

Pulmonary Rehabilitation for Patients Who Undergo Lung-Volume-Reduction Surgery or Lung Transplantation

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Introduction

Rationale for Pulmonary Rehabilitation Prior to Lung Volume Reduction Surgery or Lung Transplantation

Benefits of Pulmonary Rehabilitation Prior to LVRS or Lung Transplantation

Clinical Benefits of Pulmonary Rehabilitation Versus LVRS

Pulmonary Rehabilitation Following LVRS or Lung Transplantation

Program Content of Pulmonary Rehabilitation for LVRS or Lung Transplantation

Summary

Patients preparing for or recovering from lung-volume-reduction surgery (LVRS) or lung transplantation represent a selected group of patients with advanced chronic respiratory disease. Such patients typically have severe ventilatory limitation and disability and are at high risk of preoperative and postoperative complications. Pulmonary rehabilitation is an ideal setting in which to: address the patient's questions and knowledge-deficits regarding his or her disease and its treatment; ensure that the patient understands the nature, potential benefits, risks, and expected outcomes of the surgery relative to medical therapies, and; prepare physically and emotionally for the surgery. Pulmonary rehabilitation also may improve survival to and/or outcomes of LVRS and transplantation, at least in part by stabilizing and improving the patient's exercise tolerance and muscle function. Further work is needed to determine whether pulmonary rehabilitation can augment the benefits and outcomes of LVRS or lung transplantation, reduce postoperative complications, or improve patient survival to or following the surgery. Key words: lung-volume-reduction surgery, LVRS, lung transplantation, chronic respiratory disease, pulmonary rehabilitation. [Respir Care 2008;53(9):1196–1202. © 2008 Daedalus Enterprises]

Introduction

Pulmonary rehabilitation is now recognized widely as an important component of care of patients with chronic

obstructive pulmonary disease (COPD),¹⁻³ because it improves dyspnea, exercise tolerance, and quality of life. Patients preparing for or recovering from lung-volume-reduction surgery (LVRS) or lung transplantation repre-

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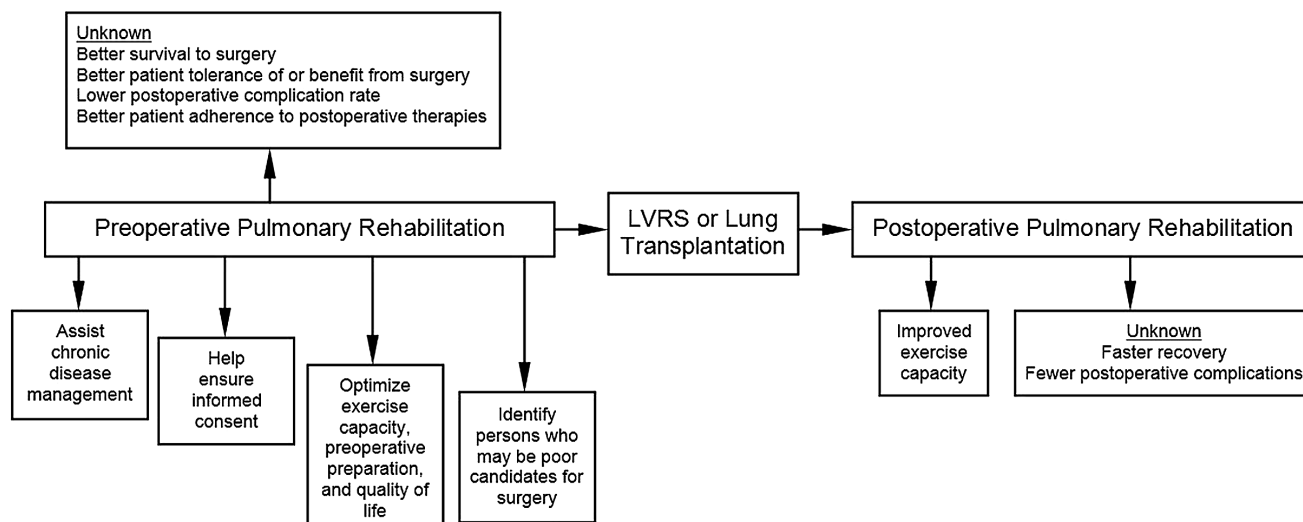


Fig. 1. Schema summarizing the rationale for and benefits of pulmonary rehabilitation for patients who undergo lung volume reduction surgery or lung transplantation.

sent a highly selected group of patients with advanced emphysema and other forms of severe chronic respiratory disease, such as pulmonary fibrosis, pulmonary artery hypertension, and cystic fibrosis (CF). Among all persons with chronic lung disease these patients tend to have the greatest degree of ventilatory limitation and disability, and are at high risk of preoperative and postoperative complications. Efforts to physically and emotionally prepare the patient for surgery may reduce the risk of complications and improve patient-centered outcomes. Postoperative rehabilitation also may hasten recovery. Preoperative and postoperative pulmonary rehabilitation is an ideal means by which these goals can be realized. Pulmonary rehabilitation is routinely provided to such patients and is recommended as a component of care in current clinical practice guidelines.^{1,3,4} This paper will discuss the role of pulmonary rehabilitation in the care of patients preparing for or recovering from LVRS or lung transplantation (Figure 1).

Rationale for Pulmonary Rehabilitation Prior to LVRS or Lung Transplantation

There are several reasons why preoperative pulmonary rehabilitation is important for patients preparing for LVRS or lung transplantation. First, patients with advanced, severe COPD and other forms of chronic lung disease are medically complex. Typically they have severe dyspnea and activity limitation, and also commonly have several medical and psychological comorbidities and must manage complicated multi-drug treatments, supplemental oxygen, and/or use noninvasive nocturnal assisted ventilation during their day-to-day lives. Optimal chronic disease man-

agement and patient adherence to a complex treatment regimen require that the patient understand the disease and the benefits and risks of their medications and oxygen therapy, and that they learn to adjust their lifestyle to manage symptoms and incorporate therapies into daily living. Unfortunately, the small amount of time allocated to routine out-patient primary care or pulmonary clinic visits is usually inadequate to address all of the patient's questions and concerns and to assure that the patient fully understands the disease and treatment.

Also, LVRS and lung transplantation are major surgical procedures that require thoracic incisions and carry substantial risk of perioperative complications and mortality.⁵⁻¹³ During LVRS, regions of non-functional lung are resected (typically from the upper lobes) to improve expiratory flow, lung elastic recoil, gas exchange, and respiratory mechanics, and to reduce work of breathing, and thus reduce dyspnea and improve exercise tolerance and quality of life.^{9,10,13} During transplantation, one (single-lung transplant) or both (double-lung transplant) lungs are removed entirely and replaced with a donor lung(s). Patients must understand the nature of the surgical procedure, the potential benefits and expected outcomes relative to their current medical therapies, as well as perioperative and postoperative risks. Following lung transplantation the patient must have frequent follow-up visits, undergo periodic bronchoscopies, and take a complex regimen of immunosuppressive medications that carry risk of both infectious and non-infectious medical complications.^{7,8,14} Lung-transplant recipients may also develop acute and/or chronic allograft rejection, including bronchiolitis obliterans, which may be debilitating and/or lead to the need for repeat transplantation or death.¹⁵ Although complete un-

derstanding of these issues is essential for the patient to provide informed consent to undergo these surgeries, again, there is little time in the routine out-patient clinical setting to address these issues as fully as needed. Pulmonary rehabilitation, wherein the patient works with a multidisciplinary team of health-care providers over a several-week period, is an ideal setting in which patients can learn about their illness, the ways it causes their symptoms, the expected benefits and potential adverse effects of their medications, and how to best prepare for and learn techniques to facilitate recovery from surgery in a way that can ensure more fully informed consent to undergo the procedure.

Third, patients with COPD and other forms of advanced lung disease have exercise limitation. Although the basis of exercise limitation in persons with advanced lung disease is multi-factorial, skeletal-muscle dysfunction (characterized by muscle fiber atrophy, reduction in type I endurance fibers, reduced capillarization, impaired oxidative capacity, and altered energy metabolism) is a major contributor to exercise impairment in patients with COPD.¹⁶ This muscle dysfunction leads to reduced muscle strength, endurance, and maximal oxygen consumption, and/or to contractile muscle fatigue,^{16,17} and contributes to early onset of anaerobic metabolism (lower lactate threshold) during exercise.^{16,18} Early-onset anaerobic metabolism in turn contributes to greater ventilatory demand. Although less studied to date, emerging evidence has identified that skeletal-muscle dysfunction is also present in patients with other forms of chronic respiratory disease. For example, some patients with CF have impaired muscle strength, reduced arm work capacity, and lower peak anaerobic power, compared to healthy age-matched persons.¹⁹⁻²¹ Also, quadriceps weakness is an important determinant of exercise capacity of persons with pulmonary fibrosis.²²

Pulmonary rehabilitation is well-known to improve exercise tolerance/capacity of patients with COPD,^{1,2,4} in substantial part by stabilizing and/or improving skeletal-muscle dysfunction and in turn by improving the pattern of breathing.^{1,23-27} Mounting evidence also indicates that pulmonary rehabilitation also improves exercise tolerance in patients with disorders other than COPD, including interstitial lung disease/pulmonary fibrosis,²⁸⁻³¹ CF,^{32,33} and pulmonary hypertension.³⁴ Importantly, impaired exercise capacity is a well-recognized and important predictor of thoracic surgical outcomes and survival among patients with COPD and other forms of advanced lung disease. Low exercise tolerance (6-min-walk distance < 200 ft, inability to climb one flight of stairs, maximum oxygen consumption < 10 mL/kg/min) is associated with poor lung-resection-surgery outcomes in patients with COPD.³⁵⁻³⁸ In patients with COPD undergoing LVRS, Szekely and colleagues found that persons with baseline 6-min-walk distance < 200 meters had greater risk of hospitalization for more than 21 days and lower survival

than did persons with better baseline exercise tolerance.³⁹ Lower exercise capacity is also associated with lower survival among patients with COPD,⁴⁰ diffuse lung disease,^{41,42} CF,⁴³ and pulmonary hypertension,⁴⁴ so low exercise capacity may impact survival to transplantation. Given its proven ability to improve exercise tolerance of patients with COPD and other respiratory disorders, pulmonary rehabilitation may potentially improve survival to LVRS and/or transplantation, and improve outcomes of these surgeries.

Finally, patient selection for LVRS and lung transplantation includes assessment of the patient's ability and willingness to adhere to the medical regimen and commitment to rehabilitation, which is particularly important in light of the limited availability of lung transplant donors. Preoperative pulmonary rehabilitation may identify persons who are non-compliant, too debilitated to complete pulmonary rehabilitation, or lack adequate family/social support, and therefore who may be poor or suboptimal candidates for surgery.

Benefits of Pulmonary Rehabilitation Prior to LVRS or Lung Transplantation

Despite severe ventilatory limitation, patients with severe emphysema can participate safely in and achieve benefit from pulmonary rehabilitation prior to LVRS. Debigaré and colleagues found that a minimally supervised, home-based pulmonary rehabilitation program undertaken 5 times per week for 12 weeks significantly improved peak work rate, 6-min-walk distance, maximum oxygen consumption, endurance time, muscle strength, and quality of life in 23 patients with COPD preparing for LVRS.⁴⁵ Similarly, Ries and colleagues found significant improvement in peak work rate (during cycle ergometry), 6-min-walk distance, quality of life, and dyspnea among the 1,218 patients with severe emphysema who underwent pulmonary rehabilitation before and after their randomization to receive either LVRS or routine medical care in the National Emphysema Treatment Trial (NETT).^{46,47} Clinical improvements following pulmonary rehabilitation were greater in patients with no prior rehabilitation experience than in persons who had undergone prior rehabilitation.⁴⁶ Interestingly and importantly, in the NETT, 20% of the patients achieved a change in exercise tolerance following pulmonary rehabilitation of a magnitude great enough so as to alter their patient subgrouping, which was subsequently found to be predictive of outcome from the surgery,⁴⁶ and some patients improved sufficiently following pulmonary rehabilitation that they opted to withdraw from the trial.⁴⁶ Indeed, a patient's decision whether to proceed with LVRS may depend on the degree of improvement in their symptoms, exercise tolerance, and quality of life following pulmonary rehabilitation alone. No particular in-

creased incidence of adverse events has been reported during pulmonary rehabilitation in persons whose COPD is severe enough that they are preparing for LVRS, as compared to persons with more moderate severity of disease.

Unlike consideration of LVRS, the benefits of pulmonary rehabilitation cannot alter the need for lung transplantation, since transplantation is considered only for persons with the most severe disease, whose survival without transplantation is expected to be limited. Nevertheless, pulmonary rehabilitation is usually required, and a majority of lung-transplantation candidates participate in preoperative pulmonary rehabilitation. Studies to date of pre-transplantation pulmonary rehabilitation have been small and uncontrolled, and various program components and outcomes measures have been used.⁴⁸⁻⁵¹ Gains in exercise endurance (assessed via 6-min-walk test) and general well-being have been reported. Randomized controlled trials of the benefits of pulmonary rehabilitation before transplantation are lacking. Given the proven benefits of pulmonary rehabilitation for patients with COPD and other forms of advanced lung disease, withholding the opportunity for pulmonary rehabilitation prior to transplantation could be considered unethical, so it is not likely that a randomized controlled trial of pre-transplantation pulmonary rehabilitation will be conducted. Currently it is not known whether pulmonary rehabilitation increases survival to surgery, increases patient tolerance of surgery, reduces postoperative complications, increases benefit from the surgery, or increases patient adherence to medications and exercise after LVRS or lung transplantation. Further research is needed to address these important questions.

Clinical Benefits of Pulmonary Rehabilitation Versus LVRS

Several studies have investigated the benefits of LVRS versus several weeks of comprehensive pulmonary rehabilitation (including exercise training and education) in patients with severe emphysema. Consistent with other pulmonary rehabilitation outcomes research, pulmonary rehabilitation significantly improved exercise tolerance,⁵²⁻⁵⁴ health status,^{47,53,54} and dyspnea,⁴⁷ in the absence of significant changes in lung function. As compared with pulmonary rehabilitation, LVRS in highly selected patients provided significantly better improvement in lung function (forced expiratory volume in the first second and/or lung volumes),^{47,52-56} walking endurance (6-min-walk distance and/or maximum exercise capacity^{52-54,56}), and patient-reported quality of life.^{53,54,56} Among patients with severe emphysema who underwent out-patient pulmonary rehabilitation prior to randomization to either LVRS or continued medical therapy in the NETT, greater gains were seen in exercise capacity and health-related quality of life in the LVRS group.⁴⁷ A significant

survival benefit from LVRS (compared to continued medical therapy alone) was also noted among patients with upper-lobe-predominant disease who also had low exercise tolerance at trial entry.⁴⁷ Notably, however, no survival benefit of LVRS was found among patients with upper-lobe-predominant disease and high baseline exercise tolerance or non-upper-lobe-predominant disease with low baseline exercise capacity, and a survival disadvantage from LVRS was identified among patients with non-upper-lobe-predominant disease and high baseline exercise capacity in the NETT.⁴⁷ Moreover, a high risk of death from LVRS was noted among candidates with forced expiratory volume in the first second < 20% of predicted who also had either homogeneous distribution of emphysema or diffusing capacity for carbon monoxide < 20% of predicted.⁵⁷ Overall, therefore, the decision as to whether a patient with COPD should consider LVRS versus pulmonary rehabilitation with medical therapy alone depends on multiple factors, including the severity and distribution of emphysema, baseline pulmonary function and gas exchange, exercise tolerance, age, comorbidities, required medical therapy, desired effects versus potential risks of the intervention and patient preference, and the clinical response to preoperative pulmonary rehabilitation.

Pulmonary Rehabilitation Following LVRS or Lung Transplantation

Exercise intolerance and functional disability often persist following LVRS. Several factors probably contribute to this continued impairment, including baseline skeletal-muscle dysfunction, time needed to achieve postoperative improvement in lung function (peak benefit following LVRS at 6–12 months after surgery), inactivity/immobility associated with the perioperative period, and/or time recovering from any complications. Although controlled data are lacking, pulmonary rehabilitation is typically administered to patients following LVRS in an effort to hasten recovery and optimize functional status. Exercise impairment also persists following lung transplantation, despite restoration of normal or near-normal lung function and gas exchange. This persistent impairment despite restoration of lung function underscores the relevance of non-ventilatory factors in exercise impairment in lung-transplantation candidates. Medications required post-transplantation can impair vasodilation and/or contribute to anemia, and cardiac denervation can contribute to exercise impairment among persons with heart-and-lung transplants.^{58,59} Importantly, skeletal-muscle dysfunction, including structural and functional alterations similar to those found in patients with stable COPD (including a lower proportion of type I fibers, impaired oxidative capacity, impaired energy metabolism, earlier fall in muscle pH during exercise, and impaired ability of skeletal muscle

to extract oxygen) have been identified in recipients of lung transplants with various lung diseases.^{60,61} Many lung-transplant patients stop exercise because of leg fatigue, as opposed to dyspnea,⁵⁸ and maximal cycle work capacity after lung transplantation correlates better with isokinetic cycling work capacity than with pulmonary function.⁶² Muscle weakness may be present for 1–3 years,^{63–66} and peak exercise capacity may be reduced to 40–60% of predicted up to 2 years after transplantation.^{58,59} Medications used in the post-transplant patient can worsen muscle function; corticosteroids may induce myopathy, and the immunosuppressants tacrolimus and cyclosporine can impair mitochondrial function and oxygen utilization.⁵⁹ Few studies have reported the outcomes of comprehensive pulmonary rehabilitation in lung-transplant recipients, but the existing data show that aerobic endurance exercise training can improve exercise capacity in those patients. Stiebellehner and colleagues found that 6 weeks of aerobic exercise training (via cycle ergometry) performed at 30–60% of each patient's baseline heart rate reserve within 6–18 months of surgery significantly improved peak oxygen uptake and peak power output among 9 lung-transplant recipients.⁶⁷ Consistent with results from exercise training in patients with stable COPD, the exercise training also reduced minute ventilation at comparable work loads. Of note, restoration of normal or near-normal lung function and gas exchange and elimination of substantial ventilatory limitation to exercise may enable lung transplant recipients to exercise at higher intensity, and in turn to achieve greater gains in aerobic fitness and exercise capacity during postoperative exercise training, as compared with gains they were able to make during pre-transplantation pulmonary rehabilitation.

Program Content of Pulmonary Rehabilitation for LVRS or Lung Transplantation

No formal guidelines exist regarding the optimal methods of exercise training or education components of pulmonary rehabilitation for patients preparing for or recovering from LVRS or lung transplantation. Most programs in the United States adhere to the current general recommendations that pulmonary rehabilitation include multimodality aerobic and strength exercise training of the lower and upper extremities 2–3 times per week for 6–8 weeks,^{1,2,4,68–70} and that the intensity of exercise be guided by patient tolerance. Data from patients with stable COPD show that high-intensity aerobic exercise training at 60–80% of maximal work capacity leads to greater physiologic gain in aerobic fitness than does lower-intensity training,^{2,18} so many pulmonary rehabilitation providers aim for such high-intensity training targets with their LVRS/transplant patients. Interval-type exercise training, wherein short periods of high-intensity exercise are alternated with

Table 1. Suggested Topics for Education Sessions in Pulmonary Rehabilitation for Patients Preparing for Lung-Volume-Reduction Surgery or Lung Transplantation

Benefits/importance of preoperative and postoperative exercise
Energy conservation
Nutritional counseling
Management of anxiety and/or depression
Familiarization with lung-volume-reduction or transplant procedure
Preparation for the perioperative period: controlled cough, incentive spirometry, pain management
Medications/immunosuppressants, benefits, possible adverse effects and events
Wound care, chest tubes, drains, and valves
Mechanical ventilation
Post-discharge issues
Breathing strategies
Monitoring for signs of infection or rejection

brief periods of lower-intensity exercise or rest,^{71,72} is an effective alternative mode of exercise training for patients who cannot sustain continuous high-intensity exercise. Stretching, flexibility, and chest-mobility exercises may also be an important component of exercise after LVRS or transplantation.⁶⁹ In the pre-transplantation period, particular attention must be paid to safety considerations that are recognized to be potential issues during exercise training for patients with various disease states.^{1,73}

Education prior to or following LVRS/transplantation should emphasize topics that facilitate and optimize the patient's understanding of his or her disease, the medications/devices used in its therapy, the surgery, and methods to hasten recovery and minimize the risks of and recognize the signs of adverse postoperative events (Table 1).^{68,69,74}

Summary

A strong scientific rationale exists for providing comprehensive pulmonary rehabilitation to patients preparing for or recovering from LVRS or lung transplantation. Existing evidence suggests that pulmonary rehabilitation for such patients is feasible, safe, and effective, provided the patient's medical therapy is optimized, the patient is monitored for any signs of adverse events, and safety precautions appropriate for the patient's disease state are undertaken during exercise training. However, much more work is needed to determine whether pulmonary rehabilitation, by improving exercise tolerance and symptom management, can improve or augment the benefits and outcomes of LVRS or lung transplantation, reduce postoperative complications, hasten recovery, or improve survival to or following LVRS or lung transplantation.

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