Grand Rounds

Pulmonary Function Tests

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ABSTRACT

Pulmonary function tests are valuable investigations in the management of patients with suspected or previously diagnosed respiratory disease. They aid diagnosis, help monitor response to treatment and can guide decisions regarding further treatment and intervention. The interpretation of pulmonary functions tests requires knowledge of respiratory physiology. In this review we describe investigations routinely used and discuss their clinical implications.

INTRODUCTION

Pulmonary function tests (PFTS) are an important tool in the investigation and monitoring of patients with respiratory pathology. They provide important information relating to the large and small airways, the pulmonary parenchyma and the size and integrity of the pulmonary capillary bed. Although they do not provide a diagnosis per se, different patterns of abnormalities are seen in various respiratory diseases which helps to establish a diagnosis. We describe the indications for performing PFTS, describe abnormal results and correlate these with underlying pathology.

GENERAL CONSIDERATIONS AND NORMAL VALUES

Guidelines for performing and interpreting PFTS have been published both by the European Respiratory and American Thoracic Societies[1-6]. Indications for performing PFTS are listed in table 1[7]. Performing PFTS is generally safe but specific contraindications exist. These are listed in table 2[7]. PFTS are effort dependent and therefore patient cooperation and understanding in performing the tests is essential in obtaining optimal results. Suboptimal results may be obtained in patients who have chest or abdominal pain or from patients who do not fully understand directions given to perform the tests.

TABLE 1

Indications for Pulmonary Function Tests

1. Investigation of patients with symptoms/signs/ investigations that suggest pulmonary disease e.g. • Cough • Wheeze • Breathlessness • Crackles • Abnormal chest x-ray
2. Monitoring patients with known pulmonary disease for progression and response to treatment e.g. • Interstitial fibrosis • COPD • Asthma • Pulmonary vascular disease
3. Investigation of patients with disease that may have a respiratory complications e.g. • Connective tissue disorders • Neuromuscular diseases
4. Preoperative evaluation prior to e.g. • Lung resection • Abdominal surgery • Cardiothoracic surgery
5. Evaluation patients a risk of lung diseases e.g. • Exposure to pulmonary toxins such a radiation, medication, or environmental or occupational exposure
6. Surveillance following lung transplantation to assess for • Acute rejection • Infection • Obliterative bronchiolitis

TABLE 2

Contraindications to performing PFTS[7]

Myocardial infarction within the last month
Unstable angina
Recent thoraco-abdominal surgery
Recent ophthalmic surgery
Thoracic or abdominal aneurysm
Current pneumothorax

Patients with active respiratory infections such as tuberculosis are not precluded from having PFTS however the tests should ideally be deferred until the risk of cross contamination is negligible. If patients with infectious disease must undergo testing then extra precautions in addition to the standard decontamination of equipment may be necessary. This may include performing PFTS at the end of the day to allow

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disassembly and disinfection of equipment, undertaking tests in the patients' room rather than the lung function laboratory and reserving equipment for sole use in patients with infections[1].

A sitting position is typically used at the time of testing to prevent the risk of falling and injury in the event of a syncopal episode, although PFTS can be performed in the standing position. Patients are advised not to smoke for at least one hour before testing, not to eat a large meal two hours before testing and not to wear tight fitting clothing as under these circumstances results may be adversely effected[1]. False teeth are left in place unless they prevent the patient from forming an effective seal around the mouth piece.

Normal or predicted ranges of values are obtained from large population studies of healthy subjects. Values are taken for people matched for age, height, sex and where appropriate ethnicity. PFTS should be performed three times to ensure that the results are reproducible (less than 200ml variation) and accurate. Dynamic studies are performed first (spirometry, flow volume curves, peak expiratory flow rates), followed by lung volumes, bronchodilator testing and finally diffusion capacity. Each of these aspects of PFTS will now be reviewed in more detail.

SPIROMETRY

Spirometry is the most frequently used measure of lung function and is a measure of volume against time. It is a simple and quick procedure to perform: patients are asked to take a maximal inspiration and then to forcefully expel air for as long and as quickly as possible (a forced vital capacity manoeuvre- figure 1). Measurements that are made include

- Forced expiratory volume in one second (FEV1)

- Forced vital capacity (FVC)
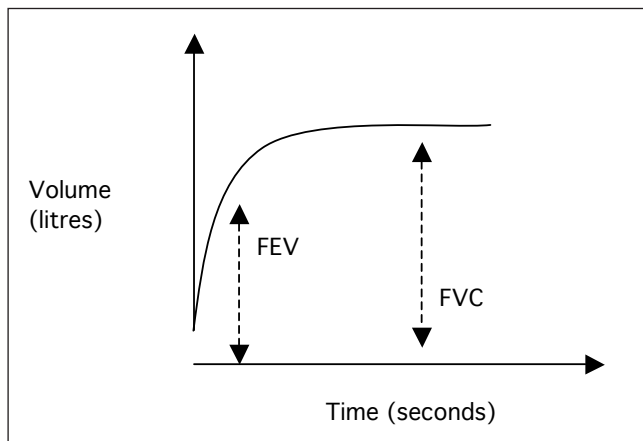
- The ratio of the two volumes (FEV1/FVC)

Fig 1. Normal Spirometry

Spirometry and the calculation of FEV1/FVC allows the identification of obstructive or restrictive ventilatory defects. A FEV1/FVC < 70 % where FEV1 is reduced more than FVC signifies an obstructive defect (figure 2). Common examples of obstructive defects include chronic obstructive pulmonary disease (COPD) and asthma. The FEV1 can be expressed as a percentage of the predictive value which allows classification

of the severity of the impairment (table 3)[8]. An FEV1/FVC > 70% where FVC is reduced more so than FEV1 is seen in restrictive defects such as interstitial lung diseases (e.g. idiopathic pulmonary fibrosis) and chest wall deformities (figure 3).
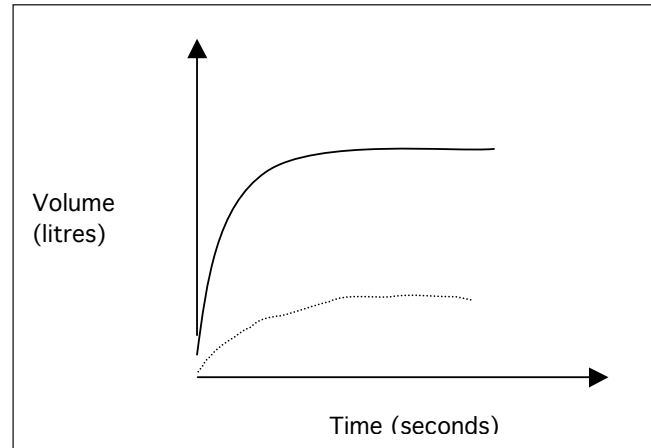

Fig 2. Spirometry in obstructive lung disease.

TABLE 3

Severity of airflow obstruction based on percentage (%) predicted forced expiratory volume in 1 second (FEV1).

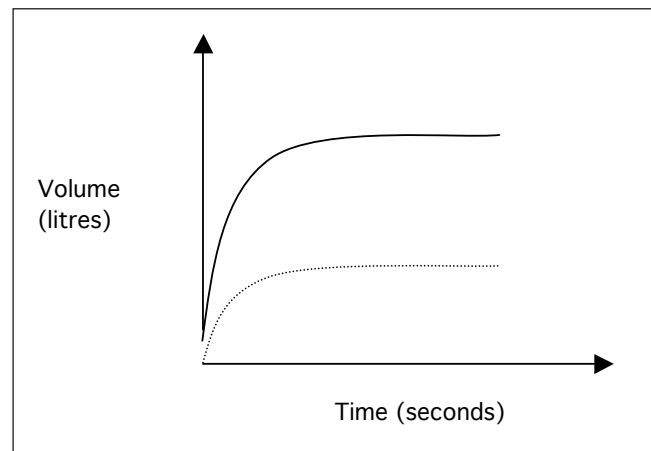| FEV1 % predicted	Stage
>80%	Mild
50-79%	Moderate
30-49%	Severe
<30%	Very severe

Fig 3. Spirometry in restrictive lung disease.

FLOW VOLUME CURVES

Flow volume curves are produced when a patient performs a maximal inspiratory manoeuvre which is then followed by a maximal expiratory effort. A graph is produced with a positive expiratory limb and a negative inspiratory limb (figure 4). The maximal flow rate during expiration can also be measured (peak expiratory flow rate PEFR). Furthermore the maximal flow rates between 25%-75% of the vital capacity (FEF25-

75%) can also be measured and these provide important information regarding small airway function.
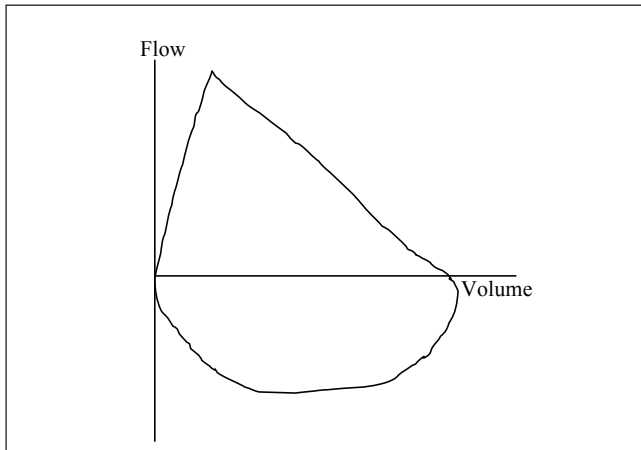

Fig 4. Normal Flow volume curve

With knowledge of the expected appearance of the flow volume loop in a normal patient, important information can be obtained from the morphology of the curve in patients with suspected respiratory disease. Patients with obstructive lung diseases with reduced expiratory flow in the peripheral airways typically have a concave appearance to the descending portion of the expiratory limb (figure 5) rather than a straight line. In patients with emphysema the loss of elastic recoil and radial support results in pressure dependent collapse of the distal airways with more pronounced "scalloping" of the expiratory limb. Even if the flow volume loop morphology is normal, a reduction in PEFR may be an indication of asthma with early airways obstruction. Similarly a reduction in FEF25-75% indicates small airways obstruction. This can also occur in patients with asthma with a normal PEFR, and is useful in providing a better overall picture of asthma control. It is also helpful in monitoring response to treatment and this may be particularly important for patients being considered for general anaesthetic and surgical intervention.In restrictive defects the expiratory limb has a convex or linear appearance because flow rates are preserved but the problem relates to a parenchymal disorder e.g. lung fibrosis which reduces lung volumes.
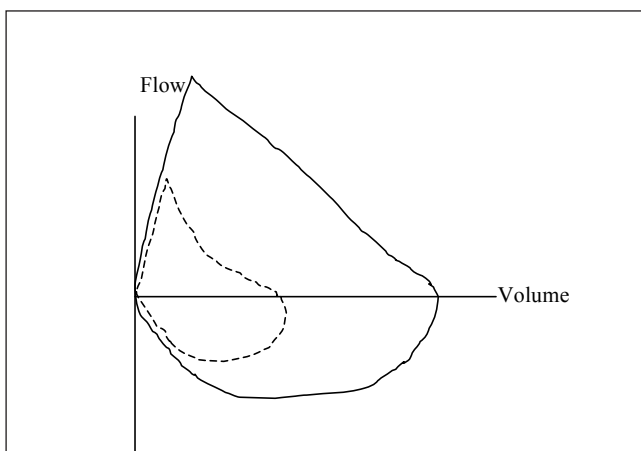

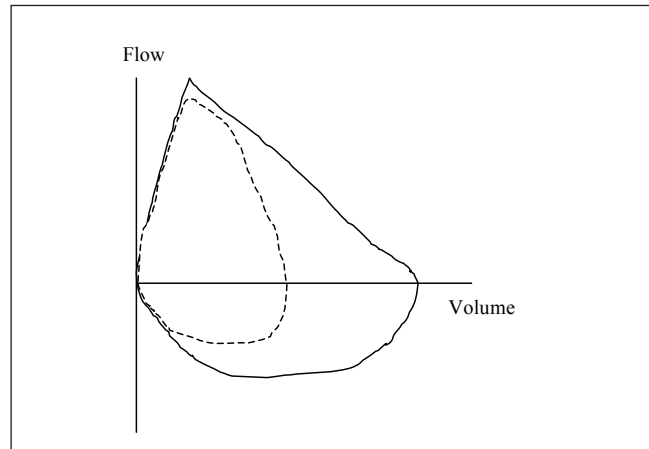*Fig 5*. Flow volume curve in obstructive lung disease e.g. COPD

Fig 6. Flow volume curve in restrictive lung disease e.g. interstitial lung disease.

Flow volumes curves are helpful in the detection of large airway abnormalities. Typically intra-thoracic large airway obstruction (e.g. from a lower tracheal or bronchial tumour figure 7) results in flattening of the expiratory limb alone with preservation of the inspiratory limb (figure 8). Normally in expiration there is a rise in intrathoracic pressure, which is transmitted to the intrathoracic airway causing some narrowing of the airway. The presence of an obstructing lesion coupled with a rise in intrathoracic pressure during expiration results in a more pronounced and pathological reduction in airflow through the obstructed or partially occluded intrathoracic airway.

In fixed extra-thoracic large airway obstruction (e.g. vocal cord paralysis or tracheal stenosis figure 9) there is symmetrical flattening of both the inspiratory and expiratory limb as airflow is limited in both directions and is not affected significantly by intrathoracic pressure changes (figure 10)[9].

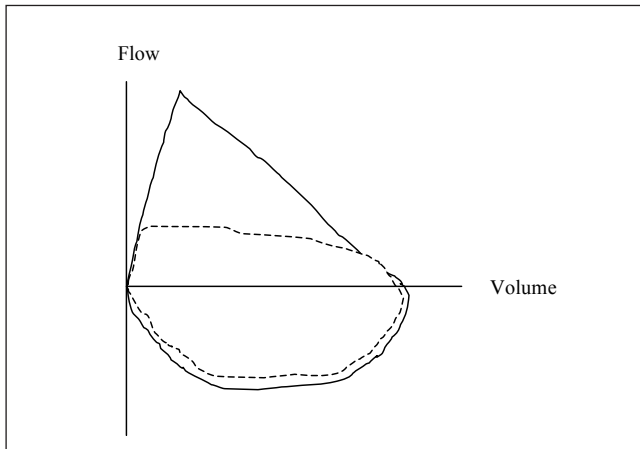*Fig 7*. A bronchial carcinoma obstructing the right main bronchus.

Fig 8. Flow volume curve seen with intra-thoracic airway obstruction.
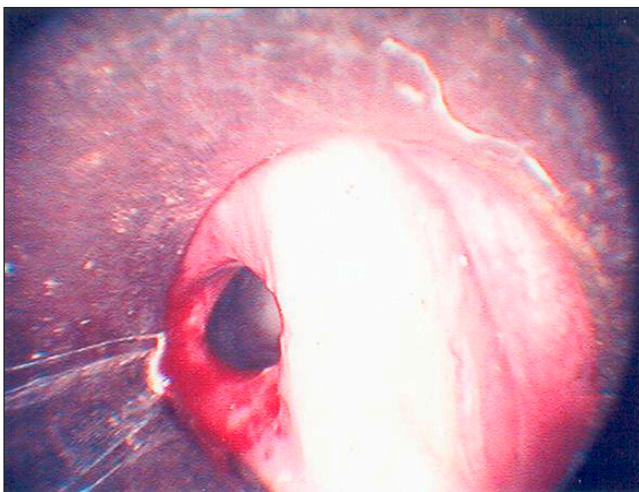

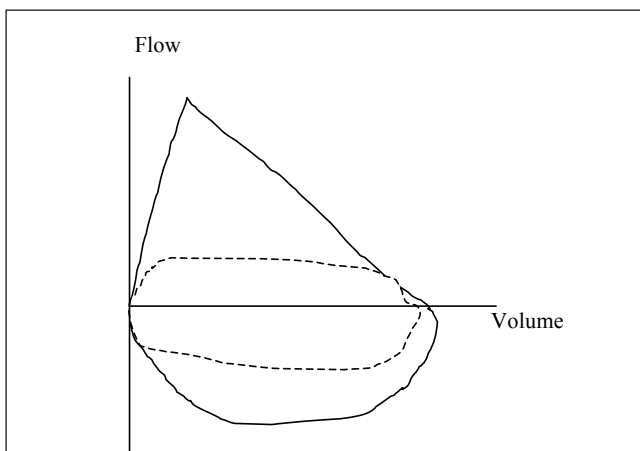*Fig 9*. Tracheal stenosis seen at rigid bronchoscopy.

Fig 10. Flow volume curve seen with fixed extra-thoracic airway obstruction

BRONCHODILATOR TESTING

The diagnostic hallmark of asthma is the presence of reversible airways obstruction. Patients with controlled or stable asthma may have apparently normal spirometry and flow volume curves. It is therefore useful to see if there is any change in the airway indices following the administration of a bronchodilator such as 2.5mg of nebulised salbutamol.

A positive response in adults is defined as a 12% increase in baseline (pre bronchodilator) FEV1 with an increase of 200mls or more following the administration of a bronchodilator. A negative test does not mean a patient will not derive any benefit from a trial of bronchodilator therapy such as inhaled salbutamol or corticosteroids. It is therefore important to use the patient's history and examination in addition to the above in formulating a diagnosis and treatment plan. In this regard home peak flow charts are helpful. Bronchial challenge testing may also be considered where a 20% fall in FEV1 in response to small doses of inhaled bronchoconstrictors such as methacholine is indicative of asthma.

LUNG VOLUMES

Static lung volumes are measured with the use of whole body plethysmography in an airtight body box. Other techniques that can be used to measure static lung volumes included nitrogen washout or helium dilution[4]. They cannot be measured by spirometry.

In body plethysmography, the patient sits inside an airtight box, inhales or exhales to a particular volume (usually FRC), and then a shutter drops across their breathing tube. The subject makes respiratory efforts against the closed shutter. Measurements are based on Boyle's law which states that at constant temperature the volume of a given mass of gas varies inversely with pressure. Therefore the increase in their chest volume slightly reduces the box volume (the non-person volume of the box) and thus slightly increases the pressure in the box. Static lung volumes can be obtained either by measuring the changes in pressure in a constant volume box or volume in a constant pressure box[4].

RESIDUAL VOLUME

Residual volume (RV) is the amount of air remaining in the lungs after a maximal expiration (normally 500mls). In patients with obstructive lung diseases where there is incomplete emptying of the lungs and air trapping, RV may be significantly increased. Patients with high RV who require surgery and mechanical ventilation require high peri-operative inflation pressures. This increases the risk of barotrauma, pneumothorax, infection and reduced venous return due to high intra thoracic pressures. The RV can also be expressed as a percentage of total lung capacity and values in excess of 140% significantly increase the risks of these complications.[7] Patients referred for lung volume reduction surgery typically have RV in excess of 180% predicted.

TOTAL LUNG CAPACITY

Total lung capacity (TLC) is the total volume of air in the lungs after a maximal inspiration. It is the sum of RV and vital capacity (the difference in volume between maximal inspiration and maximal expiration). TLC may be increased in patients with obstructive defects such as emphysema and decreased in patients with restrictive abnormalities including chest wall abnormalities and kyphoscoliosis.

FUNCTIONAL RESIDUAL CAPACITY

Functional residual capacity (FRC) is the volume of air in the lungs following normal expiration. Patterns of abnormal FRC are similar to abnormalities given above for TLC and RV.

DIFFUSION CAPACITY

The measurement of diffusion capacity (DLCO also known as transfer factor) gives important information regarding the integrity and size of the alveolar blood membrane. It measures the diffusion of gas across the alveolar membrane which is determined by the surface area and integrity of the alveolar membrane and the pulmonary vascular bed. Normally the value is corrected for the patient's haemoglobin (DLCOc). DLCOc is measured using carbon monoxide gas, which is soluble and binds to haemoglobin with its uptake limited by diffusion only. It is measured by a single breath technique where 10% helium and 0.3% carbon monoxide are rapidly inspired, held for 10 seconds and then expired with the measurement of the remaining carbon monoxide. Comparison of the inspired and expired CO fractions allows calculation of DLCO[3].

DLCOc is determined by the surface area of the alveolar membrane and as such, is impaired in conditions where the surface area is reduced e.g. pulmonary fibrosis, emphysema or pulmonary emboli. The transfer coefficient (KCO) is DLCOc corrected for alveolar volume. In patients with a pneumonectomy DLCOc will be reduced due to the loss of approximately half of the surface area of alveolar membrane but KCO will be normal as the remaining lung is normal with normal function of the alveolar blood membrane. Similarly variation can be seen in diseases that effect the lungs in a heterogeneous manner e.g. COPD or alpha 1 antitrypsin emphysema. In COPD the upper lobes tend to be preferentially damaged whereas in alpha 1 antitrypsin deficiency the lower lobes are predominantly involved. Therefore DLCOc will be lower than KCO. Pulmonary emboli should be considered in patients with an isolated reduction in DLCOc without any other obvious respiratory cause.

RESPIRATORY MUSCLE FUNCTION

A number of diseases such as motor neurone disease can result in respiratory muscle weakness, which can ultimately lead to respiratory failure. These diseases can effect not only chest wall muscles but also the diaphragm which is the major inspiratory muscle. Serial measurements of vital capacity may be necessary to detect deterioration in lung function in patients with neuromuscular disease such as Guillan Barre Syndrome. Once the vital capacity falls below 1 litre in such patients mechanical ventilatory support may be indicated. Other measures of respiratory muscle function include [7]:

Inspiratory mouth pressures – a measure of inspiratory muscle function in which subjects generate as much inspiratory pressure as possible against a blocked mouth piece[10]. The pressure generated (maximum inspiratory pressure MIP) is therefore largely a function of the inspiratory respiratory muscles rather than lung volumes which do not change significantly during the test[10]. A normal value is approximately 100 cm of water. Values of 80 cm of water or more exclude any significant inspiratory muscle weakness [11].

Expiratory mouth pressures- a measure of expiratory respiratory muscle function where patients generate a maximal expiratory pressure (MEP) against a blocked mouthpiece (a valsalva manoeuver) at TLC. The range of normal values is wide and results should be compared with published data [11].

Erect and supine vital capacity- in normal subjects there is a 5% decrease in vital capacity in the supine position. A fall of 25% or more may indicate diaphragmatic paralysis and further confirmatory tests e.g. ultrasound screening of diaphragm may be necessary.

ARTERIAL BLOOD GASES

Arterial blood gas sampling provides important information on gas exchange and oxygen delivery to the tissues. Type 1 respiratory failure is defined as a partial pressure of oxygen (PaO_2) < 8 kPa with normal partial pressure of carbon dioxide $(PaCO_2)$. Causes of type 1 respiratory failure include pneumonia and pulmonary embolism. Type 2 respiratory failure occurs when hypoxia is accompanied by hypercapnia $(PaCO_2 > 6.5$ kPa). This is seen in ventilatory failure and examples of causes include respiratory muscle weakness and COPD. Type 2 respiratory failure may also occur in patients with advanced type 1 respiratory failure as they tire and develop ventilatory failure. Such patients may require ventilatory support in the form of non-invasive or invasive ventilation.

OVERNIGHT OXIMETRY

Patients who complain of excessive daytime sleepiness (as measured by the Epworth Sleepiness Scale) and snoring with or without witnessed apnoeas should be investigated for obstructive sleep apnoea (OSA). Overnight oximetry can be used initially in the assessment of OSA. Typically 10 oxygen desaturations per hour of more than 4% would be considered to be indicative of OSA. Normal overnight oximetry does not exclude OSA and more detailed sleep studies including polysomnography should be performed in patients where there is a high clinical suspicion of OSA.

CARDIOPULMONARY EXERCISE TESTING

Cardiopulmonary exercise testing (CPET) involves patients exercising on a treadmill or cycle ergometer with measurements of variables such ventilation, heart rate, oxygen uptake $(V'O_2)$ and cardiac output. This allows causes for a reduced exercise tolerance to be identified, which may be due to ventilatory abnormalities in those with chronic lung disease or impaired cardiac output in patients with cardiac disease. It may be useful in patients who complain of excessive breathlessness and in whom investigations such as echocardiogram and pulmonary functions tests are normal. A $V'O_2$ peak standardized by body mass below 80% predicted is considered to be abnormal[12].

USING PULMONARY FUNCTION TESTS IN PRE-OPERATIVE EVALUATION OF PATIENTS

It is important to address a number of concerns in evaluating a patient prior to surgery. These include determining if a patient is [7]:

• Fit for a general anesthetic

• Appropriate for the planned surgical procedure

• Requires further treatment for any underlying respiratory problems (which may or may not have been identified prior to the evaluation).

These decisions are typically made by anaesthetists, with input

from respiratory physicians and intensive care physicians[7]. In a patient with chronic respiratory disease it is important to identify how much of their breathlessness is caused by their lung disease particularly if the patient is being considered for cardiac surgery. If their breathlessness is predominantly due to respiratory disease, this will not necessarily be improved by any corrective cardiac surgery. Surgery may also not be justified if their respiratory disease carries a poor prognosis in itself. It is important to try and identify any contributing causes for breathlessness particularly in patients with multiple co morbidities so that these can be addressed, investigated and treated as appropriate. This short history illustrates the point. A 71-year-old male smoker with COPD was referred for consideration regarding aortic valve replacement for aortic stenosis (AS). Physical examination revealed features compatible with COPD and AS but in addition he had a disproportionately loud pulmonary component to the second heart sound and a right ventricular heave. A ventilation/perfusion scan was ordered which confirmed multiple pulmonary emboli and abdominal imaging diagnosed a renal tumour involving the inferior vena cava. Cardiac surgery was postponed.

It is important to identify patients with respiratory problems that are at increased risk of peri-operative complications such as respiratory infection including ventilator acquired pneumonia, atelectasis, acute lung injury and prolonged respiratory failure with may all result in difficulty weaning from mechanical ventilation post operation. Risk factors for peri-operative pulmonary complications include increased age, COPD and smoking[13, 14]. The risk of complications is also related to the surgical site and its proximity to the diaphragm with increased complications seen following aortic aneurysm repair, and thoracic and upper abdominal surgery[13]. Procedures longer than 3 hours in duration are also associated with increased risk. Although there are no clear guidelines regarding the routine use of pre-operative PFTS, they are generally used in the assessment of symptomatic patients undergoing major thoraco-abdominal surgery. It should be remembered that pulmonary complications may occur in patients without risk factors and that strategies to reduce the risk of these complications such as smoking cessation and lung expansion techniques (e.g. deep breathing exercises) should be used in all patients with particular attention given to those at increased risk.

Patients with chronic respiratory disease or with impairment of PFTS at pre operative evaluation are challenging to assess. We recommend that where there is doubt regarding suitability for a general anaesthetic appropriate advice from anaesthetists, intensive care and respiratory physicians is sought and efforts to optimise the patient as much as possible are made.

PULMONARY FUNCTION TESTS IN PATIENTS UNDERGOING LUNG RESECTION

Resection of primary lung cancers in the form of lobectomy or pneumonectomy remains the treatment of choice in patients with early stage disease[15]. Many patients with lung cancer will also have COPD and it is important to try and determine the effect of lung resection on these patients both in terms of postoperative complications and long term disability[16, 17].

The British Thoracic Society guidelines advise that pneumonectomy can be considered in patients with FEV1 > 2.0 L and lobectomy if FEV1 > 1.5 L in the absence of any interstitial lung disease or unexpected disability due to shortness of breath[15]. As absolute values may be lower in older patients and women, patients are generally considered suitable for resection if FEV1 > 80% predicted and DLCO > 80% predicted[18]. In patients with borderline lung function the post operative predicted FEV1 and DLCO can be calculated either with knowledge of the number of lung segments to be resected or through quantitative lung perfusion scanning. Patients with a post operative predicted FEV1 or DLCO < 40% are deemed at high risk of peri-operative death and complications[17]. Further investigations including CPET may be necessary for further risk stratification.

PFTS are used in the assessment of patients for lung transplantation. Patients with PFTS below 30% predicted may potentially be considered for lung transplantation assuming no other contraindications are present[19, 20].

RIGHT HEART CATHETERISATION

Chronic respiratory diseases may result in pulmonary hypertension and eventually right-sided cardiac failure and death. Pulmonary hypertension should be considered in patients with symptoms or signs of right-sided cardiac failure or perhaps with more dyspnoea than expected on the basis of their PFTS and clinical presentation.

A Doppler trans thoracic echocardiogram is a useful non-invasive tool in screening for pulmonary hypertension. Right heart catheterisation is considered the gold standard tool and can diagnose pulmonary hypertension with the measurement of a mean pulmonary artery pressure > 25mmHg[21]. In experienced centres it can be performed safely and provide information on pulmonary haemodynamics including cardiac output, pulmonary vascular resistance and an approximation of mean left atrial pressure by measuring the mean pulmonary capillary wedge pressure[22]. Patients with pulmonary hypertension are at increased risk of peri-operative complications including pulmonary hypertensive crises where an acute rise in pulmonary pressures results in right ventricular failure and a subsequent fall in cardiac output. Knowledge of pulmonary haemodynamics allows careful pre-emptive management of these problems. Furthermore some patients with co existing pulmonary hypertension and cardiac or pulmonary disease may benefit from specific targeted therapy for their pulmonary hypertension e.g. using sildenafil[23-28].

CONCLUSION

Pulmonary function tests are an important tool in the assessment of patients with suspected or known respiratory disease. They are also important in the evaluation of patients prior to major surgery. Interpretation of the tests, which requires knowledge of normal values and appearance of flow volume curves, must be combined with the patient's clinical history and presentation.

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