Lung Pathophysiology & PFTs

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Conflicts of Interest

- I have no known conflicts of interest.
- Disclosures:
  - I have nothing to disclose.
Outline

- Lung Volumes & Capacities
- Tests defined
- Spirometry
  - Indications
  - Readouts
- Complete PFT
  - Gas dilution
  - Plethysmography
  - DL,CO

- Flow/Volume Loops
- Lung pathophysiology
  - Obstructive mechanics
  - Restrictive mechanics
- References
Lung Volumes and Capacities

Maximal inspiratory level

Resting expiratory level

Maximal expiratory level

ERV, expiratory reserve volume; FRC, functional residual capacity; IC, inspiratory capacity; IRV, inspiratory reserve volume; RV, residual volume; TLC, total lung capacity; V_T, tidal volume; VC, vital capacity.

Lung Volumes

- Tidal volume (TV) - Amount of air inhaled or exhaled with each breath during quiet breathing* (~0.5 L)
- Inspiratory reserve volumes (IRV) - additional volume inhaled after quiet inspiration (~2L)
- Expiratory reserve volumes (ERV) - additional volume exhaled after quiet expiration ~1.2L)
- Residual Volume (RV) - Amount of air remaining in lungs after maximal expiration (~2L)

*or as specified (eg. exercise)
Lung Capacities

- **TLC**: volume of gas in lungs after maximal inspiration \((RV + ERV + TV + IRV) = (FRC + IC)\)
- **FRC**: lung volume present at end-expiration during tidal breathing \((RV + ERV)\)
- **VC**: volume change at mouth between full inspiration and full expiration \((ERV + TV + IRV)\)
  - Slow inspiratory - IVC
  - Slow expiratory - EVC
  - Forced vital capacity - FVC


ERV, expiratory reserve volume; FRC, functional residual capacity; IC, inspiratory capacity; IRV, inspiratory reserve volume; RV, residual volume; TLC, total lung capacity; VT, tidal volume; VC, vital capacity.
Lung Capacities...

- **FVC** - amount forcibly exhaled from full inspiration (TLC) to full exhalation (RV).
- **IC** - (TV + IRV)

Definition of tests…

- **FEV₁**: forced exhaled volume in first second.
- **FEF<sub>25-75</sub>**: Average flow rate over mid 50% of FVC (from 25% to 75%)
- **PEF or PEFR**: Peak expiratory flow rate
  - The maximum flow rate generated with a forceful expiration (recorded as L/sec or L/min) from TLC
- **FEV₁/FVC** ratio: (FEV₁%)
  - indicator of obstruction if less than 70%. If high, may reflect restrictive disease.
Definitions of tests…

- **FEV$_1$ (% predicted):** *(don’t confuse with FEV1%)*
  - (patient FEV$_1$/ "normal" FEV$_1$) x 100
  - the FEV$_1$ of the subject as a % of predicted for the reference group; normal is $\geq 80\%$.

- **MVV:**
  - The maximum volume of air a subject can breathe over a specified period of time (12 s for normal subjects) expressed in L·min$^{-1}$ at BTPS
Lung Volumes & Capacities

Modified from Middleton’s
Allergy Principles & Practice 6th Ed. 2003
Spirometry Defined

- A physiological test that measures how an individual inhales or exhales volumes of air as a function of time.
- The primary signal measured in spirometry may be volume or flow.
- Output is numeric and graphic
  - Volume-time tracing and/or
  - Flow-volume loop
Indications for Spirometry

- **Diagnostic**
  - Evaluate Sx, signs, abnormal lab tests
  - Effect of disease on PFT
  - Screen those at risk for pulmonary disease
  - Pre-operative risk (or pre-exercise risk)
  - Prognosis

- **Monitoring**
  - Response to therapy
  - Disease progression
  - Adverse exposure/drug effect

- **Disability/Impairment**

- **Public Health**

### Spirometry:

<table>
<thead>
<tr>
<th>Measured</th>
<th>Not Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Forced Vital Capacity (FVC)</td>
<td>• RV</td>
</tr>
<tr>
<td>• Forced Expiratory Volume in One Second (FEV₁)</td>
<td>• FRC</td>
</tr>
<tr>
<td>• FEV₁ to FVC ratio (FEV₁/FVC, %)</td>
<td>• TLC</td>
</tr>
<tr>
<td>• Peak Expiratory Flow Rate (PEF)</td>
<td>• DL,CO</td>
</tr>
<tr>
<td>• MMEF (FEF₂₅₋₇₅)</td>
<td>• Compliance</td>
</tr>
<tr>
<td>• MVV (Max Voluntary Ventilation)</td>
<td>• Resistance</td>
</tr>
<tr>
<td>• Other</td>
<td></td>
</tr>
<tr>
<td>• VC (Slow)</td>
<td></td>
</tr>
<tr>
<td>• IC (Slow)</td>
<td></td>
</tr>
<tr>
<td>• ERV</td>
<td></td>
</tr>
<tr>
<td>• IRV</td>
<td></td>
</tr>
</tbody>
</table>
Normal Spirometry

Flow-Volume Loop

Volume-Time Plot

<table>
<thead>
<tr>
<th>Observed</th>
<th>LLN</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>6.00</td>
</tr>
<tr>
<td>FEV₁</td>
<td>4.80</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>80%</td>
</tr>
</tbody>
</table>

Courtesy D. Tashkin
Spirometry

Exhaled volume (L)

Time (seconds)

FEV1

Before bronchodilator

After bronchodilator

FVC

Asthma
MMEF (FEF\textsubscript{25-75})

![Graph showing volume (liters) against time (sec) and percent FVC below TLC]

- **FEV\textsubscript{1}** (liters)
- **FVC\textsubscript{1}** (liters)
- **Slope = FEF\textsubscript{25-75}**% (liters/sec)

**TLC**

**Volume (liters)**

**Time (sec)**

**% FVC below TLC**
Complete PFT

- Measures the FRC
  - Allows determination of the RV
  - Allows determination of TLC
- Diffusing capacity
  - CO uptake test (not a capacity)
- Measurement of FRC methods:
  - Gas dilution (Helium)
  - Nitrogen washout
  - Plethysmography
    - $SG_{aw}$
Determining the *Elusive* TLC

- Must assess the RV by other than exhalation maneuver.

- **Gas Dilution methods**
  - Helium Dilution (He inspired, equilibrates with lung) *
  - Nitrogen Washout (O₂ inspired washes out lung N₂)

- **Plethysmography (compressible gas vol.)**
  - Has advantage of not underestimating lung volume due to uneven ventilation and incomplete gas mixing or “trapped gas” in non-communicating or poorly communicating air spaces (e.g., bullae).

*note: inspired gas may diffuse into volume less than true lung vol. so final gas concentration too high, making volume look too low.*
Helium Dilution

**Equation:**

\[
\text{FRC}_{\text{uncorrected}} = \frac{(C_1 - C_2) \ (Vds + Vadded)}{C_2} - Vmp
\]

**Diagram:**

- **Helium Concentration Starting** = Final Volume of System
- **Helium Concentration Final** = Initial Volume of System

Fig. Courtesy D. Tashkin
Nitrogen Washout

Again, by measuring $N_2$ concentration and volume of expired gas, and knowing the original concentration of N in the lung, solve for lung gas volume.

$$
\left( \frac{\text{Concentration of nitrogen in the lungs}}{\text{volume of gas in the lungs}} \right) = \left( \frac{\text{concentration of nitrogen in expired gas}}{\text{volume of expired gas}} \right)
$$

$FRC(\text{corr}) = \left[ \frac{(V_E + V_{D1})(F_E - F_I) - (V_{D2})(F_N) - V_{TIS}}{F_{A1} - F_{A2}} \right] (K_{BTPS})$
Plethysmograph
Plethysmography Concepts

- TGV (VTG) = plethysmograph measure of intrathoracic gas at time airflow occluded.
- FRC\text{pleth} = lung gas volume with occlusion at FRC
- Other volumes (e.g., IC and ERV) by breathing maneuvers following measurement of FRC.
- Boyle’s law is underpinning

Boyle’s law is underpinning
Plethysmography 101...

Boyle’s Law (simplified):
When a constant mass of gas is compressed (or expands), gas volume decreases (or increases) and gas pressure changes such that the product of vol. and pressure at any moment is constant.

\[ P_1 \times V_1 = P_2 \times V_2 \]
Slope of Scope Readout Allows Vpleth Calculation

\[ V_{TG} = \frac{\Delta P}{\Delta P_{box}} \times P_B \]

\[ V_{TG} = \frac{\Delta V}{\Delta P} \times P_B \]
DL,CO: Diffusing capacity

- Also known as the “confusing capacity,”
- Neither a capacity nor a direct measurement of oxygen diffusion.
- A carbon monoxide transfer test.
- Measures CO uptake by Hgb in the lung.
- Any blood in the lung, intra- or extravascular, can take up CO.
Diffusing Capacity DL,CO

- Breathing minute amounts of CO
- Transfer/absorption of CO depends upon
  - Ventilation presenting CO to alveolus
  - CO transfer from alveolus through wall
  - Movement across interstitium
  - Uptake by Hgb in RBC in capillary
    - [Hgb] important (correction factor)
- Correction factors include:
  - Alveolar Volume (VA) \( DLCO/VA = KCO \) (controversial)
  - Hemoglobin concentration
Factors Affecting DL,CO

- Hgb
- Pulmonary capillary blood volume
- Lung inflation
- Carboxyhemoglobin >2% (prior to test)
- Position
- Age, gender, & height
Gas Diffusion Pathway

- **Membrane**
  - Alveolar space
  - Alveolar epithelium
  - Tissue interstitium
  - Capillary endothelium
  - Plasma layer

- **Rbc (red blood cell)**
  - Red cell membrane
  - Red cell cytoplasm
  - Hemoglobin

Modified From: Murray & Nadel Textbook of Respiratory Medicine 2nd Ed.
DL,CO: Maneuver

- Single breath of gas with low conc. of carbon monoxide, and an inert gas (He or CH₄).

- Start at RV and inhaled to TLC.
  - 10 sec. breath hold at TLS followed by full exhalation
  - exhaled alveolar gas sampled for [CO] and [He] or [CH₄].
  - drop in CO indicates how much “diffusion” has occurred, He (or CH₄) allows for the calculation of volume. Normally 20-30 mL of CO/min/mm Hg occurs.
The Flow Volume Loop
The Good, The Bad, and...The Unusual

Normal
Restrictive
Obstructive
Flow/Volume Loops: Obstructive Pattern...The Bad

Normal

Asthma - mod. obstruction

COPD – severe obstruction

nl. variant
Flow/Volume Loops…

A  Normal

B  Restrictive

C  Mixed: Restrictive - Obstructive

Eur Respir J 2005; 26
And The Unusual...

FIGURE 3. Idealised examples of a) fixed, b) variable extrathoracic, and c) variable intrathoracic airway obstruction.
Pathophysiology

- Obstructive
  - Asthma
  - COPD
- Restrictive
  - Parenchymal
  - Neuromuscular
  - Musculoskeletal
  - Extra-pulmonary
- Mixed
Mechanisms of Airway Obstruction

- Filling of Lumen
- Wall Thickening
- Loss of Tethering
Airway Resistance

\[ R = \frac{8l\eta}{\pi r^4} \]

- Airway resistance \( (R) \) varies \( (\text{inversely}) \) with the 4\(^{\text{th}}\) power of the radius of the airway.
- This is in laminar flow \( (\text{Poiseuille’s Law}) \)
- Most flow in smaller airways is laminar

\( l \) (length tube); \( \eta \) (viscosity); \( r \) (radius)
Obstructive Lung Disease Defined

- An obstructive ventilatory defect is a disproportionate reduction of maximal airflow from the lung in relation to the maximal volume (i.e. VC) that can be displaced from the lung.
- It implies airway narrowing during exhalation and is defined by a reduced FEV1/VC ratio below the 5th percentile of the predicted value.
Normal Lung vs. Emphysema
Subepithelial Collagen Deposition in Mild Asthma

Airway Remodeling

Resistance \( \propto \frac{1}{r^4} \)

Inflammation

Other factors

Expiration

Volume

Flow

Inspiration

Expiration

Volume

Flow

Inspiration
Lung volume is plotted against transpulmonary pressure. Compliance is change in volume for a given change in pressure. A patient with emphysema has much higher lung compliance in contrast to a patient with interstitial lung disease.
Restrictive Lung Diseases

- Characterized by reduction in TLC below the 5th percentile of predicted, and a normal FEV1/VC.
- Lung volumes are reduced
  - Alteration in lung parenchyma
  - Diseases of the pleura, chest wall or neuromuscular apparatus
  - Reduced compliance (pulmonary or extra-pulmonary)
Restrictive Lung Disease

- Two groups:
  - Intrinsic
    - Lung parenchyma
      - Inflammation/scarring of lung tissue (interstitial lung disease) or
      - Fill air spaces with exudate and debris (pneumonitis)
  - Extrinsic
    - Extra-parenchymal (chest wall, pleura or muscles)
High Resolution CT
Normal vs Fibrosis with Honeycombing

Schwartz & King Interstitial Lung Disease 3rd Ed. 1998
Restrictive Pattern in IPF

Schwartz & King Interstitial Lung Disease 3rd Ed. 1998
PFTs & Quality Control

Mark F. Sands MD
PFTs: Reference Ranges

- Reference equations incorporating age, height, weight, gender, & ethnicity should be utilized.¹

- **NHANES III** (National Health and Nutrition Examination Survey (8-80 y/o)²

- **Wang, et al** (<8 y/o)³

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Acceptable criteria for single maneuvers

1. Satisfactory start (EV <5% or 0.15 L whichever is greater)
2. No cough during 1st sec
3. No early termination
4. No Valsalva (e.g. glottic closure)
5. No leak
6. No obstructed mouthpiece
7. No extra breath
   (Usable curve meets 1 and 2 whereas acceptable curve meets all 7)
Normal Spirometry

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<tr>
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<tr>
<td>FVC</td>
<td>6.00</td>
<td>3.88</td>
</tr>
<tr>
<td>FEV$_1$</td>
<td>4.80</td>
<td>3.12</td>
</tr>
<tr>
<td>FEV$_1$/FVC</td>
<td>80%</td>
<td>71%</td>
</tr>
</tbody>
</table>
Insufficient inhalation – flow-volume

Good

Poor

Courtesy K Scragg, J Weiler
Hesitation

**Diagram A:**
- **Flow (L/sec)**
- **Exhaled Volume (Liters, BTPS)**

**Diagram B:**
- **Volume (L)**
- **Time (Sec)**
Hesitant start to exhalation — flow-volume

Courtesy K Scragg, J Weiler
Early Termination

Observed LLN

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>2.95</td>
<td>3.88</td>
</tr>
<tr>
<td>FEV₁</td>
<td>2.76</td>
<td>3.12</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>94%</td>
<td>71%</td>
</tr>
</tbody>
</table>
Early termination

Insufficient exhalation time (<6 sec)

Courtesy K Scragg, J Weiler
Leak at Mouth

Courtesy K Scragg, J Weiler
Obstruction of mouthpiece – flow-volume

Courtesy K Scragg, J Weiler
Submaximal Effort

Observed LLN

<table>
<thead>
<tr>
<th>Test</th>
<th>Observed</th>
<th>LLN</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>4.45</td>
<td>3.88</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>3.00</td>
<td>3.12</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC</td>
<td>67%</td>
<td>71%</td>
</tr>
</tbody>
</table>
Cough

Observed | LLN
---|---
FVC | 5.00 | 3.88
FEV<sub>1</sub> | 3.47 | 3.12
FEV<sub>1</sub>/FVC | 69% | 71%
Acceptable & Reproducible Efforts

A. Exhaled Volume (Liters, BTPS) vs. Flow (L/sec)
B. Volume (L) vs. Time (Sec)
Non-Reproducible Peak Flows

Two efforts had submaximal peak flows
Non-Reproducible End-of-Test

A) Flow (L/sec) vs. Exhaled Volume (Liters, BTPS)
B) Volume (L) vs. Time (Sec)
Non-Reproducible Exhaled Volumes

Maneuvers individually acceptable but exhaled volumes not reproducible: failure to take as deep a breath as possible before \( \geq 2 \) of the maneuvers.
Criteria for Unacceptable Maneuvers

• Individual Maneuvers should be free of:
  - Insufficient inhalation
  - Slow/hesitant start to exhalation
  - Weak effort
  - Cough
  - Glottic Closure
  - Early termination; Air leakage around mouthpiece or noseclip; Obstruction of mouthpiece
  - Extra breath

• Evaluate Shape of curves, values for acceptability & reliability
• Should not show large variation of FVC or FEV1 between maneuvers (e.g. <0.150 L)
Selected References


Thank You!