PREOPERATIVE EVALUATION FOR LUNG RESECTION

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PREOPERATIVE EVALUATION FOR LUNG RESECTION

INTRODUCTION

Patients present to the anaesthesiologist in the preoperative period for evaluation for fitness prior lung resection surgery. With the advances in thoracic surgery and anaesthetic techniques in the recent years, it is imperative for the anaesthetist to understand the intricate medical status of the patients presenting for thoracic surgery and the physiological challenges related to the proposed procedure.

Indications for lung resection surgery will vary for different patient population groups. In our environment, lung resections for infective causes like tuberculosis or pulmonary complications from the disease, are a very common phenomenon. Malignant disease as an indication for lung resection, will limit the duration of time to be spent on preoperative investigations and likewise, the duration for essential preoperative optimization of the associated medical conditions i.e. Chronic Obstructive Pulmonary Disease (COPD). The general profile of patients with malignant disease are the elderly, with an extensive smoking history and substantial cardiovascular disease that further confounds their clinical picture.

There is vast clinical evidence focusing on the postoperative outcomes for patients undergoing lung resection from malignant disease. Much of this clinical data is extrapolated by clinicians and applied to the evaluation of patients requiring lung resections from other medical conditions. The anaesthetic goals involve an evaluation of the patient’s current level of functioning and their fitness for surgery while also ensuring adequate postoperative pulmonary function after the procedure.

TYPES OF LUNG RESECTION PROCEDURES

The role of the anaesthetist is not that of gate keepers to the decision of whether or not to operate, but rather, they play a valuable role in the multidisciplinary team of professionals managing these patients in the perioperative phase. The multidisciplinary team is made up of the respiratory physician, the oncologist, the thoracic surgeon, the physiotherapist and other supporting members of staff. This team of professionals is responsible for patient selection and preparation, with a goal not deny potentially curative therapy from malignant disease that possesses 100% mortality without surgery.

This compels the anaesthetist to have sound knowledge of the types of lung resection options available and the perioperative implications of that planned intervention, for that specific patient. The extent of surgery should increase the chances cure for the patient, but at the same time, leave the patient with adequate residual respiratory function postoperatively and minimal pulmonary complications.

Resectability of a lung lesion is the anatomical staging of the disease taking into account the extent of local tissue invasion and the presence of metastatic disease.

Operability refers to the ability of the patient to cope with the operation and the subsequent residual lung volume after the procedure. These two entities are reviewed in the preoperative phase by the surgical team, and then presented to the anaesthetist for further preoperative evaluation. The operability of a lesion affects anaesthetic considerations
regarding the extent of the planned operation. For an example; tumour proximity to major vessels may lead to catastrophic intraoperative blood loss and chest wall spread of the disease will indicate chest wall resection, while tumour involving lung fissures may require intraoperative surgical escalation from a lobectomy to a pneumonectomy. Therefore these surgical concepts are important for anaesthetic safety and perioperative planning.

**Pneumonectomy**
The resection of a lung has the highest morbidity and mortality rates ranging between 5-14% compared to other types of pulmonary resections. The mortality rates associated with pneumonectomies, have improved over the years, but this procedure is still considered very high risk with a propensity to postoperative right ventricular dysfunction, acute lung injury and respiratory failure.

Right sided lung resections have a far worse postoperative outcome compared to left sided lung resections. This is due to the difference in volumes of the two lungs with the right being 10% larger than the left and therefore its higher overall contribution to pulmonary perfusion. An extrapleural pneumonectomy is a rare but extensive thoracic resection, which would include a dissection of the lymph nodes, the pericardium, the diaphragm, the parietal pleura and the chest wall. Cardiac herniation with significant haemodynamic instability and 50% mortality is a recognised complication associated with this procedure.

Sleeve pneumonectomies are performed for lesions involving proximal main stem bronchus and carina. They are an option for patients with limited pulmonary reserve that are unfit for a pneumonectomy, where parenchymal-sparing techniques can be instituted. Even though pulmonary oedema is a common postoperative problem with this procedure, it shows better postoperative outcome compared with a pneumonectomy for this high risk patient.

**Lobectomy**
This is an anatomical resection of a lung lobe. It is a standard procedure for localised disease with a morbidity and mortality risk of 2-4%, lower than that of a pneumonectomy. Sleeve lobectomy resections are performed for patients with benign lesions or patients with severe disease that cannot tolerate a pneumonectomy.

**Segmentectomy**
This is an anatomical resection, where a lung segment is removed with its supplying artery, vein and bronchus. Segmentectomies form part of limited pulmonary resections and have a lower postoperative risk compared to lobectomies. They are an alternative to patients with limited cardiopulmonary reserve to improve postoperative function. Some of the patients presenting for this resection, may have a history of previous lung resections with disease recurrence.

**Wedge resections**
Wedge resections are non-anatomical parenchymal resections where a 2cm margin around the lesion is removed. They are indicated in early localised T1 lesions, with a < 3cm diameter, excisional biopsies and disease recurrence. They form part of Lung Volume Reduction Surgery (LVRS), where the most dysfunctional part of the lung is resected, in extremely emphysematous patients, to improve respiratory function and quality of life.

**Video-assisted thoracoscopic surgery (VATs)**
VATs is minimally invasive alternative to certain lung resection procedures e.g. lung biopsies, lobectomies, segmentectomies and wedge resections and more surgeons are acquiring this skill for lung sparing procedures. This technique, has allowed patients with
advanced pulmonary disease, previously deemed functionally unfit for surgery, to undergo parenchymal sparing resection procedures with a 15% decrease in morbidity and mortality. Patients that have undergone VATs have less intraoperative blood loss, a better perioperative course, with less postoperative pain. These patients show faster recovery and are likely to mobilise early with a shortened overall postoperative hospital stay.

**POST OPERATIVE COMPLICATIONS**

There are multiple major and minor or surgical complications occurring in the postoperative period following a lung resection. Postoperative complications are defined as the adverse events occurring 30 days after a thoracotomy and they have an incidence rate as high as 49%.

The aim of the preoperative guidelines, for evaluating these patients, is to identify the group of patients at risk for poor postoperative outcomes and mortality. This is where anaesthetic and surgical consent becomes critically important as the final decision, regarding the surgical management options and risks involved, lies with the very well informed patient.

The commonest complications are listed:

<table>
<thead>
<tr>
<th>Pulmonary</th>
<th>Cardiac</th>
<th>Surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute respiratory failure</td>
<td>Arrhythmias</td>
<td>Wound infection</td>
</tr>
<tr>
<td>Reintubation</td>
<td>Pulmonary oedema</td>
<td>Empyema</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Arterial hypertension</td>
<td>Bronchopleural fistulae</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>Angina</td>
<td>Reoperation</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>Acute myocardial infarction</td>
<td>Haemothorax</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td></td>
<td>Wound dehiscence</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td></td>
<td>Chylothorax</td>
</tr>
</tbody>
</table>

Respiratory failure is the leading cause of both pulmonary morbidity and mortality with a 2-18% incidence in lung resection patients. It is characterized by postoperative hypoxemia (\(\text{PaO}_2 < 60\text{mmHg}\)), hypercapnia (\(\text{PaCO}_2 > 45\text{mmHg}\)) or requiring > 24 hours of postoperative ventilation or reintubation after initial extubation. Respiratory failure has a higher incidence in patients with poor preoperative pulmonary function, larger lung resections, the elderly and patients with cardiac comorbidities.

Atelectasis and pneumonia have a 15% incidence after lung resection and a 72 hour delay at presentation. Right sided pneumonectomies, have a higher incidence of post-pneumonectomy pulmonary oedema. Prolonged duration of surgery is also correlated with postoperative complications. Adequate postoperative pain management and the use of thoracic epidurals and physiotherapy, improves the incidence of pulmonary complications.

**PREOPERATIVE EVALUATION**

It is of paramount importance for the surgical team to determine the amount of lung that can be safely removed without expected mortality and excessive morbidity. Whilst there is much research to determine the best investigation to use to predict the adequacy of post-resection lung function, there is no single gold standard test for this purpose, in the preoperative period.
The preoperative assessment for any patient starts with a thorough history and a careful physical examination. Comprehensive cardiopulmonary evaluation of the patient assessment for lung resection builds on this initial clinical assessment. Relevant presenting complaints e.g. productive cough, fever, dyspnoea are documented together with the patients basal level of functioning. This examination should reveal any comorbid disease, for instance, a pneumonia, which must be treated with antibiotic therapy prior proceeding with surgery.

Preoperative staging for patients with non-small cell lung carcinoma is also reviewed at this stage and the questions of operability and resectability are answered. The American College of Chest Physicians (ACCP) guidelines, recommend that prior undertaking pulmonary evaluation for lung resection, the patient should undergo a cardiac assessment to uncover any underlying cardiac disease. The American Heart Association, American College of Cardiology, the European Society of Cardiology and European Society of Anaesthesiology all recommend the use of the Revised Cardiac Risk Index (RCRI) that must be recalibrated to a Thoracic Revised Cardiac Risk Index (ThRCRI) which is specific for lung resection surgery.

Patients with a score > 1.5 or impaired exercise tolerance should be referred for cardiology assessment. Patients with a high cardiac risk may require a formal Exercise Stress Test and should be managed according to the American Heart Association or American College of Cardiology guidelines.
PULMONARY RISK ASSESSMENT

Patients that receive a green light to proceed from their cardiac evaluation must have a pulmonary risk assessment. This comprises an analysis of 3 elements of respiratory function, often termed ‘the 3 legged stool’:

- Respiratory mechanics
- Pulmonary Parenchymal function, and
- Cardio-pulmonary function

Respiratory Mechanics
These tests assess the mechanical function of the lung focusing on the conduit of gasses from the atmosphere to the alveolar. Pulmonary function tests relevant to lung resection surgery, are the Force Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV₁) and the Maximum Ventilation Volume (MVV). It may often necessary to determine other lung volumes like Vital Capacity, Residual Volume and Functional Residual Capacity.

Simple Spirometry
This will determine the baseline respiratory function of the individual patient. The use of spirometry extends over 50 years for diagnosing restrictive and obstructive pulmonary disease. Pulmonary function tests as absolute values or percentages of predicted values are utilized in medical research to predict postoperative function following lung resection surgery.

Forced Vital Capacity (FVC)
It is defined as the volume of air expired after maximum inhalation at vital capacity. It is reduced in anatomically restrictive conditions and if there is restrictive pathology within the pleura or the lung itself.

Forced Expiratory Volume in one second (FEV₁)
It is the forced volume of air expired in 1 second, which will be altered in airway resistance. It shows the ability of that individual to generate an effective cough. FEV₁ must be corrected to patient’s age, height and sex and must be presented in a percentage of normal predicted values for that individual patient.

An FEV₁ > 80%, predicted, is suitable for a most lung resections including a pneumonectomy. Pulmonary complications are noted from a preoperative FEV₁ of < 80% of predicted and this value was traditionally used to identify patients requiring further investigations prior lung resection, as per the 2007 ACCP and 2009 ERS/ESTS guidelines. A FEV₁ < 30% is associated with a 43% incidence of pulmonary complications and FEV₁ > 60% has < 12% postoperative morbidity.

Absolute values for FEV₁ have previously been used to predict postoperative pulmonary function. Authors discourage the use of absolute values, unless the values are taken into context with that individual patient’s age, gender, weight and height.

Data from the 70s demonstrated a preoperative FEV₁ of > 1.5L for a lobectomy and > 2L for a pneumonectomy and these patients are still considered not requiring any further investigations unless they have evidence of interstitial lung disease or they have unexpected dyspnoea. An absolute predictive postoperative FEV₁ value of 800ml is considered a contraindication to major lung resection surgery. Patients not meeting these criteria will require prediction of their postoperative FEV₁ and DLCO values.
FEV₁/FVC ratio
An FEV₁/FVC above 80% is used to differentiate between obstructive and restrictive lung pathologies. Reversibility of the underlying pulmonary disease is demonstrated by a 12% spirometry improvement after administering a bronchodilator and repeating the test after 10 minutes. Both the FEV₁ and the FVC can be used to categorize the severity of the associated COPD, from mild to very severe, as demonstrated in the following table by the American Thoracic Society.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Postbronchodilator FEV₁/FVC</th>
<th>FEV₁ % predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>At risk</td>
<td>&gt;0.7</td>
<td>≥80</td>
</tr>
<tr>
<td>Patients who:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>smoke or have exposure to pollutants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>have cough, sputum or dyspnea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>have family history of respiratory disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild COPD</td>
<td>≤0.7</td>
<td>≥80</td>
</tr>
<tr>
<td>Moderate COPD</td>
<td>≤0.7</td>
<td>50–80</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>≤0.7</td>
<td>30–50</td>
</tr>
<tr>
<td>Very severe COPD</td>
<td>≤0.7</td>
<td>&lt;30</td>
</tr>
</tbody>
</table>

FEV₁: forced expiratory volume in one second; FVC: forced vital capacity.

If further lung volume determination is required, for values of Total Lung Capacity, Residual Volume and Functional Residual Capacity, body plethysmography, nitrogen washout and Helium dilution may be considered. Of the three, body plethysmography is the gold standard, even though it may overestimate Total Lung Capacity. Even though some of these investigations are available in our setting, it may be impractical and costly to put them into routine use in every patient assessment.

**Maximal Voluntary Ventilation (MVV)**
Also known as Maximum Breathing Capacity, MVV is an effort dependant test, where the patient is required to breathe in fast and deep for 6-12 seconds and from this effort, the maximum volume in one minute is calculated. This test has been used as a predictor of pulmonary risk and was often utilized similarly to cardiopulmonary exercise testing to assess effort tolerance in patients with limited mobility.

MVV was historically used to differentiate patients with low absolute FEV₁ scores (1000 – 600ml) considered either for wedge or segmental resection. In this group of patients, if their MVV was > 40% of predicted and their diffusional capacity was > 50% of predicted, they were considered for a segmentectomy. If the MVV was < 40% of predicted and the diffusional capacity was also < 50% of predicted, a wedge resection would be an option for that patient.
Pulmonary Parenchymal function

**Arterial blood gas data and oxygen saturation**

An arterial blood gas in room air is frequently requested in patients for lung resections. Historically, blood gas analysis has been divided into:

- **Acceptable:** $\text{PO}_2 > 90\text{mmHg}$, $\text{PCO}_2 < 42\text{mmHg}$ and Oxygen Saturation $> 92\%$
- **Borderline:** $\text{PO}_2 = 80-60\text{mmHg}$, $\text{PCO}_2 = 42-45\text{mmHg}$ and Oxygen Saturation $90-92\%$
- **Unacceptable:** $\text{PO}_2 < 60\text{mmHg}$, $\text{PCO}_2 > 45$ and Oxygen Saturation $< 90\%$

$\text{PaO}_2 < 60\text{mmHg}$ and $\text{PaCO}_2 < 45\text{mmHg}$ is traditionally used as cut-off values to lung resection, but the severity of hypoxemia is the better predictor of outcome following surgery. These numbers should not be used in isolation for prediction of poor outcome but must be used in conjunction with Pulmonary Function Tests.

**Diffusing Capacity of Carbon Monoxide ($D_L\text{CO}$)**

Since the 1980s, the $D_L\text{CO}$ has been used to examine the condition of the alveolar-capillary interface as the inhaled air crosses from the alveolar, through the interstitium and to the blood. To measure the diffusion of carbon monoxide, a single breath of a gas mixture containing 10% Helium and a low Carbon Monoxide concentration (0.3%) is inhaled and the patient holds their breath for 10-20 seconds. At full exhalation, the amount of Carbon Monoxide absorbed per minute across the alveolar-capillary membrane is calculated after dead space ventilation is discarded. Since helium is not absorbed, it is used to calculate the initial concentration of Carbon Monoxide and $D_L\text{CO}$ is measured in mmol.kPa$^{-1}.\text{min}^{-1}$. If $D_L\text{CO}$ is adjusted for alveolar volume it is then called the transfer coefficient and presented in mmol.kPa$^{-1}.\text{min}^{-1}.\text{litre}^{-1}$.

$D_L\text{CO}$ is decreased by impaired alveolar interface diffusion, a decrease in total area available for diffusion and inability to bind to haemoglobin. It was previously understood that $D_L\text{CO}$ was only indicated in patients with lung parenchymal disease, but studies have demonstrated a poor correlation between FEV$_1$ and $D_L\text{CO}$ values, indicating the need to perform both tests in each patient. Preoperative, predicted $D_L\text{CO}$ in percentages, has demonstrated a better correlation with postoperative mortality than predictive FEV$_1$.

A preoperative $D_L\text{CO}$ of 100% of the predicted value is associated with 11% risk of postoperative morbidity. A $D_L\text{CO}$ < 60% of predicted, holds a 40% risk of postoperative complications as these patients have more respiratory morbidity, worse post-resection dyspnoea scores, longer hospital stays and a higher risk of mortality.

**Predicting postoperative lung function**

In order to predict postoperative residual lung function, imaging is required to determine the segments with functional lung and those with diseased lung prior the resection. Generally, patients being assessed for lung resections have imaging already done for staging and surgical planning in the form of a chest radiograph, a computed tomographic scan and Positron Emission Tomography scans.

The lungs have 5 lung lobes with 19 segments in total, 10 on the right lung and 9 segments on the left lung. They have a total of 42 sub-segments, with 20 on the left side and 22 on the right lung. Either segments or subsegments can be used to calculate postoperative predicted values.
Radionuclide Ventilation/Perfusion lung scanning

This imaging technique, estimates the function of that region of the lung to be resected, by quantifying perfusion to that area. The patient is requested to inhale a radio-active labelled gas mixture and the chest is scanned with a Gamma camera. Then to assess perfusion, radio-active isotope is injected intravenously and the scan is repeated. Postoperative function is the product of preoperative function and the postoperative portion of lung function remaining after pulmonary resection, estimated by the scan, especially accurate for a pneumonectomy. The 2013 ACCP guidelines recommend that ventilation/ perfusion scans be used to calculate postoperative predictive values.

Quantitative Pulmonary CT scanning

CT imaging is utilized to quantify areas of normal vs abnormal lung parenchyma by examining each CT scan slice. The contribution to ventilation of each lobe, is then calculated and quantified.

Dynamic MRI

This technique estimates regional pulmonary blood volume to assess regional blood flow. It has yet to gain general favour and use in predicting postoperative values.

Predicted Postoperative-FEV1

In using spirometry for suitability for lung resection, the predicted postoperative-FEV1, (ppoFEV1) is an important test to predict postoperative morbidity. Its value in medical research has been tested from earlier work done in lung cancer resections, where an absolute ppoFEV1 of 700-800mls, is still advisable after a lung resection. PpoFEV1 presented as a percentage of predicted, is more useful in predicting postoperative outcome compared to absolute numbers. PpoFEV1 values have been used to permit individual patients with low preoperative FEV1 scores to undergo surgery successfully, provided their ppoFEV1 were acceptable.

PpoFEV1 is calculated by using imaging studies, taking into account the number segments of lung to be resected and aims to calculate the amount of post-resection lung function. The ACCP guidelines recommend separate formulae for post bronchodilator ppoFEV1 for a pneumonectomy and that for a lobectomy:
Equation for pneumonectomy:

\[ \text{PpoFEV}_1 = \text{preoperativeFEV}_1 \times (1 - \text{fraction of total perfusion for the resected lung}) \]

or

\[ \text{ppoFEV}_1\% = \text{preoperative FEV}_1\% \times (1 - \text{Functional lung tissue removed}/100) \]

PpoFEV\(_1\) for patients undergoing **lobectomy**:

\[ \text{ppoFEV}_1 = \text{preoperative FEV}_1 \times (1 - \frac{y}{z}) \]

Where: \( y \) = lung segments to be removed and \( z \) = the total number of functional segments.

For an example: A patient with a preoperative FEV\(_1\) predicted of 70% coming for a right lower lobectomy (12 subsegments), ppoFEV\(_1\) can be calculated thus:

\[ \text{ppoFEV}_1 = 70 \times (1 - \frac{12}{42}) = 50\% \]

**Predicted Postoperative-DLCO (ppo-DLCO)**

Predicted postoperative Diffusing Capacity of Carbon Monoxide (ppoDLCO), like the ppoFEV\(_1\), is an indicator of pulmonary function after resection. It is also calculated with a similar equation to that of ppoFEV\(_1\) using imaging studies. It is most useful when presented as a percentage of predicted 'normal' for that individual and is the better predictor of cardiac morbidity and postoperative mortality compared to ppoFEV\(_1\).

**Using ppoFEV\(_1\) and ppoDLCO**

There are many recommended guidelines for assessing patients for lung resections from malignant disease. The American College of Chest Physicians (ACCP) published evidence based guidelines, in 2003 and these were updated in their second edition in 2007. The third edition of ACCP guidelines was published in the chest journal in 2013, from reviewing and updating the changes in clinical evidence from 2007.

In the 2007 ACCP algorithm, as shown in the following diagram, patients with preoperative FEV1 < 80% predicted must have their ppoFEV\(_1\) and ppoDLCO values calculated.
If both ppoFEV\textsubscript{1} and ppoD\textsubscript{LCO} are > 40\%, the patient could proceed to surgery and no further investigations were required. Cardio-pulmonary Exercise testing was indicated in patients with ppoFEV\textsubscript{1} and ppoD\textsubscript{LCO} between 30-40\%, and predicted postoperative values < 30\% were high risk for surgery.

Between 2007 and 2013, published research demonstrated that carefully selected patients with a ppoFEV\textsubscript{1} and ppoD\textsubscript{LCO} 30-40\% could still undergo lung resection surgery with acceptable morbidity and mortality rates. Advancements in surgical techniques i.e. VATs, allowed many patients with postoperative predictive values < 40\%, to undergo lung resection surgery with better outcomes.

Therefore, in the 2013 ACCP guidelines, predicted postoperative values are calculated from pulmonary function tests and if both ppoFEV\textsubscript{1} and ppoD\textsubscript{LCO} values are > 60\% these patients are considered fit for surgery and no further investigations are needed. A majority of these patients can be safely extubated in the operational theatre and have an acceptable postoperative course.

If either the ppoFEV\textsubscript{1} or ppoD\textsubscript{LCO} fall within range of 60-30\%, that patient requires low technology exercise tests, like the stair climb test or the shuttle walk test. Patients with either ppoFEV\textsubscript{1} or ppoD\textsubscript{LCO} <30\% must have a formal Cardiopulmonary Exercise stress test. An algorithm of the 2013 ACCP third edition guidelines is presented in the following diagram.
Definition of risk:
- **Low risk**: patients have a < 1% risk of postoperative mortality and surgery is considered safe.
- **Moderate risk**: morbidity and mortality vary according to split lung function tests, exercise tests and extent of the resection. Risk vs benefit, should always be reviewed with the patient.
- **High risk**: mortality risk after major resections has 10% mortality and alternative treatment strategies must be explored.

Both ppoFEV$_1$ and ppoD$_L$CO of less than 30% of predicted normal is associated with significant postoperative complications, even mortality as demonstrated in current research. PpoD$_L$CO values less than 20% are considered the absolute minimum for any lung resection. It is imperative that the predictive postoperative values be calculated for all possible resections applicable to that patient prior surgery. This is uniquely necessary in patients with disease involving lung fissures and the hilar regions of the lung, in the event that the surgery must be escalated during the operation.

The values of ppoFEV$_1$ or ppoD$_L$CO are useful to the anaesthetist, but neither must be used in isolation. Predicted postoperative values attempt to estimate lung function up to 3-6 months after the resection. It should be acknowledged that the best predictor of morbidity and mortality is a measured FEV$_1$ on Day 1 postoperatively.

**Cardio-pulmonary function**
In the 2013 ACCP guidelines, cardiopulmonary exercise testing has been separated into low technology tests (Shuttle Walk Test or Stair climbing) and formal Cardiopulmonary Exercise Testing. Patients with either the ppoFEV$_1$ or the ppoD$_L$CO between 60-30%, must have a low technology exercise test and those with either ppoFEV$_1$ or ppoD$_L$CO < 30%, must receive a formal cardiopulmonary exercise test. Patients with predictive postoperative values < 30% are likely to require postoperative ventilation and have prolonged length of hospital stay.
**Formal Exercise Stress Testing and VO₂ max**

Exercise stress testing is considered the gold-standard in assessing cardiopulmonary reserve and its use has been supported for risk stratification regarding outcomes for patients undergoing lung resections. The subject is required to exercise at an increasing frequency on an exercise bike or a treadmill. The intensity of the exercise is gradually increased while the inspired and expired oxygen and carbon dioxide are measured, together with the minute volume and an electrocardiogram recording.

The (VO₂ max) maximum O₂ uptake, per Kg body weight per minute and the (DO₂ max) the maximum O₂ delivery to the tissues, indicate the physiological reserve during surgery. The anaerobic threshold is the point at which oxygen consumption exceeds oxygen delivery required to maintain aerobic metabolism and is normally 55% of VO₂ max.

VO₂ max, is calculated based on the patient’s age, sex, and height, and presented in mL/Kg/min. It can be used to differentiate patients with respiratory pathology and those with associated cardiac dysfunction.

VO₂ max > 20ml/kg/min (75% of predicted), is associated with an uneventful postoperative course following a lung resection, whilst a VO₂ max 10-15 ml/kg/min (35-75% of predicted) is linked with moderate risk of poor postoperative outcome.

A VO₂ max < 10ml/kg/min (35% of predicted) is associated with 50% postoperative mortality and is a contraindication to major lung resections, therefore requiring non-surgical options to be explored in these patients.

Likewise, an estimated postoperative VO₂ max (ppoVO₂) of < 10mL/Kg/min is also considered a contraindication for lung resection surgery.

The main limiting factor with this investigation is the cost associated with it making it impractical to use in all patients coming for lung resections in our environment. Low technology or surrogate exercise tests have been adopted by many institutions for the use to further assess patients with low FEV₁ scores.

**6 Minute Walk Test (6MWT)**

This is a low technology test where the patient is asked to walk as far as they can manage in 6 minutes at their own pace and resting during the walk is permitted.

The 6MWT has shown good correlation with the VO₂ max, which can be estimated by dividing the distance travelled in metres with the value of 30.

For instance, if the total distance travelled in 6 minutes is 400 metres,

VO₂ max =400/30 = 13mL/Kg/min

The same values of VO₂ max guiding fitness to undergo surgery can still be applied to the estimated values. It is important to note that this low technology test is not yet recommended by the European guidelines specifically for lung resections in the latest ACCP guidelines, but nonetheless, it can still give an indication to exercise tolerance for that patient.
**Stair Climbing**

This is a simple and cost effective exercise to perform but it is limited by the absence of a standard definition for ‘a flight of stairs’ in literature. Slinger et al, define a flight of stairs as 20 steps at 6 inches (15.2 cm) per step. Due to this lack of standardised definition, some authors suggest using the height of the altitude acquired during the exercise, in metres, as a more objective tool. Completing an ascent 22 metres when climbing stairs, correlates with VO$_2$ max of 15mL/Kg/min.

Despite the noted limitations, researchers have been able to demonstrate a correlation between the amount flights climbed, with FEV$_1$ and VO$_2$ max numbers. 5 flights of steps correlates with FEV$_1$ > 2L and a VO$_2$ max of greater than 20mL/Kg/min. Three flights of stairs (12-14m of stairs) indicate an FEV$_1$ of >1.7 L and 2 flights of stairs corresponds with VO$_2$ max of 12mL/Kg/min. The ideal duration for completing the stair ascent is not stated and the patient is not permitted to rest during the test. Many patients may have comorbid disease e.g. musculoskeletal disease limiting their physical ability to participate in this exercise.

**Shuttle walk test (SWT)**

Two cones are placed 10 mitres apart, and the patient is asked to walk around these cones at an increasing pace (set by the sound played from the tape recorder playing at increasing frequency) for 12 minutes.

400 metres and longer Shuttle Walk Test is equivalent to > 15mL/Kg/min of VO$_2$ max. A walk of 350m correlates with a VO$_2$ max 11ml.kg$^{-1}$.min$^{-1}$ whilst failure to achieve 250 metres is associated with a VO$_2$ max of < 10mL/Kg/min.

**SpO$_2$ during exercise**

An oxygen desaturation of >4% during any of the exercise tests, indicates that a turbulent intraoperative course must be expected and significant poor postoperative outcome must be anticipated. These high risk patients will need postoperative Intensive-Care Unit admission, with longer hospital stays and possibly postoperative home oxygen requirements. Patients that do not desaturate during exercise, have a 91-99% chance of being free of postoperative pulmonary complications after surgery.

Published ACCP guidelines state that patients for cancer related lung resection who can walk < 25 shuttles (or < 400m) on a SWT or climb < 22m in a stair climbing test, must have a formal Exercise Stress Test to measure VO$_2$ max.
ASSOCIATED MEDICAL CONDITIONS

Age
Age older than 70 years, has been shown repeatedly to be an independent risk factor in pulmonary surgery. Age alone, should however never be used as an independent contraindicating factor to lung resection, but consideration to baseline level of function and exercise tolerance, is more appropriate for the elderly population. Long term survival for elderly patients, up to 80 years, is comparable to their younger counterparts after lung resections.

Provided below is an algorithm suggested for the elderly patient for lung resection.

Cardiac
A majority of patients presenting for lung resection have associated risk factors for cardiac disease. This requires a comprehensive assessment of the cardiovascular system to determine patients with high cardiac risks as well, that will require further preoperative evaluation, risk stratification and disease optimization. There is an algorithm created by the American College of Cardiology and the American Heart Association to aid the evaluation of these patients, where patients with intermediate clinical predictors and adequate functional capacity, are progressed to surgery.

The patients with poor functional capacity, with abnormal non-invasive cardiac testing, on Electrocardiogram and Echocardiography, are evaluated for reversibility of cardiac disease. CT angiography is used in patients that require further assessment of coronary vasculature. Adequate Functional capacity of these patients is assessed as having 4 METs equivalent and greater. Patients with associated severe cardiac function, 1 MET equivalent, and those with recent myocardial infarction, present a unique challenge to the anaesthetist and these patients must be treated at their individual merit prior lung surgery.
Arrhythmias are common in the postoperative phase after thoracic surgery. Atrial fibrillation forms 60-70% of post resection arrhythmias and they are related to the extent of surgery being as high as 60% after a pneumonectomy.

Cardiac dysfunction may be either from resistance to blood flow into collapsed alveolar-capillary bed or from increased cardiac oxygen requirements and the sympathetic response during and after surgery. Atrial fibrillation can be challenging to control postoperatively in patients with COPD, especially if they have pulmonary hypertension.

Lung malignancies
Much of work on lung resection is done from lung malignant disease. It is the leading cause of cancer related deaths in both sexes in North America, where 26% of the patients diagnosed, have potentially resectable disease. Primary and secondary cigarette smoking is associated with 90% of lung cancer development.

Lung cancer is divided into two main groups: Small Cell Lung Cancer and Non-Small Cell Lung Cancer. Generally lung resections are rarely performed for small-cell carcinoma as the disease is metastasized at the time of diagnosis. When assessing patients with malignant disease, the initial assessment must explore the “4-M’s” of malignant disease:

- Mass effect
- Metabolic abnormalities
- Metastasis
- Medications
Small Cell Lung Cancer
These are neuroendocrine tumours by origin and are considered to be a medical disease rather than a surgical pathology. They regularly have metastasized by the time of diagnosis. They are classified to be either at a limited state, where surgical resection can still be offered to the patient prior chemoradiotherapy, or advanced stage, where patients require chemotherapy and palliation. The significance of these tumours, to the anaesthetist, is the paraneoplastic syndromes associated with them:

- SIADH with can lead to hyponatremia
- ACTH production leading to Cushing’s syndrome
- Lambert-Eaton myasthenia syndrome from impaired acetylcholine release, precluding the use of non-depolarizing muscle relaxants and poor response to anticholinesterase reversal agents.

Carcinoid tumours are also classified as neuroendocrine malignancies that are found in the central airways where they can present with massive haemoptysis. Intraoperative hypotension from these lesions may not respond to regular vasoconstrictors and Octreotide may be required.

Pleural tumours are usually associated with asbestosis. They present with dyspnoea and a bloody effusion. They can be easily resected with good results, but demonstrate a poor response therapy and less than a year median survival.

Non-Small Cell Lung Cancer
There are several types of cancers that fall under this group of cancers and they may also contain many subgroups of their own.

Adenocarcinoma is most common lung tumour in both sexes and is known to metastasise early in the disease course. It forms part of Pancoast disease and is associated with hypertrophic pulmonary osteoarthropathy. These tumours may have paraneoplastic metabolic factors secreting growth hormone and corticotrophin.

Bronchioloalveolar Carcinoma in a subtype of an adenocarcinoma that is not associated with cigarette smoking.
The following diagram, is a summary of common clinical considerations to common lung tumours.

<table>
<thead>
<tr>
<th>Type</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell</td>
<td>Central lesions (predominantly)</td>
</tr>
<tr>
<td></td>
<td>Often with endobronchial tumor</td>
</tr>
<tr>
<td></td>
<td>Mass effects: obstruction, cavitation</td>
</tr>
<tr>
<td></td>
<td>Hypercalcemia</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>Peripheral lesions</td>
</tr>
<tr>
<td></td>
<td>Extrapulmonary invasion common</td>
</tr>
<tr>
<td></td>
<td>Most Pancoast tumors</td>
</tr>
<tr>
<td></td>
<td>Growth hormone, corticotropin</td>
</tr>
<tr>
<td></td>
<td>Hypertrophic osteoarthropathy</td>
</tr>
<tr>
<td>Large cell</td>
<td>Large, cavitating peripheral tumors</td>
</tr>
<tr>
<td></td>
<td>Similar to adenocarcinoma</td>
</tr>
<tr>
<td>Small cell</td>
<td>Central lesions (predominantly)</td>
</tr>
<tr>
<td></td>
<td>Surgery usually not indicated</td>
</tr>
<tr>
<td></td>
<td>Paraneoplastic syndromes</td>
</tr>
<tr>
<td></td>
<td>Lambert-Eaton syndrome</td>
</tr>
<tr>
<td></td>
<td>Fast growth rate</td>
</tr>
<tr>
<td></td>
<td>Early metastases</td>
</tr>
<tr>
<td>Carcinoid</td>
<td>Proximal, endobronchial</td>
</tr>
<tr>
<td></td>
<td>Bronchial obstruction with distal pneumonia</td>
</tr>
<tr>
<td></td>
<td>Highly vascular</td>
</tr>
<tr>
<td></td>
<td>Benign (predominantly)</td>
</tr>
<tr>
<td></td>
<td>No association with smoking</td>
</tr>
<tr>
<td></td>
<td>5 year survival &gt; 90%</td>
</tr>
<tr>
<td></td>
<td>Carcinoid syndrome (rarely)</td>
</tr>
</tbody>
</table>

Squamous Cell Carcinomas are mostly associated with cigarette smoking. They are large masses that are associated with mass effects. They metastasize late in the clinical course, and may be associated with hypercalcaemia from the tumour secretion of parathyroid-like factor. Large-Cell Undifferentiated Carcinoma is the least common large tumour lesion and has a very rapid growth rate.

**TABLE 2.7. Indications for surgery in non-small cell lung cancer.**

<table>
<thead>
<tr>
<th>Stage I A and B</th>
<th>Primary resection, no postoperative chemo/radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II</td>
<td>Primary resection, adjuvant postoperative chemotherapy</td>
</tr>
<tr>
<td>Stage IIIA, N2 (for patients with N2 disease identified at thoracotomy: postoperative chemotherapy, possibly radiation)</td>
<td>Definitive chemo/radiotherapy, in select patients induction chemo/radiotherapy followed by resection in patients with stable or responding disease</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>Surgery rarely indicated. Chemo/radiotherapy</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Resection of select T4, N0–1, M0 tumors</td>
</tr>
<tr>
<td></td>
<td>Palliative therapy. Possible exception: selected patients with a resected isolated cerebral metastasis</td>
</tr>
</tbody>
</table>
**Chronic Obstructive pulmonary Disease (COPD)**
This is a common finding in patients presenting for lung resection. Severity of the disease is classified by the American Thoracic Society into 3 stages:

- Stage I is FEV₁ > 50% of predicted, including both mild and moderate COPD
- Stage II is FEV₁ 50-35% of predicted
- Stage III is FEV₁ < 35% of predicted

Patients with stage II and III disease retain Carbon dioxide from failure to maintain the work of breathing and those with stage III disease and are over 60 years have less than a 3 year life expectancy. Supplemental oxygen will likely be required for patients with stage III COPD in the postoperative period to account for the decrease in the Functional Residual Capacity. Preoperative factors for optimization in patients with COPD:

- Etelactasis
- Bronchospasm
- Respiratory tract infections
- Pulmonary oedema

Preoperative rehabilitation programmes are of benefit in these patients to as they demonstrate symptom improvement, better quality of life and improved exercise ability.

**Smoking**
This is a common habit in patients with lung cancer. Even though there is debate on the ideal time duration to stop cigarette smoking prior surgery, there is a consensus that preoperative cessation of smoking shows intraoperative and postoperative improved outcome. Smoking causes prolonged tissue hypoxia, poor wound healing and increased risk to wound infections. Limiting tobacco smoking for > 4 weeks before surgery, shows decreased pulmonary complications after surgery and evidence suggests that patients be counselled that longer is the duration of cessation, the less is the risk to pulmonary complications. Five and 10 years survival rate is worse among patients with stage 1 lung cancer who are current smokers compared to former smokers.

**Infectious diseases: Tuberculosis**
In the 1800, prior to the advanced development of anti-TB chemotherapy, surgical lung resections for diseased lung was a common procedure in an attempt to remove the mycobacterium bacilli foci in the necrotic lung tissue, alleviate symptomatology and improve pulmonary function. There were various other surgical techniques performed during those times, from lung collapse therapy and thoracoplasties, to nerve interruptions and extra-plural plombage, all with varying degrees of outcomes.

South Africa is one of the countries overburdened with the epidemic of the mycobacterial Tuberculosis, and 80% of patients TB infected patients have a Human Immunodeficiency viral coinfection. The WHO approximates that half a million new cases of MDR-TB are diagnosed per year and X-DR TB is becoming even more prevalent rendering chemotherapy ineffective. Isolated medical therapy has around 75% cure rates of MDR-TB and 40% for X-DR TB, despite the development of newer drug agents in clinical use.

Considering these statistics, adjuvant surgery for lung resection has demonstrated 75-90% cure rates for drug-resistant TB, slows conversion rates and prevention of disease spread. Lung resections for tuberculosis have demonstrated a similar risk profile to that of resections
for malignant disease. Extent for anatomical resection is guided by radiological distribution of disease. VATS in these patients could be challenging as the lung tissue adheres to the chest wall making surgical access difficult.

The anaesthetist will be met with patients presenting for lung resection in the preoperative phase, either electively as an adjunct to chemotherapy, or in an emergency scenario, from TB related complication e.g. massive haemoptysis.

Alexander et al, performed a retrospective review on 50 patients, focusing on the treatment outcomes of patient with MDR-TB and XDR-TB, comparing those with and without HIV coinfection, at King DiniZulu Hospital. They demonstrated that patients treated with adjuvant surgery had higher cure rates compared to patients treated with chemotherapy alone. They also revealed similar treatment outcomes in both HIV positive patients and those without HIV coinfection.

Patients with HIV coinfection, without established immunity as demonstrated by a low CD4 level, may need to have surgery deferred and antiretroviral therapy established to undetectable viral loads. The patients with HIV coinfection requiring emergency lung resections, are treated with the same general principles of management as HIV negative patients.

Surgical indications in Drug-resistant TB differ in different institutions but generally, authors in the field have used the following indications:

- Persistent positive smear or culture despite optimal anti-TB therapy
- Extensive drug resistance with high probability of failure or relapse
- Radiologically localized disease with high probability of near-total resection
- Expected adequate cardio-pulmonary reserve post-surgery
- Presence of sufficient drug activity to facilitate healing of bronchial stump

Patients are presented for surgery after a minimum of anti-TB chemotherapy minimum of 3-6 months. These patients will require preoperative assessment for fitness for surgery.

Preoperative work up for these patients can include:

- Karnovsky score
- Arterial blood gas on room air
- Pulmonary Function Tests
- CT scan and perfusion lung scanning, to assess post-operative lung function
- Bronchoscope
- Echocardiography to r/o pulmonary hypertension
- 6MWT
- Cardio-pulmonary assessment
- Nutritional assessment

The general principles of the preoperative assessment for TB related lung resections is similar to those for malignant disease even though the lung tissue to be resected may be not be participating in gaseous exchange. The value of ppoFEV1, is correlated with postoperative outcome in this group of patients, but is still limited by its failure to accurately reflect the actual postoperative FEV1.
Poor preoperative prognosticating factors in patients with tuberculosis include bilateral disease, XDR-TB and active disease at the time of surgery. Nutritional assessment is an important element in the preoperative evaluation of patients with chronic lung disease to undergo resection surgery. Patients with a BMI < 18, have shown to incur a worse postoperative outcome compared to patients with BMI > 18.

Albumin is a marker of nutrition and inflammation. Hypoalbuminemia has shown to be an indicator of poor postoperative outcome with regards to mortality and surgical morbidity, in patients undergoing cardiac and non-cardiac surgery. Tamoko et al, demonstrated in a cohort study of 13 000 patients undergoing cardiac transplant surgery, that albumin levels < 35g/dL were associated with higher 30 day postoperative mortality and higher incidence of wound infections and acute kidney injury after resection. In patients undergoing lung resection surgery, hypoalbuminemia is associated with higher risks of surgically related complications i.e. wound dehiscence and broncho-pleural fistulae formation.

Local units use preoperative albumin cut off of 30g/dL, and these patients are referred to the dietitian for nutritional optimization.

**Renal dysfunction**
Factors associated with increased risk of post-thoracotomy renal impairment are:
- Previous history of renal impairment
- Diuretic therapy
- Pneumonectomy
- Postoperative infection
- Requiring intraoperative blood transfusion
- Preoperative Cisplatin therapy

Patients presenting for thoracotomy with pre-existing renal impairment, are likely to require prolonged postoperative ventilation after lung resection, with prolonged length of hospital stay.

**Physiotherapy**
Preoperative physiotherapy forms part of a physical rehabilitation programme and has shown to improve both pre and postoperative pulmonary function of patients with COPD. Benefit is noted in patients having initiated physiotherapy 12 – 8 weeks prior lung resection but fewer benefits are noted if physiotherapy is started within a month of surgery. Extensively long preoperative rehabilitative programmes may not be practical in patients with malignant disease but may be of benefit in other forms of pulmonary diseases.

The breathing exercises and muscle strengthening regimes prior surgery, improves effort tolerance prior surgery and pulmonary complications after surgery. There are no established standardised rehabilitative programmes of note, but the perioperative involvement of a physiotherapist can never be overstated in this group of patients.

**Anaesthetic planning**
General measures for airway assessment must be instituted to detect patients with possible difficult endotracheal instrumentation. Expectant anatomical challenges with endobronchial intubation must be considered and diagnosed preoperatively. Previous pulmonary or airway surgery, history of local radiotherapy and infection, are all risk factors for difficult insertion of a double lumen tube and can be diagnosed from a plain chest radiograph. The CT scan
may demonstrate narrowing of the distal airways or compression of a main stem bronchus by the tumour, hinting to difficult Double Lumen Tube insertion. Patients likely to desaturate with one lung ventilation should also be identified preoperatively. The following table is from the Slinger and Darling, summarising the preoperative risks to desaturating during one-lung ventilation.

**Table 2.13. Factors which correlate with an increased risk of desaturation during one-lung ventilation.**

<table>
<thead>
<tr>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>High percentage of ventilation or perfusion to the operative lung on preoperative ( V/Q ) scan</td>
</tr>
<tr>
<td>Poor ( PaO_2 ) during two-lung ventilation, particularly in the lateral position intraoperatively</td>
</tr>
<tr>
<td>Right-sided thoracotomy</td>
</tr>
<tr>
<td>Normal preoperative spirometry (FEV1 or FVC) or restrictive lung disease</td>
</tr>
<tr>
<td>Supine position during one-lung ventilation</td>
</tr>
</tbody>
</table>

Patients with longstanding severe unilateral disease, like those with tuberculosis, generally tolerate one-lung ventilation better because they have adapted to decreased ventilation and perfusion from the diseased lung. Patients with better preoperative spirometry values desaturate more during one-lung ventilation and the reasons for this are still speculative in current studies.

Preoperative lung function and cardiopulmonary exercise testing results have an impact on the timing of extubation and planning of postoperative care. Patients with higher ppoFEV\(_1\) and D\(_L\)CO values > 60\%, may be extubated in the operating theatre and cared for in a High Care monitored ward bed.

Candidates with ppoFEV\(_1\) < 30\% may require a staged weaning approach to their timing of extubation and are likely to require admission into a High dependency Intensive Care Unit. The use of thoracic epidurals make it possible for early extubation in this group of patients but there is a 40\% failure rate to the postoperative function of epidurals. Therefore the decision to extubate, should be individualised, taking into context associated medical conditions and predicted postoperative values for the individual patient.
CONCLUSION

Any form of lung resection holds variable morbidity and mortality rates for different patient population groups. Offering surgery to patients with lung malignancy can change the outcomes of a disease with 100% mortality, and could potentially lead to a cure from Extremely-Drug resistant tuberculosis. The benefit of surgery in these patient groups, has led to a move to offer lung resection surgery to patients with lower postoperative values, with the attempt to treat as many candidates as possible.

It is the responsibility of the anaesthetist to participate in the preoperative evaluation process of these patients as miscalculations to maximum allowable resections, may imply a detrimental perioperative outcome for that individual patient. The guidelines provided by the various clinical bodies, are meant as recommendations only and each patient must still be managed as uniquely as their individual clinical presentation to the attending physicians. There is always a need to exercise vigilance in applying first world medicine in a third world environment as some advances in medical technologies and availability of medical resources may be deficient.

REFERENCES


