Surgical Options for Patients With COPD: Sorting Out the Choices

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Surgical procedures designed to improve pulmonary function and quality of life of patients with advanced emphysema have been attempted for more than a century. Of the many attempted procedures, only giant bullectomy, lung transplantation, and lung-volume-reduction surgery have withstood the test of time and are currently being practiced. This article reviews each of these procedures and also develops a rational approach to selecting appropriate candidates for these 3 interventions. *Key words: lung-volume-reduction surgery, LVRS, bullectomy, lung transplantation, emphysema, COPD.* [Respir Care 2006;51(2):173–182.

Introduction and Historical Perspective

Chronic obstructive pulmonary disease (COPD) affects as many as 14 million Americans[1] and is a growing problem worldwide. It can cause disabling symptoms of dyspnea and exercise limitation and can lead to early death.[2] The mainstay of treatment has been the use of a variety of bronchodilator and anti-inflammatory medications, oxygen supplementation, and, in some instances, a comprehensive pulmonary rehabilitation program.

A variety of surgical approaches to improving symptoms and restoring function of patients with emphysema and COPD have been described.[3] Although these were well intentioned and based on what were considered sound physiologic rationales at the time, almost none of these operations have been found useful.

In the early 1900s an over-distended and stiff chest wall was thought to cause emphysema. Accordingly, early operations were designed to increase the movement of the thoracic cage. This was accomplished by disarticulating

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the ribs from the sternum (chostochondrectomy) and performing a transverse sternotomy.[4] Despite initial reports that this approach increased the vital capacity by 500–700 mL[5,6] and relieved dyspnea,[7,8] the procedure was subsequently abandoned because of inconsistent results.

As the understanding of emphysema improved, it became clear that chest wall enlargement was the result, rather than the cause, of the condition, and operations such as phrenic nerve sectioning (phrenicectomy)[9,10] and thoracoplasty[7] were designed to decrease the size of the lungs. These operations were quickly abandoned when they were found to reduce lung function and to worsen symptoms.

Instillation of air into the peritoneum was attempted with some success, based on the rationale that it would improve the curvature, and therefore the function, of the diaphragm.[11] Unfortunately, the discomfort produced by this procedure and the need for repeated instillations of gas precluded its widespread acceptance.

The large-airway obstruction that occurs during exhalation in some patients with emphysema was thought to result from atrophy of airway cartilage. In an attempt to address this problem, a number of procedures were developed with the idea of stabilizing the trachea externally, utilizing artificial materials,[12,13] bone chips,[14] and muscle flaps.[12] Attempts to interrupt portions of the autonomic nervous system were based on the understanding that the autonomic nervous system contributed to the control of bronchial tone.[15] Sympathectomy, glomectomy, vagotomy, and total lung denervation were all attempted at one time or another in patients with asthma and COPD,[9,16–18] unfortunately with poor results.[19]

Of all the early surgical interventions, essentially the only 2 survivors are bullectomy for giant bullae and the modern version of lung-volume reduction surgery (LVRS). They will be described in further detail below.

Bullectomy for Giant Bullae

Background

Removal of giant bullae is one procedure that has withstood the test of time and the rigor of scientific evaluation. Although no randomized clinical trials have been performed, recent reviews have documented the generally positive results of the 22 cohort studies of giant bullectomy that have been published.[20,21] In appropriately selected patients it appears that removal of the giant bulla may improve the function of adjacent lung tissue that is compressed.

Removal of these bullae is therefore considered when compression of adjacent lung is thought to contribute to dyspnea and/or to exercise limitation. Other suggested indications for bullectomy are hemoptysis, complicated or repeated pneumothorax, and (occasionally) repeated infection.[22]

Surgical Technique

Bullectomy can be performed via standard lateral thoracotomy,[23] a midline sternotomy,[24] or video-assisted thoracoscopy with stapling of bullae.[25] Video-assisted thoracoscopy, a less invasive procedure, may be the preferred approach for patients thought to have excessive risk with thoracotomy. Regardless of the approach taken, full anatomic resection (ie, lobectomy or segmentectomy) is generally avoided in an attempt to preserve the maximum possible amount of lung tissue.[26] Single-lung ventilation provides an important technical advantage.

Several approaches have been used to reduce postoperative air leaks, a common and difficult postoperative problem. Buttressing of suture lines has been accomplished by everting and stapling the interior walls of the bullae, the use of bovine pericardial strip reinforcement or Teflon pledget reinforcement,[27,28] biologic fibrin glues,[29] and blood patches using the patient's own blood to seal small air leaks.[25]

Outcomes

Bullectomy in carefully selected patients appears to be beneficial and durable in terms of symptom relief and improvement of pulmonary function.[30–35] Unfortunately, all of the published reports are case series in which follow-up is incomplete and interpretation is complicated by the various methods of data presentation employed. Surgical mortality has ranged from 0% to 22.5%.[21]

In one of the largest series, FitzGerald and colleagues[30] reported the long-term results of 84 patients who underwent surgical procedures for bullous emphysema over a period of 23 years. There were 2 operative deaths (2.4%). The greatest improvement (50−200% increase in forced expiratory volume in the first second [FEV_1]) was seen in patients with giant bullae that occupied $>$ 50% of the hemithorax and in whom there were lesser degrees of emphysema elsewhere in the lung. Improvement in pulmonary function in this group frequently lasted for 5 years and was noted up to 20 years following surgery. Poorer results were seen in those in whom the bullae occupied less than one third of the hemithorax, and those with chronic bronchitis or diffuse emphysema.

Nickoladze reported results from 46 patients who underwent bullectomy.[33] Respiratory function improved during a 5-year follow-up in the subgroup of patients in whom the bulla occupied more than one third of the hemithorax, but there was no change when the resected bulla was smaller.

Patient Selection

Selecting patients who will benefit from bullectomy is difficult because their dyspnea and reduced pulmonary

Table 1. Giant Bullectomy Indications, Contraindications, and "Ideal Candidate"

Indications	Contraindications	"Ideal Candidate"
Severe functional limitation despite maximal medical therapy	Substantial emphysema elsewhere in the lung	*All of the preceding indications AND* bulla > 50% of hemithorax
Non-smoker or ex-smoker		*All of the preceding indications WITHOUT:*
Little bronchodilator responsiveness		Chronic bronchitis or recurrent infections
Bulla occupies more than one third of hemithorax		Pulmonary hypertension
Crowding of adjacent lung on CT or angiogram		Co-morbid illness
Elevated trapped gas (elevated RV) on PFTs		Older age
Normal or near-normal D_{LCO}		FEV_1 < 35% of predicted
Normal P_{aO_2} and P_{aCO_2}		

CT = computed tomography
RV = residual volume
PFT = pulmonary function test
D_{LCO} = diffusing capacity of the lung for carbon monoxide
FEV_1 = forced expiratory volume in the first second

function may be due to the giant bulla itself and/or to the emphysema distributed elsewhere in the lung. In the latter situation, bullectomy would have no effect on lung function or symptoms. The recommended preoperative evaluation aimed at identifying those patients best suited for bullectomy should include plain chest roentgenograms; computed tomography (CT); pulmonary function testing that includes plethysmographic determination of lung volumes; ventilation and perfusion lung scans; and, occasionally, pulmonary angiography.

Testing is designed to determine the extent of gas trapped in the giant bulla, whether there is compressed lung adjacent to the bulla, and the extent of disease elsewhere in the chest. Chest CT scans accurately quantify the size of bullae, and most experts suggest that the bulla occupy at least one third, and preferably one half, of the hemithorax. Both CT scan and (particularly) pulmonary angiography have been standard tests used to identify the presence or absence of relatively normal underlying compressed lung tissue.[21,36,37] CT scan of the chest is now the preferred method for evaluating compression of underlying lung.[21] Pulmonary function testing helps determine the volume of gas trapped in the bulla (plethysmographic minus helium-dilution-measured residual volume), and ventilation-perfusion scan and CT scan can assess disease elsewhere in the lung.

In summary, it appears that giant bullectomy results in subjective and objective improvement in patients who have bullae that occupy at least 30%, and preferably 50%, of a hemithorax and that compress adjacent lung, when the function of the remaining lung is relatively preserved. Table 1 has been developed by this author from data in the literature summarized in a recent American Thoracic Society/European Respiratory Society COPD diagnosis and treatment guideline.[38]

Lung-Volume-Reduction Surgery

Background

Resection of giant bullae is rarely performed, as only an extremely small fraction of patients with emphysema have giant bullae. Resectional surgery for the much more common clinical presentation of diffuse emphysema was first reported nearly 40 years ago by Brantigan and colleagues, with 33 patients.[39,40] Although they documented subjective improvement in 75% of the surviving patients, they presented no objective data in the form of physiologic measurement to substantiate their findings, and the procedure never gained widespread acceptance.

In the early 1990s there were several published reports of LVRS performed via video-assisted thoracoscopy with CO_2 laser or yttrium-aluminum-garnet (YAG) laser,[41–44] but follow-up was extremely incomplete (< 50% in some measured variables), which made objective evaluation of the procedure difficult. LVRS has since been largely abandoned. However, LVRS gained considerable momentum in April 1994, when, at the annual meeting of the American College of Thoracic Surgeons, Cooper and colleagues presented an abstract on their results with 16 patients who underwent bilateral LVRS via median sternotomy, with resection of 20–30% of each lung.[44] This group found marked improvements in FEV_1 (+82%) and forced vital capacity (FVC) (+27%) as well as improvements in oxygen levels, 6-min walk distance, and quality of life. Although the data from this and other groups appeared promising, Medicare (the primary United States insurer for this patient age-group) ceased paying for LVRS in 1995, on the basis of insufficient evidence of efficacy. A large randomized controlled trial of LVRS versus medical therapy, known as the National Emphysema Treatment Trial

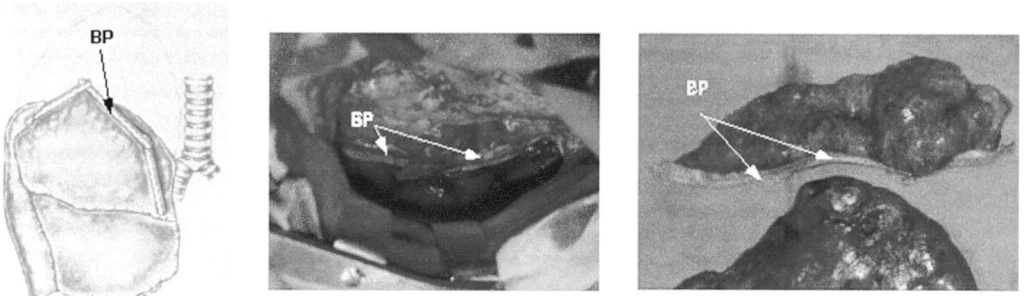

Fig. 1. Lung-volume-reduction surgery procedure. Left: Schematic of lung following typical resection. Middle: View of lung in thorax following resection. Right: View of resected emphysematous tissue. BP = bovine pericardium sealing strips.

(NETT), was undertaken to assess the efficacy of this surgical procedure. Primary outcome results from this randomized controlled trial have been published[45,46] and are detailed below.

Surgical Technique

A number of surgical approaches have been used in LVRS. In the modern era, essentially 3 approaches have been reported: (1) a midline sternotomy with stapled resection of lung tissue (Cooper, Gaissert, McKenna, and Little[2]), (2) video-assisted thoracotomy with stapled resection of tissue,[47–49] and (3) video-assisted thoracoscopy with laser ablation of bullae.[42,43,50] The latter operation has essentially been abandoned at this time because of inferior results and complications.

The midline sternotomy technique (Fig. 1) involves splitting the sternum longitudinally and exposing both lungs.[44] The upper lung zone is selected for removal in most cases, and a linear stapler, buttressed with strips of bovine pericardium, is applied, with multiple applications over the apex and a resulting inverted U-shaped margin. The surgeon aims to resect 20–30% of each lung.

In the video-assisted thoracoscopy technique, small surgical incisions in the lateral chest wall allow placement of instruments that allow resection of lung tissue without the need for larger incisions.[51] Target areas for resection are identified via inspection and analysis of preoperative studies. Resection is accomplished by placing a stapling device into the thoracic cavity. The stapler is applied repeatedly, with or without bovine pericardium buttressing, until the desired amount of tissue is resected.

Outcomes

Patients with emphysema have markedly reduced expiratory airflow, as measured by FEV_1 and FVC, which correlates with reduced exercise capacity, increased mortality, and, to some degree, dyspnea. Thus, it was a great surprise (and source of enthusiasm) that the first report of modern LVRS by Cooper and colleagues described dramatic improvements in pulmonary function in patients undergoing LVRS.[44] Subsequently, a large number of published case series have reported increases in FEV_1 and FVC, though the changes were not as large as in the initial report. In their review of the literature, Flaherty et al listed reports with average FEV_1 increases ranging between 13% and 96%.[52] Not all patients show improvements in expiratory airflow; some even show worsening after LVRS, and the durability of any improvement is unclear.

It appears that median sternotomy and bilateral video-assisted thoracoscopic approaches are similar in their ability to improve spirometry results.[48,53,54] McKenna and colleagues reported that patients who undergo bilateral procedures have a significantly greater improvement in expiratory airflow than those who undergo a unilateral procedure.[55]

Spirometry has been the most commonly used measure of severity of emphysema and response to LVRS, but lung volumes, including total lung capacity and residual volume, may also be important. Hyperinflation can lead to respiratory muscle dysfunction and dyspnea. After LVRS it is thought that decreases in lung volumes may partly be responsible for reduced dyspnea and improved exercise performance. Fewer studies have reported the effects of LVRS on lung volumes than on spirometry, but reductions in total lung capacity of 1–23% and residual volume of 9–46% have been reported.[56]

One of the most surprising effects of LVRS reported in the medical literature is improvement in P_{aO_2}. Cooper and colleagues reported a mean P_{aO_2} increase of 6 mm Hg in 18 patients.[44] This occurred despite no significant P_{aCO_2} decrease, which indicates that this effect was not the result of increased ventilation alone. The physiologic explanation for this improvement is not known. Albert and associates[57] noted widely variable changes in P_{aO_2} in 46 patients, 3 months after LVRS. On average the P_{aO_2} increased 3 mm Hg, but the changes ranged from –17 mm Hg to + 29 mm Hg. Changes in P_{aCO_2} were equally disparate, ranging from −11 mm Hg to +5 mm Hg. The investigators

hypothesized that alterations in the match of lung ventilation to lung perfusion may result from LVRS, but experimental evidence for this hypothesis is not yet available.

Improvements in pulmonary function are important only insofar as they reduce symptoms and improve function and quality of life for patients suffering with emphysema. The most commonly used measures of patient functional capacity have been the 6-min walk distance and the maximum cardiopulmonary exercise test.

Many uncontrolled studies have reported improvements in the distance covered in a timed walk.[56] Unfortunately, the reports often did not clearly describe their testing methods, and it is known that the testing protocols, the use of practice tests, and the course configuration can affect the measured outcomes.[58] The NETT[46] employed a uniform testing protocol, though varied course configurations, and compared LVRS patients to medical patients over time. The surgically treated patients were significantly more likely than the medically treated patients to show improvement in 6-min walk distance, though the mean improvement was small. In both groups, 6-min walk distance declined over time.

Cardiopulmonary exercise test is a measure of maximum exercise performance, in which the patient sits on a stationary bicycle and peddles against a graded, increasing resistance. Maximum work rate and oxygen consumption level, as well as more specific indicators of cardiac and pulmonary function, are measured.

Within the NETT,[46] exercise capacity improved by more than 10 W (compared to baseline) in 28%, 22%, and 15% of surgical patients after 6, 12, and 24 months of follow-up, respectively, compared with 4%, 5%, and 3% of medical patients.

Improvements in Dyspnea and Quality of Life

Many investigators have reported improvements in dyspnea after LVRS. Brenner and coworkers[60] used the Modified Medical Research Council dyspnea scoring system with 145 patients before and after thoracoscopic LVRS. A majority of patients experienced a reduction in breathlessness after LVRS. Yusen and colleagues, using the same dyspnea scale, reported improved scores in 81%, 52%, and 40% of patients at 6 months, 3 years, and 5 years, respectively, in a cohort of LVRS patients.[60] Within the NETT,[46] dyspnea was measured with the University of California, San Diego, Shortness of Breath Questionnaire. On average, the patients reported that shortness of breath decreased following surgery and continued to decrease through 24 months of follow-up, while the medically treated patients reported slight increases in shortness of breath over time.

The NETT investigators also assessed the effect of LVRS on health-related quality of life, measured with the St George's Respiratory Questionnaire. A lower score is associated with better health-related quality of life, and within the NETT a decrease of 8 points or more was considered meaningful. At 24 months follow-up, 33% of LVRS patients had improvement in health-related quality of life, compared to 9% of medical patients.

The most recent report by the NETT researchers provides the most complete available information on short-term and long-term mortality associated with LVRS. The 90-day mortality rate in the surgery group was 7.9%, compared with 1.3% of the medical patients. Excluding the 140 patients who made up a previously identified high-risk group ($FEV_1 < 20\%$ predicted and either a diffusion capacity for carbon monoxide [D_{LCO}] $< 20\%$ predicted or homogeneous emphysema on CT scan), the 90-day mortality was 5.2% in the 538 surgery-group patients and 1.5% in the 540 medical-group patients.[46] This operative mortality is similar to the 6% mortality reported by Geddes and colleagues[61] and the 4.5% mortality in the case series report of Yusen and colleagues.[60] Longer-term follow-up (average 29.2 mo) within the NETT found no overall difference in mortality between the surgical and medical group patients.

Patient Selection

Selection of patients for LVRS has been a topic of considerable interest. Table 2 shows a guideline developed by this author from data in the literature summarized in a recent American Thoracic Society/European Respiratory Society COPD diagnosis and treatment guideline[38] and shows indications, contraindications, and the "ideal candidate" for LVRS.

Much of the information regarding patient selection for LVRS comes from the NETT, a study that was able to identify groups of patients who had different risks of mortality and likelihood of improving quality of life and exercise capacity.[46] Those findings are summarized in Figure 2. The factors in the preoperative evaluation that were able to separate out patients with different responses were upper-lobe versus non-upper-lobe distribution of emphysema, and low versus high exercise capacity measured by cardiopulmonary exercise test after all patients had completed pulmonary rehabilitation. Low exercise capacity was defined as $\leq$ 25 W maximum exercise capacity for female patients and $\leq$ 40 W maximum exercise capacity for male patients. Patients with predominantly upper-lobe emphysema and low exercise capacity showed improved long-term survival following LVRS, compared with medically treated patients. Conversely, patients with predominantly non-upper-lobe emphysema and high exercise capacity had poorer long-term survival following surgery, compared to medically treated patients. In the remaining 2 subgroups (upper-lobe-predominant emphysema with high exercise capacity or non-upper-lobe-predominant emphysema with

Table 2. Lung-Volume-Reduction Surgery Indications, Contraindications, and "Ideal Candidate"

Indications	Contraindications	"Ideal Candidate"
Severe functional limitation despite maximal medical therapy	Co-morbid illness	*All of the preceding indications AND*
Non-smoker for at least 3 mo	Substantial untreated cardiac disease	Upper-lobe emphysema and cycle-ergometry exercise capacity $<$ 25 W (women) or $<$ 40 W (men) while breathing F_{IO_2} of 0.30
Completed pulmonary rehabilitation (6–12 wk)	Cancer other than basal cell or squamous-cell skin cancer within the last 5 years	*All of the preceding indications WITHOUT*
Post-bronchodilator $FEV_1 < 45\%$ of predicted	Diseases in other organs increasing surgical risk	Older age
RV $>$ 150% of predicted	BMI $>$ 31.1 kg/m^2 (males) or 32.3 kg/m^2 (females)	Co-morbid illness
TLC $>$ 100% of predicted	$FEV_1 < 20\%$ of predicted and either	Pulmonary hypertension
$P_{aO_2} > 45$ mm Hg	$D_{LCO} < 20\%$ of predicted or Homogeneous emphysema on CT scan	Frequent respiratory-tract infections or chronic bronchitis
$P_{aCO_2} < 60$ mm Hg	Pulmonary-artery hypertension	
Post-pulmonary-rehabilitation 6-min walk distance $>$ 140 m	Systolic $>$ 45 mm Hg or Mean $>$ 35 mm Hg	
	Prednisone $>$ 20 mg/d	

Data from Reference 38
FEV_1 = forced expiratory volume in the first second
RV = residual volume
TLC = total lung capacity
BMI = body mass index
D_{LCO} = diffusing capacity of the lung for carbon monoxide
CT = computed tomography

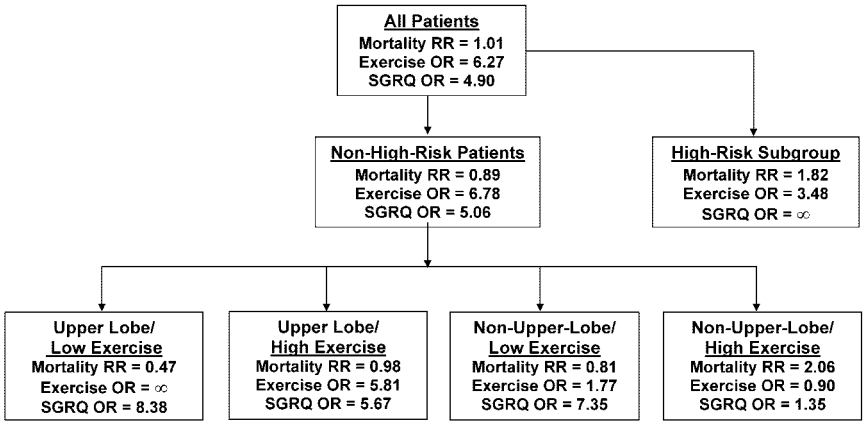

Fig. 2. National Emphysema Treatment Trial (NETT) sub-group results summary. Mortality RR = relative risk of mortality with lung-volume-reduction surgery (LVRS) versus medical arm of trial. Exercise OR = odds ratio of gaining $>$ 10-W exercise improvement on maximal cycle ergometry following LVRS. SGRQ OR = odds ratio of decrease of $\geq$ 8 points on the St Georges Respiratory Questionnaire following LVRS. Low exercise = $<$ 25 W on cycle ergometer (women) and $<$ 40 W (men). (Data from Reference 46)

low exercise capacity), long-term survival was not different between surgically and medically treated patients. There were also subgroup differences in exercise capacity and quality-of-life outcomes. There is concern about the application of these subgroup findings to clinical practice, as they were based on secondary analyses of the NETT data.[62,63]

In summary, the ideal candidate for LVRS is an individual with severe emphysema who has upper-lobe-predominant emphysema and markedly impaired exercise capacity. Other groups may benefit from the procedure, but their results are likely to be less good.

Lung Transplantation

The first human lung transplant was attempted in 1963. Unfortunately, the results from the initial efforts were poor, and it was not until the 1980s that more widespread attempts at lung transplantation were undertaken, with the development of an effective anti-rejection medication, in the form of cyclosporine. The number of programs performing single-lung transplantation, double-lung transplantation, and heart-lung transplantation around the world has grown dramatically. The major factor that currently limits

the number of lung transplants is the shortage of donor organs. Currently, COPD is the most common indication for lung transplantation.

Surgical Procedure

Both single-lung transplantation and double-lung transplantation are potential procedures for patients with COPD. Exercise functional capacity after transplant is not significantly different between those who undergo single-lung transplantation versus double-lung transplantation, and because unilateral transplantation allows the potential for 2 recipients from a single donor, unilateral lung transplantation has been the preferred procedure. However, more recent data suggest that there may be a reduced incidence of primary graft failure and perhaps better overall outcomes in younger individuals with emphysema.[64] Patients with COPD and associated purulent lung disease (bronchiectasis or marked daily sputum production) must undergo double-lung transplantation because of the risk of infection of the allograft by secretions from the native lung.[65] Single-lung transplantation is a simpler procedure, performed via lateral thoracotomy incision. The bilateral procedure is performed either via median sternotomy or via a subcostal "clam shell" incision. About 20% of patients undergoing bilateral transplantation will require cardiopulmonary bypass.[66]

Outcomes

Survival rates for patients undergoing lung transplantation for COPD appear to be somewhat better than for those with other lung diseases.[67] Reports about survival differ, but it appears that 1-year survival is approximately 90%,[68] 2-year survival is 65–90%, and 5-year survival is as low as 41–53%.[69] Most early deaths following lung transplantation are related to infectious processes. Late mortality is related to obliterative bronchiolitis, a process thought to be a form of chronic rejection. Whether lung transplantation in COPD provides a survival benefit remains unclear. Hosenpud and colleagues[70] compared survival curves of COPD patients waiting for transplant to those who underwent transplant and found that the survival curve following transplant was never greater than for those who continued to wait on the transplant list. Although this is not a scientific controlled trial, it is the best data available. Therefore, benefits from lung transplantation must be looked at in terms of functional and quality-of-life benefit.

Substantial improvements in pulmonary function,[64,71] exercise capacity,[72] and quality-of-life assessments[73] have routinely been found. Spirometric improvement has been seen almost uniformly following lung transplantation. Single-lung transplantation appears to result in less spirometric improvement than double-lung transplantation.[69] Near-normal values can be expected in lung function following double-lung transplantation.[68] It is interesting to note, how-

Table 3. Lung Transplant Indications, Contraindications, and "Ideal Candidate"

Indications	Contraindications	"Ideal Candidate"
Advanced COPD	Active malignancy within 2 years (except basal or squamous-cell skin cancer)	*All of the preceding indications AND*
Symptomatic despite maximal medical therapy	Substance addiction within 6 mo	Highly motivated individual
High risk of death within 2–3 y	Substantial dysfunction of extrathoracic organs	Excellent social support
COPD-specific (one or more)	HIV infection	*All of the preceding indications WITHOUT*
FEV_1 < 25–30% of predicted	Hepatitis B antigen positive	Symptomatic osteoporosis
Pulmonary-artery hypertension	Hepatitis C with biopsy-proven evidence of liver disease	Oral steroids > 20 mg/d
Right-ventricular failure		Invasive mechanical ventilation
P_{aCO_2} > 55 mm Hg		Colonization with fungi, resistant organisms, or atypical mycobacteria
Severe functional limitation, but preserved ability to walk		
Suggested Age Limitations		
Age < 55 y for heart-lung transplantation candidates		
Age < 60 y for bilateral-lung-transplantation candidates		
Age < 65 y for single-lung-transplantation candidates		

Data from Reference 38
LVRS = lung-volume-reduction surgery
COPD = chronic obstructive pulmonary disease
FEV_1 = forced expiratory volume in the first second
HIV = human immunodeficiency virus

Table 4. Proposed Criteria for Selection of LVRS Versus Lung-Transplant in Patients With COPD

Lung Transplant	LVRS	LVRS or Lung Transplant, or LVRS followed by Lung Transplant
Purulent Obstructive Disease Bronchiectasis More than 1/4 cup of phlegm per day Associated pulmonary-artery hypertension and/or right-heart failure Absence of hyperinflation: TLC < 100% of predicted or RV < 150% of predicted FEV_1 < 20% of predicted with either homogeneous emphysema or D_{LCO} < 20% of predicted (NETT high-risk subgroup) Non-upper-lobe emphysema with low exercise capacity P_{aCO_2} > 55 mm Hg P_{aO_2} < 50 mm Hg 6-min walk distance < 300 feet	Age > 65 y, with upper-lobe emphysema and low exercise capacity Age > 65 y, with upper-lobe disease and high exercise capacity Age > 65 y, with non-upper-lobe disease and low exercise capacity Age < 65 y, with FEV, 30–45% of predicted but disabling symptoms despite maximal medical therapy	Age < 65 y and meets criteria for both transplant and LVRS

LVRS = lung-volume-reduction surgery
COPD = chronic obstructive pulmonary disease
TLC = total lung capacity
RV = residual volume
FEV_1 = forced expiratory volume in the first second
D_{LCO} = diffusing capacity of the lung for carbon monoxide
NETT = National Emphysema Treatment Trial

ever, that exercise performance is essentially equivalent for those who receive either single-lung transplantation or double-lung transplantation.[68,74] It appears there is exercise limitation due to peripheral muscle function impairment, which may be caused by cyclosporine.[75]

Regarding quality of life and health status following lung transplantation among patients with COPD, Gross et al noted significant improvements in scores on the Medical Outcome Study Health Survey, the Index of Well-Being, and the Karnofsky Performance Status Index at 6 and 12 months following transplantation.[73] TenVergert et al found scores on the Nottingham Health Profile at 4 months after lung transplantation that were comparable to the general population.[76]

Patient Selection

Individuals with COPD who are candidates for lung transplantation are those who are predicted to have a survival of 2 years or less. Natural history data for COPD are imprecise, but generally accepted criteria include those whose FEV_1 falls below 25–30% of predicted, or when there is a rapid decline in lung function, substantial hypoxemia, hypercapnia, and secondary pulmonary hypertension despite maximal medical therapy. Table 3 details indications, contraindications, and the "ideal" lung-transplant candidate, and was developed by this author from data in the literature summarized in a recent American Thoracic Society/European Respiratory Society COPD diagnosis and treatment guideline.[38] Candidates for single-lung transplantation should be less than 65 years of age, and double-lung transplant candidates should be less than 60 years of age. Candidates should be free of other important comorbidities. Optimal candidates should 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. The preoperative weight should ideally be between 70% and 130% of predicted, and pre-transplant osteoporosis (a common finding among COPD patients) must be aggressively corrected to reduce the risk of postoperative fractures. Patients who are mechanically ventilated have been shown to do poorly and are generally not considered to be candidates for lung transplantation.[77] Candidacy for those who have undergone previous thoracic surgical procedures must be reviewed on a case-by-case basis. Previous talc instillation or pleurectomy are relative contraindications because of the risk of operative bleeding. Oral steroid therapy prior to transplant should be no greater than the equivalent of 20 mg of prednisone daily, as greater amounts impair postoperative healing.

There is substantial overlap between candidates for lung transplant and LVRS, with some individuals being candidates for both procedures. Guidelines on this are lacking. Table 4 shows one possible approach to this issue. In summary, it appears that lung transplantation can provide

symptom and functional improvement for those with severe emphysema who qualify and are motivated to undergo this difficult procedure. Whether there is a survival benefit for those with COPD who undergo lung transplantation remains unclear.

Conclusion

The 3 surgical options currently available for patients with advanced COPD are (1) giant bullectomy, (2) LVRS, and (3) lung transplantation. Each of the options has different indications, although there is some overlap, particularly between LVRS and lung transplantation. It is quite likely that further scientific evaluation of these surgical techniques will lead to more clearly defined indications for the procedures.

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