abstract

Chronic obstructive pulmonary disease (COPD) often has a profound effect upon the quality of life and mortality of the older adult. Despite numerous medical treatments, surgery may be considered for the symptomatic patient with medically-optimized, end-stage COPD. Bullectomy, lung volume reduction surgery (LVRS), and lung transplantation have all proven to be important surgical therapies. This article reviews the current state of these interventions, and the criteria when deciding on the best surgical option for a given patient.

Key words: emphysema, COPD, lung transplant, lung volume reduction surgery, bullectomy

Surgical Interventions for COPD

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Introduction

Approximately 710,000 Canadians suffer from chronic obstructive pulmonary disease (COPD),[1] and hundreds of thousands more may have this disease but have never been diagnosed. COPD is largely a disease of older adults; in individuals older than 75 years the prevalence is approximately 6.9%,[1] compared with 4.6% in individuals aged 55 to 74.

COPD is a slow and irreversible process that progresses over several years, often punctuated by exacerbations and eventually leading to death. According to the 1998/9 National Population Health Study (NPHS), 51% of individuals with COPD reported that shortness of breath caused some restriction in their home, work, and social activities. In Canada, COPD is the seventh most common cause of hospitalization for men and the eighth for women, with a rehospitalization risk of approximately 40%.[2] It is also the fourth leading cause of death in Canadian men and the fifth leading cause of death in Canadian women. However, these figures may be underestimates and the listed cause of death of COPD patients may instead reflect the often-associated pneumonia or congestive heart failure. Economic impact studies suggest that the cost of COPD on Canada's health care system now exceeds $3.2 billion each year,[3] a figure that is expected to rise exponentially over the next several years.

Etiopathology

COPD is a heterogeneous respiratory disorder encompassing emphysema and chronic bronchitis. In emphysema, there is destruction of pulmonary parenchyma causing a reduction in functioning lung tissue, that results in a decrease in the amount of gas exchange that occurs. As more lung tissue is destroyed it loses elastic recoil and expands in volume, resulting in a hyperexpanded chest with flattened diaphragms and widened intercostal spaces. This destruction and expansion of the abnormal lung occurs in a nonuniform manner, crowding the relatively healthy lung tissue and preventing ventilation of the normal lung.

Chronic bronchitis is clinically defined as a persistent cough with sputum production present on most days for three months in two consecutive years. There is obstruction of the small airways caused by a combination of reversible bronchospasm and irreversible loss of elastic recoil by adjacent lung parenchyma. This loss of mechanical advantage and functioning pulmonary parenchyma leads to increased work of breathing. In addition to the primary effects in the lung, the chronic inflammatory process of COPD is associated with numerous effects on other systems such as skeletal muscle dysfunction,[4] right heart failure,[5] secondary polycythemia,[6] malnutrition,[7] and depression.[8]

Management

Once a diagnosis has been made, an effective management program for severe COPD centres on adequate management of symptoms and maintenance of a reasonable quality of life. The diagnosis and treatment of COPD was
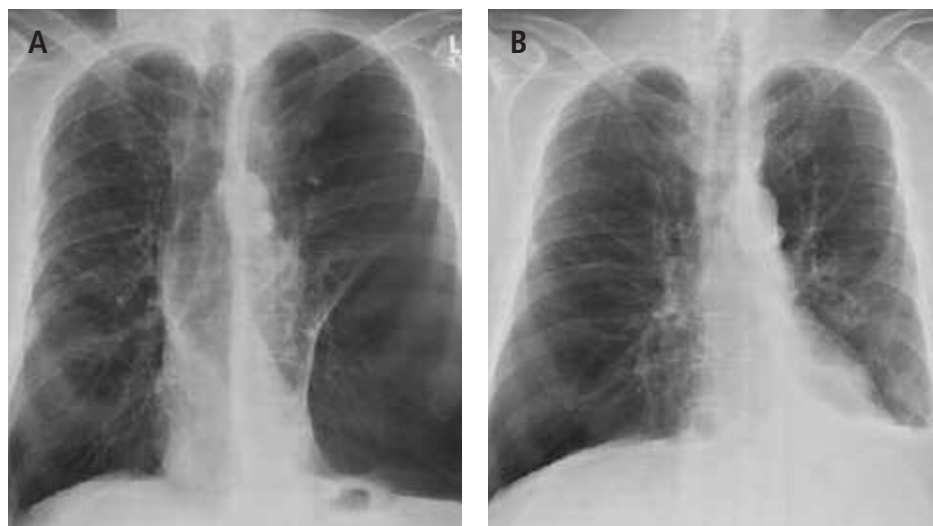
Figure 1: Chest X-ray of an Individual With a Giant Bulla (A) Before bullectomy, the bulla is occupying more than 30% of the left hemi-thorax. (B) Two years after bullectomy, reduction is apparent.

recently reviewed by Bourbeau in *Geriatrics & Aging's* January issue on lung disease.[36] Medical management includes smoking cessation, exercise, vaccinations, home oxygen for hypoxic patients, bronchodilators, and antibiotics during infectious exacerbations. Systemic corticosteroids are used during acute exacerbations and for individuals with poorly controlled end-stage COPD despite being optimally medically managed. All COPD patients who have activity-related shortness of breath are likely to benefit from pulmonary rehabilitation, resulting in a reduction of symptoms and improved quality of life.

Surgical interventions have a risk of both morbidity and mortality, so they are directed only to patients who remain symptomatic despite optimal medical treatment. There are numerous surgical interventions for the treatment of the hyperexpanded and poorly perfused emphysematous lung; these include costochondrectomy, phrenic crush, pneumoperitoneum, pleural abrasion, lung denervation, and thoracoplasty. Unfortunately, these interventions have largely been unsuccessful.

This article will review three surgical procedures that have gained prominence in the management of medically optimized, end-stage COPD: bullectomy, lung volume reduction surgery, and pulmonary transplantation.

Bullectomy

Bullae are markedly dilated (>1cm) air spaces within the lung parenchyma that are commonly secondary to COPD. It is believed that bullae arise from a ball-valve mechanism, wherein obstruction of a bronchiole or bronchus leads to progressive distention of the areas of lung tissue where alveolar walls are already damaged. Air may flow into these areas but is unable to escape, resulting in increased pressure and further enlargement of the air space.

Although bullae increase physiological dead-space, they rarely compromise

pulmonary function. Unfortunately, giant bullae can exert substantial compressive effects on underlying normal lung tissue, which in turn may reduce blood flow and ventilation to potentially normal functioning lung parenchyma.

The natural history of bullae is one of enlargement, causing worsening dyspnea. Excision of bullae has the following effects:
– expansion of the underlying compressed lung,
– reductions in airway resistance, functional residual capacity (FRC), pulmonary vascular resistance, and physiologic dead space,
– increase in the elastic recoil pressure of the lung,
– improvement in dynamic compliance,
– restoration of the mechanical linkage between the chest wall and normal lung,
– upward movement of the diaphragm to a more efficient position.

The most common indications for bullectomy are severe dyspnea in the setting of a large bulla occupying at least 30% of the hemithorax, pain, or spontaneous pneumothorax. Other indications may include hemoptysis or repeated infection of the bullae, but both may be better managed medically. The preoperative evaluation should include chest
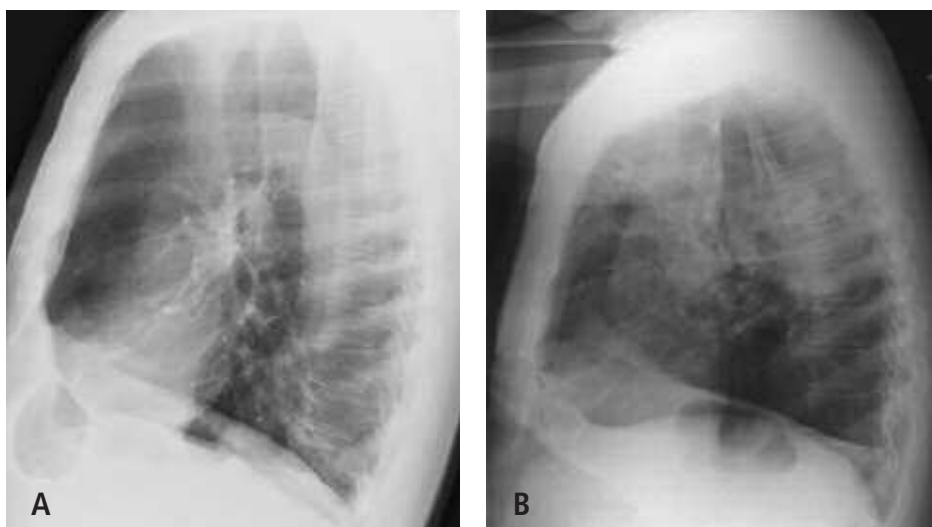

Figure 2: Lateral Chest X-ray of an Individual with COPD (A) Before LVRS, the lungs appear to be hyper-inflated with flattened diaphragms. (B) After LVRS, the lungs appear to be less hyper-expanded and the diaphragms (particularly the left diaphragm) are less flattened, improving the mechanical function of the respiratory system.
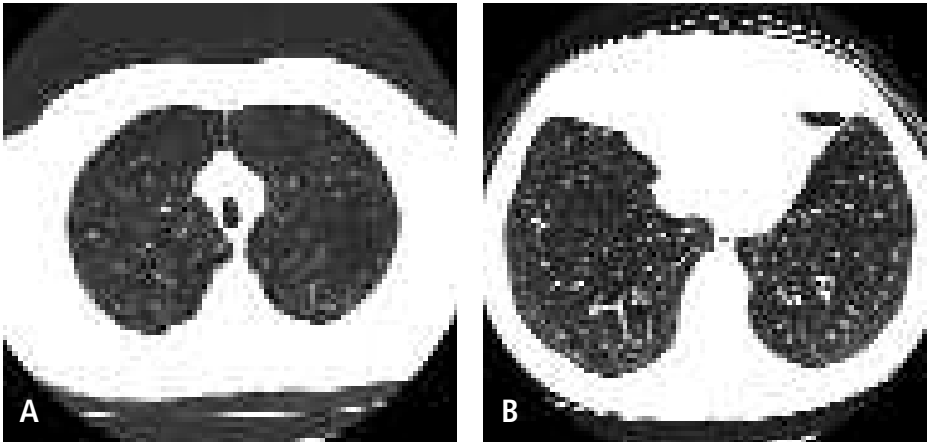
Figure 3: CT Scan of Emphysema with Upper Lobe Predominance (A) In the upper lobes, there are numerous focal areas of lucency compared to the background of the normal lung. (B) In the lower lobes, emphysema is much less severe.

x-ray, CT of thorax, full pulmonary function testing (PFTs), ventilation/perfusion (V/Q) scan, and, for some patients, angiography of the pulmonary circulation.

Figure 1 illustrates the chest x-rays of an individual with a giant bulla, before (A) and after (B) bullectomy.

Factors that make bullectomy less appealing include the presence of multiple smaller bullae, advanced emphysema in the nonbullous adjacent lung, and significant comorbidities. Surgical risk is increased when the forced expiratory volume in one second (FEV1) is less than 40% of predicted or less than 500ml. The presence of severe dyspnea, hypercapnia, or cor pulmonale makes the risk of surgery almost prohibitive.[9]

Numerous surgical techniques have been used for bullectomy including muscle-sparing thoracotomy, video-assisted thoracoscopy, and large stapled wedge resection if numerous bullae merge indistinctly with the comparatively normal adjacent lung. Thoracoscopy is generally favoured for unilateral bullous disease, whereas median sternotomy is utilized in the resection of bilateral bullae. If the lobe is near completely destroyed, lobectomy may be implemented. Prolonged air leaks, pulmonary infections, and respiratory failure are the most common complications. In carefully selected individuals, the mortality for bullectomy has been reported to be 2.3%[10] with statistically significant improvements of

FEV1, diffusing capacity (DLCO), and health-related quality of life that were maintained three years postbullectomy; however, recent series have reported a mortality of 6.9–12.5%[9,11] with thoracoscopy. These mortality rates have varied greatly because of differences in patient selection and bullectomy techniques.

Lung Volume Reduction Surgery (LVRS)

Lung volume reduction surgery (LVRS) involves the surgical reduction of lung volume by multiple wedge excisions. LVRS was initially described by Brantigan in 1959; it consisted of a unilateral thoracotomy of 20–30% of the most diseased-appearing portion of the lung, coupled with lung denervation.[12] It was proposed that LVRS increased elastic recoil of the lung by improving the size mismatching of the chest and the hyperinflated lungs. This would restore the outward circumferential pull on the bronchioles, thereby improving expiratory airflow. It was also suggested that LVRS improved the mechanical function of the diaphragm and intercostal muscles by decreasing the functional residual capacity and returning the diaphragm to a more normally curved and lengthened configuration (Figure 2). In addition, there may be changes in cardiopulmonary interdependence, decreased central respiratory drive, and ventilatory response to CO_2. Unfortunately, the tech-

nique was abandoned because of the high reported surgical mortality rate of 16%.

In the 1990s, LVRS was conducted via video-assisted thoracoscopy with CO_2 laser or yttrium-aluminum garnet laser.[13,14] Despite suggestions of benefit in some nonrandomized series, the studies were plagued by incomplete follow-up. Additionally, several reports and trials demonstrated an appreciable operative mortality without substantial improvements in lung function or symptoms.[15]

In 1994, based on the extensive experience in lung transplantation for patients with end stage emphysema, JD Cooper re-evaluated Brantigan's LVRS operation.[16] He modernized the procedure by resecting areas of severe emphysema of both lungs through a median sternotomy and then buttressing the staple lines with bovine pericardium to reduce air leaks.[17] He reported that LVRS significantly improved spirometric values, oxygenation, and exercise tolerance.

The controversy around the risks, benefits and long-term outcomes of LVRS led to the randomized controlled trial, National Emphysema Treatment Trial (NETT).[18,19] The study enrolled 1,218 patients with severe emphysema and randomized them to either LVRS or ongoing best medical therapy after each group had received six to ten weeks of standardized pulmonary rehabilitation. This was a study of US Medicare recipients, thus many older patients were included. The mean age of the LVRS group was 66.5±6.3 years whereas the medical group was 66.7±5.9 years. Overall mortality did not differ between patients undergoing LVRS versus those assigned to medical therapy only; however, in the surgical group there was a significant improvement in exercise capacity, FEV1, general and health-related quality of life, and degree of dyspnea. The researchers found only two characteristics that helped predict whether a participant would benefit from LVRS: whether the emphysema was localized in the upper lobes of the lung and whether the functional capacity was low or high.

Table 1: Evaluation of Patients for LVRS

	Inclusion Criteria	Exclusion Criteria
General Evaluation	Disability despite medically optimized and maximal rehabilitation Tobacco cessation >6 months	Poor medical compliance and inability to participate in pulmonary rehabilitation Continued tobacco use Significant comorbidity Previous pleurodesis or thoracotomy Severe obesity or cachexia Age >75 (American Thoracic Society)*
Radiographic Features	Marked emphysema Heterogeneously distributed emphysema where there are target zones of poorly perfused lung and areas of better preserved lung Marked thoracic hyperinflation	Bronchiectasis Homogeneously distributed emphysema with no target zones or preserved lung tissue Chest wall or thoracic cage abnormalities
Physiologic Testing	Marked airflow obstruction Marked hyperinflation Cardiovascular function: normal ejection fraction	Minimal to moderate airflow obstruction Minimal to moderate thoracic hyperinflation Markedly disordered alveolar gas exchange: DLCO<10% $PaCO_2$>60mmHg Impaired cardiovascular function: Left ventricular ejection fraction <40% Mean pulmonary artery pressure >35mmHg Significant coronary artery disease

*This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, May 1996.[35]

Patients with predominantly upper-lobe emphysema and low exercise capacity had a lower mortality after LVRS than the corresponding medical-therapy group. The trial also demonstrated that patients with FEV1 <20% and homogenous lung disease (or a diffusing capacity of carbon monoxide [DLCO] that was less than 20%) had a high risk of death with little functional benefit. Therefore, success of LVRS is dependant upon meticulous selection of patients with upper lobe predominance (Figure 3) and low exercise capacity, methodical patient preparation with reduction of risk factors, and attentive postoperative care.

The eligibility criteria for LVRS are summarized in Table 1. For patients who are unable or unwilling to undergo LVRS, a potential alternative is the use of one-way endobronchial valves bronchoscopically placed into areas of severe emphysema. Air is prevented from enter-ing into these segments, but distal bronchial secretions are allowed to escape, resulting in atelectasis of these diseased portions of lung. Airflow is then redirected to the relatively healthier areas of the lung, improving ventilation-perfusion mismatch. Preliminary small-scale studies of endoscopic lung volume reduction have been promising,[20,21] and a recent study by Yim *et al.*[22] demonstrated short-term improvements in FEV1, functional status, quality of life, and relief of dyspnea. A larger multicentre study with long-term follow-up is being organized (the International Endobronchial Valve for Emphysema Palliation Registry).

For patients with severe homogenous emphysema, another experimental alternative to LVRS is the bypassing of collapsed and obstructed small airways of emphysematous lung with noncollapsing extra-anatomic stents.[23,24] These stents would connect lung parenchyma to large airways, which would assist expiration and decrease dynamic hyperinflation. This may improve respiratory mechanics, exercise tolerance, and dyspnea. However, the safety of the procedure needs to be established since there may be significant risk of hemorrhage or production of pneumothorax with the insertion of bronchopulmonary stents. At present, there are ongoing long-term animal studies in the development of the ideal stent for maintaining long-term efficacy.

Lung Transplantation

While lung transplantation was initially used as a treatment for pulmonary fibrosis and pulmonary hypertension, the indications have evolved such that emphysema is the most common diagnosis leading to transplantation, accounting for 39% of transplants

worldwide.[25] Approximately 50% of lung transplant recipients are older than 50 years, which is the age group characteristic of COPD and interstitial pulmonary fibrosis.

According to the published international guidelines for the selection of lung transplant recipients,[26] patients who are less than 65 years old with end-stage pulmonary disease in the absence of other significant organ dysfunction should be considered for lung transplant referral. Recently, some programs have been transplanting individuals older than age 65 in the absence of comorbidity. However, many older patients are found to have significant cardiac disease during lung transplant candidacy evaluation, given the high prevalence of prior smoking in this group of patients. Older patients are also more likely to have significant dysfunction of other organs.

Lung transplantation should be offered to patients with diffuse disease who have any of the following: FEV1 <20% predicted, hypercapnia, associated pulmonary hypertension, or a predicted survival of less than the expected post-transplant survival. Recent COPD survival prediction models such as the BODE score[27] may assist in identifying suitable candidates for transplantation. Potential lung transplant recipients must be ambulatory and have a preoperative weight of 70–130% of predicted. Candidates should also be motivated, have adequate social support to deal with the rigorous pre- and post-transplant activities, and have undergone a comprehensive preoperative pulmonary rehabilitation program.

Previous bullectomy or LVRS is not a contraindication to lung transplantation, and these procedures have been successfully used to bridge patients to transplantation. This is important as the early benefits of bullectomy and LVRS may not be sustained beyond a few years (Figure 4).

Either single or double lung transplantation may be used for patients with emphysema. Both procedures result in substantial improvements in pulmonary

function, exercise capacity, and quality of life. Disadvantages of pulmonary transplantation include a lack of available donor lungs and mortality rates of 5–15% in the first 30 days. Survivors require lifelong immunosuppression, which increases the risk of neoplasm and infection compared with nonimmunosuppressed individuals. Lung transplant recipients are also at risk of developing bronchiolitis obliterans, manifested by chronic allograft dysfunction, which reaches a cumulative incidence of 50–60% at five years post-transplantation. The cumulative five-year survival is 50%, and whether lung transplantation provides a survival benefit to COPD patients remains unclear.

In 1998, Hosenpud *et al.*[28] compared the survival curves of COPD patients waiting for transplant to those who underwent transplant. The study concluded that the risk of death for patients following transplant was never lower than the risk for those who continued to wait on the transplant list. This finding may have been due to premature listing of American lung transplant candidates, since European data do suggest a survival benefit of transplantation.[29,30] However, this remains an area of controversy and underscores the importance of functional and quality of life benefit in assessing outcomes of transplantation.

The choice of bilateral or unilateral transplantation for COPD patients is con-

troversial. Numerous authors have described a higher perioperative risk from bilateral operation without a demonstrable functional benefit when compared to unilateral lung transplantation.[31,32] There were also no differences in hospital stay, ICU stay, and duration of mechanical ventilation. However, five-year survival has been reported to be 66.7% for bilateral lung transplant recipients versus 44.9% for single lung transplant recipients.[33]

Accrued from the data of 17,128 lung transplant recipients, the registry from the International Society of Heart and Lung Transplantation has demonstrated that the age of the transplant recipient does not have an effect on six-month or one-year survival.[25] Thereafter, recipients greater than 50 years of age have a more rapid decline in survival when compared to younger recipients. This is likely due to the comorbidities associated with aging and the effect of immunosuppressants on these age-related conditions.[25] These findings are similar to the experience of the Toronto Lung Transplant program, where lung transplant recipients older than 60 years had increased mortality even after adjusting for their expected higher age-related mortality.[34]

Conclusions

COPD carries a large individual and societal burden, and may have profound effects upon the quality of life of the older
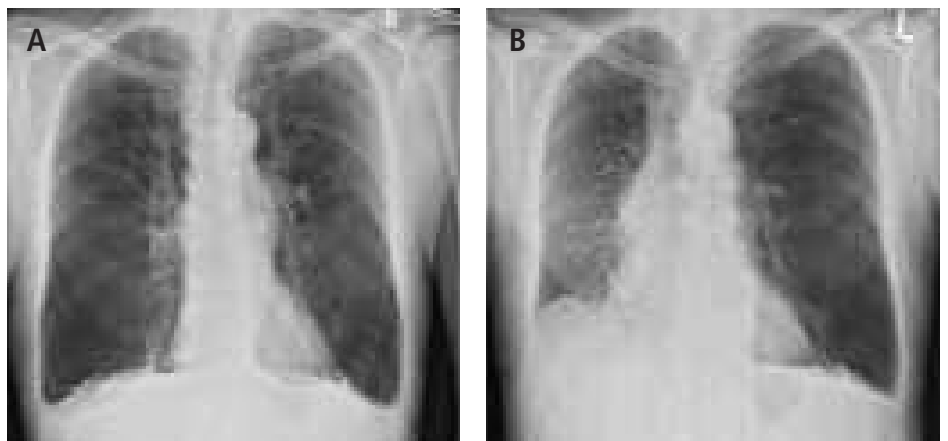
Figure 4: Advanced Symptoms of COPD (A) This chest x-ray demonstrates the parenchymal hyperlucency and low-set flat diaphragms that may be associated with advanced COPD. This patient had previous LVRS of both lungs seven years prior to single lung transplantation. (B) This chest x-ray is of the same patient after his right single lung transplant.

patient. Despite numerous medical treatments to improve the quality of life and mortality of the COPD patient, surgery may be of benefit to the patient with end-stage COPD. Bullectomy, LVRS, and lung transplantation have all proven to be important surgical therapies, and the use of meticulous selection criteria is essential when deciding the best option for a given patient. Patients with severe dyspnea in the setting of a large functionless space-occupying bulla should be assessed for thoracoscopic or open bullectomy. In contrast, patients with hyperinflation, heterogeneous distribution of disease predominantly in the upper lobes, FEV1 >20%, and a normal PaO2 should be assessed for LVRS. Lastly, patients with diffuse disease should be considered for lung transplantation if they have clinical predictors of reduced survival such as FEV1 <20% predicted, hypercapnia, or associated pulmonary hypertension.

Although there is controversy as to whether mortality improves with these surgical interventions, symptomatic and functional improvements have been demonstrated in individuals who are carefully selected and who are motivated to undergo these procedures.

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