver or Muller maneuver. Exhalation should be rapid with total exhalation lasting 4 seconds or less.

An interval of at least 4 minutes should be lapsed between the two repeated tests. Not more than 5 single breath maneuvers should be performed at a time for a patient. Repeatability criteria average of two or more tests should be reported in which two acceptable tests should be performed within 2 ml per minute per millimeters of mercury of each other. Now what are the potential problems that we may face while performing the test that the patient may not cooperate or may not be able to perform the technique correctly. First and foremost, problem which may arise is patient not reaching the residual volume and TLC.

If residual volume and TLC are not reached properly during inhalation and exhalation it may lead to reduction in DLCO value. The other problems are slow inhalation, slow exhalation, stepwise inhalation, stepwise exhalation, transient overshoot or gas leak while exhalation. All this will result in a DLCO report that is not ideally interpretable. Before

interpreting the diffusion capacity report, we are supposed to make certain adjustments to the DLCO. Those factors that are going to affect the DLCO report those are age, gender, height, race especially the hemoglobin because anemia affects the DLCO.

When there is 1 gram per deciliter fall in the hemoglobin there is going to be 4 percent fall in the DLCO. Hence it has to be corrected. Also, lung volume has to be corrected. Carboxyhemoglobin is another factor which is going to reduce the DLCO. And then oxygen in the inspired air is again a factor that is going to affect DLCO.

For example, in high altitude where the oxygen tension is going to be low there is going to be less competition from the oxygen for carbon monoxide binding. So, carbon monoxide diffusion increases. Also, presence of pCO2 decreases the DLCO. Exercise and body position will also affect the DLCO. Hence the test should be performed in a sitting position.

Now what are the diseases associated with altered DLCO? Let us take a look at this picture to understand the basic pathophysiology in different conditions where DLCO will be reduced. So, this first one is a normal image where the alveoli are normal. Alveolar capillary membrane is normal and capillary is normal with red blood cells. Here the diffusion is normal. But when we look at a case of emphysema the alveoli are destructed resulting in inadequate distribution of the gas resulting in air trapping.

So, there will be less diffusion. In case of anemia where the circulating RBCs are low or hemoglobin is low the diffusion is going to be affected. In case of pulmonary emboli where there is going to be an embolus in the vessel that is going to obstruct the blood flow there is going to be reduction in diffusion capacity. In case of diseases like interstitial lung disease where there is going to be fibrosis pneumonitis there is going to be thickening of the interstitium, thickening of the alveolar capillary membrane resulting in reduction in the diffusion capacity of the lung. In cases where there is going to be reduction in area like pneumonectomy or atelectasis there is going to be reduction in diffusion capacity.

So let us see few conditions where we are going to get reduction in diffusion capacity. Next is isolated reduction in diffusion capacity that is the lung volumes remain normal only the diffusion capacity will be reduced. It occurs in conditions like pulmonary vascular disease, congestive cardiac failure, anemia, early emphysema, morbid obesity, cirrhosis of liver and diabetic lung. Let us see conditions where there is low DLCO with obstruction. It occurs in bronchiolitis, combined pulmonary fibrosis and emphysema, cystic fibrosis emphysema and then sarcoidosis.

Conditions where there will be low DLCO with restrictive pattern occurs in interstitial lung disease pneumonitis. Conditions where there will be both restriction and obstructive pattern along with a DLCO low DLCO occurs in sarcoidosis and asbestosis. And there are few conditions where there will be increase in diffusion capacity of the lung like when there is recruitment of blood in the alveolar capillary blood like when the patient is lying

in supine position, when there is hyperdynamic circulation, when there is bronchial asthma, when the patient is performing Muller s maneuver, left to right cardiac shunts, early congestive cardiac failure and also in certain miscellaneous conditions like polycythemia, alveolar hemorrhage where there will be blood in the alveolar space that will take up the carbon monoxide, obesity due to some uncertain mechanisms, high altitude because of low PIO2 following bronchodilator in obstructive disease in correct reference range. Now let us see the interpretation of DLCO report. If we take solely the diffusion report alone, it is difficult to interpret because the only information that will be available is whether the DLCO is reduced or not.

In order to identify the underlying respiratory disease, we need a complete PFT report which is composed of the spirometry report lung volumes and then a body plethysmograph report or then we have to finally interpret the DLCO report. Now let us look at the report severity classification of DLCO. So, diffusion, abnormality, DLCO value of more than 140 is considered abnormally high, 76 percent to 140 percent is considered normal, 61 to 75 percent is considered mild impairment, 41 to 60 percent is considered moderate impairment and less than 40 percent is considered as severe impairment. Before interpreting a DLCO report, we all should understand three components. One is DLCO per se, next is KCO that is the rate of uptake of carbon monoxide by the blood and VA that is alveolar volume.

We have to understand the relation that DLCO is KCO into VA where KCO is DLCO by VA that is corrected DLCO to alveolar volume. KCO is otherwise called as the transfer coefficient determines whether the currently available alveolar spaces are functionally normal. Now this is an algorithm for stepwise interpretation of DLCO report. In a DLCO report, first we should see the value of DLCO. If DLCO is more than the upper limit of normal or more than the 140 percentage, then it is considered abnormally high.

What could be the underlying cause? It could be increased blood flow, example left to right shunt, asthma or obesity or erythrocytosis or alveolar hemorrhage. When DLCO is less than lower limit of normal or less than 76 percent, then next we have to look at the value of VA. If DLCO is low, but VA is normal, then underlying condition may be a pulmonary vascular abnormality like pulmonary hypertension, pulmonary embolism or pulmonary vasculitis. Sometimes there might be an emphysema with preserved lung volume like in early ILD or anemia. If DLCO is low and VA is low, next we should look at the KCO.

If KCO is low or normal, then we have to suspect some loss of alveolar capillary structure with loss of lung volume like an emphysema or interstitial lung disease. If DLCO is low, VA is low, but KCO is high, then we have to suspect underlying localized loss of lung volume like in pneumonectomy, incomplete lung expansion, example atelectasis and neuromuscular dysfunction. The next step is looking at the relationship between VA and

TLC. TLC is total lung capacity. So, we all know that VA is accessible alveolar volume that is available for the diffusion.

So, VA is not total lung capacity, VA is a fraction of the total lung capacity, but it should be within 15 percent of the total lung capacity. When VA is very much less than the total lung capacity, it is understood that there is poor distribution of ventilation. Let us look at another algorithm where this relationship between VA and TLC is used. When TLCO or DLCO is low, look at VA. If VA is low, then look at the VA by TLC ratio.

If VA is very low when compared to TLC and ratio falls below 0.8, then it might suggest that the underlying is obstructive disease. If the VA by TLC is preserved and it is approximately more than 0.8 percent, then it is suggestive of an underlying restrictive disease. So next we have to look at the value of KCO whether it is normal, low or high.

Now let us start interpreting the report by implying what we have seen so far. So, this is the first report of a patient who came with breathlessness. First let us start interpreting the lung volume. So, here we have a pre and post bronchodilator response lung volume. So FVC of this patient is 58 percent pre and 51 percent post.

FEV1 is 52 percent pre and 52 percent post. FEV1 is 107 percent. And we also see there is no significant bronchodilator reversibility. So, this lung volume report, spirometry report is suggestive of a restrictive defect. Now let us take a look at the body plethysmograph report. TLC is reduced and this confirms the restrictive disease.

Now let us take a look at the diffusion study of the same patient. DLCO corrected to hemoglobin is 42 percent. Next step is looking at the VA. This is again reduced.

Next step is looking at the KCO is fairly normal. Let us take a look at the algorithm. So, in this report, DLCO is reduced, VA is reduced. Next, we are looking at the KCO. KCO is again fairly normal. So, this could be either emphysema or ILD, but in view of restrictive disease, this is of the case of interstitial lung disease.

Let us look at the second report. Spirometry values are given here. So FVC pre is 96 percent, post is 98 percent. FEV1 pre is 83 percent, post is 87 percent. There is no significant bronchodilator reversibility.

FEV1 by FVC is 69 percent. So, this is suggestive of a mild obstruction with no significant bronchodilator reversibility. Now let us take a look at the body plethysmograph report. This shows that the TLC is increased as well as residual volume is increased that confirms that this is an obstructive disease with air trapping. Now let us take a look at the diffusion study.

DLCO is reduced to 55 percent. Second step is looking at VA. This is again reduced 71 percent. KCO is again reduced 46 percent. So, this is a case of COPD emphysema. One

point to note here is that VA is very much reduced than the TLC telling us that there is small distribution or inadequate distribution of ventilation throughout the alveolar membrane.

Let us move on to case 3. Case 3 we have the spirometry values here where the pre FVC is 88 percent, post is 98 percent, pre FEV1 is 47, 59 percent is post, FEV1 by FVC ratio post is 62 percent which tells that there is a obstructive disease. Let us look at the percentage change. It is 12 percent and 24 percent in FEV1. So, this is an obstructive disease with significant BDR.

Let us see the body plethysmograph report. TLC is 101 percent; residual volume is increased 177 percent. Let us take look at the diffusion studies. Diffusion capacity is normal, VA is normal and KCO is normal. So obstructive disease with significant bronchodilator reversibility and a normal DLCO we can infer that this is a case of bronchial asthma.

The last report, let us report the last case. So, FVC pre is 74 percent, FVC post is 64 percent, FEV1 pre is 61 percent, FEV1 post is 64 percent, FEV1 by FVC post is 105 percent. So, this is suggestive of a restrictive defect. To confirm it let us look at the body plethysmograph report. TLC is reduced, RV is reduced.

So, this tells us this is a restrictive disease. Now let us take a look at the diffusion study to come to a conclusion. So DLCO is 68 percent reduced, VA is 63 percent reduced, KCO is 111 percent which is increased. When coming across such a situation it is ideal to look at VA by TLC ratio as we have already seen this algorithm where VA is low, VA by TLC has to be looked out.

If it is more than 0.8 percent, if it is more than 0.8 percent then it is suggestive of restriction. Where KCO is high it is suggestive of extra parenchymal. Like in our report here we see that VA by TLC 3.49/3.92 is more than 0.8 suggestive of a restrictive disease where KCO is high. So, it is mostly suggestive of an extra parenchymal disease like a neuromuscular disease. So, to summarize we have for interpreting diffusion capacity of the lung we need spirometry lung volume reports, TLC report and we have to look into three components DLCO, VA and KCO and in certain situations we have to look into VA by TLC.