

# Long-Term Nonpharmacologic Management of Patients with Chronic Obstructive Pulmonary Disease

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A comprehensive treatment plan for managing patients with chronic obstructive pulmonary disease (COPD) involves appropriate use of nonpharmacologic as well as pharmacologic interventions. Nonpharmacologic intervention begins with an aggressive effort toward smoking cessation, which has been proven to slow the accelerated rate lung function that characterizes COPD and to decrease all-cause mortality in patients with COPD. Proper nutrition and regular exercise are vital for all patients. Some patients with documented hypoxemia from more severe disease may require long-term oxygen therapy. Pulmonary rehabilitation benefits most patients, and even surgical intervention with lung volume reduction surgery or lung transplantation may help a limited number of patients. This article reviews the nonpharmacologic interventions that may be used in conjunction with maximized pharmacologic therapy in the long-term management of patients with COPD. (*Clinical Cornerstone*®. 2004;6[Suppl 2]: S29–S34) Copyright © 2004 Excerpta Medica, Inc.

The treatment goals related to the management of chronic obstructive pulmonary disease (COPD) emphasize decreasing symptoms, improving exercise tolerance, slowing the accelerated annual decline in FEV<sub>1</sub> (forced expiratory volume in 1 second), preventing acute exacerbations, preventing and treating disease complications, and reducing both COPD-related and all-cause mortality. A significant first step in achieving many of these treatment goals is initiating an effective smoking cessation program. While smoking cessation does not lead to recovery of lost lung function, it does cause the accelerated annual rate of decline in FEV<sub>1</sub> to revert toward that of a

nonsmoking subject.<sup>1</sup> Smoking cessation or even a significant decrease in exposure to tobacco smoke also diminishes the patient's risk of mortality from other tobacco-related disease (heart attack, stroke, and cancer). Consequently, abstaining from or decreasing smoking also lowers all-cause mortality. Smoking cessation interventions should include physician counseling as well as pharmacologic interventions and behavioral modification.<sup>2</sup> Antidepressants such as bupropion, used alone or in combination with nicotine replacement products, are effective smoking cessation aids. Use of nortriptyline, though not approved by the US Food and Drug Administration for smoking

cessation, has successfully led to tobacco abstinence in patients and is also considered a first-line treatment for smoking cessation.<sup>3</sup> All forms of nicotine replacement products increase long-term rates of smoking cessation and relieve nicotine cravings and withdrawal symptoms. Smoking cessation rates increase further when antidepressant and nicotine replacement therapy is combined with formal behavioral counseling.

### KEY POINT

**Smoking cessation or a significant decrease in smoking does not lead to recovery of lung function; however, it does cause the accelerated annual rate of decline in FEV<sub>1</sub> to revert toward that of a nonsmoking subject and it reduces mortality.**

In addition to smoking abstinence or reduction, several other nonpharmacologic therapies have been shown to be beneficial when included in the treatment paradigm for long-term management of COPD. These nonpharmacologic modalities are used in addition to optimal daily dose of 1 or more bronchodilators and vaccines, and include continuous long-term oxygen therapy, pulmonary rehabilitation, optimization of nutrition and maintenance of body mass index (BMI), and in the small percentage of patients with severe COPD and emphysema who qualify, surgical therapy with lung volume reduction surgery (LVRS) or lung transplantation.<sup>4</sup>

### LONG-TERM OXYGEN THERAPY

There are well-established criteria for long-term oxygen therapy in COPD patients with significant hypoxemia. Patients who meet these criteria derive substantial benefit from long-term oxygen therapy. Specifically, if patients are compliant with the regimen prescribed (ie, 15–18 hours a day minimum for those on continuous oxygen therapy), long-term oxygen therapy has been shown to prolong survival, lower red blood cell mass, and improve hemodynamics, cognitive function, and exercise capacity. These improvements do not occur when long-term oxygen therapy is administered to patients who do

not meet the specific hypoxemia criteria. In a randomized trial, 55% of patients with hypoxemia who were treated with oxygen continuously for 15 hours per day were alive after 5 years of follow-up compared with only 33% of hypoxemic patients who did not receive oxygen therapy.<sup>5</sup> The daily duration of oxygen therapy is also an important determinant of survival. Results of a randomized study showed that survival was twice as high in patients who received oxygen for 24 hours per day compared with those who received it for 12 hours per day.<sup>6</sup> Thus, patients with a resting PaO<sub>2</sub> <55 mm Hg (SaO<sub>2</sub> <88%)—or <60 mm Hg (SaO<sub>2</sub> <89%) for patients with cor pulmonale, right ventricular failure, or erythrocytosis—should receive long-term continuous oxygen therapy for 15 to 18 hours per day. If the requisite PaO<sub>2</sub> occurs only during exercise or sleep, oxygen supplementation should be provided only during these activities. Patients should be reminded that the purpose of long-term oxygen therapy is not to relieve their dyspnea, but rather to prolong their survival.<sup>5–7</sup>

### PULMONARY REHABILITATION

Regular personal exercise should be recommended for all patients with COPD, regardless of severity, including those with an FEV<sub>1</sub> of just under 80% of predicted. A comprehensive pulmonary rehabilitation program involves more than just scheduled exercise; it includes education about COPD, work and acts of daily living simplification and energy conservation, smoking cessation, breathing strategies, and end-of-life issues. The benefit of patient education is reflected not so much in improvements in lung function or exercise performance but rather in patients being able to adapt to their limitations, to cope effectively with their illness, and to deal with sensitive issues surrounding end-of-life care. A monitored (SaO<sub>2</sub>, EKG), supervised, individualized exercise program in which oxygen supplementation is provided for *documented* SaO<sub>2</sub> <88% during exercise is also a part of pulmonary rehabilitation programs.<sup>8–10</sup> The exercise component of pulmonary rehabilitation should occur at least 3 times per week for at least 2 months. Although high-intensity endurance and strength training are preferred,<sup>11</sup> low-intensity exercise is also effective.<sup>4,8,10,12</sup> The concentrated program must be followed by long-term maintenance exercise or the beneficial effects of the pulmonary

rehabilitation program may diminish within months.<sup>9</sup> Documented outcomes of pulmonary rehabilitation include reduced dyspnea,<sup>12,13</sup> increased exercise capacity,<sup>13</sup> improved health-related quality of life,<sup>12,13</sup> reduced acute exacerbation rate<sup>14</sup> and hospitalizations,<sup>8</sup> reduced mortality,<sup>15</sup> and improved maximal oxygen consumption. Significant reductions in mortality as a result of pulmonary rehabilitation plus long-term maintenance treatment are achievable; in a single-center study survival was ~45% higher over 3 years in patients undergoing pulmonary rehabilitation with long-term maintenance compared with patients who refused pulmonary rehabilitation

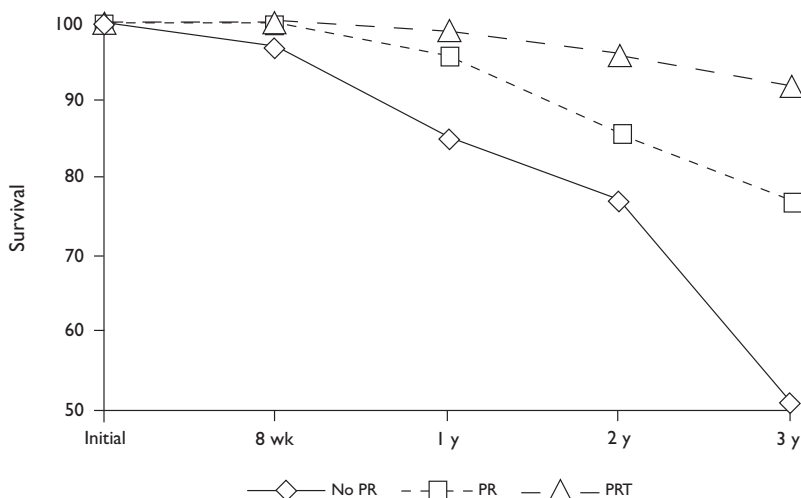
### KEY POINT

**Pulmonary rehabilitation plus long-term maintenance exercise and optimized medical treatment can lead to significant reductions in the frequency of acute exacerbations, hospitalizations, and premature mortality.**

(Figure 1).<sup>15</sup> However, pulmonary rehabilitation does not improve arterial blood gases or pulmonary function (FEV<sub>1</sub>, forced vital capacity [FVC]) testing results.<sup>10</sup>

### NUTRITION AND WEIGHT MANAGEMENT

Good nutrition is very important in the management of COPD patients. Patients with COPD who are obese may experience more dyspnea on exertion or even at rest, but patients who lose lean body mass are at increased risk for mortality. There are multiple reasons for low BMI in COPD patients, with pulmonary cachexia, including decreased appetite and caloric intake due to breathlessness, increased caloric use by respiratory muscles and high work of breathing, an imbalance of hormones, such as leptin, which control satiety and hunger, and inflammatory mediators that are highly catabolic, such as tumor necrosis factor- $\alpha$ . A low BMI is a predictor of mortality in patients with COPD.<sup>16</sup> In pulmonary cachexia, the cross-sectional area of the quadriceps muscle on MRI is a better predictor of prognosis than is the FEV<sub>1</sub>; however, the FEV<sub>1</sub> remains the most cost-effective and sensitive modality for the early detection of COPD, long before this stage of the disease is manifested.



**Figure 1.** Relationship between pulmonary rehabilitation (PR) and survival in patients with chronic obstructive pulmonary disease. Adapted with permission.<sup>15</sup>

- ◇— No PR: Patients declined pulmonary rehabilitation
- -□- - PR: Completed pulmonary rehabilitation program
- -△- - PRT: Completed pulmonary rehabilitation program, and continued long-term maintenance exercise

Nutritional support, while desirable in COPD patients who are losing weight, may result in only fat increase for some patients.<sup>16,17</sup> An increase in fat-free mass, which is presumed to be muscle, is required to improve prognosis for patients with a low BMI. High caloric intake plus exercise can improve muscle mass in some patients, and adding anabolic steroids can increase fat-free mass with corresponding significant increases in survival, particularly in those patients with low BMI at baseline (Figure 2).<sup>16-18</sup>

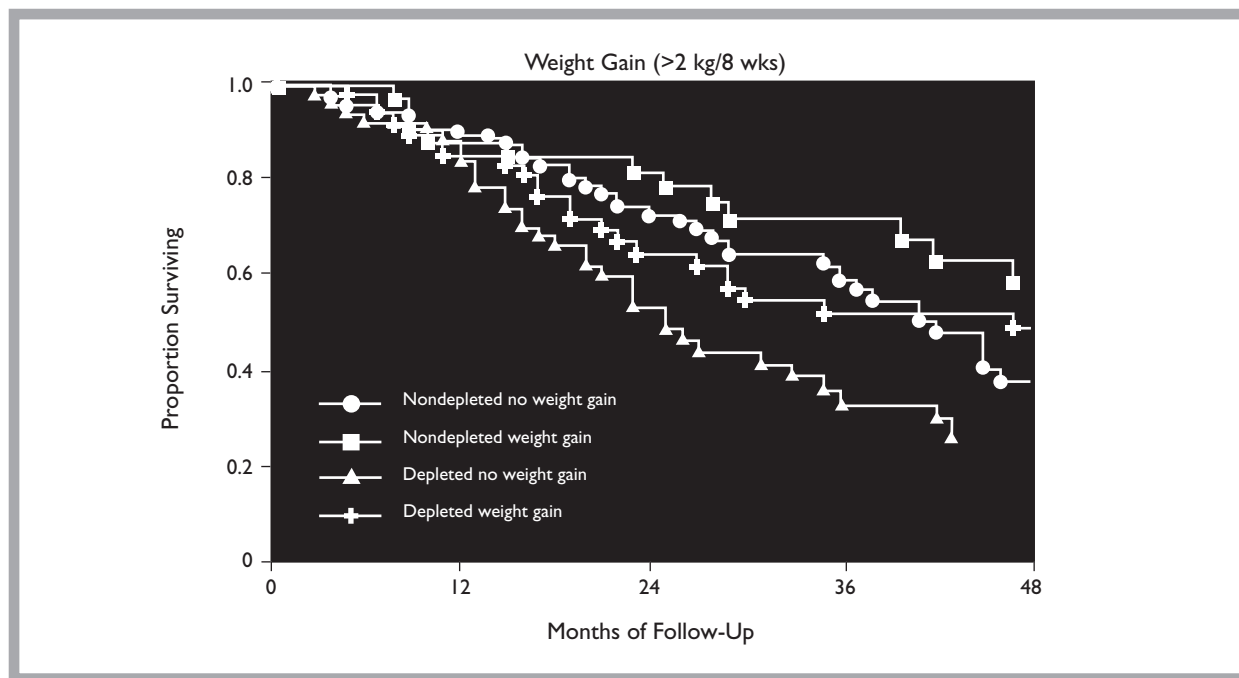
**SURGERY**

Surgical interventions such as LVRS or lung transplantation may be beneficial for some patients with COPD who have advanced disease and significant emphysema, though this is a small group of patients.

**Lung Volume Reduction Surgery**

The National Emphysema Treatment Trial (NETT), sponsored by Medicare and the National Institutes of Health, was a 60-month trial that compared outcomes in patients with COPD managed with comprehensive medical treatment versus those managed surgically with LVRS in addition to comprehensive medical management.<sup>19</sup> These patients with CT scan and physiologically documented sig-

nificant emphysema, completed a comprehensive pulmonary rehabilitation program and underwent evaluation of postpulmonary rehabilitation exercise capacity before being randomized to medical or surgical treatment groups. Results indicate that LVRS benefits some patients, but at a cost of \$190,000 per quality adjusted life-year salvaged.<sup>20</sup> The mortality probability of LVRS was similar to that of aggressive medical therapy at 60 months, although early mortality was higher in the surgical treatment group. A group of unacceptably high-risk patients with diffuse emphysema and an FEV<sub>1</sub> <20% of predicted or a diffusion capacity <20% of predicted were identified as having an unusually high mortality risk associated with surgery; therefore, LVRS is not appropriate for patients with these pulmonary indices.<sup>21</sup> Patients with predominantly upper-lobe emphysema who had low postrehabilitation exercise capacity had better outcomes with LVRS than those patients with other characteristics; however, patients with nonfocal emphysema and/or higher exercise capacity did less well. Compared with medical therapy, LVRS improved exercise capacity in all patient groups, and improvement was more pronounced for patients with predominantly upper-lobe emphysema and low exercise capacity.<sup>22,23</sup>



**Figure 2.** Relationship between weight gain and mortality risk in patients with chronic obstructive pulmonary disease who have low body mass index. Adapted with permission.<sup>16</sup>

**KEY POINT**

**Increased caloric intake plus exercise and anabolic steroids can increase fat-free mass (muscle mass) in COPD patients, which increases BMI and significantly improves survival.**

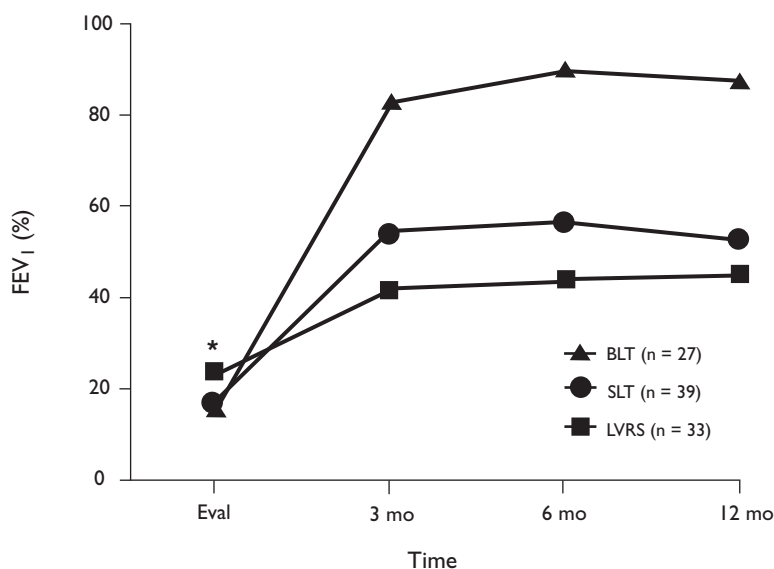
**Lung Transplantation**

COPD patients with far advanced disease, an FEV<sub>1</sub> <25%, and/or frequent acute exacerbations despite maximized medical therapy and pulmonary rehabilitation, may benefit from lung transplantation. Patients who are <65 years old and able to walk well enough to complete a pulmonary rehabilitation program are candidates for transplantation, provided they have no severe comorbidities. Approximately 20% of centers will now transplant COPD patients aged >65 years if comorbidities do not disqualify them for the transplant. The presence of comorbidities is common, and often limits patients' access to lung transplant rosters. Data from most lung transplant centers show that lung

transplantation improves FEV<sub>1</sub> and quality of life and probably prolongs survival. Comparison of 12-month postsurgery FEV<sub>1</sub> after LVRS, single-lung transplantation, or bilateral transplantation strongly favors bilateral lung transplantation. Even single-lung transplantation, which is performed more often than bilateral transplantation because of the shortage of donor organs, produces greater improvement in FEV<sub>1</sub> at 1 year than does LVRS (Figure 3).<sup>24,25</sup>

**SUMMARY**

Nonpharmacologic therapies play an important role in the management of COPD. Long-term continuous oxygen supplementation is of considerable benefit in selected patients. Virtually all patients with COPD, as early as Stage II (moderate COPD; FEV<sub>1</sub> <80% of predicted but >50% of predicted) by GOLD criteria, can benefit from a comprehensive pulmonary rehabilitation program, which should be combined with a follow-up maintenance exercise program; unfortunately this approach is rarely used in asymptomatic disease and, in general, is underutilized. Nutritional support is another important component of an aggressive COPD management program. Increased caloric intake plus exercise and anabolic steroids can increase fat-free mass in COPD patients, which in



**Figure 3.** Effect of lung volume reduction surgery (LVRS) versus single lung transplantation (SLT) or bilateral lung transplantation (BLT) on forced expiratory volume in 1 second (FEV<sub>1</sub>). \**P* < 0.05 for LVRS vs SLT; *P* < 0.001 for LVRS vs BLT; *P* < 0.001 for LVRS vs LVRS eval; *P* < 0.001 for LVRS vs SLT and BLT. Adapted with permission.<sup>25</sup>

turn increases BMI and significantly improves survival. Recently published results from a large clinical trial suggest that LVRS may improve outcomes compared with medical therapy in a small highly selected subgroup of patients, but at a significant cost. In patients with advanced disease, low FEV<sub>1</sub>, and frequent exacerbations despite maximized medical therapy, lung transplantation provides greater benefit than LVRS in terms of FEV<sub>1</sub>. Nonpharmacologic therapies, in combination with smoking cessation, aggressive daily bronchodilator therapy, and vaccines can help achieve most of the treatment goals of long-term COPD management.

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