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FCA REFRESHER COURSE

Lung function testing and interpretation

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"Remember, when life gets too much… take a spirometric breath." – Farriel Desai

Introduction

Pulmonary function tests (PFTs) are non-invasive tests that indicate how well or poorly an individual's lungs are functioning. PFTs aid the diagnoses of symptomatic disease, screen for early asymptomatic disease, monitor any response to pharmacological therapy, and provide a prognosis for a known disease. PFTs can only provide a physiological diagnosis and not a clinical diagnosis of pulmonary disease. It is important to recognise that a PFT is not a standalone test. A combination of the clinical picture of a patient with other diagnostic tests (arterial blood gases, chest X-rays, etc.) must be made to make a clinical diagnosis of pulmonary disease, particularly if there is a high index of suspicion for disease but PFTs are interpreted as normal.[1]

A major limitation of PFTs is how they are interpreted. Firstly, a knowledge of whether the PFT is acceptable to interpret is important. Secondly, there are many values in the report, therefore it is important to have an organised approach to interpreting these values. Finally, an appreciation that the reference values in PFTs are not absolute cut-off values for confirmed disease is important. A task force appointed in 2022 by the European Respiratory Society (ERS) and the American Thoracic Society (ATS) has updated the 2005 guidelines on PFT interpretation.[2] This refresher will highlight the important updates on reference values, bronchodilator responsiveness interpretation, and the grading of severity of pulmonary disease.

PFTs can comprise six different tests: spirometry, spirometry pre- and post-bronchodilator, flow-volume loop, lung volumes, diffusing capacity for carbon monoxide/transfer factor for carbon monoxide (DLCO/TLCO), and a bronchoprovocation challenge.[1] The number of tests a PFT report may contain will depend on the result of the first basic PFT, namely spirometry.

Reference equations in PFTs (important to understand)

The crux of interpreting PFTs lies in comparing an individual's PFT result to a set of reference values. Reference values are based on reference equations obtained from a population of healthy individuals, which adjust for standing height, biological sex, and age.[2] Ideally, an individual should be compared to their ancestral population of reference equations.

Previously, a major limitation of reference equations was that they were not standardised, adjustment factors were used for black and Asian people and over 100 different reference equations were used for different populations and each PFT. This created uncertainty when interpreting PFTs.[2]

The 2022 ERS/ATS guidelines have now recommended the use of the Global Lung Function Initiative (GLI) reference equations for spirometry, DLCO, and lung volumes. The GLI reference equations consist of five population groups: black, white, North Asian, South Asian, and "other", facilitating a consistent and standardised approach to PFT interpretation across a wider age range than before (3–94 compared to 8–80 years).[2]

Limits of normal

In a healthy population, according to the normal distribution curve, an individual may fall on the fifth percentile of normal, i.e. there is a 5% chance an individual has a low PFT score, which is normal for that individual and not pathological (false positive). This emphasises the uncertainty in interpreting PFTs and allows for a trade-off in incorrectly labelling a low PFT score in a healthy individual as pathological. A fifth percentile equates to a z-score of -1.645, which is considered the lower limit of normal (LLN) in PFTs. The LLN is considered the "cut-off" value in PFT. Conversely, a 95th percentile equates to a z-score of +1.645, which is the upper limit of normal (ULN) for PFTs.[2]

Reference equations for PFTs should be reported as z-scores/LLN and the specific reference equations used should be specified in the PFT reports. For ease of reference in this refresher, LLN and ULN will be used in the discussion below.

PFTs

Spirometry

- Definition: The volume of air (litres) maximally exhaled is measured over different points of time (seconds) after a maximal inhalation to provide peak expiratory flow (PEF),

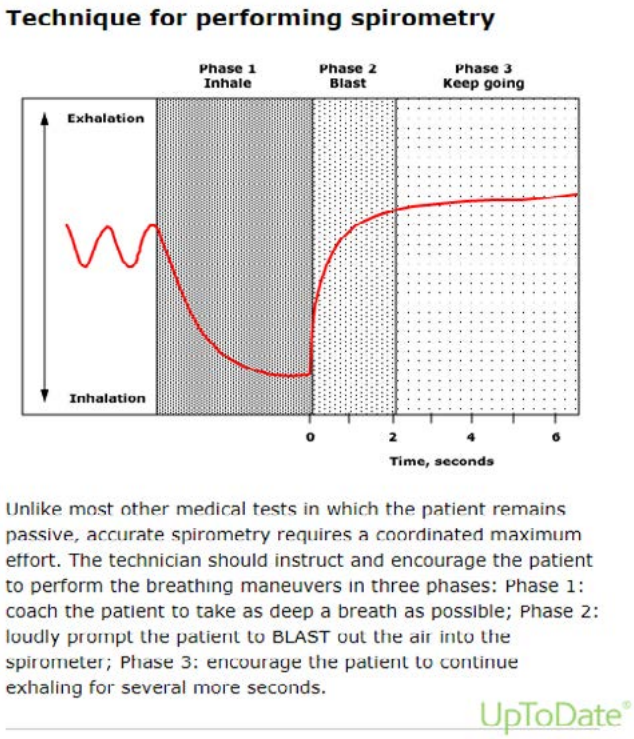

Figure 1: Technique for performing spirometry

forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), the ratio of FEV_1:FVC, and forced mid-expiratory flow ($FEF_{25–75\%}$).

- The technique has three phases (Figure 1):

Phase 1: A nose clip is applied to the nose to prevent an air leak, the patient is coached to inhale as deeply as possible, and a mouthpiece is then placed into the mouth.[3]

Phase 2: The patient exhales forcefully.[3]

Phase 3: The patient continues to exhale forcefully until either a plateau in exhalation or 15 seconds is reached. The spirometry must be acceptable and reproducible.[3]

- Acceptability
  - Good effort with a demonstrable rapid increase in airflow as exhalation begins.
  - The patient must complete the manoeuvre with exhalation lasting at least six seconds to end in a plateau.
- Reproducibility
  - Three efforts are recorded with all three FEV_1 and FVC within 200 ml of each other.
- Interpretation
  - Obstructive lung disease
    - FEV_1:FVC ratio < LLN and PEF < LLN.
    - Note the use of a fixed ratio FEV_1:FVC < 70% to define obstruction and > 80% to define normal is no longer recommended.[2]
    - Spirometry has a "scooped" shape in early obstructive airway disease where the FEV_1:FVC ratio may be normal. $FEF_{25–75\%}$ < LLN.[2]

The current recommendation for the severity of obstruction is to use an FEV_1 z-score if available; the FEV_1 percentage predicted is used, as before, if the FEV_1 z-score is not available (Figure 2).[2]

Spirometry pre- and post-bronchodilator (BDR)

- Indication: To evaluate obstructive lung disease.
- Technique: Chronic pre-existing BDR medication is omitted before spirometry, according to Table I:

Table I: Omission of bronchodilator use prior to PFT

Bronchodilator	Time omitted before PFT
Short-acting β2 agonists (salbutamol)	4–6 hours
Muscarinic antagonists (ipratropium)	12 hours
Long-acting β2 agonists (salmeterol)	24 hours
Ultra-long-acting β2 agonists (indacaterol)	36 hours
Long-acting muscarinic antagonists (glycopyrrolate)	36–48 hours

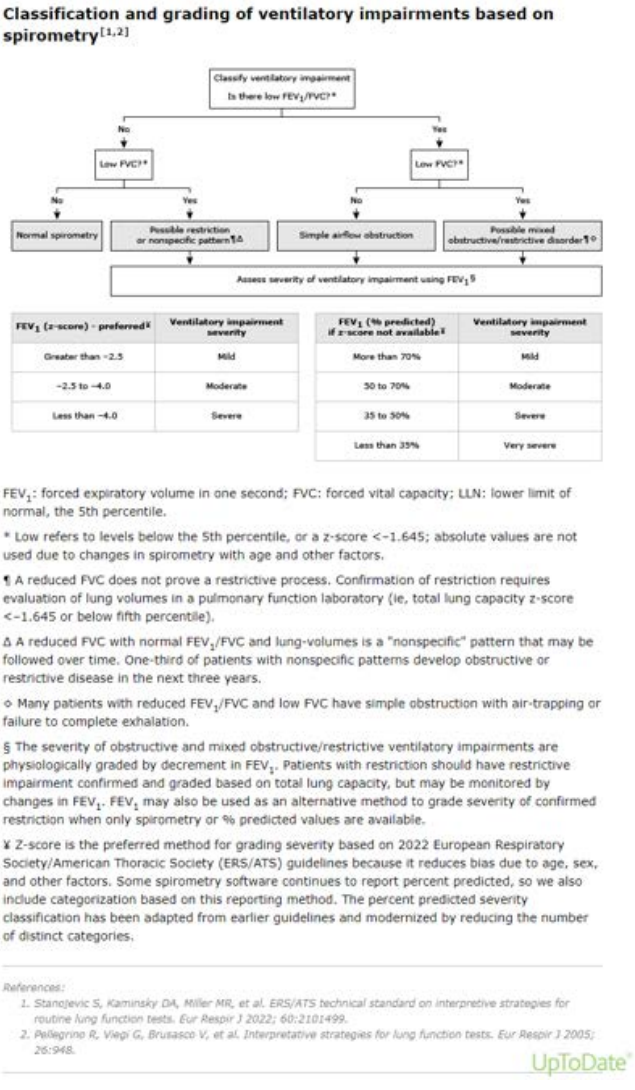

Figure 2: Classification and grading of ventilatory impairments based on spirometry

Albuterol via a spacer/chamber/nebuliser is administered to the patient to assess for reversibility or responsiveness. Spirometry is then repeated after 10–15 minutes.

- Interpretation
  - If a patient has symptoms of asthma but their spirometry is normal, a bronchoprovocation test is done (see bronchoprovocation).[1]
  - Some patients with asthma improve to normal spirometry values post-BDR, these patients have reversible airway disease.
  - Some patients with asthma show an improvement in spirometry values post-BDR, these patients are BDR-responsive.
  - Some patients experience a subjective improvement in symptoms post-BDR; however, their spirometry values do not show an improvement post-BDR. This could be due to an improvement in small airway resistance in response to BDR with no improvement in larger airway resistance post-BDR. These patients should still benefit from a trial of BDR and glucocorticosteroid therapy despite no change in spirometry.
  - Patients with chronic obstructive pulmonary disease (COPD) do not show reversibility in spirometry values post-BDR.
  - Significant response
    - ERS/ATS define a significant post-BDR response as either an FEV_1 or an FVC ≥ 10% of predicted values, respectively. This has changed from greater than 12% and greater than 200 ml. This new ULN is based on worldwide data, excludes age and height as confounders, and is associated with mortality.[2]

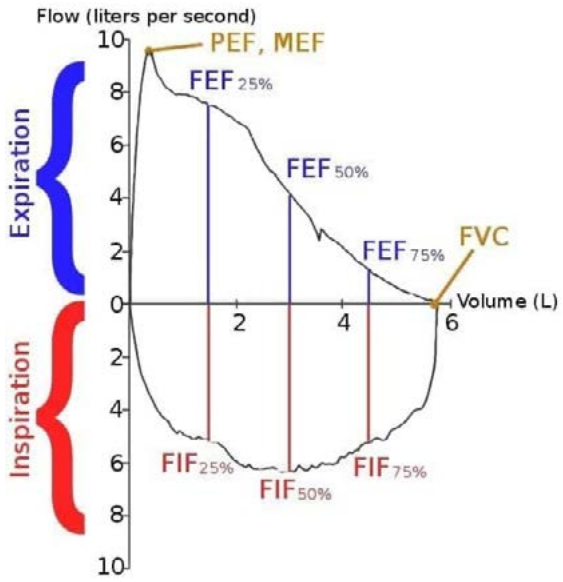

Figure 3: Flow volume loop showing upper exhalation phase (top part of loop) and lower inhalation phase (bottom part of loop). Source: Life in the Fast Lane

    - Equation:

$$\text{BDR response} = \frac{(\text{post-BDR predicted value [L]}) - (\text{pre-BDR predicted value [L]}) \times 100}{\text{Predicted FEV1/FVC value (L)}}$$

*Note that the *actual* BDR predicted value in litres is used, *not* the percentage predicted value for BDR

Flow volume loop

- Definition: The flow of air (litres/second) is measured against lung volumes (litres).
- Technique: The same spirometry technique described above with an additional deep *inhalational* manoeuvre, which must be reproducible, reflecting forced inspiratory vital capacity (FIVC). This is performed at the end of Phase 3 of spirometry, and therefore, a flow volume loop must be specifically requested. Otherwise, a request for spirometry may only provide an exhalation phase (top part of the loop, Figure 3).
- Indication: This PFT assists in determining the cause of stridor/upper airway obstruction/extrathoracic airway obstruction, i.e. pharynx, larynx and trachea above the thoracic inlet.
- Result
  - Variable upper airway obstruction. There is limited airflow during forced inhalation (box-shaped inspiratory pattern on flow-volume loop, Figure 5). During spontaneous ventilation, the negative intraluminal pressure (relative to atmospheric pressure) causes the extrathoracic pathological site to collapse on inhalation (Figure 4A).[1]
  - Variable lower airway obstruction. There is limited airflow during forced exhalation (box-shaped expiratory pattern on flow-volume loop, Figure 5). During spontaneous ventilation, positive intrapleural pressure (relative to intraluminal pressure) causes the intrathoracic pathological site to collapse on exhalation (Figure 4B).[1]
  - Fixed airway obstruction. There is limited airflow during both forced exhalation and inhalation (box-shape inspiratory and expiratory patterns on flow-volume loop).

It is important to note that a pathological tracheal lumen diameter of < 1 cm is required before this pattern is seen on a flow-volume loop, therefore the flow-volume loop has poor sensitivity to diagnose a fixed-upper airway obstruction.[1]

Lung volumes

An understanding of respiratory physiology is needed to relate why changes in certain lung volumes indicate certain lung pathology.[4] Respiratory physiology will not be discussed in this refresher.

- Definitions
  - Volumes (Figure 6)
    - Tidal volume (TV): Normal breathing (± 500 ml).
    - Inspiratory reserve volume (IRV): Extra air which can be inhaled beyond a TV breath (± 3 000 ml).

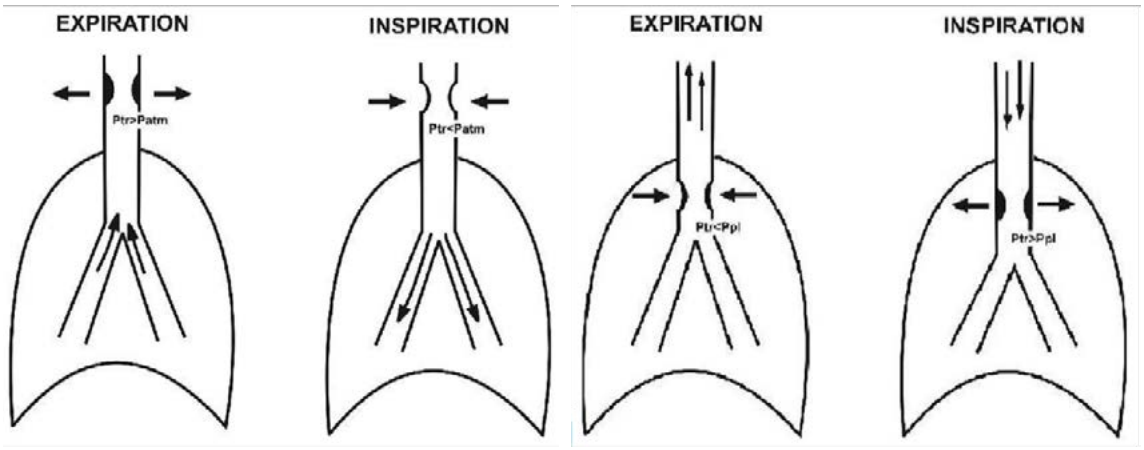

Figure 4.A (left): Variable upper airway obstruction, **Figure 4.B** (right): Variable lower airway obstruction. Source: Researchgate

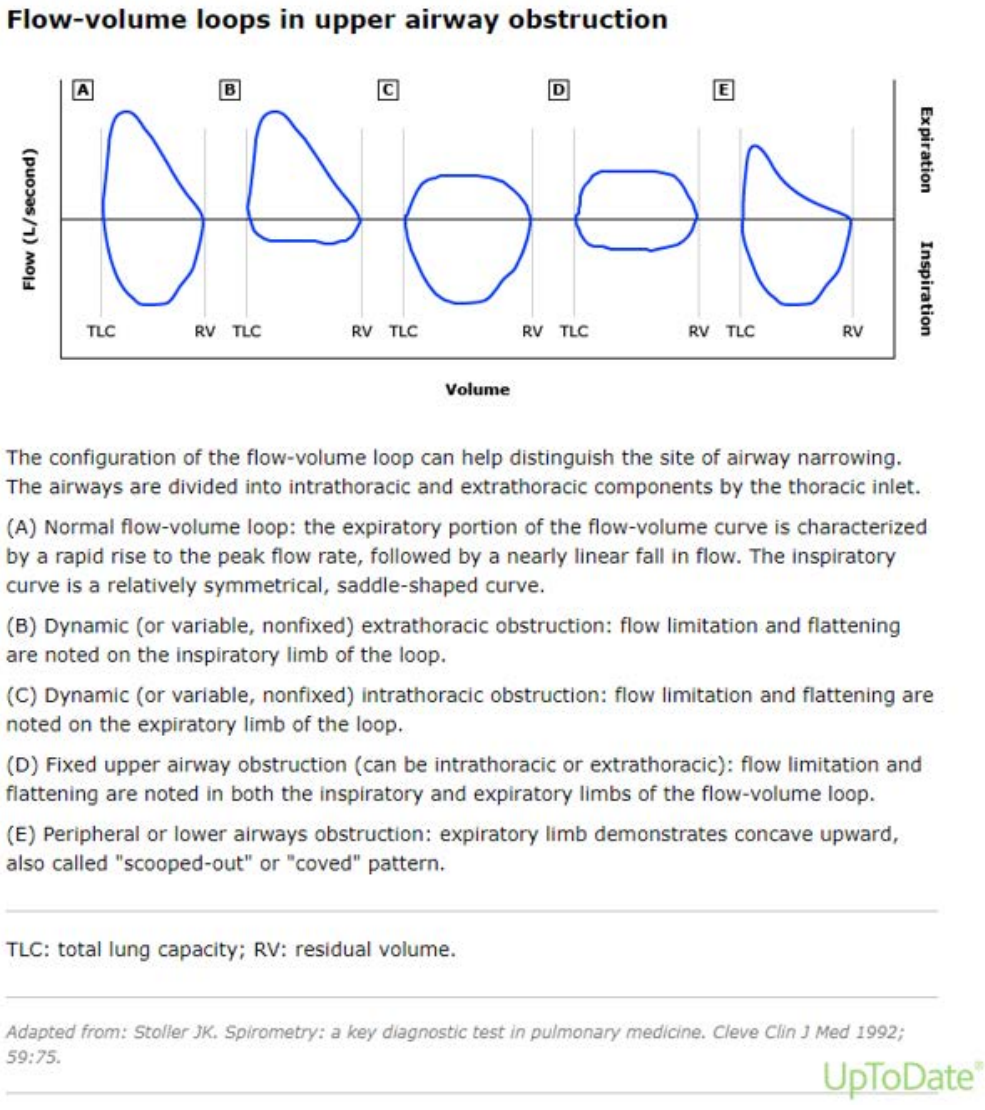

Figure 5: Flow-volume loops in upper airway obstruction

- Expiratory reserve volume (ERV): Extra air which can be forcefully exhaled beyond a TV breath (± 1 100 ml).
- Residual volume (RV): Volume of air remaining in the lung after a maximal exhalation (± 1 200 ml).

◦ Capacities (sum of volumes, Figure 6)

- Inspiratory capacity (IC): TV + IRV.
- Expiratory capacity (EC): TV + ERV.
- Functional residual capacity (FRC): ERV + RV.
- Vital capacity: IRV + TV + ERV (total amount of exchangeable air).
- Total lung capacity (TLC): IRV + TV + ERV + RV (total amount of air in the lung after a maximal inhalation effort).

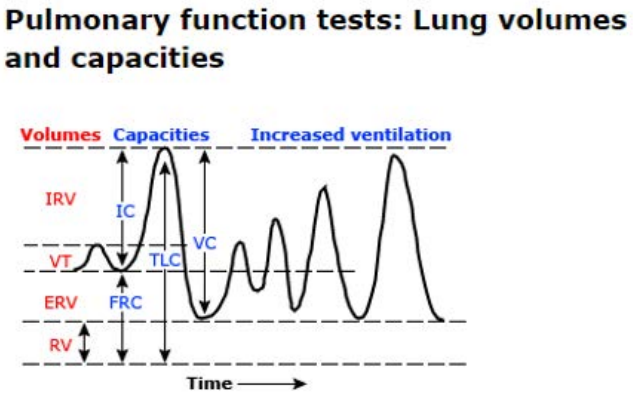

Figure 6: PFTs: lung volumes and capacities. Source Life in the Fast Lane

- Indication: When there is a decreased FVC on spirometry, this PFT is done to determine if a low FVC is due to a restrictive lung disease, severe obstruction, neuromuscular disease or poor effort from the patient. It also differentiates between chronic bronchitis and emphysema as the cause of airway obstruction.[1]
- Technique: There are four ways to measure lung volumes, namely body plethysmography (the gold standard and may overestimate lung volumes), helium dilution, nitrogen washout (may underestimate lung volumes), and chest imaging. These techniques are topics to be studied under physics and will not be discussed in detail here.
- Interpretation
  - Restrictive lung disease: TLC < LLN.
  - Mixed disease (obstructive and restrictive pattern): FEV_1:FVC ratio < LLN plus TLC < LLN.
  - Air trapping (clinically precedes hyperinflation): RV > ULN with a normal TLC or RV:TLC ratio is increased.
  - Hyperinflation: FRC and/or TLC > ULN.
  - Non-specific pattern: FVC is low but FEV1:FVC ratio and TLC are both normal.

Diffusing capacity for carbon monoxide quantitation (DLCO) or transfer factor for carbon monoxide (TLCO)

- Indication
  - Evaluate whether obstructive lung disease (FEV_1:FVC < LLN) is due to emphysema or chronic bronchitis.
  - Evaluate if restrictive lung disease (TLC < LLN) is due to intrinsic lung disease or extrinsic lung disease.
  - Evaluate if there is pulmonary vascular disease.
- Technique
  - A single breath test where the patient exhales deeply to RV and a device connected to a test gas (0.3% carbon monoxide [CO], tracer gas, oxygen, and nitrogen) is placed in the patient's mouth. The patient then inhales to TLC in four seconds, holds their breath for 10 seconds and then exhales to RV rapidly. An alveolar gas sample is taken, dead space is washed out, and CO uptake is calculated.
  - Adjustments are made for anaemia (low haemoglobin reduces the carrying capacity for CO in blood, resulting in poor CO uptake) and smoking (carboxyhaemoglobin reduces the carrying capacity of haemoglobin for CO).
- Interpretation (Figure 7)
  - Emphysema: DLCO < LLN.
  - Chronic bronchitis: DLCO is normal.
  - Intrinsic lung disease: DLCO < LLN.
  - Extrinsic lung disease: DLCO is normal.
  - Pulmonary vascular disease: Normal spirometry plus DLCO < LLN.

Bronchoprovocation challenge

(This topic will not be discussed in detail in this refresher.)

- Indications
  - Reversible airway disease is suspected but normal spirometry is obtained.
  - Variable airflow limitation is present (only after certain triggers are encountered).
  - Airway hyperresponsiveness due to inflammation or specific external triggers.

Interpretation of diffusing capacity of the lungs for carbon monoxide (DLCO)

Increased DLCO
Altitude
Asthma
Polycythemia
Severe obesity
Pulmonary hemorrhage
Left-to-right intracardiac shunting
Mild left heart failure - increased pulmonary capillary blood volume
Exercise just prior to the test - increased cardiac output
Mueller maneuver
Supine position
Low DLCO with normal spirometry and normal lung volume
Anemia - mild decrease
Pulmonary vascular disease - mild to severe decrease
Early interstitial lung disease - mild to moderate decrease
Valsalva maneuver
Low DLCO with obstruction with or without concomitant restriction
Bronchiolitis
Combined pulmonary fibrosis and emphysema (CPFE)
Cystic fibrosis
Emphysema
Interstitial lung disease in patient with COPD
Lymphangioleiomyomatosis
Sarcoid
Low DLCO with restriction
Interstitial lung disease
Pneumonitis
Other
Carboxyhemoglobin - reduces DLCO
Supplemental oxygen - reduces DLCO
Bronchodilator - increases DLCO

UpToDate

Figure 7: Interpretation of diffusing capacity of the lungs for carbon monoxide (DLCO)

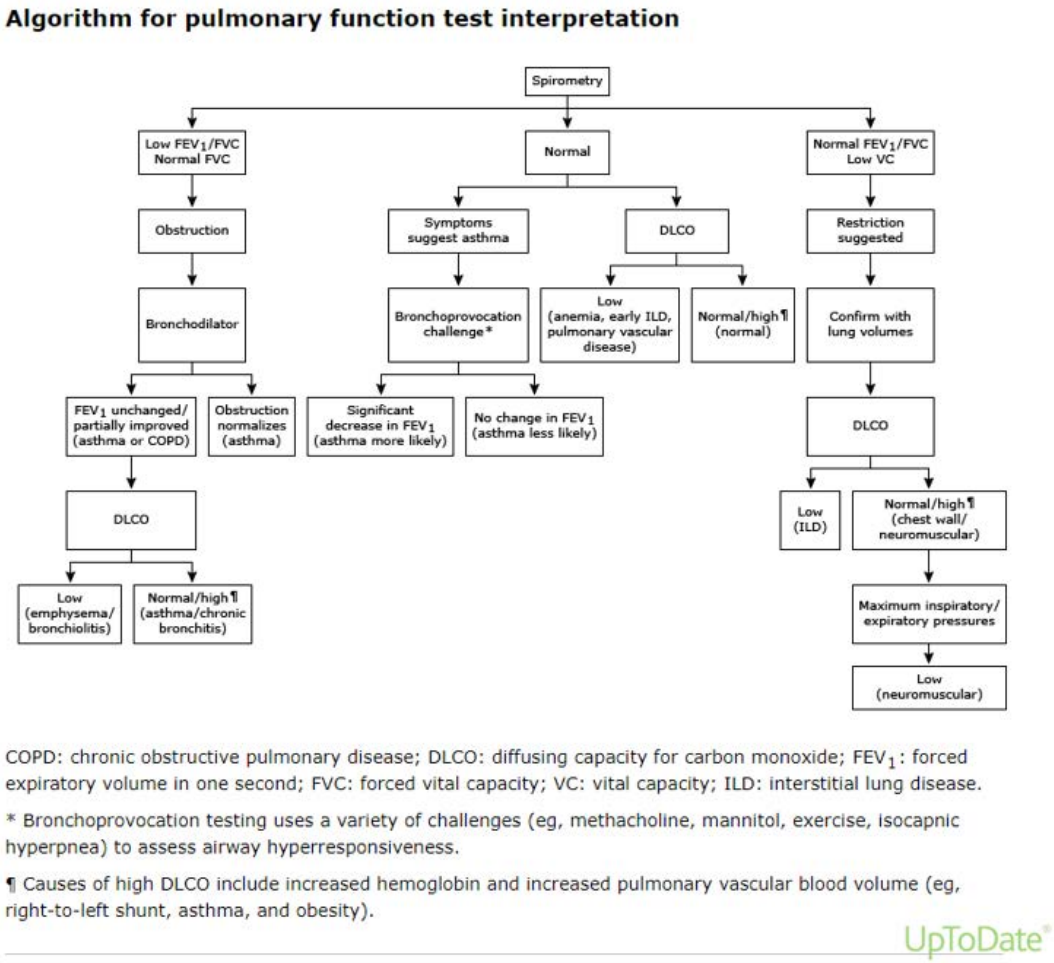

Figure 8: Algorithm for PFT interpretation

- Methacholine, mannitol, and exercise are used to stress the airways.

Practise (remember to have a system, Figures 8 & 9)

1. What is the clinical scenario of the patient? Look at the demographics (this is important).
2. Start with analysing the flow-volume loop and the volume-time curve.
3. Identify any obvious patterns; is the loop acceptable and reproducible?
4. Are the reference equations mentioned in the report?
5. Look at the values of FEV_1 and FVC compared to LLN and work out BDR response if BDR is used.
6. Work out FEV_1:FVC ratio.
7. Are lung volumes available? Assess the TLC for restrictive lung disease.
8. Is there a DLCO available?

COVID-19

PFTs are aerosol-generating procedures. With the recent COVID-19 pandemic, it is recommended to only perform PFTs if they are vital to aiding diagnostic and management decisions (e.g. pneumonectomy).[1] There are several strategies to limit the spread of aerosols.

- Patient
  - Select appropriate patients for PFTs.
  - Patients should not be queued for prolonged periods.
  - A delay of 20 minutes to three hours between patients to allow for the elimination of aerosols.
- Staff
  - Hand washing and use of personal protective equipment (N95 mask, apron, face shield, and gloves).
- Equipment
  - Single-use mouthpieces and disposable filters.
  - Negative pressure rooms with frequent air changes.

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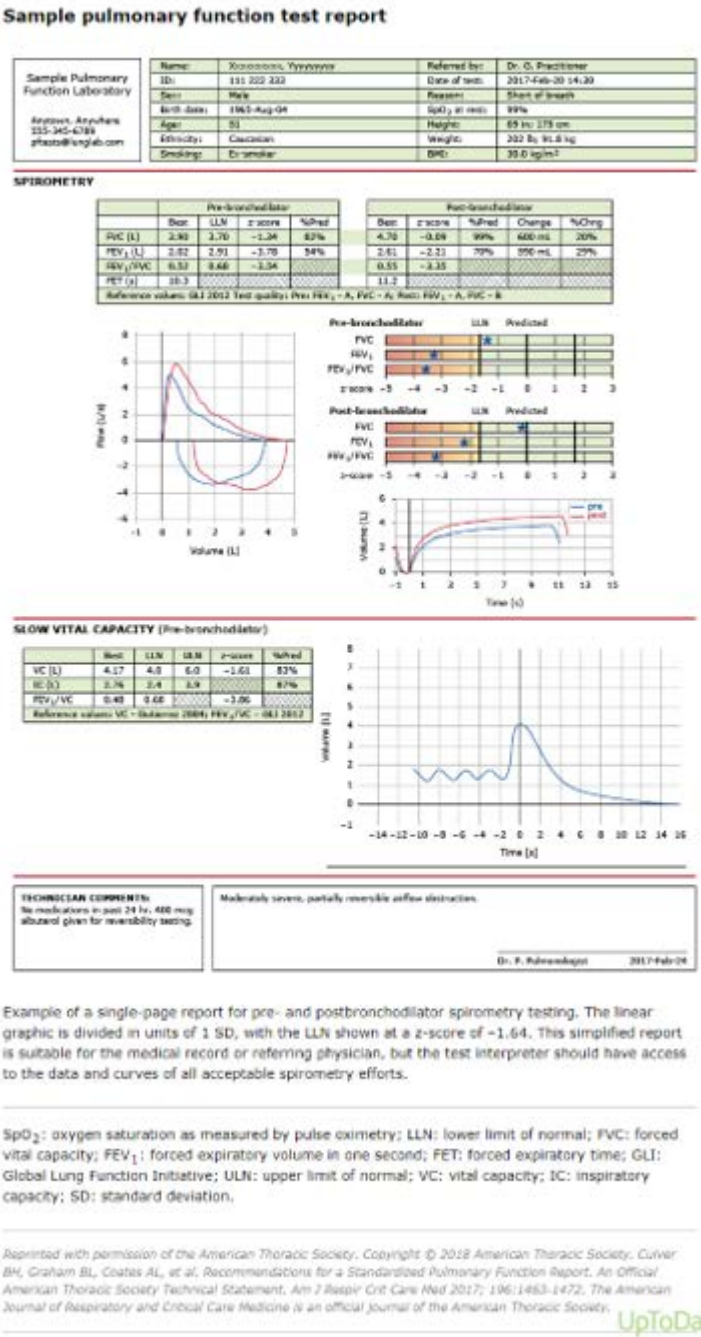

Example of a single-page report for pre- and postbronchodilator spirometry testing. The linear graphic is divided in units of 1 SD, with the LLN shown at a z-score of −1.64. This simplified report is suitable for the medical record or referring physician, but the test interpreter should have access to the data and curves of all acceptable spirometry efforts.

SpO_2: oxygen saturation as measured by pulse oximetry; LLN: lower limit of normal; FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; FET: forced expiratory time; GLI: Global Lung Function Initiative; ULN: upper limit of normal; VC: vital capacity; IC: inspiratory capacity; SD: standard deviation.

Figure 9: Sample PFT report