

Surgical Management for Chronic Obstructive Airway Disease

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (**COPD**) is common, usually progressive and is a leading cause of mortality and morbidity globally. The World Health Organization (**WHO**) [1] estimates that COPD is responsible for 5% of annual deaths. Whilst 835,000 people in the UK have been diagnosed with the disease, it is estimated a further 2 million may be unidentified [2]. COPD kills about 25,000 people per annum in England and Wales, is the fifth biggest killer in the UK and the only major cause of death on the increase [2,3]. Despite being primarily a medical disorder, Patients with COPD have various presentations for which the surgeon plays a pivotal role: Spontaneous pneumothorax, Bullous disease, Heterogeneous emphysema and end stage COPD requiring lung transplantation.

BULLOUS DISEASE AND SECONDARY PNEUMOTHORAX

Aetiology (Origin and Pathophysiology)

Blebs are sub-centimeter collections of air that escaped from the alveoli into the interstitial. They are covered by visceral pleura. Bulla are coalesced alveoli from destroyed lung tissue either over distended elastic fibers or air trapping from destroyed reticular fibers that strut open the small to medium size airways during exhalation. If the Bulla occupies over one third of the thoracic cavity then it is called a giant Bulla [4].

Blebs and apical Bulla play an important role in the development of primary and secondary spontaneous pneumothorax [5]. Pneumothorax in itself maybe life threatening due to respiratory failure or hemodynamic implications of a tension pneumothorax, especially in the context of increasing atmospheric pressures as during pilot landing and diving. In these situations indications for resection and pleurodesis are obvious. Bulla may also cause dyspnea by virtue of being space occupying, compressing underlying normal lung tissue and decreasing elastic recoil to nearby airways causing air trapping and disease progression. In these cases indications for surgery are less clear cut and require more in depth assessment of the risks of surgery versus quality of life improvements from relief of dyspnoea. The wide spread availability of VATS has allowed a much lower threshold for operating on patients compared to open thoracotomies [6].

Patient Selection and Indications to Operate

Pneumothorax in a patient with underlying lung disease is secondary spontaneous pneumothorax. Indications to operate on these patients according to the BTS guidelines are:

1. Failure of the lung to expand or prolonged air leaks beyond 48 hours after first attack. If the patient is unfit and the lung has expanded then medical pleurodesis with talc has acceptable low risk of infection and ARDS (**Figure1**).
2. Second attack of pneumothorax on the same or contra lateral side
3. Bilateral pneumothorax
4. Tension Pneumothorax

Special Circumstances

Pregnancy: Where the risks on the mother and fetus from both the pneumothorax and surgery need to be considered. Pregnancy exaggerates pneumothorax. In most instances conservative measures as observation if the patient is asymptomatic and there is no evidence of fetal distress, simple aspiration and assisted delivery if near term is adequate. VATS pleurodesis is also feasible with adequate short term control. If drains are inserted and bedside pleurodesis is indicated, Blood pleurodesis is the safest substrate to be used [7] (**Table 1**).

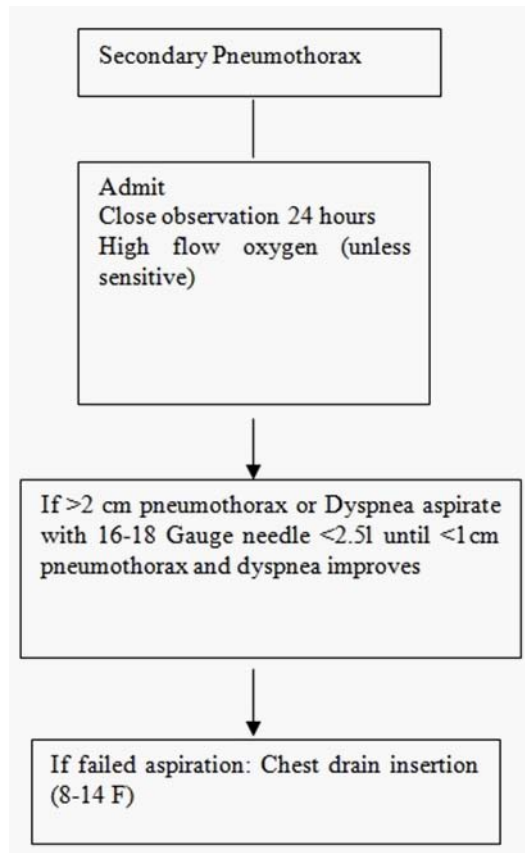


Figure 1: Flow Chart for Management Of Secondary Pneumothorax Based On BTS Guidelines 2010.

Table 1: Predictors of outcome according to the ATS guidelines following bullectomy

Parameter	Favourable	Unfavourable
Clinical	Smoking cessation>6weeks	Elderly
	Progressive Dyspnea	Underweight/Weight loss
		Co morbidities
		Chronic bronchitis
		Frequent chest infection
		Pulmonary hypertension
Investigations	FEV1>40%	FEV1<35%
	Large volume of trapped lung	Po2<6
	Transfer factor near normal	PCO2>8
	Normal Blood gases	
Imaging	Giant bulla well defined	Multiple ill defined bullae
	Well defined perfusion defect at site of bulla	Disrupted vasculature in remaining lung

SURGICAL MANAGEMENT

Preoperative Preparation

Patients with secondary pneumothoraces need proper clinical assessment as they are at risk of other co morbidities that share smoking as a risk factor with COPD. Particular attention should be given to ischemic heart disease which may preclude general anesthesia. Underlying chest infection ideally should be controlled prior to surgery. Performance status and pulmonary function tests quantify overall pulmonary reserve and fitness for surgery. Medications for associated co morbidities, such as antiplatelets need to be stopped 5 days prior to surgery.

Chest X rays are usually diagnostic of the pneumothorax; however some thoracic surgery units will not proceed without a CT scan to exclude underlying lung cancer. Also, occasionally these patients have partial pleural adhesions resulting in excessive surgical emphysema which make diagnosing the pneumothorax particularly challenging and require a CT scan. CT scans also allow assessment of the underlying lung condition and mapping of Bullae which helps plan the procedure and avoids missing out Bullae which may cause later recurrence.

Intraoperative Considerations and Techniques

Anesthetic

The induction of anesthesia is collaborated with the surgeon to perform bronchoscopy. This is essential in all cases to allow exclusion of endobronchial lesions and pulmonary toilet (cultures may be sent for microbiologic assessment if necessary) which will aid with Intraoperative ventilation and post operative recovery. Double lung ventilation is essential for VATS approach and preferable for open thoracotomies. Non invasive blood pressure monitoring is adequate.

Surgery

Patients are positioned in the lateral decubitus, in the prayer position with the operating table flexed to expand the rib spaces. Poster lateral thoracotomies are performed in the standard 4th -5th intercostals space. If the procedure is by VATS, usually 3 ports are used (**Figure 2**).

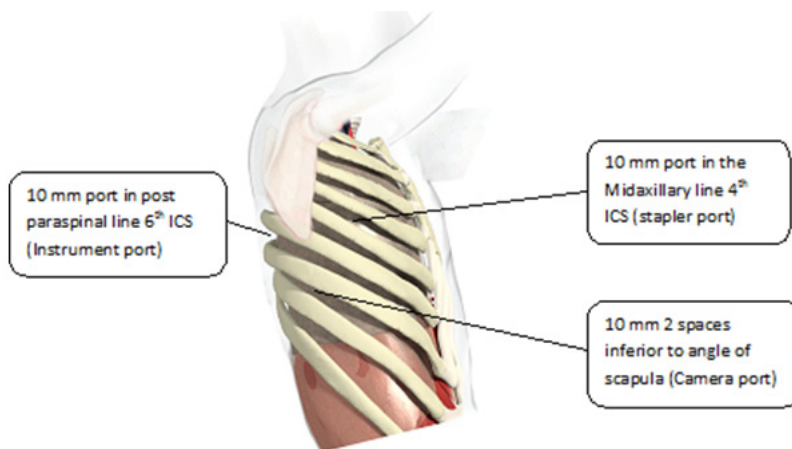


Figure 2: Positioning the ports for VATS bullectomy.

The initial assessment is aimed at localizing significant Bullae and blebs and excluding any masses. Most Bullae arise at the apices of the lobes. Occasionally there are adhesions to the chest wall which maybe vascular. Bullae are stapled with commercially available staples. If there is concern about the underlying emphysematous lung, buttressed staples are preferred to avoid prolonged postoperative air leaks. With extensive heterogeneous emphysema or multiple Bullae that would leave limited lung behind if stapled, the surgeon may opt not to staple off any Bullae (**Figure 3**).

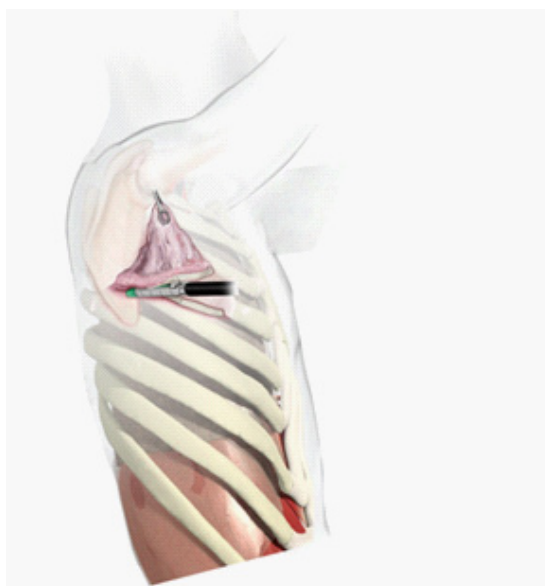


Figure 3: Bullectomy with buttressed staples. Bullae, usually detected in the apices of the upper and occasionally the lower lobes are stapled at the site of relatively normal lung tissue to minimize air leaks.

Pleural symphysis is essential to obliterate the pleural cavity. This will prevent any pneumothorax and lung collapse from blebs or Bullae that are left behind or develop later. This may be by parietal pleurectomy or pleural abrasion. The pleura are stripped/abraded from the ribs. Care should be taken around the apex of the lung to avoid injuring the subclavian vessels. The pleura on the diaphragm is adherent and only abrasion can be performed. These patients may have highly vascular pleura and talc pleurodesis may be preferable to a pleurectomy if excessive bleeding is expected.

A single apical drain is inserted in one port and the lung is inflated. With open thoracotomies, testing for air leaks at 30 cm H₂O is performed and any leaks are dealt with, usually with topical aero-sealants. With VATS a defect of up to 200 ml per breath on positive ventilation will usually resolve upon extubation. An Epidural or paravertebral catheter is used for adequate analgesia postoperatively in thoracotomies while Local anesthetic infiltration to the ports in VATS procedures. All patients are sent to recovery for a couple of hours and a chest x-ray to ensure lung expansion and drain position is performed.

Postoperative Care

Patients are kept on suction (3-5Kpa) to allow maximum apposition of the lung to the chest wall and initiate fibrinous adhesions. On day 2 postoperatively patients are taken off suction if no air leaks are identified. The drain is taken out on the same day or a day later and patient discharged home. Pain control (with opioids, NSAIDs and paracetamol) and chest physiotherapy is important to avoid infection and maintain expanded lungs. Prolonged air leaks are managed depending on severity. Mild to moderate air leaks where the lung remains expanded off suction, patients are managed as outpatients on flutter bags. With severe air leaks, mobile suction devices allow mobilization which improves the resolution of air leaks and the patients psyche rather than being bed bound to wall suction. Occasionally further talc pleurodesis through the drain is needed to seal the air leaks.

LUNG VOLUME REDUCTION SURGERY (LVRS)

History

Surgeons have always been tempted to operate on this ever growing population of COPD patients. Many innovations have been attempted in vain. Targeting the increased lung volumes by paralyzing the diaphragm, resecting costal cartilages and thoracoplasty all failed. Pulmonary denervation aimed at tackling dyspnea and again had no sensible reported results. Excising more severely emphysematous portions of lung showed promising results by Cooper and this led to a multicentre randomized controlled study which laid the foundations for LVRS [8-11].

Principles of LVRS

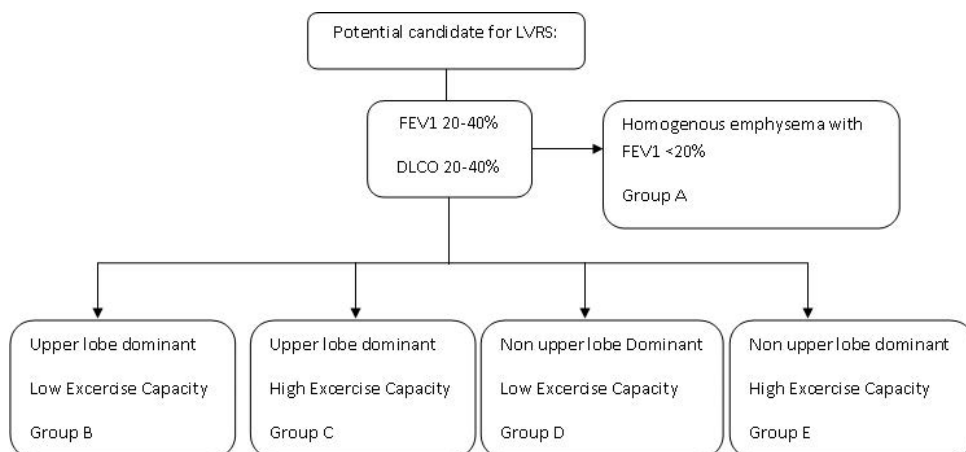
Resecting the least functioning lung allows better chest wall mechanics with improved ventilation secondary to less hyperinflation. The strut diaphragm is allowed to return to its dome

shape. Hence upon inspiration the longitudinal chest dimensions increased. Also the ribs and sternum are allowed to descend which allows the transverse and anteroposterior diameters to increase. Also, the remaining relatively normal lung expands and better ventilation perfusion matching further improves respiration. The elastic recoil in the remaining lung improves allowing better expiratory flows and less air trapping in the remaining lung [9,12].

Patient Selection

Patient selection criteria remain debatable. Multidisciplinary approach will allow proper selection and preoperative optimization of these high risk operations with optimal results. From the NETT trial, we know that the patients with upper lobe dominant emphysema and low exercise tolerance have both prognostic and symptomatic benefits from bilateral LVRS compared to medical therapy [13]. Hence the work up for these patients, although variable amongst different units, aims at identifying this category of patients.

The algorithm for patient selection in the NETT trial:



Results of the surgical population in comparison to the medical population in the different groups:

Group A:

Group	Prognostic	Symptomatic
A	Worse	N/A
B	Better	Better
C	No Difference	Marginally Better
D	Marginally Better	Better
E	Worse	No difference

Broadly speaking (ATS guidelines) favorable and unfavorable parameters are:

Table 2: Predictors of outcome according to the ATS for LVRS

Parameter	Favourable	Unfavourable
Clinical	Smoking cessation>6weeks	Elderly
	Refractory Dyspnea	Underweight/Weight loss
		Co morbidities
		Chronic bronchitis
		Frequent chest infection
Investigations		Pulmonary hypertension
	FEV1<45% post bronchodilator	FEV1 & TLC<20%
	Hyperinflation	
	RV>150%, TLC >100% pred.	
	Post rehabilitation low exercise tolerance	
Imaging	Po2<6kpa, PCO2>8kpa	
	Heterogeneous upper lobe dominant emphysema	Homogenous emphysema

The study also compared outcomes depending on surgical technique used: bilateral VATS versus sternotomy. No significant difference was found in the outcomes between the two for bilateral LVRS.

INTRAOPERATIVE CONSIDERATIONS AND TECHNIQUES

Anesthetic

After induction, bronchoscopy is necessary for pulmonary toileting and to exclude endobronchial pathology. Mucus samples are sent for culture and sensitivity. These patients have varying degrees of associated chronic bronchitis and a mintracheostomy may be used to side post operative physiotherapy. Double lumen tube to allow for single lung ventilation while operating on the contra lateral lung is essential, whichever approach (VATS vs. sternotomy) is used. The emphysematous lung is overinflated and even upon isolation is difficult to deflate. Insufflating the side that needs deflation with CO₂ will aid in deflating but at the expense of hypercarbia. Arterial lines are necessary for blood gas monitoring.

Surgery

The inferior pulmonary ligament is released to aid the remaining lung in mobilizing to the apex. Also any adhesions, from previous pneumonia are released. Identifying the fissure and demarcating the most emphysematous portions for resection is done while the lung is inflated. Technically, the emphysematous lung may be further deflated by diathermy to the upper lobe in the parts that will be resisted, along with the anesthetic maneuvers mentioned earlier. Staplers with pericardial strips are used to support the underlying lung tissue and minimize postoperative air leaks. About 20-35 % of the lung volume should be resisted. The staple line is tested for air leaks. Aero sealants may be used to reinforce the staple margin. The lung is allowed to inflate. Once the anesthetist is satisfied, the procedure is repeated on the other side.

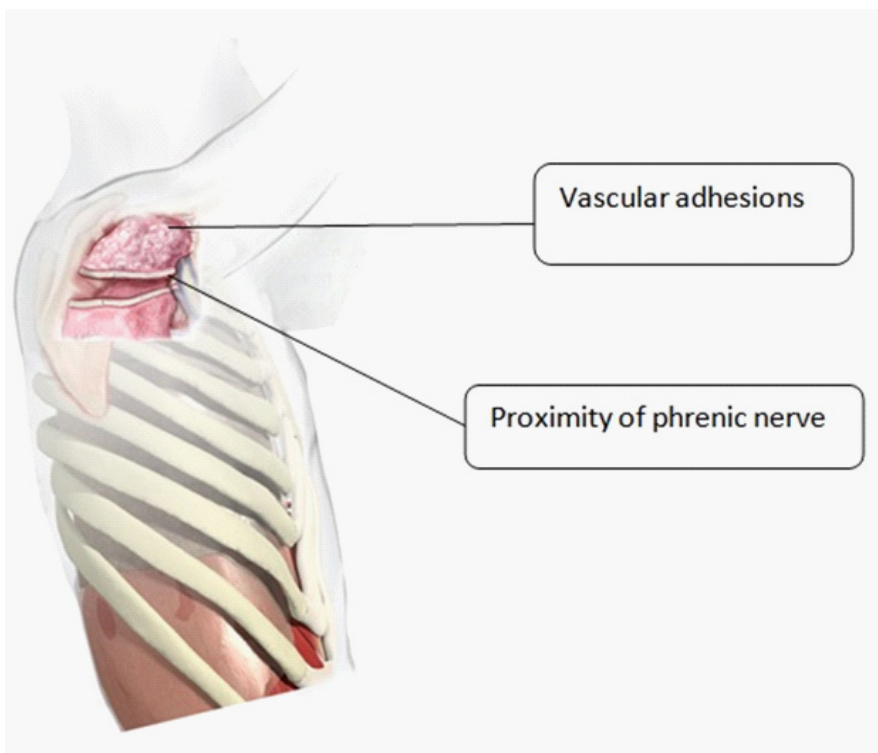


Figure 4: Caution during LVRS due to adhesions from prior infection as they may be vascular and due to proximity of vital structures such as the phrenic nerve and subcalvian vessels.

Postoperative Care

An x ray in recovery is performed to assess lung expansion and drain position. If the lung is expanded, even if an air leak is present, the temptation to put the patient on suction should be avoided as this will increase the flow across any pores in the staple margin and potentially delay healing. The patient is sent to the ward and extensive physiotherapy is started 2 hours post op by sitting the patient out. Adequate pain control cannot be overstressed. Minitracheostomies are used if inserted in theatres. If the patient develops any signs of infection, a minitracheostomy is inserted at very low thresholds and empirical antibiotics are started till culture results are retrieved. Prevention of chest infection is extremely important in this group of patients as there reserve is low and they easily go into respiratory failure.

Postoperative Results

LVRS has been proven to provide both symptomatic benefit and more importantly, prognostic benefit in a subgroup of patients with upper lobe dominant emphysema and poor exercise tolerance and FEV1 and DLCO >20%. These benefits are at the cost of 2.9% 90 day mortality, 30% major pulmonary (respiratory failure) and 20% major cardiac incidents (myocardial infarcts) [10,13-15].

ENDOBRONCHIAL PROCEDURES

overview

Emphysema basically involves destruction of the alveoli leading to a number of changes that decrease exercise tolerance. Firstly the residual surface area for diffusion is decreased. None of the available treatments addresses this factor. Secondly the elastic recoil on the remaining lung is decreased causing less expiratory flows which leads to air trapping. This is more pronounced during exercise when the expiratory time becomes even less. Finally the voluminous lungs suppress the diaphragm and splay the ribs, interfering with respiratory mechanics (12, 16). The last 2 elements are addressed by LVRS and other endobronchial techniques.

Endobronchial Valves (EBV)

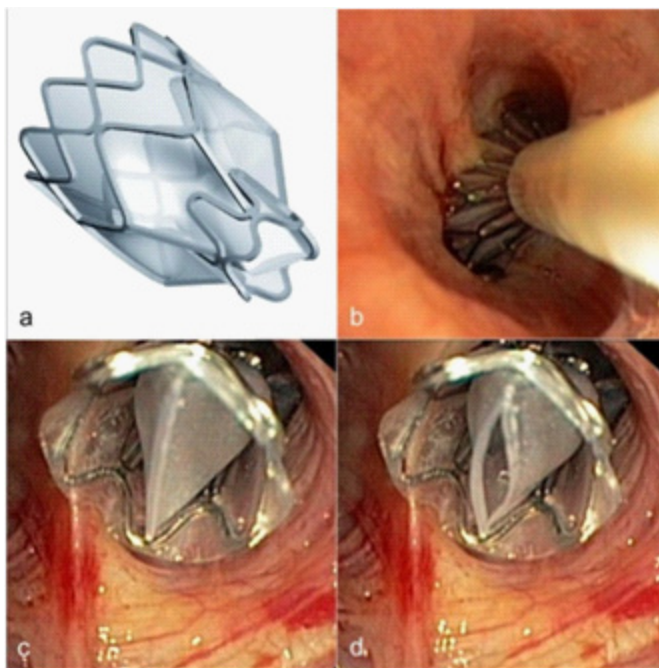


Figure 5: Zephyr Valves

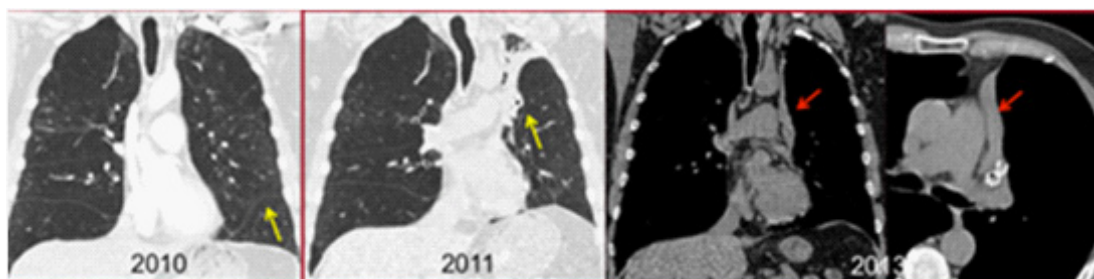


Figure 6: Effects of Endobronchial valves

The EBVs are designed as one way valves letting air and mucus out during exhalation, not allowing inhalation of air into the segment/lobe with the valve. The valves come in sizes and are removable. They are the most studied form of endobronchial modalities treating COPD patients. The VENT trial [17] has provided the following important recommendations to attain the best results:

1. Heterogenous emphysema
2. Completeness of fissure
3. Minimal collateral ventilation (tested by catheters occluding the target bronchus and measuring exhaled volume collateralized from surrounding lung) [18]
4. Complete isolation of segment/lobe with the appropriate size valve

The one way valves targets the same patients selected for LVRS that are unfit for surgery. The results from the VENT (European) trial revealed an increased FEV1 up to 26% and a decrease in the target segment/lobe volume of $80\% \pm 30\%$. Also there was $>50\%$ met minimal clinical difference threshold. Contrary to LVRS the atelectatic lung left behind caused complications: haemoptysis, pneumonia and pneumothorax.

Other Separation valves which attempted to address the complications of atelectatic lung by allowing partial inspiration failed to show any positive results compared to patients that underwent sham bronchoscopes only [19].

Airway Stents

Patients with homogenous emphysema have significant air trapping. Airway stents at least theoretically were thought to maintain airway patency and allow deflation and less trapping [Figure 7]. The initial data showed improvement in patients with $RV/TLV > 67\%$ and these patients were randomized in the Exhale Airway Stents for Emphysema (EASE) trial [208 stent vs. 107] sham bronchoscopy) [20]. The day one physiologic parameters in the stented group were very impressive (FEV1, RV and RV/TLC). Unfortunately most of the stents migrated and occluded at 6 months leading to no significant improvement over time.



Figure 7: Endobronchial stents. (With permission from Paulo F.G. Cardoso MD, PhD)

Biologic and Polymeric Lung Volume Reduction and Thermal Vapour Ablation

These are released in the segments targeted causing inflammatory response and scarring occluding both the bronchi alveolar and collateral ventilation leading to lung volume reduction. The effects are irreversible and not related to fissure development. Anecdotal data has not shown any benefit from biodegradable agents. Ongoing trials are assessing the effects of polymeric agents. Thermal vapour ablation has shown promising results following an inflammatory response with COPD exacerbation at 6 months with a mean improved FEV1 by 17% [21-26].

Endobronchial coils

Coils act on the principle of reducing the volume of lung hence reestablishing the elastic recoil. Initial pilot studies showed improvements in spirometric and lung volumes [Figure 8]. Trials in the UK revealed initial 90 day improvement in 6MWT by 70 meters, improved st George questionnaire score and FEV1 by 13% [27].

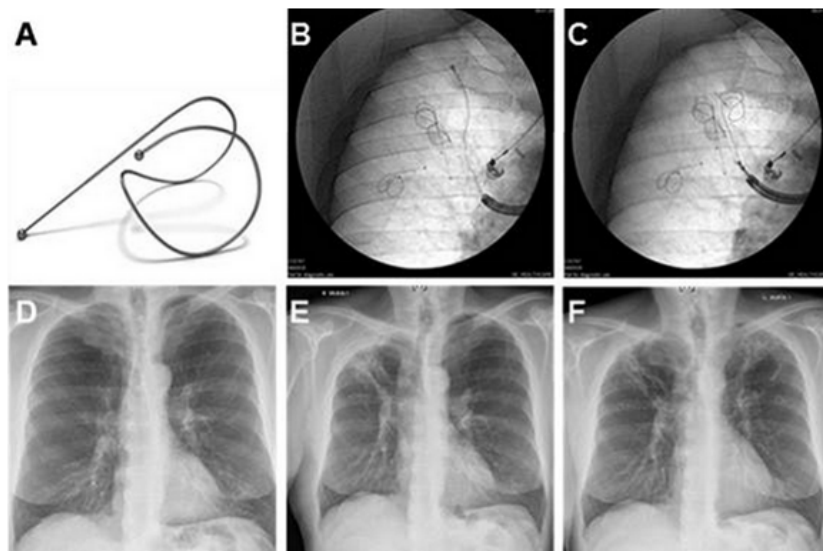
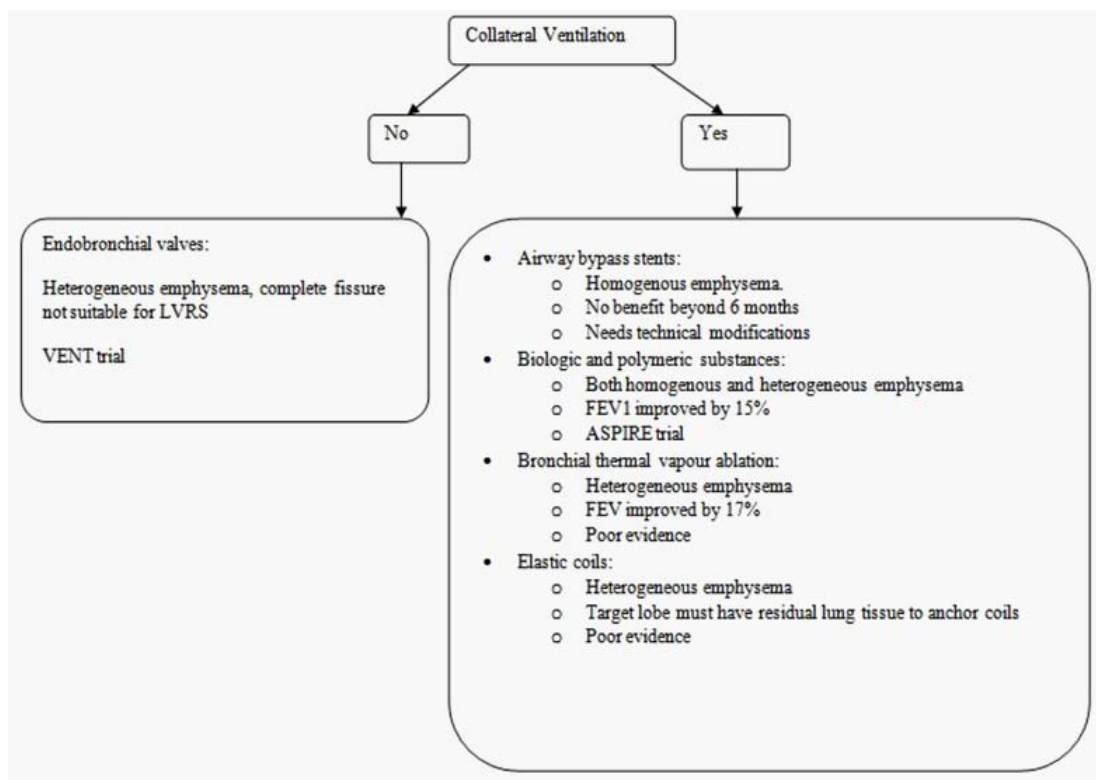


Figure 8: A : Coil, B: coil within the catheter, C : coil deployed once the catheter has been retrieved, D : Chest X ray before treatment, E : Chest X ray 3 months after right upper lobe treatment, F : Chest X ray 6 months after bilateral treatment (upper lobes).

Summary of Endobronchial procedures [28]



LUNG TRANSPLANTATION

Overview

Lung transplantation theoretically solves all the COPD problems. It provides the patient with normal sized lungs allowing better chest wall mechanics. The alveolar-capillary surface area is not broken down allowing normal diffusion. The elastic recoil and compliance is normal avoiding air trapping and hyperinflation. Unfortunately, the lungs are both part of the reticuloendothelial system (RES) and exposed to the external atmosphere. Unlike the cornea, not part of the RES, lungs are rich in immune cells needing more aggressive immunosuppression to be accepted by the recipient. On the other hand, unlike other internal organs such as the liver (part of the RES), it is in contact with the external environment, which makes it, more vulnerable to infection, and hence more severe infection with immune suppression. This has led to poor median survival of 5.6 years following lung transplantation [29] this factor has its impact on criteria for lung transplantation in COPD (see later).

Patient selection

Age: 65 is the cut off age in the UK but there have been lung transplants for fit 75 year old patients in USA.

1. Smoking cessation over 6 months
2. Life expectancy less than 2 years secondary to severe functional disability (NYHA 3-4) from the lungs and no other organ failure.
3. Five year clearance from malignancy
4. Patients on high dose steroids are excluded [30, 31]

Preoperative Evaluation

Patients undergoing lung transplantation must have single organ-system failure (cardiopulmonary). Hence, extensive evaluation to rule out other organ dysfunctions and co morbidities (Echocardiogram, left and right heart catheterization to exclude ischemic heart disease and evaluate pulmonary hypertension) are used. Also quantitative lung functions (V/Q scan) help plan which lung to transplant (the worst) first [30, 31].

Due to the long waiting lists the Lung allocation score (LAS) has allowed better utilization to the most needy patients on the waiting list and has lowered mortalities on the waiting list at the expense of higher acuity at the time of transplantation. The reason for this continuing analysis is the need to balance on one hand the desire to help those patients in direct need, versus the statistical likelihood of the patient to survive the procedure, as well as the post-operative risks of infection and transplant rejection [30]

The LAS involves the following steps [32]:

1. Calculate the waiting list survival probability during the next year
2. Calculate the waitlist urgency measure
3. Calculate the post-transplant survival probability during the first post-transplant year
4. Calculate the post-transplant survival measure
5. Calculate the raw allocation score
6. Normalize the raw allocation score to obtain the LAS

Lung transplantation provides approximately 50 % 5 year survival, hence patients having COPD (42% of lung transplants) [30] must have significantly poor performance status to be accepted for transplantation. Specific criteria for COPD patients to be included on the waiting list are:

1. FEV1<20-25% predicted
2. PO2 <55mmHg and PCO2>55mmHg at rest
3. Onset of secondary pulmonary hypertension

There is a small but statistically significant advantage in bilateral lung transplantation in COPD patients; therefore the trend is for bilateral transplantation [30, 31].

Donor Criteria

Donor lungs should be within 25-30% of the predicted size of the recipient's lungs. Ideally, patients who have COPD should be matched with donors who are between 3 and 5 cm of the recipient height. Other criteria include: Less than 20 pack year smoking history, ABO compatibility, and evidence of good gas exchange, normal chest x-ray and normal bronchoscopy. Preferably, the lung should not have been exposed to >5cmH2O PEEP [31].

TECHNICAL CONSIDERATIONS

Incision

For bilateral transplantation either a clamshell incision, bilateral anterior thoracotomy or sternotomy if (CPB needed). For Single lung transplantation posterior or anterior thoracotomies suffice. If CPB needed on the left side than Femoral bypass is used. On the right side, central cannulation is feasible [33].

Bronchial Anastomosis

By far, bronchial anastomosis has caused the commonest complications due to poor circulation. Either stenosis or dehiscence is secondary to poor circulation. The donor bronchus receives minimal back flow from the pulmonary circulation. Attempts at micro vascular anastomosis of

the bronchial arteries have not lead to any improvements in outcomes. Allowing a short donor stump (no more than 2 cartilaginous rings beyond the lobar carina) [30, 34].

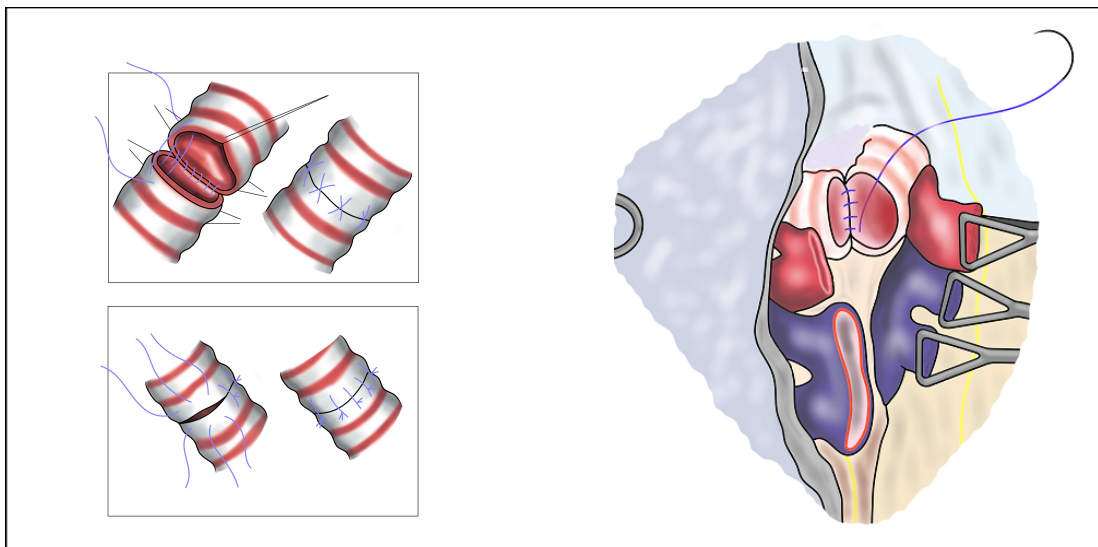


Figure 9: Bronchial anastomosis: A. Continuous suturing to membranous portion and
B. interrupted to cartilaginous portion

Vascular anastomosis

Pulmonary anastomosis rare cause complications but should be considered with high PA pressures and hypoxia. Pulmonary vein stricture occurs usually secondary to a small atrial cuff and should be suspected with high PA pressures and unilateral edema [30].

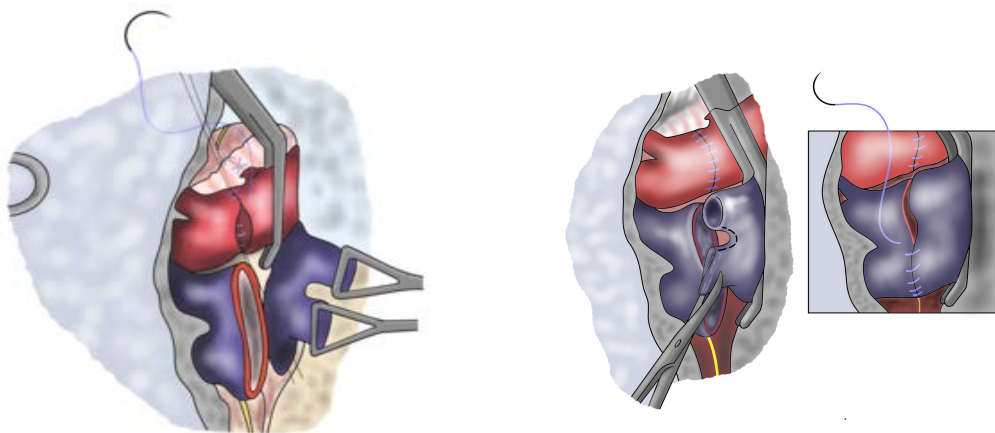


Figure 10: A. Pulmonary artery (right) and B. Pulmonary vein anastomosis (left) Postoperative care

Post operative ventilation in single lung transplant patients with COPD in the remaining lung is a challenge. The difference between the hyper compliant native lung and the low compliance post transplant edematous lung causes hyperinflation of the native lung with suboptimal distending pressures of the transplanted lung [30]. Maneuvers to avoid this include: prolonged expiration, near zero positive pressures and early extubation. Double lumen ventilation with separate ventilator parameters may also be considered.

Postoperative Complications

Immunologic complications are the main compromise to survival and outcome both in the short and long term. Bacterial infections are commonest in the early stages while CMV is commoner in the long term.

Primary graft dysfunction, mainly from ischemia reperfusion has an incidence up to 25%. Acute graft rejection, up to 75%, should be suspected with fever, dyspnea, fatigue, a drop by 10 or more in the FEV1 and chest x ray showing infiltrates. One of the risk factors for bronchiolitis obliterans and chronic rejection is acute rejection. Chronic rejection can be slowed down by immune modulation but is inevitably progressive and irreversible [31].

Outcomes

According to ISHLT 1 year survival following lung transplantation is 79% and 5 year survival is 52% [29]. These low figures need to be taken into account when placing emphysema related patients on the waiting list.

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