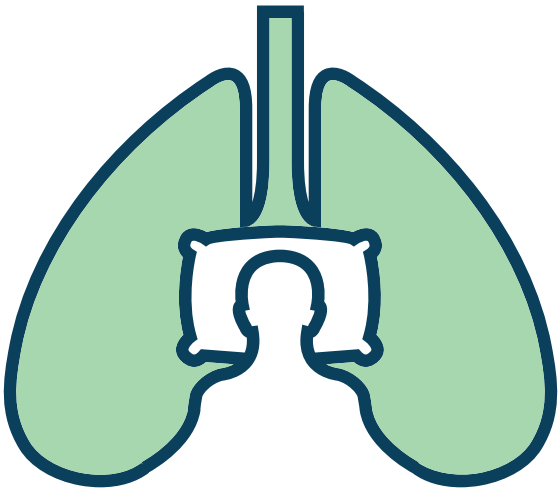


RSDC

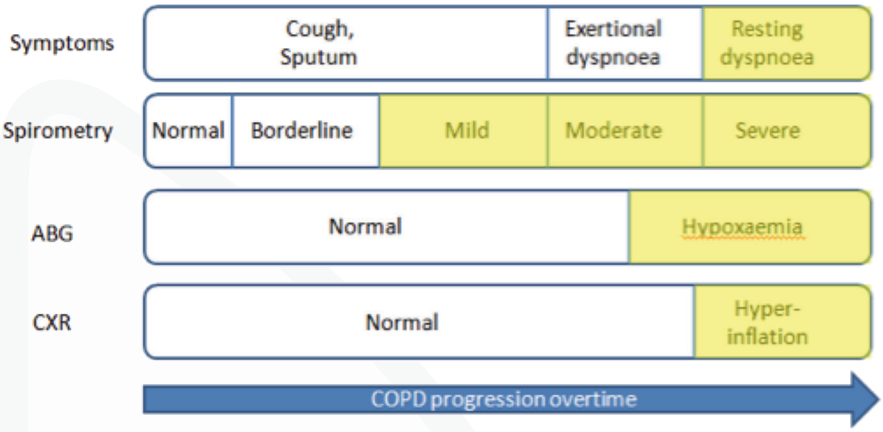
Respiratory Sleep Disorder Centre

A practical approach to respiratory function testing

Introduction

Although respiratory function tests are an integral part of diagnosis and management of respiratory diseases, they are not diagnostic for any given disease. Respiratory function tests may be able to identify and quantify respiratory system functional abnormalities years before other investigations become abnormal or patients become worry about their symptoms (figure 1).

Fig 1. RFT may be useful in detection of COPD before other investigations and symptoms



Despite their ability to answer many clinically relevant questions (table 1), they are underused to a great extent. There are patients who have had invasive cardiac tests to assess their symptoms before a respiratory function test reveals the real cause of their complaint. Lack of confidence in interpretation of respiratory function tests may be one of the reasons for this. The purpose of this article is to improve general practitioners' abilities to identify the indications and interpretation of these tests.

Table 1- Respiratory Function Test is indicated in:

Investigation of the cause of respiratory symptoms (cough, dyspnoea, wheeze)
Assist in diagnosis of obstructive, restrictive, mixed obstructive and restrictive ventilatory defect, respiratory muscle weakness, or upper airway diseases
Assessment of the severity of impairment and prognosis
Investigate response to bronchodilators
Detection of gas exchange abnormalities
Follow up and assess progression of chronic lung diseases
Efficacy of therapeutic interventions

Pre-operative risk assessments
Screening for chronic lung disease in high risk groups (smokers or ex-smokers, occupational lung disease)
Pre-employment screening (scuba divers, military/ police staff)
Objective assessment of disability

(the evidence for screening spirometry in asymptomatic high risk population is controversial)

Respiratory Function Test

Respiratory function tests may have different parts including spirometry, diffusing capacity, measurement of lung volumes, tests of respiratory muscle strength and bronchial provocation tests. Spirometry is to measure dynamic lung volumes, body plethysmography to measure static lung volumes and diffusion capacity to measure gas transfer abilities of the lung.

Lung Volumes and capacities

Figure 2 shows static lung volumes and capacities. Summation of two or more volumes is called capacity.

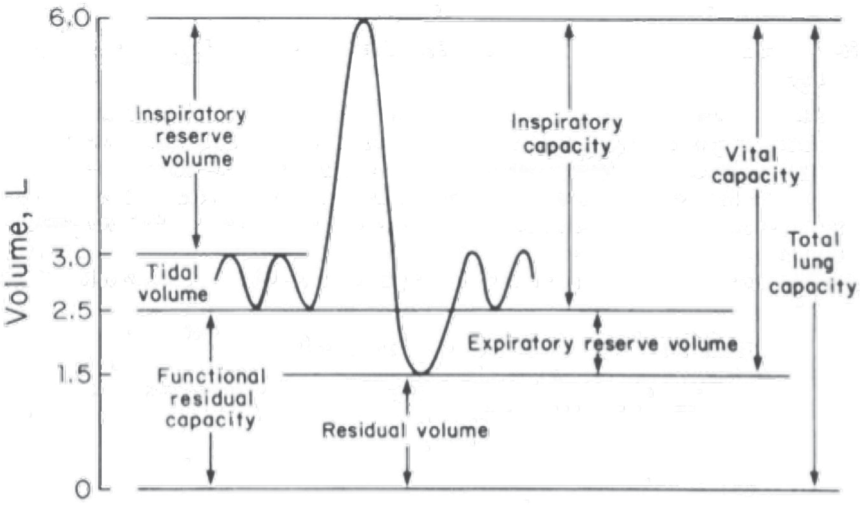


Fig 2. Static lung volumes.

Spirometry

Testing

Spirometry is a tool to assess ventilatory function by measurement of inspired and expired volumes over time (i.e. dynamic lung volumes). A subject is asked to inspire maximally and then exhale forcefully and completely into a spirometer.

Some devices can also measure airflow. These measurements can be illustrated into volume –time curves or flow volume loops (Fig.3).

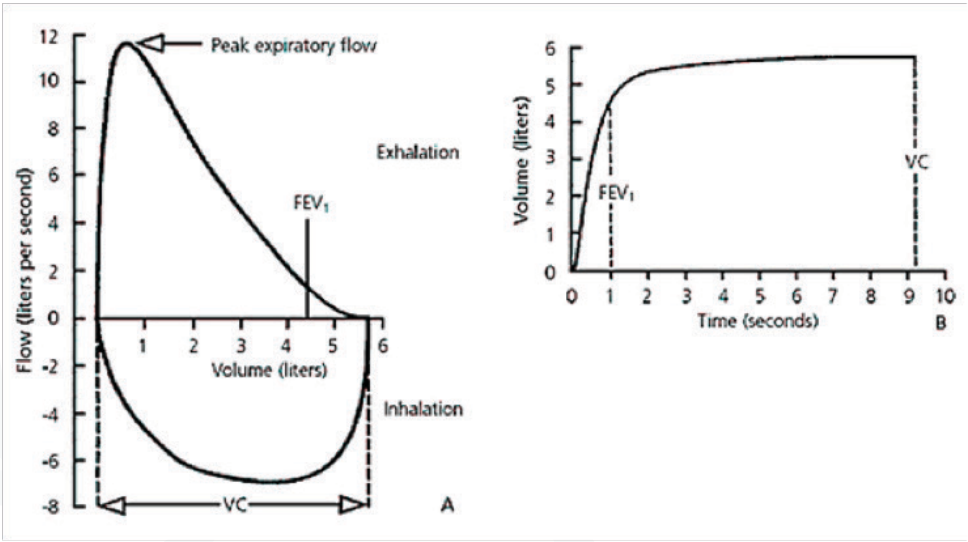


Figure 3. Flow- Volume loop (A) and Volume-Time curve (B).

Volume measurements

The volume of air exhaled in the first second of forceful expiration(forced expired volume in one second= FEV1) and the total volume exhaled forcefully after maximal inspiration (the forced vital capacity= FVC) are recorded and the FEV1: FVC ratio (forced expiratory ratio= FER) calculated.

Flow measurements

During FVC manoeuvre, peak expiratory flow (PEF), which is the maximum flow generated during forceful exhalation, may also be measured. PEFR (peak expiratory flow rate) is reliable and easy to be measured by patient at home and can be valuable in asthma management.

Average of expiratory flow over the middle 50% of forced expiration is called $FEF_{25\%-75\%}$. This value compared to volume measures (i.e. FEV1), may be considered as a more sensitive measure of small airways disease to detect early obstruction in COPD and asthma.

Because flow measurements are more dependent on patient efforts compared to volume measurements (FEV1 and FVC), they are highly variable and not specific for small airways disease.

Baseline values

The baseline values for each patient are determined by patient age, sex, height and ethnicity. After entering these parameters to the device, the baseline (normal) predicted values for a particular patient are calculated and the results of patient's test are compared with these normal values and presented as percentages and also raw numbers. The baseline values have been well validated in population studies for Caucasians. In non-Caucasian population a correction factor is used. These baseline values are validated for patients between 8–80 years of age and values beyond these age groups are extrapolated. This may cause some degree of inaccuracy in interpretation of lung function tests in these age groups.

Test performance

It is very important to direct the patient to perform the test properly. The patient must reach to maximum inspiration before rapid expiration starts. Expiration is continued with maximum effort until the patient cannot exhale any more air.

There are criteria for start and end of the test. For an acceptable performance, the reproducibility criteria must be met and a minimum of 3 acceptable attempts is required. Artefacts may also occur during the test, which can make interpretation difficult. These artefacts include: cough, glottis closure, submaximal effort, air leak and obstructed mouthpiece. Reproducibility of the tests and presence of artefacts are assessed by the technician. These are evaluated while the patient is performing the test and also by observation of different flow-volume loops or volume-time curves.

Poor test performance may resemble disease patterns and causes misinterpretation. As an example, FVC is underestimated after a submaximal effort and spirometry may be suggestive of a restrictive ventilatory defect or an obstructive defect may be

missed (lower FVC causes higher FEV1/FVC ratio).

Interpretation

An approach to interpretation of spirometry is illustrated in Fig.4. The first step is to look at FEV1: FVC ratio (FER) and compare it to the predicted value for the patient. If FER is less than lower limit of normal for the patient, there is an obstructive ventilatory defect. However in other classification systems specifically for research purposes airflow obstruction is defined by FER less than 70%. If FER is more than lower limit of normal, the patient does not have obstructive defect.

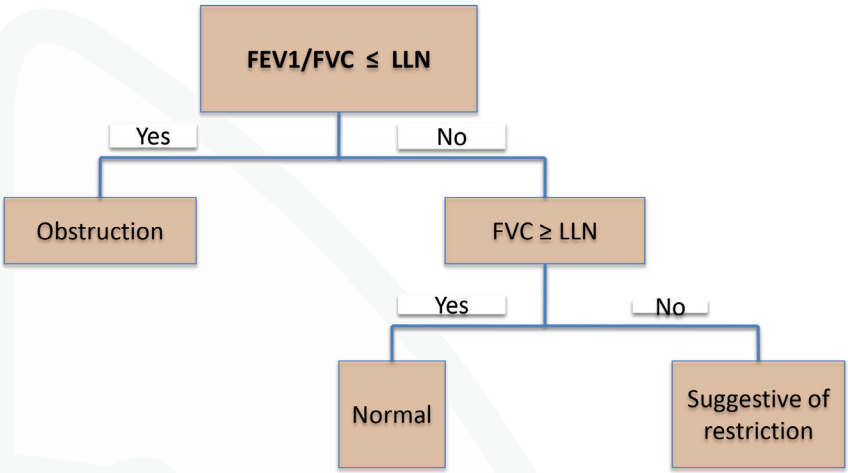


Fig.4 Algorithm for interpreting spirometry

If FER is not reduced to less than what is predicted for the patient, then an obstructive ventilatory defect is ruled out. This result can be seen in a normal patient or patients with restrictive defects. Looking at vital capacity (VC) or FVC is the next step to differentiate between these two. If FVC or VC is less than lower limit of normal for a particular patient and FER is normal, spirometry is suggestive of restrictive ventilatory defect. This finding has to be confirmed by measurement of total lung capacity which is the gold standard for diagnosis of restriction. Normal VC or FVC rules out restrictive defect.

Reduced FVC when FER is reduced most likely indicate hyperinflation as a result of severe airflow obstruction. It may also be due to a mixed ventilatory defect. Measurement of lung volumes is necessary to differentiate between these. A mixed obstructive and restrictive ventilatory defect is present when both FER and TLC are reduced.

There are patients who do not follow the above algorithm. Normal spirometry does not exclude severe lung disease. For example in a subgroup of patients with combined Emphysema and Interstitial Lung Disease there is a relative preservation of lung volumes with normal spirometry and marked reduction in DLCO . However, these group of patients will have severe limitation in gas transfer properties, which will be discussed later in this article.

After one is diagnosed with airflow obstruction (FER< lower limit of normal), the next step is to classify the severity of obstructive defect and to assess for presence of bronchodilator response (suggestive of current asthma).

Severity of limitation

To classify the severity of a ventilatory defect one needs to look at FEV1% predicted for the patient. According to ATS/ERS task force, the degree of severity is as shown in table 2.

As an example if a patient has FER< predicted LLN and FEV1=100% predicted, by definition this patient has mild obstructive ventilatory defect (although this can be considered a normal variant depending clinical information). However, this can be sometimes considered normal especially in young population.

Degree of severity	FEV_1 % pred
Mild	>70
Moderate	60-69
Moderately severe	50-59
Severe	35-49
Very severe	<35

Table 2. Severity of ventilatory defects Based on FEV1% predicted.

Bronchodilator response

Spirometry can be performed before and after the administration of an inhaled bronchodilator to test for a significant response, which is suggestive of reversible airflow obstruction. To assess bronchodilator response the patient is given 400 microgram of inhaled salbutamol (four separate puffs with 30 seconds intervals) via spacer and spirometry is repeated after 15 minutes. If FEV1 and/or FVC is improved by more than 200 millilitres and 12% after salbutamol use, bronchodilator response is positive. This is suggestive of bronchial hyper-reactivity. In an appropriate setting this result can be consistent with un-controlled asthma. Bronchial hyper-

responsiveness has clinical implications. It may suggest benefit from further treatment with inhaled corticosteroids or addition of long acting bronchodilators.

If the clinician is looking for reversibility in lung function to investigate their patient for possible asthma, the patients should not take their short acting bronchodilator 4-6 hours before spirometry and long acting bronchodilator 12-24 hours prior to testing.

Review of flow volume loop (FVL)

Some practitioners review flow volume loop even before looking at the results of spirometry. FVL can give critical information regarding patient performance and can also show characteristic features for lesions in trachea or upper airway.

Pathologic FVLs

As mentioned previously, useful information regarding test performance and artefacts during spirometry can be obtained by looking at FVL. Flow volume loops are also valuable in diagnosing upper airway (intrathoracic or extrathoracic) pathologies.

Diffusing capacity

Carbon monoxide is the gas used to measure diffusing capacity of the lung ("window on the pulmonary microcirculation"). Because of its high affinity to haemoglobin, carbon monoxide is considered a diffusion-limited gas. Nitrogen and oxygen are considered perfusion limited and both perfusion/diffusion limited gases retrospectively.

Carbon monoxide has 200 times more binding affinity to haemoglobin compared to oxygen. This property of carbon monoxide prevents high concentration of the gas in the capillary blood and tension across membranes does not occur. So gas concentration is not usually a limiting factor for its transfer across alveolar capillary membrane. The causes of limitation in diffusing capacity for carbon monoxide (DLCO) are listed in table 3.

Table-3.Causes for reduced DLCO (TLCO)

Interestitial lung disease
Emphysema
Pulmonary hypertension
Pulmonary embolism
Anaemia
Neuromuscular disease
Chest wall abnormalities
CCF
Pleural abnormalities

(TLCO = Transfer factor for carbon monoxide)
Similar to normal values for spirometry, DLCO predicted values determined by patient's sex, age, height, ethnicity and altitude (inspired oxygen concentration). There are many other factors that can affect DLCO including circadian rhythm, menstrual cycle, smoking, bronchodilator use, exercise, haemoglobin concentration, carboxyhaemoglobin concentration, body position and obesity in women (due to overestimation of the normal value for DLCO in obese women).

In many respiratory laboratories haemoglobin concentration is measured by a finger prick test and measure DLCO is corrected for haemoglobin. Clinicians always look for corrected DLCO to assess diffusion limitation.

It is also important to correct DLCO for alveolar (lung) volume (VA). In most cases with reduced lung volume DLCO is also reduced. It is not clear whether the reduction in diffusion capacity is due to extrathoracic causes (including chest wall and pleural abnormality, neuromuscular disease or poor test performance) or real reduction in diffusion capacity.

If DLCO corrected for alveolar volume (KCO= DLCO/VA) is also reduced it is suggestive of paranchymal or pulmonary vascular disease.

The degrees of severity of DLCO is mentione in table 4.

Degree of severity	**DLCO % predicted**
Mild	60-80%
Moderate	40-60%
Severe	<40%

Lung volumes

Measurement of absolute lung volumes including RV, FRC and TLC (Fig.2) is more challenging and their use is limited in clinical practice. However they are sometimes strictly necessary for a correct diagnosis. The definition of restrictive lung disease is based on reduced total lung capacity (TLC), which is the amount of air in the lung after maximum inspiration. The amount of air in the lungs after maximum expiration is residual volume (RV).

In a patient with reduced FVC (or VC) on spirometry, measurement of lung volumes is necessary to exclude or confirm restriction. A normal TLC rules out true restriction. Increased TLC in a patients with reduced FER (obstruction) and reduced FVC, confirms hyperinflation related to severe airflow obstruction. Reduced TLC in a patient with reduced FVC and normal FER (restriction) confirms the diagnosis of true restriction. Reduced TLC in a patient with reduced FER (obstruction) and reduced FVC confirms mixed obstructive restrictive defect. These findings are summarised in table 5.

Table- 5

FER (FEV1/FVC)	FVC	TLC	Interpretation
▼	▼	▲	hyperinflation related to airflow obstruction
►	▼	▼	true restriction
▼	▼	▼	mixed obstructive restrictive defect

Measurement of RV is informative in some patients. An increased RV/TLC ratio more than predicted in a patient with obstructive ventilatory defect is indicative of gas trapping. In a patient with neuromuscular disease with a restrictive ventilatory defect, reduced TLC is typically associated with increase RV.

Bronchial Challenge Tests

There are two types of bronchial challenge tests. Indirect challenges which activate mast cells to release histamine and other bronchoconstrictor mediators (e.g. mannitol, hypertonic saline, eucapnic voluntary hyperventilation, exercise challenge). Direct challenges, which directly constrict airway smooth muscle via receptors on smooth muscle (e.g. methacholine, histamine). These tests are considered positive if a known dose of stimuli can cause a 20% (direct challenge) or 15% (indirect challenge) reduction in FEV1. These test are useful in excluding, rather than confirming, a diagnosis of asthma.

There are 2 components of airway hyper-responsiveness, inflammation and persistent airway remodelling. A greater change in responsiveness to indirect

stimuli (e.g. mannitol, hypertonic saline) is suggestive of more inflammatory component and need for treatment with inhaled corticosteroids. On the other hand greater response to direct airway stimuli (methacholine, histamine) is suggestive of persistent airway remodelling. Response to direct stimuli may decreases during treatment with ICS but it does not resolve.

A positive indirect test is consistent with a diagnosis of active asthma (high specificity) and predicts respond to treatment with inhaled steroids. They are also used in diagnosing exercise-induced bronchoconstriction (EIB) and identifying individuals who may experience "airway narrowing" while SCUBA diving.

Table-6 shows some clinical advantages of mannitol challenge test in diagnosis and management of patients with respiratory disorders.

Mannitol POSITIVE		Mannitol NEGATIVE	
Not on ICS	Using ICS	Not on ICS	Using ICS
Asthmatic with active airway inflammation	Asthmatic with poorly controlled asthma, consider increasing ICS dose or assess adherence to treatment or device technique	Consider other diagnosis eg. Post nasal drip, reflux, ILD, lung cancer	Asthmatic who is well controlled airway inflammation

In an asthmatic patient with a normal lung function and negative indirect challenge test a regular long-acting b 2 –agonist is probably not warranted.

Patients follow up and repeat RFTs to assess progression of disease

One of the main indications for respiratory function tests is in following up the patients and screening for progression of chronic lung diseases. In obstructive lung disease a decline in FEV1 by more than 12% and 200ml is considered significant. As a general rule a decline in DLCO by more than 3 units is considered significant.

A positive bronchodilator response or a positive bronchial challenge test in an asthmatic suggest current airway hyper-responsiveness and need for further therapy.

In idiopathic pulmonary fibrosis, FVC and TLC correlate poorly with morphologic extent of disease on HRCT and are less predictive of outcome than DLCO. A 10% change in FVC or 15% change in TLCO is considered significant in management of interstitial lung disease.

DLCO is a good parameter in following up of patients with combined emphysema and interstitial lung disease and ILD combined with pulmonary hypertension.

About Us

At RSDC we have a particular interest in quick approach and triaging patients with suspected lung malignancy, management of pleural diseases, sleep disorders of obstructive sleep apnoea and other more complex sleep disorders, airways disease including asthma and COPD. We use a comprehensive approach to interstitial lung disease in addition to occupational and environmental lung disease.

Locations

- 719 Burwood Hwy
  Ferntree Gully VIC 3156
- Suite 2A, Knox Private Hospital
  262 Mountain Hwy, Wantirna VIC 3152
- 55 Whitehorse Rd
  Deepdene VIC 3103

Contact Us

Phone: 1300 773 210

Fax: 1300 773 220

Email: admin@RSDC.com.au

Email: info@RSDC.com.au

Website: www.RSDC.com.au

RSDC

Respiratory Sleep Disorder Centre