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Invited Review

Is there a role of pulmonary rehabilitation in extrapulmonary diseases frequently encountered in the practice of physical medicine and rehabilitation?

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ABSTRACT

There is a group of diseases such as low back pain, osteoporosis, fibromyalgia and obesity for which pulmonary rehabilitation can be applied. Although these diseases do not directly impact the lungs, respiratory dysfunction occurs through various mechanisms during the disease process and complicates the underlying primary disease. Respiratory dysfunction and spirometric abnormalities have been observed from the early stages of these diseases, even without obvious signs and symptoms. These patients should be carefully evaluated for pulmonary problems as a sedentary lifestyle may hide the presence of respiratory symptoms. Once pulmonary problems have been detected, pulmonary rehabilitation should be added to the routine treatment of the primary disease.

Keywords: Pulmonary rehabilitation, respiratory dysfunction.

Although most research on the effects of Pulmonary Rehabilitation (PR) has focused on chronic obstructive pulmonary disease (COPD), respiratory societies recognize that PR has an important role in all patients with respiratory symptoms associated with decreased functional capacity and quality of life.

Although there may not be primary involvement of the pulmonary system, many extrapulmonary diseases such as neurological diseases, osteoporosis (OP), fibromyalgia (FM), and low back pain (LBP), cause varying degrees of respiratory disorders. Respiratory dysfunction in these diseases occurs for various reasons, complicates the primary disease, and causes disability by impairing activity, decreasing social participation, and reducing quality of life, and increasing morbidity and mortality. Respiratory problems in these patients may be a direct result of disease, disease progression and/or medication.

In addition to the findings of the primary diseases, respiratory dysfunction can cause many signs and symptoms such as dyspnea, cough, difficulty coughing, retention of secretions, atelectasis, pneumonia, hypoxia, hypercapnia, sleepdisordered breathing, respiratory failure, deconditioning, early fatigue, reduced exercise tolerance and functional capacity, and thereby quality of life in these patients is significantly diminished.

However, little attention is generally paid to the respiratory system during the examination of these diseases, probably because these patients are usually free from respiratory symptoms or significant lung disease. It should be considered that most of these patients can reduce respiratory symptoms by limiting

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their physical activity, so respiratory symptoms can be masked. Nevertheless, respiratory dysfunction and spirometric abnormalities may be present from the early stages of these types of diseases, even without significant respiratory symptoms and signs.

Conditions and diseases that cause respiratory dysfunction in particular are neuromuscular diseases (NMDs), stroke, Parkinson's disease (PD), multiple sclerosis (MS), spinal cord injury (SCI), LBP, OP, FM, and obesity.

Furthermore, rheumatological disease with primary lung involvement should also be kept in mind. The lung is an important target in many rheumatological diseases such as rheumatoid arthritis, ankylosing spondylitis, scleroderma, myositis, and systemic lupus erythematosus. As extraarticular manifestation of rheumatological diseases, lung involvement may occur years after the musculoskeletal system findings, or it may be the first finding. These diseases can involve the parenchyma, pleura, airways, respiratory muscles, chest wall and vascular structures in the lung, resulting in severe morbidity and even mortality. Rheumatological diseases with pulmonary involvement are beyond the scope of this chapter.[1,2]

This review will first examine how respiratory problems occur in these diseases. Then, PR applications to prevent, reduce, and treat respiratory problems in these patients will be reviewed based on the literature.

CLINICAL AND RESEARCH CONSEQUENCES

Neuromuscular disease

As a heterogeneous group of disorders, the umbrella term of NMD includes a variety of diseases such as motor neuron diseases (e.g., amyotrophic lateral sclerosis [ALS] and Post-polio); motor nerve root (e.g. hereditary motor sensory neuropathy [HSMN]) and peripheral nerve disorders (e.g. chronic peripheral neuropathy); neuromuscular junction diseases (e.g. myasthenia gravis), and muscle disorders (myositis, myopathies and dystrophies).

Although it is an extrapulmonary disease, NMD may affect the respiratory system leading to respiratory failure. Respiratory muscle weakness (inspiratory, expiratory, bulbar and accessory muscles), the mechanical effects of progressive scoliosis or rigid spine, and the decreased central respiratory drive in this disease result in respiratory problems.[3,4] The most common pulmonary problems seen in these patients are alveolar hypoventilation and gas exchange abnormality, upper airway obstruction, reduced efficiency of cough, secretion retention and increased risk of lower airway infection, aspiration lung disease, and reduced chest wall compliance.[3,4]

Pulmonary function test parameters such as slow vital capacity (VC), total lung capacity (TLC) and functional residual capacity (FRC) are found to be decreased and restrictive lung disease is observed in patients with NMD. The severity of restrictive ventilatory defect increases with the worsening of scoliosis. Due to the respiratory, peripheral (muscle weakness, fatigue and pain) and cardiac limitation, NMD patients have reduced exercise capacity. Initially, respiratory symptoms such as dyspnea and fatigue may occur only during exercise, but in later periods, they may occur during activities of daily living or at rest.[3,4]

Traditional PR exercise programs may not be appropriate for these patients because of the nature of NMD. It has also been postulated that exercise may have harmful effects by increasing muscle damage in this disease. Attention should be paid to the follow-up of the harmful effects of exercise such as pain, myoglobinuria and serum creatine kinase concentration. Thus, PR should be prescribed on an individual basis depending on the type of neuromuscular disease, the rate of disease progression, and the type of exercise.[3-11]

A PR program for this patient population may include airway clearance techniques, respiratory muscle training, peripheral muscle exercises (aerobic, strengthening and combined aerobic and strengthening), breathing retraining (diaphragmatic breathing (DB), pursed lips breathing, glossopharyngeal breathing), neuromuscular electrical stimulation (NMES), and assisted ventilation. Respiratory muscle training is contraindicated in hypercapnic NMD patients, and those with vital capacity <25% predictive and very rapidly progressive NMD such as ALS. Pulmonary rehabilitation exercises should be performed under close supervision as there may be cardiac involvement in some NMDs, such as muscular dystrophies. Balance and proprioceptive training could be included in a PR program as balance and posture are affected in patients with NMD. The PR exercise program should also aim to increase task-specific performance. Varying levels of evidence have shown peripheral (aerobic, strengthening and

combined) and respiratory muscles exercise training to be effective in PR for NMD.[3-11]

Parkinson's disease

Parkinson's disease is a progressive neurodegenerative disease associated with symptoms such as tremor, postural instability, bradykinesia and rigidity. The symptoms can be of motor and non-motor character such as impaired gait and balance, frequent falls, muscle stiffness, sensory and cognitive deficits. Respiratory abnormalities have been observed in patients with PD since its first description. Possible causes of pulmonary problems in PD are the stiffness of the chest inhibiting mechanical respiratory movements, deficiency of dopamine, which is effective in facilitating respiration at the central level, and the extrapyramidal involvement of the striated upper airway musculature limiting airflow. The medications used to treat this disease can also result in respiratory dysfunction.[12-14] For all these reasons, lung volume and ventilation decrease in these patients and a wide variety of respiratory problems can develop. These include restrictive and obstructive ventilatory defects, upper airways obstruction, respiratory muscle weakness (inspiratory and expiratory muscles), abnormal ventilatory control (reduced response to hypercapnia), diaphragmatic dyskinesia and pleuropulmonary complications, and sleep breathing disorder.[12-14] Respiratory problems have been reported to contribute to morbidity and mortality in these patients.[12-15] The important point to consider is that most patients are asymptomatic despite having abnormal pulmonary function tests.

The patient may have symptoms such as exercise dyspnea, fatigue, cough and sputum production, daytime sleepiness due to nocturnal hypoxia, and acute stridor without evident clinial respiratory dysfunction. A higher proportion of patients with PD die from pneumonia than in the general population.[12-15]

Respiratory muscle training (inspiratory and expiratory), breathing strategies (lung recruitment maneuvers, glossopharyngeal breathing, incentive spirometry, DB, air-shifting techniques), posture training, and aerobic, strength, and combined exercise training applications have been used for PR in these patients. After the training program, positive effects have been observed on pulmonary function test parameters (minute ventilation [VE], tidal volume [TV], VC, and maximal inspiratory pressure (MIP) and maximal expiratory pressure [MEP] as measures the strength of respiratory muscles, positive expiratory pressure levels, peak cough flow, inspiratory muscle endurance, perception of dyspnea, chest amplitude, lung expansion, the ability to produce an effective cough and exercise capacity. Moreover, a significant correlation has been reported between improvement in MIP and inspiratory muscle endurance and decreased perception of dyspnea with inspiratory muscle training.[12-18]

Multiple sclerosis

Multiple sclerosis is a chronic demyelinating disease of the central nervous system and manifests with different symptoms according to the plaque location in the nervous system. Degeneration of motor neurons causes weakness and atrophy of the peripheral muscles and similar changes also occur in the respiratory muscles. Consequently, respiratory complications can occur early during the course of the disease and are associated with the neurological impairment. Both acute and chronic respiratory failure can be encountered in the MS process. Infections and respiratory complications are the main causes of mortality in this population.[19-22] A variety of respiratory problems including respiratory muscle weakness and spasticity, sleep disorder breathing, central sleep apnea, central respiratory dysregulation or neurogenic swallowing disorders have been demonstrated in these patients. Respiratory muscle weakness and spasticity may lead to reduced lung volume, inefficient ventilation, impaired carbon monoxide diffusion capacity, ineffective cough and retention of secretions. The decrease in expiratory muscle strength is more significant compared to inspiratory muscles, which impairs cough efficiency and increases the risk of lung infection, atelectasis and acute respiratory failure.[20,23] A restrictive ventilatory pattern is obtained on pulmonary function test of these patients. Respiratory dysfunction in patients with MS is also a contributing factor to the worsening of motor performance and/or spasticity, fatigue, cognitive impairments, exercise capacity and cardiorespiratory fitness.[24]

Respiratory muscle training (expiratory and inspiratory muscles), lung recruitment maneuvers (active, passive or mechanically asssisted techniques), breathing strategies (slow deep breathing, DB, air-shifting techniques, positive expiratory pressure device),upper extremity training (accessory muscles training), and aerobic, strength and combined exercise training have been used to improve

respiratory dysfunction in the MS population.[16,24-26] These rehabilitation approaches have been found to be beneficial on pulmonary function test parameters (forced expiratory volume in one second [FEV1], forced vital capacity [FVC], peak expiratory flow rate [PEF], MIP, MEP), peak cough flow, balance tests, six-minute walk test, cardiorespiratory fitness, mobility, and symptoms of fatigue and depression.[16,24-26]

Stroke

There are varying degrees of weakness in the upper and lower extremities, trunk and respiratory muscles on the hemiplegic side following stroke. Partial or total weakness of the diaphragm, intercostal and abdominal muscles have also been reported after stroke. Due to the weakness, chest wall kinematics are altered and an atypical breathing pattern is observed. The diaphragm is elevated with less movement on the affected side.[27-30] EMG activities of diaphragm and intercostal muscles have been reported as reduced and diaphragm muscle thickness measurement with ultrasound has shown diaphragm dysfunction. Ventilatory dysfunction is associated with reduced VC, inspiratory capacity (IC), TLC, maximum inspiratory capacity and especially expiratory residual volume (ERV) in these patients. Due to the respiratory muscle weakness and altered chest wall kinematics, cough is impaired, which is responsible for an increased risk of aspiration and chest infection.[31] Nearly half of patients with stroke report dyspnea.[28,30] Significant correlations have been found between measures of inspiratory strength and dyspnea and quality of life in this population.[27-30]

Respiratory muscle training (expiratory and inspiratory muscles), controlled breathing techniques (DB, air-shifting techniques, pursed lip breathing, segmental breathing/lateral costal breathing), airway clearance techniques (incentive spirometry), posture exercises, and aerobic, strength and combined training are the modalities applied for PR in these patients. It has been reported that pulmonary function test results (FVC, FV1, IC, TV, MIP, MEP and maximum voluntary ventilation [MVV] as a measure of the endurance of respiratory muscle), exercise capacity (peak oxygen consumption [VO_{2peak}]), inspiratory muscle endurance, fatigue level, respiratory muscle strength, lung volume, respiratory flow, and trunk control ability have been reported to be improved after the training program.[16,27-34]

Spinal cord injury

Pulmonary problems are one of the important causes of morbidity and mortality in this population. Denervation of the respiratory pump (reduced respiratory muscle force and fatigue), impaired cough, increased secretions and bronchial tone, impaired ventilatory control, and decreased chest wall and lung elasticity are the main causes of deterioration of pulmonary functions and complications in these patients.[35-45] While the lifetime rate of all pulmonary complications is 50-67%, this rate has been found to be 85% in tetraplegics and 65% in paraplegics.[39] Pneumonia, lung collapse and respiratory failure are the three most common complications in the early period.[37,39] Respiratory problems such as dyspnea, impaired cough, respiratory failure, pneumonia, atelectasis, pulmonary thromboembolism and sleep respiratory disorders also persist in the chronic phase of the injury.[37,39]

The degree of respiratory impairment is strongly related with the severity of neurological impairment and the time since injury. Respiratory problems are more common in high level complete SCI.[40,42] Reduced lung function and lower respiratory muscle strength following SCI mechanically restrict ventilation and lead to a decrease in cardiorespiratory fitness and maximum exercise capacity. It has been suggested that respiratory muscle training in the early stages following spinal cord injury may reduce pulmonary complications, increase exercise capacity, and preserve respiratory functions by delaying thoracic stiffening.[43-45]

Respiratory muscle training (voluntary isocapneic hyperpnoea, inspiratory resistive loading, inspiratory threshold loading), controlled breathing techniques (DB, air-shifting techniques, pursed lip breathing, glossopharyngeal breathing), airway clearance techniques (active cycle of breathing techniques, autogenic drainage, forced expiratory techniques, postural drainage, incentive spirometry, assisted cough, mechanical insufflation-exsufflation [MI-E] machine), lung recruitment maneuvers (active, passive or mechanically asssisted techniques), neuromuscular electrical stimulation [NMES] (abdominal muscles, phrenic nerve or diaphragm), upper extremity training (resistance training, circuit resistance training, cycle ergometer, wheelchair propulsion), abdominal muscle training maneuvers (abdominal belt, abdominal drawing-in maneuver), and aerobic, strength and combined exercise training

have been investigated extensively as a PR mode in SCI patients.[35-45] It has been reported that these rehabilitative approaches have varying degrees of beneficial effect on pulmonary function parameters (FVC, VC, IC, TV, FEV1 and VE peak), diaphragm thickness, respiratory muscle strength and endurance, resting and exercising respiratory function, and peak aerobic exercise performance (power output and VO_{2peak}).[35-45]

Osteoporosis

In patients with OP, kyphosis (dowager hump) may be a sign of multiple vertebral compression fracture, particularly wedge fractures. The progressive collapse of the fractured osteoporotic vertebral body causes an increase in the kyphosis angle (anteroposterior diameter of thorax), narrowing of the distance between the xiphoid and pubis, and a change in the position of the thoracic cage, all of which reduce the amount of space in the chest, mobility of the rib cage, and expansion of the lungs. Spinal and thoracic cage deformities impair the mechanics of the respiratory system and put the respiratory muscles at a mechanical disadvantage, which in turn, leads to a decrease in respiratory muscle efficiency. Consequently, pulmonary function, rib mobility, and respiratory muscle strength and endurance are significantly impaired in patients with OP due to the vertebral deformities, increased kyphotic angle, respiratory muscle activity impairment, postural deviation and pain.[46-51] Pulmonary function test parameters such as FVC, VC, IC and PEF have been found to be decreased in patients with OP.[46-51] The measurements of the respiratory muscles strength and endurance have also been determined to be reduced.[49,51,52] The decline in pulmonary function may be greater in patients with more severe kyphosis.[48] It has been shown that as the number of fractured vertebrae and the degree of kyphotic deformity increase, pulmonary function is more affected.[50] Results of the pulmonary function test in OP show a restrictive ventilatory pattern.[46,50,51] Disturbances in pulmonary function may cause dyspnea, fatigue and reduced exercise capacity in this population. Previous studies have shown a significant negative correlation between kyphosis and FEV1, FVC and aerobic exercise capacity. These studies suggested PR to prevent and reduce pulmonary dysfunctions.[48,51]

Although there are many studies investigating the presence and nature of respiratory problems in OP, research on preventing and reducing pulmonary dysfunction is scarce. In those studies, it has been shown that respiratory muscles and spinal exercise training (thoracic expansion, stretching, range of motion and posture exercises) improve respiratory muscle strength and endurance, dyspnea, exercise capacity, posture, chest expansion, spine range of motion, and angle of kyphosis.[52,53]

Fibromyalgia

Multiple symptoms and comorbidities such as fatigue, sleep disturbance, impaired cognition, anxiety, irritable bowel, headache, and respiratory symptoms have been reported associated with FM.

Compared with healthy control subjects, respiratory problems such as dyspnea, decreased thoracic mobility, impaired respiratory mechanics, decreased respiratory muscle endurance and strength, and reduced cardiorespiratory fitness have been reported in these patients. Furthermore, it has been found that the inspiratory muscle strength is associated with the number of active tender points, fatigue, and thoracic mobility.[54-62]

Controlled studies have determined that spirometric values such as VC, FVC, and FEV1, are decreased despite normal lung functions in patients with FM. Moreover, MIP, MEP, and MVV, as measures of the strength and endurance of respiratory muscles, have been found to be lower than in healthy subjects.[57,58,59] Other studies have also found FEV1 and FEV1/FVC to be low. These results suggest that there may be an obstructive respiratory pattern in patients with FM.[57,58]

Although the exact mechanism of respiratory muscles dysfunction in patients with FM is not known precisely, it has been suggested that factors such as central nervous system dysfunction, impaired control mechanism at the supraspinal level, changes in neurohumoral activity, reduced thoracic mobility, physical inactivity, and reflex inhibition due to pain or fear of pain may play a role. It is thought that pain and tenderness in the thoracic and spinal muscles, especially the pain and stiffness of the upper half of the body, may impair the functions of the muscles involved in respiration, leading to the emergence of respiratory symptoms.[57,58]

Dyspnea and early fatigue in the achievement of activities that should be performed at maximum respiratory pressures limit the patient's performance and functional capacities. Adaptation to rest and a sedentary lifestyle due to the pain, fatigue, and dyspnea, and restriction of physical activity

and level of participation are the factors that contribute to the decrease in cardiorespiratory fitness. Furthermore, reduced respiratory muscles strength and endurance and restricted thoracic mobility are other factors that contribute to decreased cardiorespiratory fitness. Therefore, not only the pain and musculoskeletal system, but also respiratory problems should be considered in the rehabilitation of these patients.

Although there is no study directly showing the effects of respiratory training on lung function parameters in patients with FM, it has been shown that a breathing exercise program such as slow and deep breathing, air shifting techniques, pursed lip breathing, DB and thoracic expansion exercises have positive effects on pain, respiratory symptoms such as dyspnea, fatigue, anxiety, quality of sleep, functional capacity and quality of life. These results indicate that breathing exercises are an effective intervention in patients with FM.[54-56,60-62]

Low back pain

As a common movement system problem, LBP lasts longer than three months in 10% of cases, and chronic LBP develops. A significant correlation has been found between chronic LBP and the presence of dyspnea, asthma, non-specific respiratory disorders, allergies, and respiratory infections.[63]

Inspiratory muscles, specifically the diaphragm, in combined action with the abdominal and pelvic floor muscles, control intra-abdominal pressure and reduce stress on the spine. Therefore, inspiratory muscles play a key role in both breathing and posture control, and trunk stability.[64-68] Decreased postural control is associated with the presence of LBP. It has been shown that the diaphragm is in suboptimal function and in a higher position, exhibiting less excursion during inspiration in patients with LBP. Furthermore, it has been found that patients with LBP have decreased chest wall expansion and a predisposition to diaphragmatic fatigue compared to healthy people.[64-68]

Altered breathing patterns have been observed during lumbopelvic control tests in patients with chronic LBP. The breathing pattern changes when the trunk stabilizer muscles need to work in these patients. It is thought that the diaphragm's participation in respiration decreases when it helps postural control in patients with chronic LBP.[64-68]

The transversus abdominis (TA) and multifidus muscle together stabilize the spine during inspiration and the TA muscle alone during expiration. Biomechanically, these two muscles pull the ribs along their margins and increase the internal abdominal pressure, thereby helping the respiratory muscles to generate effective respiratory force. Approximately 20% of the work of breathing is done by the abdominal muscles.[65,67]

Studies have shown that co-contraction of abdominal muscles and the diaphragm stabilises the trunk by increasing intra-abdominal pressure and reducing stress on the spine, especially in the lumbar region. In chronic LBP, the coordination function between the TA muscle and the diaphragm is decreased.[64-68]

The imbalance and weakness of these muscles cause an increase in lumbar lordosis, and these postural changes and spinal instability impair the generation of effective respiratory forces, leading to alterations in maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) and respiratory dysfunction.[65] Moreover, pain and kinesiophobia indirectly contribute to the deterioration of pulmonary functions by causing plastic adaptations in the muscles without affecting maximum force production. In the long-term, plastic changes occur in the lung and chest wall in patients with LBP, and a pattern of restrictive lung disease may develop.

Compared with healthy control subjects, it has been reported that patients with LBP have lower MVV, FEV1 and FVC values and show restrictive type of ventilatory disorder. Despite these findings, there is no study in the literature directly showing the effects of respiratory training on lung function in patients with LBP.[66]

It has been reported that stabilization exercises alone will not increase the activation of the TA and multifidus muscles in patients with LBP, and it is also necessary to do breathing exercises. Previous studies have shown that respiratory exercises increase the activities of the abdominal muscles, with significant improvements in posture control and the severity of LBP as a result of training the inspiratory muscles.[64,67,68]

Obesity

Obesity disrupts the lung function by changing the physiology of the respiratory system with mechanical effects due to the accumulation of adipose tissue in the chest wall, abdomen and upper respiratory tract, and the effects of systemic inflammation.[69-72]

Obesity has been shown to be a risk factor for diseases such as obstructive sleep apnea syndrome, obesity hypoventilation syndrome, asthma, pulmonary embolism and aspiration pneumonia. Moreover, studies have shown that it is associated with chronic respiratory system diseases such as COPD.[70,72,73]

In normal breathing, the diaphragm contracts and pushes the abdominal contents down and forward, while the external intercostal muscles contract, pulling the ribs up and forward.[70,72]

In obese people, this mechanism is disrupted due to the accumulation of adipose tissue in the chest and abdomen, thereby limiting diaphragm mobility and rib movement. This causes a decrease in lung and chest wall compliance, changing the respiratory system dynamics, decreasing lung capacity, and creating a mechanical disadvantage in the movement of respiratory muscles (length-tension disadvantage) and deterioration in respiratory muscle functions.[69-72] The rapid and shallow breathing pattern in these individuals also results in increased respiratory oxygen consumption and respiratory workload.[70,71,73]

Changes in the diaphragm, chest cavity, and lungs cause restrictive pulmonary dysfunction. While FRC and ERV decrease in moderate weight gains, TLC, FEV1 and FVC decrease only in morbidly obese patients.[70,72-74] Respiratory muscle strength (MIP and MEP) is also decreased.[70-72,74] These changes become more pronounced as weight and BMI increase.

In general, obese individuals have decreased lung compliance, decreased lung volumes, increased airway resistance, decreased respiratory muscle strength, heterogeneity in ventilation distribution, increased pulmonary diffusion, and hypercapnic respiratory failure.[69-74]

All these factors together lead to an increase in inspiratory load and inspiratory effort, oxygen consumption, carbon dioxide production, and respiratory energy expenditure. Ventilatory needs increase during exercise. Exercise capacity is decreased due to respiratory muscle weakness and rapid fatigue, decrease in lung volumes and dyspnea.[69-75]

Many studies have shown that respiratory muscle training improves strength and endurance of respiratory muscles, exercise capacity (VO_{2peak}), functional exercise capacity (6 min walking test), quality of life, and dyspnea sensation in obese individuals.[69,71,75]

CONCLUSIONS

It should be taken into account that pulmonary function test impairments and respiratory problems may be present from the early stages in these diseases. Respiratory dysfunction in these patients causes shortness of breath and early fatigue during activities of daily living, limits cardiorespiratory fitness and exercise tolerance, and leads to a sedentary lifestyle. Therefore, the primary disease itself, respiratory problems, and a sedentary lifestyle may together contribute to reduced physical, recreational and social activities, and impaired health-related quality of life. These patients should be carefully evaluated for pulmonary problems, as a sedentary lifestyle may hide the presence of respiratory symptoms. Once pulmonary problems have been detected, pulmonary rehabilitation should be added to the routine treatment of the primary disease in order to eliminate respiratory symptoms and fatigue, and improve exercise capacity, physical activities, functional status and quality of life.

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