Measurement of Lung Volumes in Patients with Obstructive Lung Disease

A Matter of Time (Constants)

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In Brief

The total lung capacity of a 57-year-old man with chronic obstructive pulmonary disease is measured by both nitrogen washout and body plethysmography. One measured volume is considerably larger than the other. Which one is more accurate and best reflects the patient's actual total lung capacity?

The Clinical Challenge

A 57-year-old man with chronic obstructive pulmonary disease complains of increasing shortness of breath on exertion over the preceding 3 months. He experiences dyspnea after walking approximately 100 m, a mild productive cough, and wheezing, and he has recently gained 5 kg (11 pounds) in body weight. Physical examination demonstrates abdominal obesity, mild expiratory wheezing with a few inspiratory crackles at the lung bases, and mild lower extremity edema. He weighs 86.4 kg, and his height is 171 cm. Posterior-anterior and lateral chest radiographs (Figure 1) are suggestive of hyperinflation. Pulmonary function test results are shown in Table 1.

Questions

Does This Patient Have Combined Obstruction and Restriction?

This patient's FEV₁/VC is below the fifth percentile of predicted, which meets the ATS definition for expiratory airflow obstruction. When measured using the nitrogen washout technique, his TLC is also below the fifth percentile, which indicates a mixed obstructive and restrictive pattern. When determined by body plethysmography, however, the TLC is 115% of the predicted value, indicating no restrictive pattern.

Why Is There a Large Difference between TLC Measurements Using Nitrogen Washout and Body Plethysmography?

FRC can be measured using either nitrogen washout or body plethysmography. TLC is the sum of FRC and inspiratory capacity (IC), which is measured by spirometry. The accuracy of the nitrogen washout technique depends on all nitrogen (N₂) being "washed out" of the lungs. This technique may underestimate FRC in patients with obstructive lung disease because of poorly ventilated lung regions that still contain N₂ at the end of the test.

Theoretically, body plethysmography should provide a more accurate measurement of lung volume in patients with airway obstruction because it measures the total volume of gas in the thorax, not just the gas that can be exhaled. More than 50 years ago, Tierney and Nadel (1) found that the mean FRC in 13 patients with emphysema was on average 0.99 L higher when measured by body plethysmography than by nitrogen washout. Their assumption was that this difference reflected the amount of gas that was "trapped" in the lungs. In fact, however, body plethysmography may overestimate FRC and TLC in patients with obstructive lung disease, because high airway resistance can contribute to underestimation of alveolar pressure changes. Suboptimal patient technique will exaggerate this error.

The Clinical Solution

The clinician must recognize the potential for both under- and overestimation of FRC and TLC in patients with obstructive lung disease. The large difference found in the patient presented here was likely due to errors generated by both techniques. The accuracy of nitrogen washout can be improved by prolonging the washout period. Errors associated with body plethysmography can be reduced by instructing the patient to support his or her cheeks during the panting maneuver and by having the patient make small respiratory excursions at a frequency of no greater than one per second. In this patient, the hyperinflation on chest radiograph, the lack of evidence of neuromuscular weakness, and normal lung parenchyma on chest CT scan suggested that only obstruction and not restriction was present, and the TLC from...
Body plethysmography was judged to be more correct.

The Science behind the Solution

Measurement of Lung Volume by Nitrogen Washout

This technique is based on the concept that N\textsubscript{2} can be "washed out" of the lungs by breathing 100% oxygen. If the volume of exhaled N\textsubscript{2} (V\textsubscript{N2}) is measured, the original volume of gas in the lungs (V\textsubscript{L}) can be calculated by dividing V\textsubscript{N2} by the initial fractional concentration of N\textsubscript{2} (F\textsubscript{IN2}).

\[ V_L = \frac{V_{N2}}{F_{IN2}} \quad (1) \]

For example, if 2.34 L of N\textsubscript{2} is exhaled and F\textsubscript{IN2} is 0.78\textsuperscript{1}, the initial lung volume must have been 2.34 \div 0.78, or 3.0 L.

A more detailed description of this technique is shown in Figure 2. The patient performs normal tidal breathing and is switched to 100% O\textsubscript{2} once a stable end-expiratory volume (FRC) has been reached. Exhaled gas flow (V) is measured with a pneumotachograph and integrated to provide exhaled volume, while exhaled F\textsubscript{N2} is continuously sampled with a rapidly responding nitrogen analyzer. The test typically lasts for 4 to 7 minutes and ends only when the exhaled F\textsubscript{N2} is less than 0.015 for three consecutive breaths.

Before washout begins (Figure 2A), the (initial) volume of N\textsubscript{2} in the lungs (V\textsubscript{IN2}) is equal to the product of the initial lung volume (FRC) and F\textsubscript{IN2}.

\[ V_{IN2} = FRC \times F_{IN2} \quad (2) \]

After several minutes of breathing 100% O\textsubscript{2} (Figure 2B), the volume of N\textsubscript{2} remaining (V\textsubscript{F2}) is equal to FRC multiplied by the final F\textsubscript{N2} (F\textsubscript{FN2}).

\[ V_{IN2} = FRC \times F_{IN2} \quad (3) \]

Because the total volume of exhaled nitrogen (V\textsubscript{N2}) is the difference between V\textsubscript{IN2} and V\textsubscript{FN2}, Equations 2 and 3 can be combined and solved for FRC.

\[ V_{N2} = V_{IN2} - V_{FN2} = FRC \times (F_{IN2} - F_{FN2}) \quad (4) \]

\[ FRC = \frac{V_{N2}}{F_{IN2} - F_{FN2}} \quad (5) \]

In practice, V\textsubscript{N2} is measured by summing the product of exhaled flow, time interval, and F\textsubscript{N2} for each breath (Figure 2). That is:

\[ V_{N2} = \int V F_{N2} \, dt \quad (6) \]

Because nitrogen is washed out of the body tissues as well, a standardized correction is applied.

\[ V_{N2} = \int \dot{V} F_{N2} \, dt - N_{2 \text{ washed out of tissues}} \quad (7) \]

Combining Equations 5 and 7 gives:

\[ \text{FRC} = \frac{\int \dot{V} F_{N2} \, dt - N_{2 \text{ washed out of tissues}}}{(F_{IN2} - F_{FN2})} \quad (8) \]

Underestimation of Lung Volume in Patients with Obstructive Lung Disease

If regions of the lungs poorly or slowly communicate with the central airways, N\textsubscript{2} from these regions may not be completely

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\textsuperscript{1}In the fasting state with a low R (gas exchange ratio), F\textsubscript{N2} is closer to 0.80, rather than the usually assumed 0.78 of room air, because of unequal exchange of O\textsubscript{2} for CO\textsubscript{2} [alveolar F\textsubscript{N2} = inspired F\textsubscript{N2} + alveolar F\textsubscript{CO2} \times (1 - R)/R]. In fact, alveolar F\textsubscript{N2} can be somewhat different throughout the lungs, depending on regional ventilation-perfusion ratios.

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*Figure 1. Chest radiograph of patient showing evidence of hyperinflation, especially on lateral view.*
washed out when the test is ended, and VN2 will be falsely low. FN2 may also be falsely low because of dilution from better-ventilated regions. As shown by Equation 8, both problems cause FRC (and TLC) to be underestimated. Slow communication and washout most commonly occur in patients with obstructive lung disease and are caused by local regions with high airway resistance, high lung compliance, or both. This is best understood by introducing the concept of the time constant.

If we consider the lungs to be a single, uniform compartment, during nitrogen washout FN2 falls with each breath by a factor of 1 – (V/(V + VT)), where V is the volume of the compartment and VT is the volume exchanged. For example, if V = 3.0 L and VT = 0.5 L, each breath will decrease FN2 by about 14% from its previous value. Because FN2 repeatedly falls by a constant fraction, it can be modeled as an exponential function with a time constant (τ), which is expressed in seconds. As shown in Figure 3, FN2 falls by approximately 63, 95, and 99% after 1, 3, and 5 time constants, respectively. So, the longer the time constant, the longer it takes to wash N2 from the lungs.

The time constant is calculated by dividing the volume of the lung compartment by the rate at which this volume is exchanged:

\[ \tau = \frac{V}{f \times V_T} \times 60 \]  

Here, f is the respiratory rate in breaths per minute, and multiplying by 60 converts the units to seconds. It is apparent from this equation that τ will be high if V is large relative to the rate of volume exchange.

Let us consider one more, very useful way of calculating the time constant. Notice in Equation 9 that rate multiplied by tidal volume equals flow. Because lung volume is equal to the product of compliance (C) and pressure (P), and flow is equal to pressure divided by airway resistance (R), we can rewrite Equation 9 as:

\[ \tau = \frac{C \times P}{P/R} = C \times R \]  

That is, the time constant is simply equal to the product of compliance and resistance. Because we express compliance as ml/cm H2O and flow as ml/s, the time constant still has units of seconds (s).

The relationship between compliance, resistance, and the rate at which FN2 falls during nitrogen washout is best understood by examining a balloon and straw model of the respiratory system (Figure 4). The rate at which the balloon empties is inversely related to both the compliance of the balloon and the resistance of the straw.

Table 1. Pulmonary function test results for a 57-year-old man with chronic obstructive pulmonary disease

<table>
<thead>
<tr>
<th></th>
<th>Predicted</th>
<th>Pre-bronchodilator</th>
<th>Post-bronchodilator</th>
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<tr>
<td>VC, L</td>
<td>3.62</td>
<td>2.43</td>
<td>2.48</td>
</tr>
<tr>
<td>IC, L</td>
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<td>FEV1, L</td>
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<td>FEV1/VC, %</td>
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<td>Body plethysmography</td>
<td></td>
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<tr>
<td>FRC, L</td>
<td>3.19</td>
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</tr>
<tr>
<td>TLC, L</td>
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<tr>
<td>N2 washout</td>
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<tr>
<td>FRC, L</td>
<td>3.19</td>
<td>2.91</td>
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<tr>
<td>TLC, L</td>
<td>6.24</td>
<td>4.55</td>
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<tr>
<td>DLCO, ml/min/mm Hg</td>
<td>26.4</td>
<td>13.4</td>
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</tbody>
</table>

Definition of abbreviations: DLCO = diffusing capacity of carbon monoxide; ERV = expiratory reserve volume; IC = inspiratory capacity.
In other words, the balloon will deflate quickly if it is very stiff (low compliance) and the straw has a large radius (low resistance). On the other hand, the balloon will empty much more slowly if it has little elastic recoil (high compliance) and the straw is narrow (high resistance). In the same way, the rate at which FN₂ falls in our single lung compartment model will be inversely related to the product of its resistance and compliance.

Of course, the lungs are not a single compartment and must instead be considered to have many parallel compartments. Because each has a different value of \( \tau \), the overall washout is the sum of multiple monoexponentials (Figure 5).

**Measurement of Lung Volume Using Body Plethysmography**

The body plethysmograph is a nearly airtight box with a volume of about 600 L. A patient sits in the plethysmograph and performs regular, tidal breathing through a mouthpiece. When a stable end-expiratory volume has been reached, a shutter occludes the mouthpiece so that no inspiratory or expiratory flow can occur. The patient is instructed to pant, and the pressure in front of the shutter (mouth pressure \( [P_m] \)) and inside the plethysmograph (box pressure \( [P_{box}] \)) are continuously measured. The relationship between these two pressures is then used to calculate the lung volume (FRC) during the panting maneuver.

But, how is FRC calculated? The answer starts with Boyle’s Law, which states that at a constant temperature, the product of the pressure and volume of a gas are constant. This can be expressed mathematically as:

\[
P_1 \times V_1 = P_2 \times V_2
\]

where the subscripts refer to the same quantity of gas at different pressures and volumes.

Now look at what happens during the panting maneuver (Figure 6). When the patient pants against the closed shutter, the volume of the thorax changes by a small amount, which we will call \( \Delta V \). According to Boyle’s Law, this causes a change in alveolar pressure (\( P_{alv} \)), which will be referred to as \( \Delta P_{alv} \). If \( P_1 \) and \( V_1 \) refer to \( P_{alv} \) and lung volume (\( V_L \)) when the shutter closes, and \( P_2 \) and \( V_2 \) denote \( P_{alv} \) and \( V_L \) while panting, Equation 11 can be rewritten as:

\[
P_{alv} \times V_L = (P_{alv} + \Delta P_{alv}) \times (V_L + \Delta V)
\]

Multiplying the right side of the equation gives:

\[
P_{alv} \times V_L = (P_{alv} \times V_L) + (P_{alv} \times \Delta V) + (\Delta P_{alv} \times V_L) + (\Delta P_{alv} \times \Delta V)
\]

Ignoring the very small final term and rearranging yields:

\[
-\Delta P_{alv} \times V_L = P_{alv} \times \Delta V
\]

Solving for \( V_L \) gives:

\[
V_L = -\left( \frac{\Delta V}{\Delta P_{alv}} \right) \times P_{alv}
\]

Because the shutter is closed at end-expiration, \( V_L \) is FRC, and because \( P_{alv} \) equals barometric pressure (\( P_B \)), our final equation becomes:

\[
\text{FRC} = -\left( \frac{\Delta V}{\Delta P_{alv}} \right) \times P_B
\]

But how do we get \( \Delta V \) and \( \Delta P_{alv} \) from our simultaneous measurements of \( P_m \) and \( P_{box} \)? First, it is assumed that \( \Delta V \) is the change in volume of both the thorax and

![Figure 3.](image-url) The exponential fall in fractional concentration of nitrogen (\( F_{N2} \)) with a time constant (\( \tau \)) of 20 s. After one time constant (20 s), \( F_{N2} \) has fallen by 63%, or to 37% of its initial value. After three (60 s) and five (100 s) time constants, \( F_{N2} \) has fallen by 95% and 99%, respectively.

![Figure 4.](image-url) A balloon and straw model of the respiratory system. (A) Normal resistance (\( R \)) and compliance (\( C \)) produce a normal time constant (\( \tau \)) and normal expiratory flow (\( \dot{V} \)). (B) Elevated resistance (\( R_1 \)) and compliance (\( C_1 \)) prolong the time constant and reduce expiratory flow (\( \dot{V}_1 \)).
the gas in the plethysmograph. Before use, a piston pump produces small, known volume changes in the box while $\Delta P_{\text{box}}$ is measured. This allows $\Delta V$ to be estimated by measuring $\Delta P_{\text{box}}$ and using the appropriate calibration factor. Second, because the glottis is open and there is no flow, $P_{\text{alv}}$ is assumed to equal $P_m$. Thus, during the panting maneuver, the slope of $P_m/P_{\text{box}}$ is assumed to be equal to $\Delta P_{\text{alv}}/\Delta V$, which is the reciprocal of $\Delta V/\Delta P_{\text{alv}}$ in Equation 16.

The body plethysmograph was first used to measure lung volumes by Arthur Dubois and colleagues at the University of Pennsylvania in the mid-1950s (3). Dubois solved several problems by asking subjects to pant at a relatively high frequency, which minimized artifacts from small leaks in the box and helped to keep the glottis open. He also emphasized the importance of having the patient press on his or her cheeks to avoid any pressure difference and gas flow between the alveoli and the mouth.

Overestimation of Lung Volume in Patients with Obstructive Lung Disease
The body plethysmograph would seem to be preferred for determination of FRC and TLC in patients with obstructive lung disease because it does not depend on communication of gas with the measurement system. Unfortunately, whereas nitrogen washout may underestimate FRC in patients with airflow obstruction, FRC measurements using body plethysmography may be falsely high.

The main source of error is that $\Delta P_m$ does not always equal $\Delta P_{\text{alv}}$. When the volume of gas in the lungs changes during the panting maneuvers, $P_{\text{alv}}$ also changes and creates the potential for gas to flow between the alveoli and the mouth. If flow occurs, $P_{\text{alv}}$ does not equal $P_m$, and measurement errors occur. The difference between $P_{\text{alv}}$ and $P_m$ and the magnitude of the measurement error depend on two factors—the compliance of the mouth and total airway resistance. If mouth compliance is high, flow from lung to mouth is more likely to occur during the panting maneuver. If airway resistance is high, even a small amount of flow must be driven by a difference between $P_m$ and $P_{\text{alv}}$. Once again, it can be useful to think in terms of the time constant ($\tau$), which is the product of compliance and resistance (see Equation 10). As $\tau$ increases, so does the measurement error.

This is illustrated in Figure 7, which shows both a schematic diagram of the lungs and an electrical analog circuit. Between the alveoli and the mouth, both small and large airways contribute resistance ($R_{\text{aw}}$), and the mouth acts as a capacitor with a variable compliance ($C_m$). In the absence of flow, any change in the input pressure ($P_{\text{alv}}$) is exactly and instantly reflected by a change in $P_m$, but any flow through the circuit attenuates the change in downstream $P_m$. The difference between $P_{\text{alv}}$ and $P_m$ increases with $R_{\text{aw}}$, $C_m$, and $\tau$, and the frequency ($f$) of panting.\footnote{For a sinusoidal pattern of $\Delta P_{\text{alv}}$, $\Delta P_m = \Delta P_{\text{alv}}/\left[2 \pi f R_{\text{aw}} C_m \right]^{1/2} + 1$\textsuperscript{-1/2}. Therefore, $\Delta P_m$ most closely approximates $\Delta P_{\text{alv}}$ when $f$, $R_{\text{aw}}$, and $C_m$ are small.}

When $\tau$ and $f$ are low, $\Delta P_m$ closely approximates $\Delta P_{\text{alv}}$ and the FRC measurement is most accurate. If $R_{\text{aw}}$ is large (as seen in obstructive lung disease), $C_m$ is large (the cheeks move in and out), or $f$ is high, $\Delta P_m$ will be systematically smaller than $\Delta P_{\text{alv}}$, and FRC will be falsely high (see Equation 16, substituting $\Delta P_m$ for $\Delta P_{\text{alv}}$). Mouth compliance can be substantially reduced by having patients support their cheeks while panting. The effect of high airway resistance can be decreased by instructing the patient to pant using small excursions at a frequency slightly less than one per second, although errors may still occur when obstruction is severe (4).
Figure 7. Schematic of the lungs and a series RC (resistance-capacitance) circuit showing airway resistance (Raw), compliance of the mouth (Cm), and flow between the lungs and the mouth. Palv = alveolar pressure; Pbox = plethysmograph pressure; Pm = mouth pressure; Raw = airway resistance.

References


Recommended Reading


