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Diffusing Capacity

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Abstract The diffusing capacity for carbon monoxide (DL_{CO}) is a commonly performed and clinically useful pulmonary function test that provides a quantitative measure of gas transfer in the lungs. It is valuable for evaluating and managing patients with a wide variety of pulmonary disorders, especially patients with interstitial lung disease, pulmonary vascular disease, and obstructive lung disease. Important aspects of the DL_{CO} test are discussed including the physiologic principles governing diffusion, testing technique and equipment, technical and physiologic factors influencing DL_{CO} variability, DL_{CO} test interpretation, and the clinical utility of DL_{CO} measurement.

Keywords Diffusing capacity · Pulmonary function test · Respiratory disease

Abbreviations

DL_{CO}	diffusing capacity for carbon monoxide
CO	carbon monoxide
COPD	chronic obstructive pulmonary disease
ATS	American Thoracic Society
ERS	European Respiratory Society
Hb	hemoglobin
$\dot{V}$gas	gas transfer per unit time
D_M	membrane component of diffusion
θ	rate at which carbon monoxide binds with hemoglobin
VA	alveolar volume
V_C	pulmonary capillary blood volume
STPD	standard temperature, pressure, dry conditions

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Introduction

The diffusing capacity for carbon monoxide (DL_{CO}) is a common and clinically useful test that provides a quantitative measure of gas transfer in the lungs. Diffusing capacity, along with spirometry and arterial blood gas measurement, are core pulmonary function tests used to evaluate and manage patients with respiratory diseases. Diffusing capacity is often abnormal in patients with interstitial lung disease, pulmonary vascular disease, and chronic obstructive pulmonary disease (COPD). In patients with obstructive lung disease, it may be useful in distinguishing asthma from COPD [1, 2]. Because it is able to measure the transfer of gas from the airways to the reaction with hemoglobin (Hb) in the pulmonary capillaries, DL_{CO} has been called a "window on the pulmonary microcirculation [3]." Diffusing capacity is influenced by processes in addition to diffusion and is usually obtained at rest when it is submaximal—it is not a true capacity measurement. *Transfer factor*, the term commonly used outside of North America, is a more accurate term. However, because of its historical use and for the sake of uniformity, the European Respiratory Society (ERS) and the American Thoracic Society (ATS) continue to endorse the expression DL_{CO} [4].

Diffusing capacity was first measured and reported by Krogh in 1914 [5]. Ogilvie introduced the single-breath technique in 1957, adding an inert gas to the inhaled gas mixture, allowing the concomitant measurement of lung volume [alveolar volume (VA)] and the use of a single alveolar gas sample [6]. The single-breath technique is the most common method to measure DL_{CO}

around the world and will be the focus of this review. Diffusing capacity can be measured using other techniques including the steady state method, rebreathing method, intrabreath method, and multiple inert gas technique. These are more technically demanding and are reviewed elsewhere [7].

Physiology of diffusing capacity

The purpose of measuring DL_{CO} is to provide information on the transfer of gas from the airways to Hb. This is depicted in Fig. 1. The biologically important gas essential to cellular metabolism is oxygen (O_2). Why then is the diffusion of carbon monoxide (CO) measured rather than the diffusion of O_2? Both CO and O_2 readily diffuse across the alveolar capillary membrane and bind tightly with Hb. However, CO has a binding affinity for Hb 200 to 250 times greater than that of O_2. Because of the high affinity of CO with Hb and the abundance of CO binding sites on the Hb molecule, the pulmonary capillary CO tension remains near zero when low concentrations of CO are inhaled. Carbon monoxide uptake is entirely diffusion-limited. In contrast, the pulmonary capillary O_2 tension or partial pressure rises along the length of the capillary, creating appreciable back tension. Oxygen is perfusion limited in normoxic conditions and perfusion and diffusion limited in hypoxic conditions. Despite the fact that O_2 is the primary gas of interest, technical factors preclude measurement of DL_{O2}. At the present time, CO is the best gas to measure the diffusion properties of the lung.

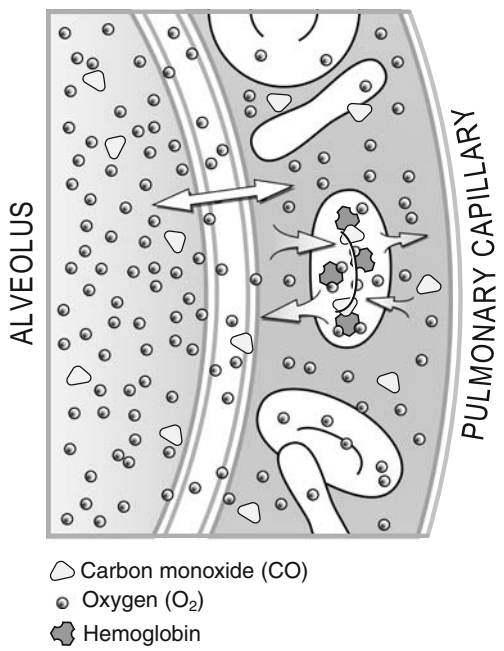

Fig. 1 The transfer of carbon monoxide and oxygen from the alveolus, across the alveolar–capillary membrane, and the reaction with hemoglobin is represented

Fick's law explains the diffusion of a gas through tissue. The amount of gas transferred across a sheet of tissue is directly proportional to the tissue surface area, diffusion constant, and the difference in gas partial pressure and inversely proportional to the tissue thickness. The 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. This relationship is exhibited in Fig. 2. It is not possible to determine the tissue area or thickness of the alveolar capillary membrane for the entire lung, so area, thickness, and the diffusion constant are replaced by a single constant DL, representing the diffusing capacity for the lung.

$$\dot{V}_{\text{gas}} = D_{\text{L}} \times (P_1 - P_2)$$

Where D_{L} is the diffusing capacity of the lung and P_1 and P_2 are the gas concentrations in the alveolus and pulmonary capillary, respectively. When CO is the gas being measured, P_2 is assumed to be small and is ignored. The equation then becomes

$$\text{DL}_{\text{CO}} = \dot{V}_{\text{CO}} \Big/ \text{PA}_{\text{CO}}$$

This equation states that the quantity of CO transferred from the alveolar gas to the capillary blood, or the diffusing capacity for CO (DL_{CO}), is equal to the volume of CO transferred per minute per millimeter of mercury of alveolar partial pressure of CO. The traditional units for DL_{CO} are millimeters CO at standard temperature, pressure, and dry (STPD) conditions, per minute, per millimeter Hg; SI units are moles CO per minute per kilopascal [4].

As illustrated in Fig. 1, the pathway for diffusion of CO and O_2 involves diffusion across the alveolar capillary membrane (consisting of the alveolar cell, the basement membrane, a potential interstitial space, and the capillary endothelium), across a thin layer of plasma, across a red blood cell membrane, and within the red blood cell until they bind with Hb. Roughton and Forster simplified this process into two stages: (1) diffusion of CO from the alveolus to the red cell interior, described as the membrane component (D_M), and (2) the uptake of CO by binding with Hb in the red cells per millimeter Hg CO tension (θ) and the blood volume of the pulmonary capillary bed (V_C) [8]. The basic equation for DL_{CO} is a conductance, flow divided by pressure change ($\dot{V}/\Delta P$). The reciprocal of conductance is resistance, and resistances can be added in series. Therefore, Roughton and Forster proposed the following equation to describe the diffusion of CO in the lung:

$$1/\text{DL}_{\text{CO}} = 1/D_{\text{M}} + 1/\theta V_{\text{C}}$$

The relative importance of each component can be determined by measuring DL_{CO} with high concentrations

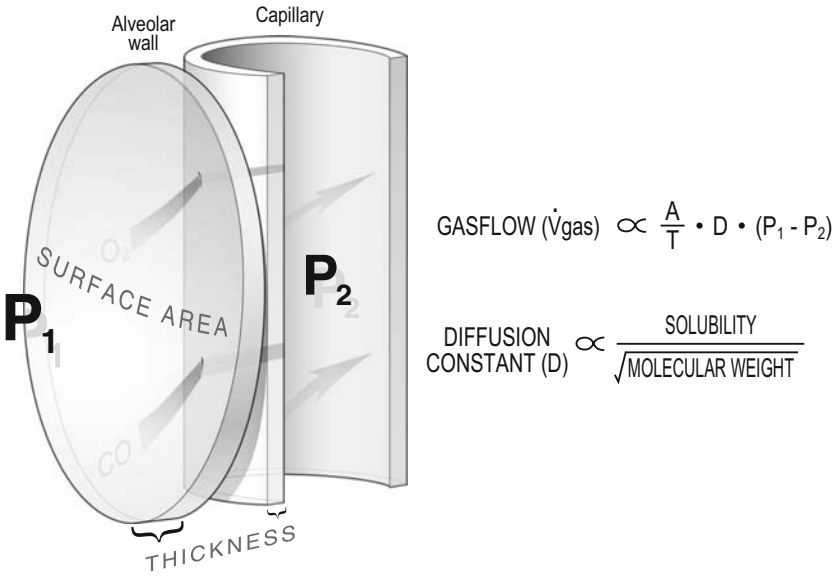

Fig. 2 Fick's law describes the factors that determine diffusion of a gas (V_{gas}) through tissue including tissue surface area (A), tissue thickness (T), a diffusion constant (D), and the difference in gas partial pressure across the tissue (P_1–P_2). The diffusion constant (D) is determined by the solubility of a gas and the molecular weight of the gas

of inspired O_2. With increasing partial pressure of O_2, CO competes with O_2 for Hb binding, reducing the θV_C component. While this is conceptually important in determining the pathophysiologic mechanism for reduced DL_{CO} in various conditions, it has not been found to be clinically useful because of technical difficulties and poor reproducibility [9].

The single-breath DL_{CO} technique requires a subject to inhale a gas mixture containing a low concentration of CO and an inert gas, usually helium, methane, or neon. The inert gas is essentially insoluble and cannot cross the alveolar capillary membrane. The inhaled concentration of inert gas is known, and by measuring the exhaled concentration, the VA can be determined. The initial alveolar concentration of CO (PA_{CO}) can be determined by making the assumption that CO is diluted to the same extent as the inert gas. The advantage of this method is that it only requires knowing the concentration of the inhaled CO and inert gas and the concentration of the same gases in an alveolar sample. This method allows the measurement of VA, as well as DL_{CO}.

Testing technique and equipment

The single-breath method of measuring DL_{CO} is the most commonly used technique. Its advantages are that it has been standardized by the ATS and ERS, there are well-defined reference values for healthy subjects, and the majority of clinical studies have used this method [4]. The three-equation method of measuring single-breath DL_{CO} has been reported to be more accurate, precise, and easy for the patient to perform, but it has not been widely adopted. It is more complicated and not available on most commercial instruments [10].

Single-breath DL_{CO} measurement is more complex than spirometry and requires a higher level of commitment and expertise for test performance, maintenance, and quality control. In addition, the instrument is considerably more expensive than a spirometer, often costing greater than $30,000. For these reasons, DL_{CO} is not commonly performed in the outpatient office setting. The basic instrument consists of a source of test gas, a device for measuring inspired and expired volume, and gas analyzers. The test gas is usually a mixture of 0.3% CO, an inert gas often either 0.3% methane, 10% helium or 0.5% neon, 17% or 21% O_2, and the balance nitrogen. At altitudes above sea level, gas mixtures with a higher concentration of O_2 are often used to achieve an inspired O_2 partial pressure similar to that at sea level [11, 12]. The gas analyzer can be a single-sample slow responding analyzer or a continuous high-speed analyzer. The high-speed analyzers allow the washout volume and alveolar sample volume to be adjusted. Using a system with a continuous high-speed analyzer that allows visual adjustment of the washout volume appears to improve the accuracy and reproducibility of DL_{CO} measurements [13].

Performance standards for DL_{CO} equipment and quality control measures are discussed in detail elsewhere [4]. As is the case for spirometers, the volume measuring accuracy should be within +/− 3.5% over an 8-L volume range. The gas analyzer must produce a linear response for CO and the tracer gas over their expected concentration ranges with a maximum error of 0.5% [4]. The methods for determining instrument accuracy vary from instrument to instrument and specific instructions provided by the manufacturer must be followed. Standard recommendations suggest that, before each test, the gas analyzer should be zeroed. Each day, volume accuracy should be tested with a 3-L syringe. In

addition, the system should be tested weekly with a biological control or a commercially available DL_{CO} simulator (Hans Rudolph, Kansas City, MO, USA).

Standardizing test performance is important to minimize variability. The patient should be instructed to not smoke or exercise vigorously on the day of the test and should discontinue supplemental oxygen for 10 min prior to testing, if clinically acceptable. With a nose-clip in place, the patient breathes quietly through the mouthpiece. After the technician sees a stable breathing pattern, the patient is instructed to exhale completely. The valve to the test gas is then opened and the patient instructed to take a full breath. Inspiratory time should be less than 4.0 s. The inhaled volume should be at least 85% of the largest known vital capacity. The patient then holds his or her breath for 10 (+/−2) s, maintaining near atmospheric pressure during the breath hold (performing neither a Valsalva or Muller maneuver). Breath-hold time is calculated using the Jones–Meade method (two-thirds of the time for inspiration and continuing until half-way through the sample collection) [14]. The Jones–Meade method for calculating breath-hold time is depicted in Fig. 3C. After the breath hold, the patient is instructed to exhale smoothly without hesitation. Total exhalation time for clearing the washout volume and collecting the alveolar sample should not exceed 4 s. Measurement of DL_{CO} requires a good alveolar sample. The alveolar sample is the gas volume obtained after the anatomic and mechanical dead space volumes are cleared or "washed out." It is the volume of gas used to analyze the CO and tracer gas concentrations. The washout volume needed to confidently clear the dead space is 0.75–1.0 L [13]. In patients with a vital capacity less than 2.0 L, the washout volume may be reduced to 0.50 L. If all lung units emptied simultaneously, it would not matter where the alveolar sample was collected as long as the dead space was appropriately cleared. However, in patients with lung units that empty with different time constants, a suitable volume is needed to represent multiple lung units. The recommended alveolar sample gas volume collected for analysis is 0.50–1.00 L. In patients with a vital capacity of less than 1.0 L, an alveolar sample gas volume of less than 0.50 L is acceptable if the dead space volume has been adequately cleared. This can be done by visually adjusting the alveolar sample collection at a point where the inert gas concentration has started to plateau and requires a system with a rapid gas analyzer. The single-breath DL_{CO} maneuver is illustrated in Fig. 3A, B.

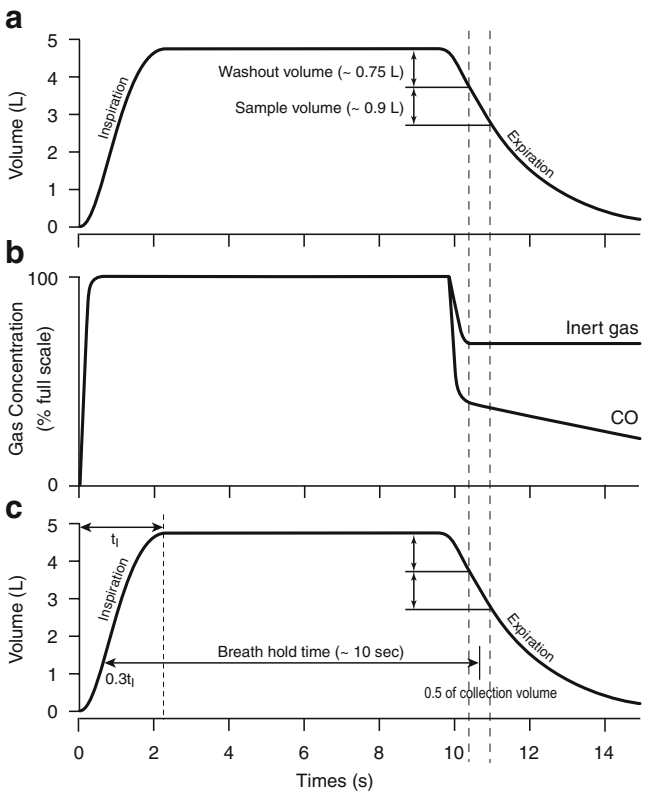

Fig. 3 The single-breath DL_{CO} maneuver with recommended washout and sample collection volumes is represented (**a**). Typical inert gas and carbon monoxide (CO) gas concentration curves are shown (**b**). Note that the sample volume should be collected when there is a "plateau" of the inert gas concentration. The Jones-Meade method for calculating breath-hold time is illustrated (**c**)

The DL_{CO} maneuver should be repeated until there are at least two technically acceptable and reproducible tests. The ATS/ERS guidelines suggest the average of at least two acceptable tests be reported; acceptable tests are repeatable within 3 ml CO (STPD) min^{-1} mm Hg^{-1} of each other or within 10% of the highest value [4]. Many laboratories require a higher degree of intersession reproducibility. In a large university-based laboratory study, 91.5% of patients were able to meet a repeatability criterion of 2 ml CO (STPD) min^{-1} mm Hg^{-1} [15]. The DL_{CO} maneuver checklist used in our laboratory reviewing key points in test performance is included as Table 1.

Diffusing capacity variability

Many technical and physiologic factors influence DL_{CO} variability. These sources of variability must be minimized to obtain clinically useful results. As noted above, the ATS/ERS guidelines recommend that two acceptable tests be within 3 ml CO (STPD) min^{-1} mm Hg^{-1} of each other or within 10% of the highest value, and laboratories should strive to meet a repeatability criteria of 2 ml CO (STPD) min^{-1} mm Hg^{-1}. Strict adherence to guideline recommendations will reduce variation. Interlaboratory variability for DL_{CO} can be very large and caution should be used when comparing an individual patient's results obtained at different laboratories [16]. However, if technical factors

Table 1 DL_{CO} maneuver checklist

VI is at least 85% of largest VC
Rapid inspiration—VI inspired in <4.0 s
Breath-hold time of 10 +/− 2 s; no evidence for air leak during breath-hold
Intrapulmonary pressure during breath-hold is near atmospheric; no Valsalva or Muller
Smooth unforced exhalation in <4 s
Washout (deadspace) volume is 0.75–1.0 L (0.50 L is acceptable if VC<2.0 L)
Sample (alveolar) volume is 0.50–1.0 L and collected on plateau of inert gas tracing (<0.50 L is acceptable if VC<2.0 L)
A minimum of 2 acceptable tests within 2 units

VI inhaled volume, *VC* vital capacity

are tightly controlled, intraindividual variability can be within 5%. This is comparable with the accepted intra-individual variability for forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) [15, 17].

The most important technical sources of variation in the measurement of DL_{CO} include the measurement of inspired and expired volume, inspired volume of the test gas, rate of inspiration, breath-hold duration, method of calculating breath-hold time, the condition of the breath-hold, dead-space washout volume, and gas analysis. The measurement of inspired and expired volumes must be accurate. Inspiratory volume can be compared to another independent measure of vital capacity and should be within 85%. A submaximal inspiratory volume will reduce the DL_{CO} [18]. Prolonging inspiration beyond 4 s will reduce DL_{CO}. Breath-hold time should be 10±2 s and measured using the Jones–Meade method described above. An under-reported breath-hold time will result in an overestimation of DL_{CO}. During the breath-hold, intrapulmonary pressure should be near atmospheric; a Valsalva maneuver (expiratory efforts against a closed airway) will decrease venous return and thoracic blood volume resulting in a decrease in DL_{CO} of up to 17% [19]. A Muller maneuver (inspiratory efforts against a closed airway) will have the opposite effect on venous return and thoracic blood volume and may increase DL_{CO} up to 6% [19]. The deadspace washout volume must be cleared and an alveolar gas sample collected. Contaminating the alveolar gas sample with dead space gas will result in an underestimation of DL_{CO}. Gas analyzer instability is a frequently unrecognized technical source of increased variability.

Physiologic sources of variability may be more difficult to control than technical sources of variability but must be considered when interpreting DL_{CO} changes in an individual. The most important physiologic sources of variability in the measurement of DL_{CO} are listed in Table 2. Cross-sectional reference studies have shown that DL_{CO} is primarily influenced by age, height, sex and race [11, 20]. Diffusing capacity is lower with advancing age and shorter height. It is lower in women than men for any given height and Hb level. African-American's DL_{CO} is lower by an average of 1.96 ml CO (STPD) min^{-1} mm Hg^{-1} compared to Caucasians for a given height [21]. Reduced Hb (anemia) results in a reduction in DL_{CO}, and an adjustment for Hb concentration is important for interpretation [4]. Elevated carboxyhemoglobin (COHb) reduces DL_{CO} by reducing the available Hb binding sites and by increasing the back pressure of CO in alveolar capillary blood. In general, a 1% increase in COHb reduces the measured DL_{CO} by 1% [4]. Because cigarette smoking is the most common reason for increased COHb, patients should not smoke on the day of the test. Changes in inspired oxygen concentration, either by the use of supplemental O_2 or altitude, affect DL_{CO}. Diffusing capacity increases with decreasing inspired O_2 pressure (PO_2) as O_2 and CO compete for the same binding sites on the Hb molecule. The altitude effects on DL_{CO} can be corrected by either increasing the test gas O_2 concentration or by using an altitude adjustment equation [12]. For example, in Salt Lake City, UT (altitude 1,400 m), 25% O_2 is commonly used in the DL_{CO} test gas mixtures to produce a PO_2 similar to that at sea level (150 mm Hg) [11].

Diffusing capacity decreases from morning to evening, a finding likely explained by small changes in Hb during the course of the day [22]. Diffusing capacity can vary about 9% throughout a woman's menstrual cycle, with the highest level occurring just before menses and the lowest occurring

Table 2 Physiologic sources of variability

Age
Gender
Ethnicity
Hb concentration
COHb concentration
Altitude and inspired oxygen concentration
Circadian rhythm
Menstrual cycle
Smoking history
Exercise
Body position
Bronchodilation

5–10 days after the onset of menses. This monthly variation is not explained by changes in Hb concentration [23]. Current and past cigarette smokers have small reductions in DL_{CO} compared with never smokers. The reduction is proportional to the number of pack years [21]. The effects of exercise on DL_{CO} are complex. During exercise, DL_{CO} increases and is associated with increased capillary blood flow [24, 25]. Following intense exercise, DL_{CO} falls below pre-exercise levels perhaps representing a redistribution of pulmonary capillary blood volume to peripheral muscles [26]. Because diffusing capacity decreases as a patient moves from the supine to sitting to standing positions [24], it is recommended that patients remain in the sitting position during and at least 10 min prior to testing. Bronchodilator administration increases DL_{CO} as much as 6% in patients with obstructive lung disease [27]. The use of a bronchodilator prior to testing should be noted during the interpretation.

Diffusing capacity interpretation

As with spirometry, the first step in interpreting a DL_{CO} study is to review test quality and reproducibility. The results from two acceptable tests should be within 3 ml CO (STPD) min^{-1} mm Hg^{-1} of each other and the mean value reported. Any adjustments for Hb and COHb should be reported.

If previous tests are available, the results should be compared with them, as well as with reference values based on healthy subjects. There are limited data regarding intraindividual variability in DL_{CO} over time. The ATS/ERS guidelines state that changes of greater than 10% from year to year are significant [28].

When DL_{CO} is compared to reference values, care should be taken to use reference values from populations of comparable biologic characteristics and performed using similar technical standards [28]. The test is judged abnormal if it is below the lower fifth percentile of the reference population. The ATS/ERS criteria [28] for grading the severity of reductions in DL_{CO} are listed in Table 3.

A common practice is to adjust or "correct" DL_{CO} for lung volume by using DL_{CO}/VA. The clinical utility of this measurement is questionable primarily because the relationship between DL_{CO} and VA is not linear. In some circumstances, including patients postpneumonectomy and normal subjects with incomplete inhalation, the reduction in DL_{CO} is less than the concomitant decrease in VA, and the DL_{CO}/VA will be increased. In patients with pulmonary vascular disease and some patients with hyperinflation, the reduction in DL_{CO} is greater than the concomitant change in VA, resulting in a decrease in DL_{CO}/VA [29, 18]. When ventilation is maldistributed and VA is altered, it cannot be assumed that the diffusion properties of the maldistributed lung units are the same as the more normal lung units. The measurement of DL_{CO}/VA is commonly misleading and cannot be relied upon to make clinical decisions.

Table 3 Degree of severity of decrease in DL_{CO}

Degree of severity	DL_{CO} % predicted
Mild	>60% and <LLN
Moderate	40–60%
Severe	<40%

LLN lower limits of normal

The single-breath DL_{CO} test requires the measurement of VA. VA minus dead space volume approximates total lung capacity (TLC). However, VA is determined by the inert gas dilution method and only measures those areas of the lung that communicate with the mouth. Lung units that contain trapped gas are not measured. In patients with obstructive lung disease, VA results in significant underestimation of TLC measured by the more accurate body plethysmography technique [30, 31]. Reliance on VA to assess lung volumes may result in falsely classifying patients with obstructive lung disease as having a mixed obstructive/restrictive abnormality.

The final step in interpretation is to provide useful information to help answer the clinical question for which the test was ordered. Diffusing capacity interpretation is most clinically useful when it is done in conjunction with measurements of spirometry and lung volumes. A low DL_{CO} with normal spirometry suggests pulmonary vascular disease, early interstitial lung disease, emphysema associated with a restrictive lung process, anemia (reduced Hb), or elevated COHb level. Pulmonary vascular diseases such as idiopathic pulmonary artery hypertension, pulmonary embolism, chronic thromboembolic pulmonary hypertension, and pulmonary vasculitis should be considered in a patient with a significant reduction in DL_{CO} and normal spirometry and lung volumes [32, 33]. Early interstitial lung disease can cause mild to moderate reductions in DL_{CO} before the development of abnormal spirometry. A reduced DL_{CO} is often an early manifestation of interstitial lung disease, and a low DL_{CO} in a patient with dyspnea should lead to further evaluation such as a high-resolution computed tomography scan of the chest [34]. Emphysema with a concomitant restrictive process such as idiopathic pulmonary fibrosis (IPF), amiodarone-induced interstitial lung disease, or hypersensitivity pneumonitis has been associated with a reduced DL_{CO} and normal spirometry and lung volumes [35].

A low DL_{CO} in the setting of obstruction, defined as a FEV_1/FVC ratio below the lower limits of normal, suggests

a diagnosis of emphysema. In emphysema, the magnitude of the reduction in DL_{CO} correlates with the severity of airway obstruction, exercise capacity, and the degree of emphysema scored pathologically or radiologically with CT scans [36–38].

The clinical value of DL_{CO} in diagnosing COPD in an individual patient is limited because patients can have early emphysema while DL_{CO} is preserved and the chronic bronchitis phenotype is often associated with a normal DL_{CO} [36]. In addition, DL_{CO} has not been proven to be better than FEV_1 in predicting symptoms or mortality. In children and young adults, a low DL_{CO} with obstruction should raise the possibility of cystic fibrosis or alpha-1-antitrypsin deficiency. One of the uses of DL_{CO} measurement in patients with obstructive lung disease is distinguishing asthma from COPD. Diffusing capacity is preserved and often elevated in asthma [1, 2]. This is likely due to improved ventilation perfusion relationships in the apices of the lungs [39].

A low DL_{CO} in the setting of restriction, defined as a FVC or TLC below the lower limits of normal, is seen in various interstitial lung diseases, neuromuscular disease, chest wall abnormalities, and severe congestive heart failure. Most interstitial lung diseases, such as IPF, [40], nonspecific interstitial pneumonitis, [40], sarcoidosis, [41] cryptogenic organizing pneumonits [42], and drug-induced pulmonary toxicity (e.g., amiodarone, bleomycin, cyclophosphamide, methotrexate, and nitrofurantoin) [43, 44], are associated with a disproportionately larger reduction in DL_{CO} than in lung volumes. Pulmonary processes associated with significant restriction that do not affect the lung parenchyma, such as neuromuscular disease, chest wall abnormalities, and pleural abnormalities, generally cause only a small reduction in DL_{CO}.

Diffusing capacity is valuable in monitoring for disease progression in patients with IPF and sarcoidosis [45, 46]. While commonly used to screen patients for amiodarone pulmonary toxicity, serial DL_{CO} measurement may not be effective due to poor specificity [47].

Congestive heart failure has variable effects on both DL_{CO} and lung volumes, depending on disease severity. In advanced heart failure, DL_{CO} and lung volumes are often reduced [48]. In early heart failure, lung volumes are preserved and DL_{CO} is also usually normal, although it may be mildly elevated because of increased pulmonary capillary blood volume [49].

Most disease processes reduce DL_{CO}. A few disorders are associated with an elevated DL_{CO}, defined as a DL_{CO} greater than 140% of predicted value. The most common cause of an elevated DL_{CO} is obesity, likely due to increased pulmonary capillary blood volume [50]. Other disease processes associated with an elevated DL_{CO} include pulmonary hemorrhage syndromes (e.g., Wegener's granulomatosis, Goodpasture's syndrome, idiopathic pulmonary hemosiderosis), polycythemia, left-to-right intracardiac shunts, and asthma [50–52].

Conclusion

DL_{CO} is a widely used, clinically important pulmonary function test that provides information about gas transfer in the lungs. It is useful for evaluating and managing patients with a wide variety of pulmonary disorders. It is most clinically useful in managing patients with interstitial lung disease but also has a role in the evaluation of patients with obstructive lung disease where it may be of benefit in distinguishing asthma from COPD. It is more technically demanding than spirometry, but if performed properly, the test's coefficient of variation is similar to that of FEV_1 and FVC.

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