Using and Interpreting Carbon Monoxide Diffusing Capacity (DLCO) Correctly

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Objectives for Diffusing Capacity

- What is diffusing capacity and why do we do this test?
- Diffusing capacity physiology
- Diffusing capacity test performance
- Variability in diffusing capacity measurements
- Diffusing capacity interpretation
- Clinical utility of diffusing capacity
Animated DLCO test

Special thanks to nddmed

https://www.youtube.com/channel/UC94tvJZBjJVjqRxcpovAA-A
Why do we need this test

To evaluate respiratory symptoms
To determine severity of impairment in patients with known respiratory disease
To follow the course of disease in a patient, including the response to therapy
To screen for subclinical disease
DLCO — Indications

- Differentiate asthma from emphysema
- Evaluation and severity of restrictive lung disease
- Disability/impairment evaluations for ILD or COPD
- Anemia
- Pulmonary fibrosis
- Early stages of pulmonary hypertension
- Sarcoidosis
- Pulmonary vascular disease
- Interstitial lung disease
- Alveolar hemorrhage
- COPD
What is diffusing capacity?

Measure's ability of lungs to transport inhaled gas from alveoli to pulmonary capillaries

Carbon monoxide is carrier gas because of binding affinity to hemoglobin (0.3%)
200-250 greater affinity than oxygen
Inert gas such as 10% helium

Used to diagnose various pulmonary diseases

Depends on:
- alveolar—capillary membrane
- hemoglobin concentration
- cardiac output
Diffusing capacity pathway

- Pathway for diffusion of CO and O₂ involves diffusion across the
  - Alveolar capillary membrane
  - Alveolar cell basement membrane
  - Potential interstitial space
  - Capillary endothelium
  - Across a thin layer of plasma
  - Across a red blood cell membrane
  - Red blood cell until they bind with hemoglobin.
$D_L$CO-Nice picture!

Diagram: Diffusing Capacity for Carbon Monoxide ($D_L$CO)

- $D_L$: overall throughput or conductance
- $D_M$: diffusing capacity of membrane
- $P_{ACO}$: partial pressure of arterial carbon dioxide
- $PCO$: partial pressure of carbon dioxide
- $HbCO$: carbon monoxide bound to hemoglobin
- $\Theta \cdot V_c$: rate of reaction with Hb

Conditions:
- Normal
- Emphysema
- Anemia
- Alveolar Hemorrhage
Diffusing capacity physiology

- Gas crosses the alveolar-capillary membrane
- CO has greater affinity to binding to hemoglobin than oxygen (200-250)
  - Greater number of CO binding sites on hemoglobin molecule
  - CO so far is best gas for test
- WARNING! FOR GEEKS ONLY - Fick's law describes the diffusion of a gas through tissue
  - Amount of gas transferred across a membrane is directly proportional to
    - Tissue surface area
    - Diffusion constant
  - Difference in gas partial pressure and is inversely proportional to the tissue thickness.
  - Diffusion constant is proportional to the solubility of a gas and is inversely proportional to the square root of the molecular weight of the gas.
Grades of severity in DLCO reduction

- Normal DLCO: >75% of predicted, up to 140%
- Mild: 60% to LLN (lower limit of normal)
- Moderate: 40% to 60%
- Severe: <40% LLN: lower limit of normal

\[
\begin{align*}
\text{Men : } & \quad \text{DLCO} = 0.3504H - 0.2156A - 23.168 \\
& \quad \text{DLCO/VA} = -0.0205H - 0.0283A + 9.0919 \\
\text{Women : } & \quad \text{DLCO} = 0.2491H - 0.1533A - 11.662 \\
& \quad \text{DLCO/VA} = 0.0140H - 0.0216A + 3.413
\end{align*}
\]
Diffusing Capacity

- **Decreased DLCO** (<80% predicted)
  - Obstructive lung disease
  - Parenchymal disease
  - Pulmonary vascular disease
  - Anemia

- **Increased DLCO** (>120-140% predicted)
  - Asthma (or normal)
  - Pulmonary hemorrhage
  - Polycythemia
  - Left to right shunt
Normal Diffusing Capacity

- Average DLcosb value 25 ml CO/min/mm Hg (STPD)
- Should always be done with spirometry
• Diffusion and perfusion are the two main processes which govern the rate of alveolar-capillary gas transfer

• **Perfusion limited**
  - Reduced cardiac output or anemia will impede oxygen transport
  - Less uptake of oxygen by hemoglobin

• **Diffusion limited**
  - Oxygen transfer is impeded by physical barrier
  - Examples include
    - Atelectasis
    - Pulmonary fibrosis
    - Emphysema
    - Pneumonia
    - Interstitial edema
Diseases With Decreased DLCO

- Emphysema
  - Obstructive pattern

- Interstitial lung disease
  - Thickening of the alveolar-capillary membrane with restrictive pattern

- Idiopathic pulmonary fibrosis
  - Restrictive pattern with autoimmune diseases

- Sarcoidosis
  - Mixed pattern with anemia due to noncaseating granulomas and absent iron stores in the bone marrow

- HIV infection (PCP) – new studies emerging
  - Obstructive pattern with inflammation
More Diseases With Decreased DLCO

- Pulmonary vascular disease
  - DLCO is an independent predictor of death
- Pulmonary arterial hypertension
  - DLCO was strongly associated with survival in patients with PH across different etiologies
- Pulmonary embolism
  - Reduction of DLCO provides a useful and simple screening test for PE and responsiveness of anticoagulant responsiveness
- Left-sided heart disease
  - Restrictive pattern and reduction in the alveolar–capillary membrane surface area available for gas exchange
- Anemia
  - Positive linear correlation between the hemoglobin content of the blood and DLCO
Cases of Increased DLCO

- Pulmonary hemorrhage (pulmonary vasculitis)
- Polycythemia
- Asthma
- Obesity
- Pregnancy (if not anemic)
A 65-year-old man undergoes pulmonary function testing as part of a routine health-screening test. He had no pulmonary complaints. He is a lifelong nonsmoker and had a prior history of asbestos exposure while serving in the Navy. His pulmonary function test results are as follows:
# Spirometry

<table>
<thead>
<tr>
<th>Test</th>
<th>Actual</th>
<th>Predicted</th>
<th>% Predicted</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>4.39</td>
<td>4.32</td>
<td>102</td>
<td>-1</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>3.20</td>
<td>3.37</td>
<td>95</td>
<td>7</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>73</td>
<td>78</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>FRC (L)</td>
<td>3.17</td>
<td>3.25</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>ERV (L)</td>
<td>0.63</td>
<td>0.93</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>RV (L)</td>
<td>2.54</td>
<td>2.32</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>TLC (L)</td>
<td>6.86</td>
<td>6.09</td>
<td>113</td>
<td></td>
</tr>
<tr>
<td>DLCO uncorr</td>
<td>25.69</td>
<td>31.28</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>DLCO corr</td>
<td>26.14</td>
<td>31.28</td>
<td>84</td>
<td></td>
</tr>
</tbody>
</table>

DLCO is measured in ml/min/mmHg
Flow Volume Loop
Case 1 Interpretation

- Is this a normal or abnormal PFT test?
  - The FVC and the FEV1 are 102% and 95% of predicted, respectively, values well above the lower limit of normal and the FEV1/FVC ratio is greater than the predicted value minus 8.

- What are your observations about the flow volume loop?
  - The flow-volume loop also corresponds quite nicely to the predicted values for this patient (darkened circles). Based on this normal spirometry pattern, you would conclude that there is no evidence of air-flow obstruction. The patient also has normal total lung capacity, indicating that there is no evidence of restriction, and a normal diffusing capacity for carbon monoxide, indicating that the alveolar-capillary surface area for gas exchange is normal.

- Was there a significant change in the bronchodilator response?
  - There is no bronchodilator response.

- Was her DLCO normal or abnormal?
  - Normal
Case study 2

- A 41-year-old woman presents to the General Internal Medicine Clinic at Harborview Medical Center complaining of dyspnea with mild exertion.
- She has a 10 pack-year history of smoking and a history of using intravenous drugs including heroin and ritalin.
- Her pulmonary function tests are as follows:
## Spirometry

<table>
<thead>
<tr>
<th>Test</th>
<th>Pre-Bronchodilator (BD)</th>
<th>Post-BD</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>Actual</td>
<td>Predicted</td>
<td>% Predicted</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>0.90</td>
<td>3.09</td>
<td>29</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>0.49</td>
<td>2.57</td>
<td>19</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>54</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>RV (L)</td>
<td>3.83</td>
<td>1.49</td>
<td>257</td>
</tr>
<tr>
<td>TLC (L)</td>
<td>4.78</td>
<td>4.44</td>
<td>108</td>
</tr>
<tr>
<td>RV/TLC (%)</td>
<td>80</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>DLCO corr</td>
<td>0.75</td>
<td>24.85</td>
<td>3</td>
</tr>
</tbody>
</table>
Flow Volume Loops

Her flow volume loop is as follows:
Case 2 Interpretation

- Is this patient demonstrating air-flow obstruction?
  - Yes- her FEV1, FVC and her FEV1/FVC are all decreased

- Does her flow volume loop demonstrate the characteristic scooped-out appearance seen in obstructive lung disease?
  - Yes- and also demonstrates markedly reduced peak expiratory flows.

- Based on her FEV1 of 19% predicted would this would be classified as “very severe” obstructive lung disease?
  - The patient also has evidence of air-trapping, as her RV is 257% predicted. She would not be classified as being hyper-inflated because her TLC is only 108% predicted.

- Was there evidence of a bronchodilator response?
  - There is no evidence of a bronchodilator response as her FVC and FEV1 both values decline following bronchodilator administration.
Case 2 Interpretation

- Was her DLCO decreased?
  - Her DLCO is decreased, indicating a loss of alveolar-capillary surface area for gas exchange.

- Is it likely that she has asthma?
  - Asthma is an unlikely diagnosis given the absence of reversibility with bronchodilator administration.

- Her chest x-ray provides some clues to the diagnosis- do you know what it is?
  - There is marked hyperlucency at the bases, suggesting that this is a basilar-predominant form of emphysema. The lower lobes are over-inflated.
Decreased Diffusing Capacity with Emphysema

- Decreased *DLCO is associated with* airflow obstruction
  - Diagnosis of emphysema is to be considered
- Emphysema with a restrictive process such as idiopathic pulmonary fibrosis
  - Reduced DLCO
  - Normal spirometry and lung volumes
Diffusing Capacity and Interstitial lung disease

- Decreased DLCO with restrictive process
- Elements of fibrosis with biopsies
- Reduced lung volumes
- Patchy distribution of ground glass, reticular, nodular, or cystic opacities on radiographic images
- Monitored over time to determine severity of disease process
Diffusing Capacity and Sarcoidosis

- Airway obstruction and lower DLCO
- Symptoms related to the lung, skin, eyes, peripheral nerves, liver, kidney, heart, and other tissues.
- North American blacks and European white people
- More common in women
- Noncaseating granulomas in a biopsy specimen
- Bilateral hilar adenopathy
- Diffuse reticular infiltrates
Diffusing Capacity and COPD

- Obstructive pattern with spirometry
- Normal DLCO unless complicated by emphysema
- In patients with COPD, DLCO less than 50% of predicted is accompanied by O2 desaturation during exercise
- Low resting DLCO (<50% - 60% of predicted) may indicate the need for assessment of oxygenation during exercise
Summary

- DLCO is a valuable test when done with conjunction of PFT
- Obstructive and restrictive disorder can be identified
- Monitor the progress of lung disorders
• *Pulmonary function in case of rheumatoid arthritis at a Tunisian population*. Tunis Med. 2013 Apr;91(4):248-53 Fredj,B

• *Disease Progression in Idiopathic Pulmonary Fibrosis Without Pulmonary Function Impairment*. Respirology. 2013 Mar 12,Kondoh,Y

• *The rise in carboxyhemoglobin from repeated pulmonary diffusing capacity tests*. Respir Physiol Neurobiol. 2013 Mar 1;186(1):103-8,Zavorsky,GS
