Interstitial Lung Disease (ILD) is a heterogeneous group of pulmonary disorders characterized by inflammation and/or fibrosis of lung parenchyma. These diseases generally result in restrictive physiology and substantial gas exchange abnormalities. Common manifestations of ILD include exertional dyspnea, hypoxemia, which is often worse with activity or exercise, fatigue, deconditioning, and diminished quality of life.1-3

Patients with ILD may experience significant dyspnea and hypoxemia that inhibit normal function and safe exercise. Causes of dyspnea may include neuro-mechanical dissociation with reduced compliance and increased elastic recoil. Other factors associated with dyspnea in ILD include cardiovascular limitations, anxiety, depression, and ventilatory muscle weakness.1,4,5 Hypoxemia may occur in response to ventilation-perfusion abnormalities and diffusion impairment caused by capillary bed destruction. Exercise may increase ventilatory demand leading to shallow, rapid breathing. Reduced lung compliance and increased elastic recoil may limit increase in tidal volume, which normally occurs during exercise.1 The resulting decrease in length of respiratory cycle may reduce time for adequate inspiration resulting in dynamic hypoinflation.1 Similar to patients with chronic obstructive pulmonary disease (COPD), skeletal muscle dysfunction and weakness may occur in patients with ILD and emerging evidence suggests that this weakness may improve with exercise training.6-13

KEY WORDS

exercise training
interstitial lung disease
pulmonary rehabilitation

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INTERSTITIAL LUNG DISEASE AND PULMONARY REHABILITATION

Most of the evidence supporting the effectiveness of pulmonary rehabilitation (PR) and guideline development comes from studies of persons with obstructive
disorders such as COPD. Growing evidence also supports the effectiveness of PR in ILD and that PR is associated with significant improvement in dyspnea and function in this population. The American Thoracic Society/European Respiratory Society (ATS/ERS) defines PR as an “evidence based, multidisciplinary, comprehensive intervention for patients with chronic respiratory disease who are symptomatic and often have decreased daily life activities.”\textsuperscript{13} PR confers significant gains in symptom control, exercise capacity, and health-related quality of life despite negligible changes in pulmonary function by stabilizing or reversing systemic manifestations of chronic lung disease.\textsuperscript{13} Although the ATS/ERS consensus statement on PR includes chronic respiratory disease regardless of cause, the research base for PR effectiveness is primarily from studies of patients with COPD, where PR has been found to improve symptoms, quality of life, function, and healthcare utilization.\textsuperscript{14–20} Growing evidence also supports the effectiveness of PR in ILD.

**IMPACT OF PR ON ILD**

Although ILD is often refractory to conventional medical treatments, PR targets several areas of morbidity that can contribute to disability and impaired quality of life in ILD including deconditioning and symptoms of dyspnea (Table 1).\textsuperscript{6–13} A recent retrospective multicenter trial of 99 patients found significant improvement in dyspnea and 6-minute walk distance (6MWD) after PR, consistent with established clinically significant differences.\textsuperscript{13} In a separate randomized trial of 57 patients with ILD, patients receiving exercise training had statistically significant improvement in 6MWD and dyspnea compared with those receiving weekly telephone support.\textsuperscript{8} Nishiyama et al\textsuperscript{7} randomized 30 patients with idiopathic pulmonary fibrosis, a form of ILD, to 10 weeks of outpatient PR or standard therapy. They found significant improvement in 6MWD and the St. George’s Respiratory Questionnaire in the PR group. In a 2008 Cochrane review, Holland and Hill\textsuperscript{12} identified physical training as safe in patients with ILD and found improvement in 6MWD, dyspnea, and health-related quality of life after PR. Most studies have used multidisciplinary, outpatient programs including supervised exercise training and educational activities for 6 to 9 weeks.

Collectively, these trials demonstrate benefits of PR similar to those found in patients with COPD. The factors that determine responders versus nonresponders to PR in patients with ILD have yet to be established. One trial identified PR as beneficial regardless of age and baseline pulmonary function and was more pronounced in persons with lower baseline 6MWD.\textsuperscript{13} This is an area requiring additional research.

Safe and effective PR requires a multidisciplinary team approach that emphasizes collaborative patient self-management. A complete medical evaluation by a pulmonary specialist familiar with ILD diagnosis and management should be performed before beginning PR. Patients should be evaluated

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<th>Study</th>
<th>Subjects</th>
<th>Design</th>
<th>Results</th>
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<tr>
<td>Ferreira et al\textsuperscript{13}</td>
<td>99 ILD</td>
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<td>Ferreira et al\textsuperscript{8}</td>
<td>330 total (43 ILD)</td>
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**Table 1: STUDIES OF IMPACT OF PULMONARY REHABILITATION ON INTERSTITIAL LUNG DISEASE**

Abbreviations: BDI, Baseline Dyspnea Index; CRQ, Chronic Respiratory Disease Questionnaire; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; MRC, Medical Research Council; 6MWD, 6-minute walk distance; RCT; randomized control trial; SGRQ, St. George’s Respiratory Questionnaire; Shuttle, Shuttle walk test.
for comorbidities including pulmonary hypertension (PH), concomitant obstructive lung disease, cardiac disease, gastroesophageal reflux disorder, and mood disorders. Consideration should be given to consultation with a university-based ILD clinic or clinical center specializing in ILD. If significant PH is present that is out of proportion to the severity of ILD, consultation with a PH specialist should be considered for optimal treatment and exercise recommendations.

**STRUCTURE OF PR PROGRAMS IN ILD**

PR programs should be individualized to address the clinical needs, goals, and safety of each patient with ILD. PR clinicians should perform a thorough evaluation including medical history, assessment, and management of comorbidities, current exercise, oxygen use, and knowledge deficits in disease self-management strategies. PR staff should be familiar with physiologic and clinical features and interventions of ILD and PH including symptom management. Pre- and post-PR evaluation and testing should include objective measures of function such as the 6MWT or shuttle walk test with continuous oxygen saturation monitoring during testing to detect desaturation. Cardiopulmonary exercise testing may be recommended prior to PR particularly in patients with suspected underlying cardiac disease.

**EXERCISE TRAINING IN PATIENTS WITH ILD**

Optimal strategies for exercise training for patients with ILD have not been established. Patients with ILD require monitoring of oxygen saturation, dyspnea, and heart rate at rest and with exercise. Options for measuring dyspnea include the Borg scale, modified Borg scale, and visual analog scale. Many programs perform telemetry monitoring during the first exercise session and ongoing telemetry monitoring in patients with significant PH or cardiac abnormalities such as arrhythmias. Although exercise protocols have not been established for patients with ILD, progressive exercise routines should be based on patient symptom level including dyspnea and fatigue; physiologic findings such as adequate oxygenation, stable heart rate, and blood pressure; and results of 6MWT or cardiopulmonary exercise testing. With ongoing monitoring of clinical findings, multimodal exercise routines are generally appropriate including the use of treadmill, leg and arm ergometry, and other modes of aerobic and resistance training. Exercise should be stopped if the patient develops significant signs or symptoms (Table 2).

According to the American College of Chest Physicians/American Association for Cardiovascular and Pulmonary Rehabilitation evidence-based guidelines, exercise should include training of muscles of ambulation and strength training to increase muscle strength and muscle mass. Supplemental oxygen should be used during rehabilitative exercise training in patients with severe exercise-induced hypoxemia. General goals for exercise are to exceed 30 minutes per session. The individualized patient exercise prescription should include aerobic, resistance, and flexibility training; mode, intensity, duration; and home recommendations. Aerobic options may include walking or leg ergometry. Low-intensity exercise is recommended in the initial stages of exercise until clinical findings such as dyspnea levels, oxygen saturation, and heart rate support the safety of incremental increase in intensity to a moderate level based on clinical stability. Patients may initially exercise for up to 5 to 10 minutes duration depending on the level of deconditioning and clinical

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<th><strong>Table 2</strong> • INDICATIONS FOR CESSION OF EXERCISE IN PATIENTS WITH INTERSTITIAL LUNG DISEASE</th>
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<tr>
<td><strong>Chest pain</strong></td>
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<td><strong>Exertional hypertension</strong></td>
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<td><strong>Dizziness</strong></td>
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<td><strong>Severe dyspnea</strong></td>
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<td><strong>Significant hypoxemia</strong></td>
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**Abbreviation**: PVC, premature ventricular contraction.
response to exercise. Increased conditioning may allow many to progress to 30 or more minutes per day. Exercise parameters and home exercise programming should be established and communicated to the patient once these have been established in the PR setting. Patients also need instructions regarding indications for stopping exercise and the reporting of symptoms to their care providers. Interval training exercise routines require investigation in ILD to determine safety and effectiveness.

**OXYGEN MONITORING AND DELIVERY**

During PR sessions, patients with ILD should be regularly monitored for hypoxemia and dyspnea at rest and with exercise to detect oxygen desaturation. In hypoxemic COPD patients, oxygen has been found to improve survival, exercise, sleep, and cognitive performance with a therapeutic goal of oxygen saturation level of more than 90% during rest, sleep, and exertion.21 It seems reasonable to apply these parameters to patients with ILD in order to maintain adequate oxygen saturation in exercising muscles as well as to prevent exercise hypoxemia-induced increases in pulmonary artery pressure. For hypoxemic ILD patients, PR staff should facilitate patient use of safe and effective stationary and portable oxygen systems based on ongoing oxygen saturation monitoring at rest and with exercise. Patients with ILD require monitoring during physical activity while using ambulatory systems to ensure adequate oxygenation. Patients may require use of high-flow oxygen systems to adequately oxygenate during exercise. Patients with ongoing desaturation despite the use of high-flow oxygen require medical evaluation and management before resuming exercise.

**PATIENT EDUCATION**

Patient education should be individualized to meet the specific needs and goals of the patient and should focus on collaborative disease self-management, adherence to treatment, and transference of learning to the home setting.25 An individualized curriculum should be based on knowledge deficits identified during the initial evaluation. Areas of focus may include the following:

- oxygen use, safety, appropriate flow rates with exercise, ongoing monitoring, and use of portable systems;
- prevention, recognition, and management of exacerbations and pulmonary infections;
- energy conservation, pacing, and management of activities of daily living;
- symptom management including control of cough and symptoms of gastroesophageal reflux disorder;
- management of anxiety, panic, and mood disorders with identification of support system and community resources;
- medication actions, schedule, side effects, and adherence;
- preparation for lung transplantation and post-transplant rehabilitation; and
- advance directives and end-of-life care.

Most dyspnea control techniques have been developed to address dynamic hyperinflation associated with obstructive lung disease. It remains unclear if these techniques are effective in ILD.

An exacerbation is a sustained worsening of patient symptoms beyond normal day-to-day variation, often requiring a change in treatment. Patients should be instructed in strategies to prevent pulmonary infections, such as frequent hand-washing and appropriate vaccination, and to contact their physicians early in the course of an exacerbation. In addition, body composition abnormalities are common in chronic lung disease. Nutritional intake and physical activity habits should be addressed and an individualized intervention provided to enhance the benefits of formal PR.

Mood disorders such as major depressive disorder and general anxiety disorder are common in obstructive lung disease27,28 and should be assessed during the initial evaluation and subsequent rehabilitation sessions. These disorders often result in impairment in quality of life, function, and ability to perform activities of daily living. Psychosocial interventions can effectively reduce distress and facilitate adaptive coping. Interventions include breathing retraining, relaxation techniques, and stress management to reduce the anxiety and dyspnea. Establishing an adequate patient support system is recommended. Individuals experiencing substantial impairment in psychological functioning should be identified and referred to a mental health provider for further evaluation and treatment.

Adherence to therapeutic interventions and transfer of education and exercise to the home setting is a crucial health behavior in the management of chronic respiratory disease. Interventions should focus on maximizing patient self-management capabilities and quality of life. Tools for evaluation of health-related quality of life include the St. George’s Respiratory Questionnaire,29 Chronic Respiratory Disease Questionnaire,30 and the Medical Outcomes Study Short Form–36.31
Patients with respiratory failure whose disease is not potentially reversible may have poor outcomes after mechanical ventilation. Palliative care and hospice services are often poorly understood and underutilized in patients with chronic lung disease. Patients with ILD should be advised of options for end-of-life decision making including advance care planning and palliative care options to promote effective and appropriate decision making and the use of healthcare resources.

Patients who have undergone lung transplantation require heightened caution regarding prevention of infection because of their immunosuppressed state. This includes avoidance of persons with signs or symptoms of infection, frequent hand-washing of both patient and staff, and regular cleansing of exercise and monitoring equipment. Posttransplant patients normally use surgical facemasks while in the PR facility until discontinued by the transplant team. Following surgery, patients are normally advised not to lift more than 5 lbs; to avoid abducting arms above the shoulder; and avoid excess twisting, pushing, or pulling for 12 weeks following surgery or when otherwise permitted by the transplantation team.

PH IN THE REHABILITATION SETTING

The incidence of PH in ILD has been reported to range from 4% to 43%. PH is associated with progressive elevation in pulmonary vasculature resistance, worsening pulmonary vasoconstriction, poor right ventricular response to rapid increase in afterload, and greater oxygen defect resulting in dyspnea and activity limitation. An echocardiogram is a useful tool for screening for PH. However, accurate diagnosis requires right heart catheterization.

Historically recommendations have been to limit exercise in this population. Availability of multiple target medical therapies may allow increase in functional ability in patients with PH. The exercise recommendation should be based on cardiopulmonary exercise testing and monitoring of signs and symptoms such as dyspnea and fatigue, tachycardia, oxygen saturation, and hypotension or hypertension. Patients should be undergoing regular medical follow-up and treatment of PH. Exercise should begin at low intensity and short duration, with careful, incrementally progressive submaximal levels. Sun et al demonstrated that symptom level may be used to determine safe submaximal exercise. Interval training should be avoided because of rapid changes in pulmonary hemodynamics and risk of syncope. Light-intensity resistance training is employed only with appropriate breathing patterns, avoiding the Valsalva maneuver. Exercise should not be performed if dizziness, presyncope, or chest pain is present. If the patient is undergoing vasodilator medication infusion, care must be taken not to disrupt the infusion.

SUMMARY

PR offers potential for improved function and symptom control in patients with ILD. A collaborative self-management approach provided by a multidisciplinary team is recommended. There is a need for larger trials of the impact of PR on ILD, including the impact on healthcare utilization, outcomes after lung transplantation, and survival. Future goals include the development of international guidelines for evidence-based practice of PR in ILD.

References


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