Pulmonary Function Tests and Assessment for Lung Resection

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INTRODUCTION

The aim of this article is to describe the tests available for the assessment of patients presenting for lung resection. The individual tests are explained and we describe how patients may progress through a series of tests to identify those amenable to lung resection.

Pulmonary function testing is a vital part of the assessment process for thoracic surgery. However, for other types of surgery there is no evidence that spirometry is more effective than history and examination in predicting postoperative pulmonary complications in patients with known chronic lung conditions. Furthermore specific spirometric values (e.g. the FEV_1) cannot be taken as prohibitive for non-cardiothoracic surgery.[1-3] Exercise testing of cardiopulmonary reserve is increasingly used to assess patients undergoing major surgery.

In addition to preoperative assessment for lung resection surgery, pulmonary function testing is also indicated for assessing suitability for coronary artery bypass grafting and to formally diagnose chronic obstructive pulmonary disease (COPD).

THE ROLE OF LUNG RESECTION IN THE MANAGEMENT OF LUNG CANCER

In the UK the incidence of lung cancer is 77 per 100,000 males and 52 per 100,000 females, whilst the death rates are 54 and 30 per 100,000 respectively. There are 2400 lobectomies and 500 pneumonectomies performed in the UK each year, with in-hospital mortality 2-4% for lobectomy and 6-8% for pneumonectomy.[4]

Lung resection is most frequently performed to treat non-small cell lung cancer. This major surgery places large metabolic demands on patients, increasing postoperative oxygen consumption by up to 50%. Patients presenting for lung resection are often high risk due to a combination of their age (median age is 70 years)[5] and co-morbidities. Since non-surgical mortality approaches 100%, a thorough assessment of fitness for surgery is essential in order to ensure that none are denied a potentially life-saving treatment.[6]

Lung cancer treatment is primarily dictated by the histological diagnosis, i.e. whether it is a small cell or non-small cell (squamous cell, adenocarcinoma, large cell) tumour. Small cell cancer is more aggressive and at presentation has often already metastasized. Therefore outcome is poor and surgery is only rarely an option. The options for non-small cell cancer depend upon its stage or how advanced it is (see Table 1). A tumour is staged using information about its size, position and invasion of structures locally, whether any lymph nodes are involved, and if it has spread to other areas within or outside the thorax. Stage 1 is the least advanced and stage 4 the most advanced.

Summary

This article describes the steps taken to evaluate patients' fitness for lung resection surgery. Examples are used to demonstrate interpretation of these tests. It is vital to use these tests in conjunction with a thorough history and examination in order to achieve an accurate assessment of each patient's level of function. Much of this assessment for surgery will be conducted by the surgeon and a multidisciplinary team. Involvement of the anaesthetist at an early stage and good communication with the surgeon are important. The particular features of each patient and their disease dictate the extent of surgery and therefore the requirements for their perioperative care.

Table 1. *Overview of the treatment options in lung cancer*

Type of lung cancer	Stage	Treatment
Non-small cell *(e.g. squamous cell, adenocarcinoma, large cell)*	1 and 2	**Surgery** +/- chemotherapy Radiotherapy if unfit for surgery
	3	**Surgery may be possible** + chemo/ radiotherapy or chemo/radiotherapy alone
	4	Radiotherapy +/- chemotherapy
Small cell		Chemotherapy +/- radiotherapy *(Rarely surgery)*

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ASSESSMENT OF PATIENTS FOR LUNG RESECTION

Each patient's management requires planning by a multi-disciplinary team (MDT), which includes a respiratory physician, a thoracic surgeon, an oncologist and other staff such as physiotherapists and respiratory nurses. If the MDT feels that surgery is appropriate, then the surgeon will decide if the tumour is technically resectable based on chest Xray and CT scan images (Figure 1). Important factors include tumour that impinges on the chest wall, traverses the fissures between lobes or is in close proximity to major vessels. In some cases, and where available, a PET scan (positron emission tomography) may be performed to further identify the anatomy of the tumour and to clarify whether nodal spread or metastasis has occurred (Figure 2). As an anaesthetist it is important to view these scans in order to understand the planned surgery. For example:

- chest wall resection may be necessary,

- close proximity to the pleura with pleural resection may make paravertebral analgesia impossible,

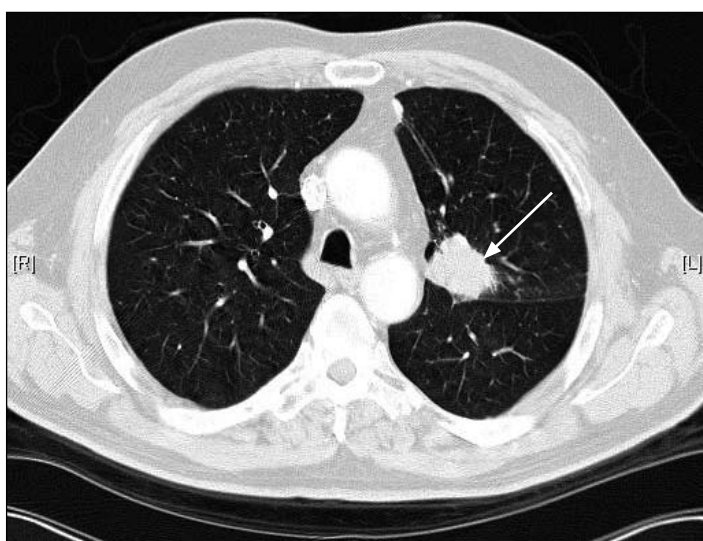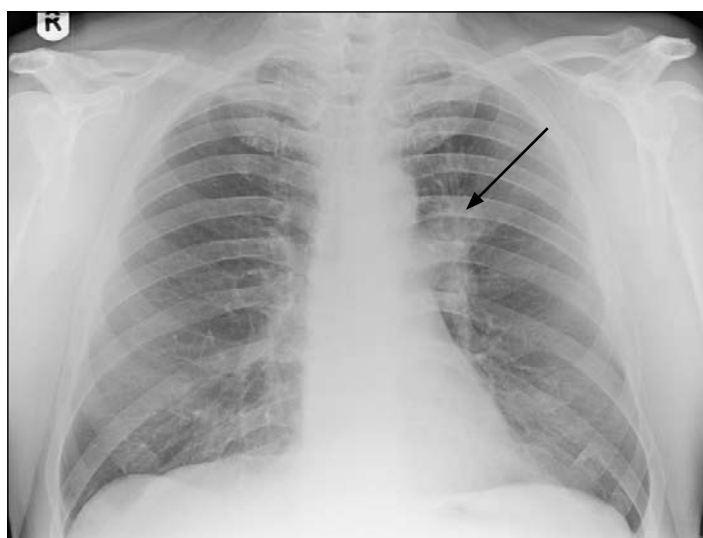- proximity to the pulmonary vessels or aorta makes major blood loss more likely.

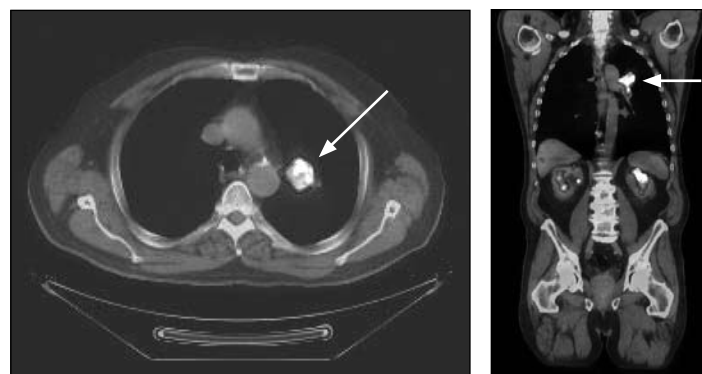**Figure 1**. *Chest Xray and CT scans showing a left upper lobe tumour*

Figure 2. *A PET (positron emission tomography) scan shows the functional status of the body tissues and so highlights neoplastic tissues with a high rate of metabolism. Scans may be combined with CT images to reconstruct three dimensional images*

Where it is unclear whether mediastinal or hilar nodes are involved, superior (or cervical) mediastinoscopy, under general anaesthesia, may be performed. This requires a relatively straightforward anaesthetic that may contribute some information for the anaesthetist when assessing the patient's fitness to undergo major lung resection. Where a tumour is unresectable, the patient may be reassessed after *neo-adjuvant* chemotherapy.

PULMONARY FUNCTION TESTS

Whilst these investigations give an indication of a patient's fitness to undergo a surgical procedure, a thorough history and examination is essential to build up a true clinical picture. A patient's exercise tolerance may demonstrate that their functional ability has been underestimated by pulmonary function tests. Poor technique gives misleading results that may conflict with your clinical assessment. A more formal assessment of this is obtained by measuring oxygen saturations before, during and after a stair climb (see below). A history of chronic sputum production suggests that the ability of the patient to expectorate in the postoperative period will be critical.

Pulmonary function tests can be divided into those of ventilation and those of gas exchange. Exercise tests that assess cardiopulmonary reserve are also considered.

Indications for pulmonary function tests

- Diagnosis of a disease process
- Monitoring the response to therapy
- Documentation of the course of a disease process
- Preoperative assessment for lung resection, cardiac surgery or non-cardiothoracic surgery
- Evaluation of disability
- Evaluating disease prognosis.

ASSESSMENT OF VENTILATION

Peak Flow

This is the easiest test of ventilation to perform and an inexpensive portable peak flow meter is used. It is a measure of the peak expiratory flow rate during forceful expiration from vital capacity (i.e. at full inspiration). The main role for peak flow is to follow the course of obstructive diseases such as asthma and COPD, which

lead to a reduction in flow through the airways (and a reduced peak flow). It may be useful during exacerbations of these conditions and in assessing the response to treatment. The value obtained is assessed in comparison to the patient's previous results or to a predicted value, calculated using the patient's sex, age, and height. There is a normal diurnal variation of peak flow with the lowest levels occurring during the early hours of the morning.
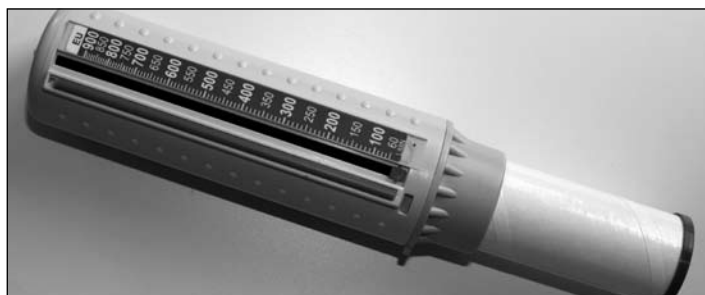

Figure 3. *A simple peak flow meter*

Spirometry

Basic measurements of the forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) can be obtained using a vitalograph, which is a relatively cheap and portable piece of equipment (Figure 4).

Figure 4. *A vitalograph consists of a bellows attached to a pen, with a motor, which moves a sheet of paper under the pen tip, as the subject exhales and fills the bellows. A typical reading is shown in Figure 5*
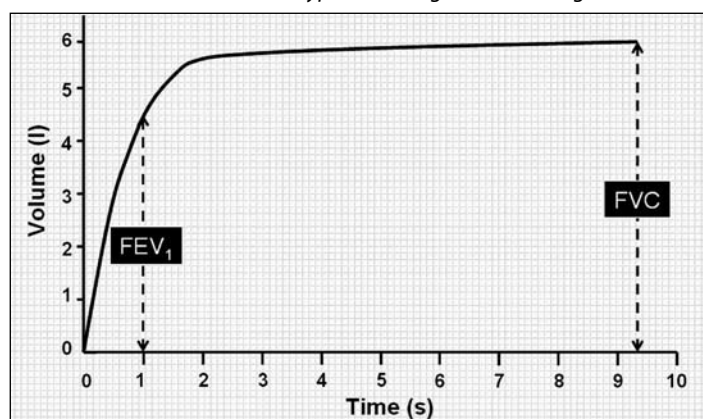

Figure 5. *A vitalograph recording from a normal subject. The arrows indicate the values for the forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC)*

The principle values obtained are:

The forced vital capacity (FVC)

The subject exhales from maximum inspiration (vital capacity) as quickly and completely as possible, and the total volume of air expired is measured. This tests the lungs ability to act as a bellows and is reduced by restrictive conditions affecting the thoracic cage (e.g. kyphoscoliosis), neuromuscular conditions (e.g. polio), changes within the pleura, or the lung itself (e.g. lung fibrosis).

The forced expiratory volume in one second (FEV_1)

The subject expires forcefully from vital capacity and the volume of air expired in the first second of expiration is measured. This value is altered by changes in airway resistance and, to a lesser extent, by respiratory effort. It is reduced in conditions such as asthma and COPD where the airways are narrowed. It clinical terms it provides some indication of how effectively an individual can generate a forceful outflow of air from the airways - i.e. a **cough**.

The FEV_1/FVC ratio

This is useful to differentiate between obstructive conditions where the ratio is reduced and restrictive conditions where it is not. The normal ratio is around 80%. In obstructive conditions, such as COPD, both FVC and FEV_1 are reduced, but the reduction in FEV_1 is greater.

The FEV_1 and FVC are expressed as absolute values and also as percentages of predicted values. The latter are more useful as they take height, age and sex into account. Spirometry may be performed before and after a dose of bronchodilator (or even a course of steroids) in order to determine the reversibility of the airway disease.

Some hospitals have more advanced equipment in a pulmonary function unit or laboratory (Figure 6). This equipment can be used to obtain additional information such as flow-volume loops (Figure 7). Other data on airflow at different lung volumes such as the FEF_{50} (the forced expiratory flow at 50% of vital capacity in $l.s^{-1}$), FEF_{75} and FEF_{25-75} (forced expiratory flow rates) may be more sensitive to detect airflow obstruction earlier in the disease process. A reduction in the FEF_{50} for example is a measure of small airway disease.

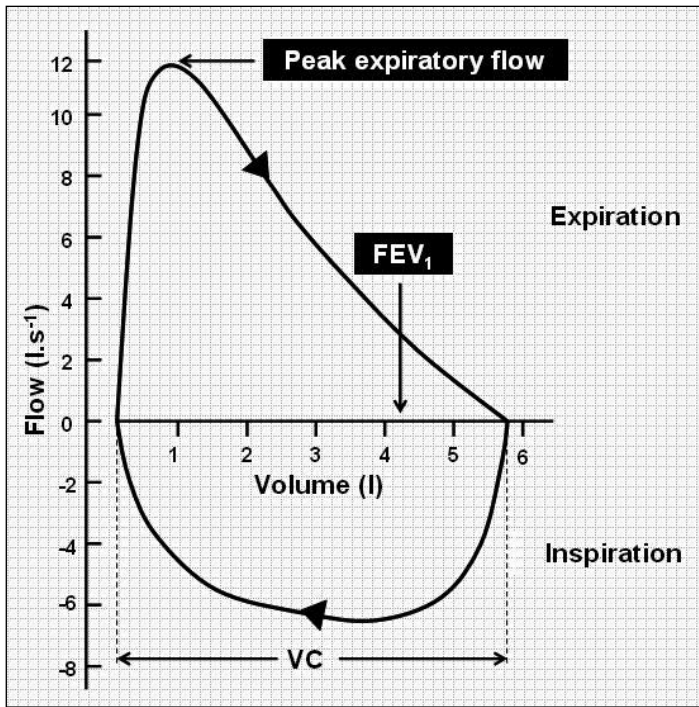**Figure 6**. *Laboratory spirometry*

Figure 7. *A typical flow-volume loop for a normal subject obtained using a laboratory spirometer*

Some of the lung volumes that cannot be directly measured using spirometry can be estimated using body plethysmography. Examples are the total lung volume (TLV), the functional residual capacity (FRC) and the residual volume (RV). Figure 8 demonstrates these volumes and capacities. Patients with obstructive lung disease, who demonstrate an increased residual volume (RV) have hyperinflated lungs and are prone to gas-trapping (due to airway collapse) at the end of expiration during positive pressure ventilation (Table 1).
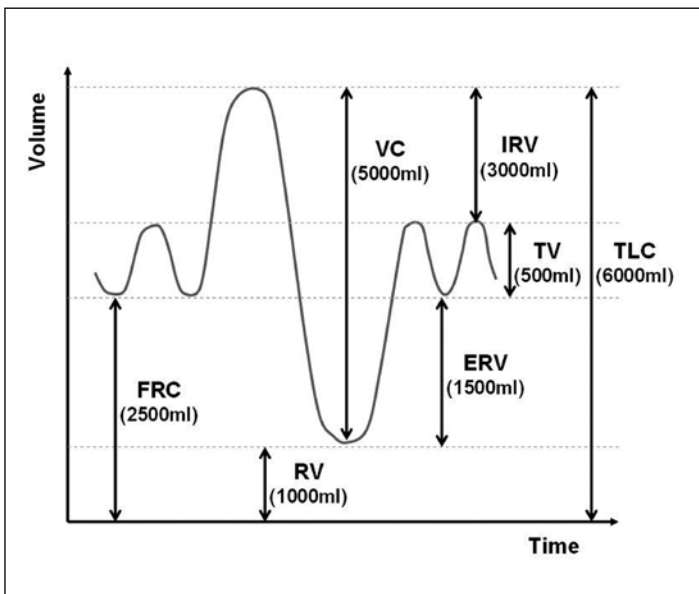

Figure 8. *Lung volume measurements. VC – vital capacity; IRV – inspiratory reserve volume; TV – tidal volume; TLC – total lung capacity; FRC - functional residual capacity; ERV – expiratory reserve volume; RV - residual volume*

Table 1. *An example of spirometry values for a patient with COPD. Note that both the FEV_1 and FVC are reduced, with the FEV_1 reduced to greater extent, resulting in a low FEV_1/FVC ratio. Note that the residual volume is increased suggesting hyperinflation and a tendency to 'gas-trapping' at end expiration.*

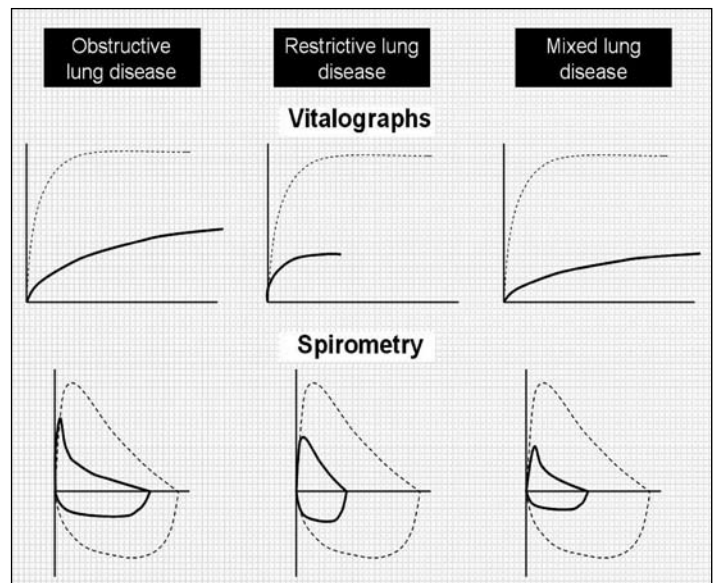| Parameter	Measured value	% of predicted value
FEV_1	1.17	44.6
FVC	2.60	74.9
Residual volume	2.93	112
FEV_1/FVC	45%	

Figure 9. *Examples of typical spirometry loops seen with obstructive, restrictive and mixed (obstructive and restrictive) lung disease*

ASSESSMENT OF GAS EXCHANGE

Transfer factor (TLCO)

This is also referred to as diffusion capacity (DLCO - more accurately the D_LCO, the diffusion capacity of the lungs for carbon monoxide) and provides a measurement that indicates the functional surface area of the bronchial tree and the efficiency of the gas diffusion across the alveolar-capillary membrane. It must be performed in a laboratory, most commonly using a single breath of a mixture containing 10% helium and a low concentration of carbon monoxide (0.3%). The patient holds their breath for ten to twenty seconds and then exhales. The first 750ml of exhaled (dead space) gas is discarded and the following litre is analysed. Helium is not absorbed by the lungs, so the helium concentration in the expired gas can be used to calculate the initial concentration of carbon monoxide. Therefore the amount that has been absorbed across the alveolar-capillary membrane per minute is calculated. This represents the diffusing capacity in mmol. $kPa^{-1}.min^{-1}$. Carbon monoxide is used because of its high affinity for haemoglobin. This maintains low partial pressures in the blood so its uptake is primarily determined by diffusion across the alveoli.

TLCO is reduced by:

• Impaired diffusion - i.e. increased thickness (lung fibrosis),

- Decreased area (lung resection, emphysema),

- Reduction in the ability to combine with blood (e.g. anaemia).

The TLCO value is adjusted for alveolar volume and termed the transfer coefficient (KCO), with units of $mmol.kPa^{-1}.min^{-1}.litre^{-1}$. Where TLCO and KCO are reduced by similar amounts, the disease process is homogenous throughout the lungs. If TLCO is reduced more than KCO, it suggests that some areas of the lung have relatively preserved function, for example in smokers or those with emphysema.

Arterial blood gases and oxygen saturation

These give a picture of respiratory function as a whole and are affected by central mechanisms, cardiac function and metabolism as well as lung function. Absolute values of $PaCO_2$ do not correlate well with outcome, but hypoxia (O_2 saturation <90%) and oxygen desaturation on exercise (>4%) are associated with worse outcomes.

PULMONARY FUNCTION TESTS AND LUNG RESECTION

Broadly speaking, in terms of the FEV_1, the following patients require no further investigation, provided there is no evidence of interstitial lung disease or unexpected disability due to shortness of breath:[7,8]

FEV_1 > 1.5l	Suitable for lobectomy
FEV_1 > 2.0l or >80% predicted	Suitable for pneumonectomy

Below these values further interpretation of the spirometry readings is needed and a value for the predicted postoperative (ppo-) FEV_1 should be calculated. As the FEV_1 decreases, the risk of respiratory and cardiac complications increases, mortality increases and patients are more likely to require postoperative ventilation.

Calculating the predicted postoperative FEV_1 (ppoFEV_1) and TLCO (ppoTLCO)

Radiological imaging (usually a CT scan) identifies the area of the lung that requires resection. There are five lung lobes containing nineteen segments in total with the division of each lobe shown in Figure 10.
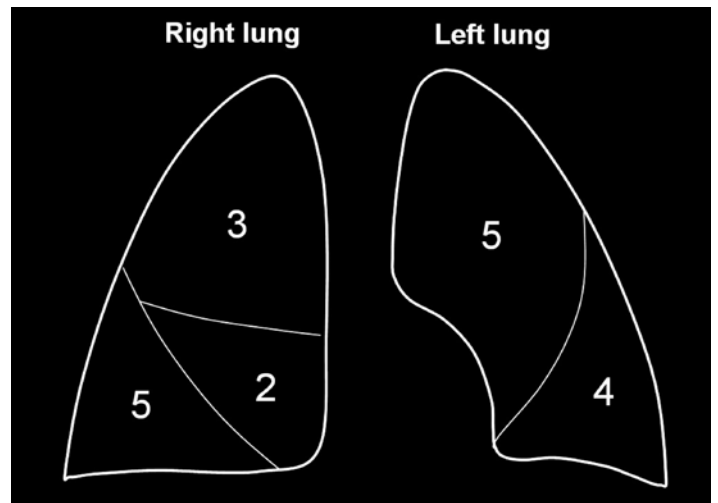

Figure 10. *The number of segments within each lung lobe*

Knowledge of the number of segments of lung that will be lost by resection allows the surgeon and anaesthetist to estimate the post-resection spirometry and TLCO values. These can then be used to estimate the risk to the patient of undergoing the procedure (Table 2). Note that resection of the left upper or right lower lobe, both of which have five segments, has the greatest impact on predicted post-resection values.

$$ppoFEV_1 = preoperative\ FEV_1 \times \frac{number\ of\ segments\ left\ after\ resection}{19}$$

In some instances, for example when the tumour is near to the hilum or in close proximity to the fissure between lobes, it may remain unclear whether surgery will involve single lobectomy, bi-lobectomy or pneumonectomy, until the surgeon has gained surgical access to the patient's chest. In this situation the anaesthetist and surgeon must have estimated in advance, which of these procedures the patient will be able to tolerate peri- and postoperatively.

Table 2. *Using ppoFEV$_1$ and ppoTLCO as a screening tool to assess suitability for lung resection*

ppoFEV_1 (% of predicted)	Interpretation
> 40	No or minor respiratory complications anticipated.
< 40	Increased risk of perioperative death and cardiopulmonary complications.[8]
< 30	Likely to require postoperative ventilation[9] and further increased risk of death/complications. Non-surgical management should be considered.[8]

ppoTLCO (% of predicted)	Interpretation
> 40%, ppoFEV_1 > 40% and O_2 saturation > 90% on air	Intermediate risk, no further pulmonary investigation required.
< 40%	Predicted represents increased respiratory and cardiac morbidity.[7,10]
< 40% and ppoFEV_1 < 40%	High risk-require cardiopulmonary exercise testing.
< 30%	Patient is likely to be hypoxic without supplementary oxygen.

All other combinations require cardiopulmonary exercise testing[7]

Case example 1

A 57-year-old man is booked for right thoracotomy and lung resection. He has lost 8kg in weight but is otherwise fit and well. Chest Xray and CT chest show a large right upper lobe mass with distal collapse/consolidation of most of the right upper lobe (Figure 11). Transmural biopsies from the right main bronchus via flexible bronchoscopy have confirmed the mass is a carcinoma.

His pulmonary function tests (Table 3) show that his spirometry values are near normal, but that his TLCO is significantly reduced to 55.5% of the predicted value for his sex, age and height.

The surgeon plans to perform a right upper lobectomy, but may consider upper and middle bi-lobectomy or pneumonectomy depending on his findings at thoracotomy. In terms of his ventilatory function, as indicated by his spirometry readings, he would be expected to tolerate lobectomy, or pneumonectomy without too much difficulty. However the calculations in Table 4a show that his predicted postoperative TLCO after pneumonectomy mean that adequate oxygenation will not be achievable without oxygen therapy.

However, his CT scan shows that the majority of his right upper lobe is severely affected by the disease process and so contributed little to his preoperative performance. Therefore the denominator in the calculations can be changed to 16 (the 3 segments of the right upper lobe are discounted). The new predicted post-pneumonectomy TLCO value is 31.2% (Table 4b) suggesting that although he is at high risk of preoperative complications, independent survival post-pneumonectomy is possible.

Figure 11. *(A) Chest Xray and (B) CT showing right upper lobe collapse/consolidation secondary to a right upper lobe tumour*

Table 3

	Actual	**Predicted**	**% predicted**
FEV$_1$	2.76	3.04	91%
FVC	3.74	3.80	98%
TLCO			55.5%

Table 4a

Extent of lung resection	Lung remaining post resection	Predicted post-resection TLCO
R U lobectomy	16/19 segments remaining	46.7%*
R U & M lobectomy	14/19 segments remaining	40.9%
R pneumonectomy	9/19 segments remaining	16.1%

* calculated as 16/19 x preoperative TLCO (55.5%).

Table 4b

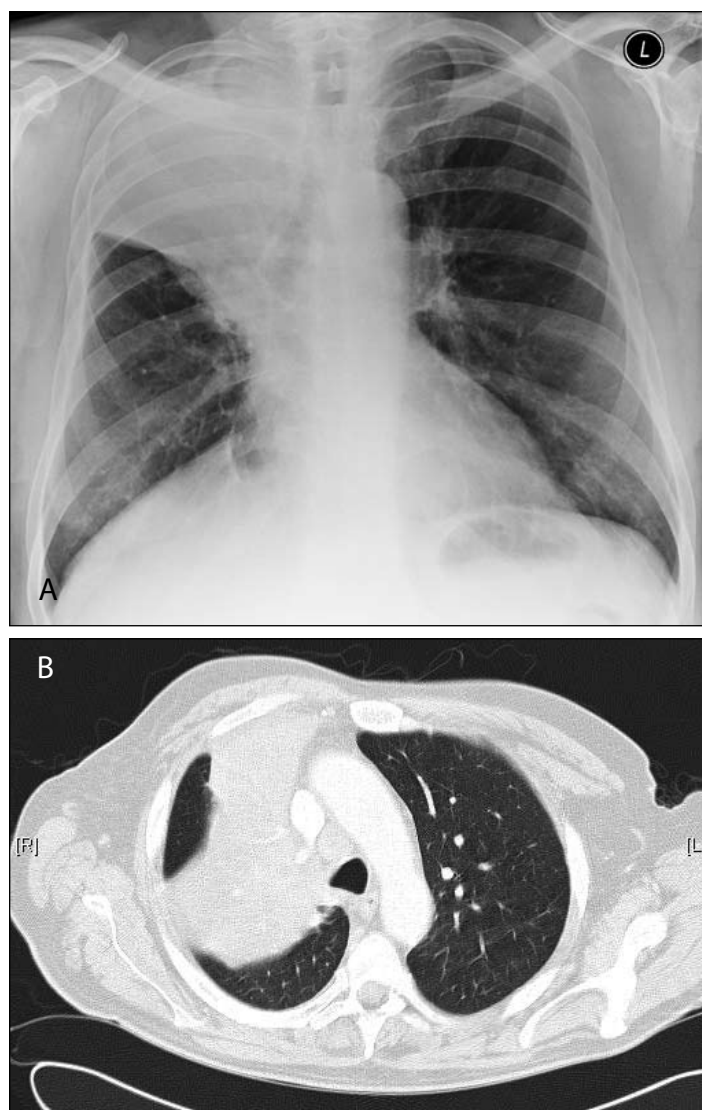| Extent of lung resection	Lung remaining post resection	Predicted post-resection TLCO
R U lobectomy (and assume RU lobe non-functional)	14/16 functional segments remaining	48.6%
R pneumonectomy (and assume RU lobe non-functional)	9/16 functional segments remaining	31.2%

Use of ventilation isotope scans to calculate the predicted postoperative FEV₁ (ppoFEV₁) and TLCO

Where the relative contributions of the diseased and non-diseased lungs to overall function is unknown, ventilation scans (the ventilation part of a V/Q isotope scan) can be used. The patient inhales a radioactive labelled gas (xenon) mixture and the chest is scanned using a gamma camera. (For the perfusion part of the scan, as used to detect pulmonary emboli, a radioactive isotope is also injected and the lung scan repeated).

Case example 2

A 65-year-old woman requires pneumonectomy for non-small cell carcinoma of the right lung. Her preoperative pulmonary function tests are shown in Table 5 and predicted post resection levels of FEV_1 and TLCO are borderline.

However her CXR and CT suggest that significant parts of her right lung may be non-functional. This can be determined using a ventilation scan, which demonstrates that the relative contribution of her right and left lungs to ventilation (and therefore to spirometry testing) is 36% to 64%. Her predicted post-pneumonectomy values for FEV_1 and TLCO can then be calculated by multiplying the pre-resection values by 0.64 (64%). These values are 41.6% for the FEV_1 and 45.4% for the TLCO, representing far more acceptable values to proceed with pneumonectomy.
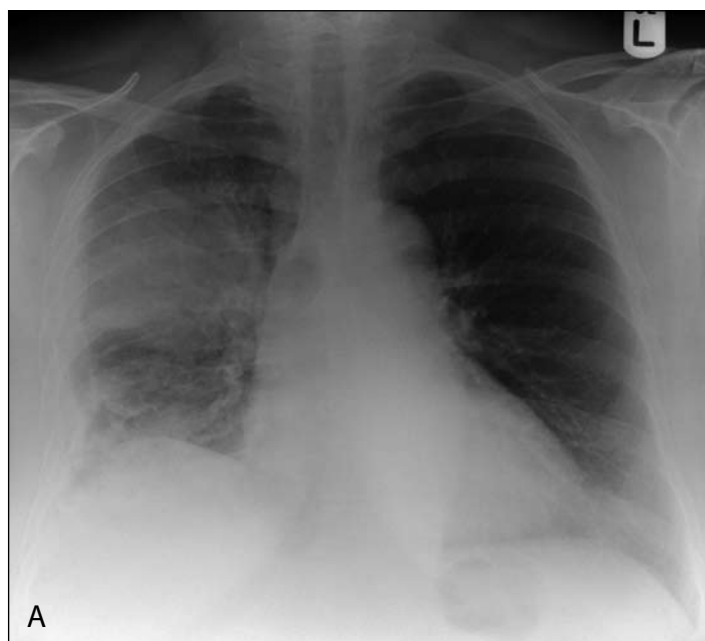
OTHER TESTS

Maximum breathing capacity

Otherwise known as maximum voluntary ventilation this is the maximum volume of air that can be breathed when the subject inspires and expires as quickly and forcefully as possible. Less than 40% predicted represents a high risk for surgery.[11]

Exercise tests and oxygen uptake (Cardiopulmonary exercise testing)

The various tests outlined below give information on cardiopulmonary reserve. They range from simple tests requiring no equipment to complex tests requiring expensive machines.

Stair climbing and 6-minute walk test

This is a simple test that is easy to perform with minimal equipment required (see Table 6).

Shuttle walk

The patient walks between cones 10 meters apart. A tape player sets the pace by beeping at reducing intervals (increasing frequency). The subject walks until they cannot make it from cone to cone between the beeps, or 12 minutes has passed. Less than 250m or decrease SaO_2 > 4% signifies high risk.[7,8] A shuttle walk of 350m correlates with a VO_2 max of 11ml.kg⁻¹.min⁻¹. A study looking at mortality after oesophagogastrectomy found zero 30-day mortality in patients who were able to shuttle walk at least this far.[14]

The obvious advantages of this technique are that it is cheap and easy to perform and gives reliable information that is directly related to clinical outcomes.
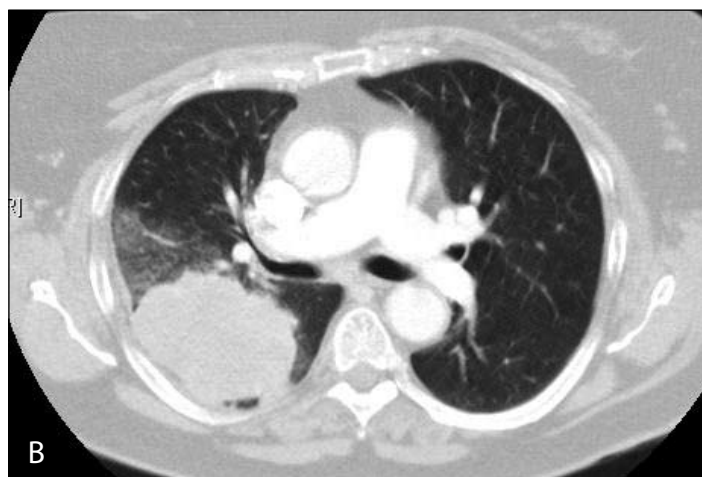
Figure 12. *(A) Chest Xray and (B) CT showing right upper lobe collapse/consolidation secondary to a right lung tumour*

Table 5

	Actual value	Predicted for age, sex, height	% predicted	Predicted post right pneumonectomy (9/19 segments remaining)
FEV₁	1.48	2.28	65%	30.8%
FVC	1.96	2.70	72%	34.1%
TLCO			71%	33.6%

Table 6. *Summary of stair-climbing assessment of performance*

Performance	VO_2 max equivalent	Interpretation
>5 flights of stairs	VO_2 max > 20ml.kg^{-1}.min^{-1}	Correlates with, FEV$_1$ > 2l and low mortality after pneumonectomy
>3 flights of stairs		Correlates with FEV$_1$ of 1.7l and low mortality after lobectomy
<2 flights of stairs		Correlates with high mortality
<1 flight of stairs	VO_2 max < 10ml.kg^{-1}.min^{-1} [12]	
6min walk test < 600 meters	VO_2 max <15ml.kg^{-1}.min^{-1} [13]	

Cardiopulmonary exercise testing - CPEX

This provides a functional assessment of cardiopulmonary reserve. The subject exercises at increasing intensity on an exercise bike or treadmill, whilst inspired and expired O_2 and CO_2 are measured and an ECG is recorded. It is also possible to measure flow volume loops. The main values of interest are the maximum O_2 uptake (VO_2 max), and the anaerobic threshold (the level at which anaerobic respiration begins).

VO_2 max is the maximum oxygen uptake per kg body weight per minute. It is the most useful predictor of outcome in lung resection. The maximum oxygen uptake (VO_2 max) and maximum oxygen delivery to the tissues (DO_2 max) give us information about the body's physiological reserve and our ability to deal with the extra metabolic demands of surgery. VO_2 max and DO_2 max are dependent on the body's cardiac and respiratory systems. The point at which oxygen consumption exceeds oxygen uptake is known as the anaerobic threshold. It is the level at which the oxygen delivery required by the tissues to maintain aerobic metabolism is no longer met and anaerobic metabolism occurs. Above this level, energy production is much less efficient and lactic acid is produced, causing metabolic acidosis.

The information gained from CPEX testing allows quantification of the predicted risks of surgery, however this information is of limited value in the context of a disease process where mortality approaches 100% without surgery.

Table 7. *Interpreting the VO_2 max*

VO_2 max	Interpretation
20ml.kg^{-1}min^{-1} or >15ml.kg^{-1}min^{-1} and FEV$_1$ > 40% predicted	No increased risk of complications or death[15,4]
< 15 ml.kg^{-1}min^{-1}	High risk[7,8]
< 10 ml.kg^{-1}min^{-1}	40-50% mortality,[8] consider non-surgical management.[4]

CONCLUSIONS

We have described, with examples, the pulmonary function tests commonly performed to evaluate patient's fitness for lung resection surgery. It is valuable for the anaesthetist to understand the interpretation of these test results and also to know how they fit into the overall approach taken in the preparation of patients for thoracic surgery. Figure 13 shows a suggested sequence for these tests. These tests do not always give the full picture and anaesthetic assessment

for lung resection surgery should include a thorough history and examination and, above all, good communication with the surgical team.
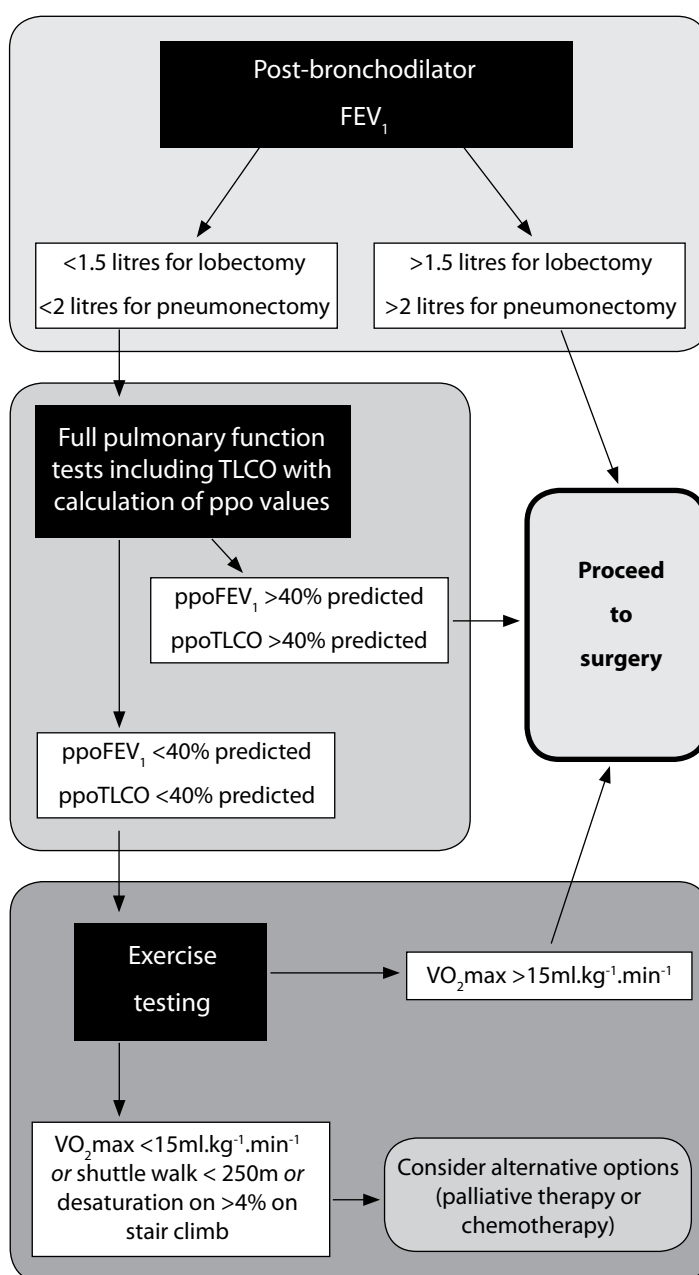

Figure 13. *An approach to assessment of suitability for lung resection (adapted from reference 4)*

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