Fatigue in Cardiopulmonary Disease

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A very prominent symptom in most cardiac and pulmonary conditions is fatigue. It is present in up to 69% to 82% of patients with cardiac disease and up to 68% to 80% of patients with pulmonary disease.[1–4] This is second only to breathlessness in patients with both cardiac and pulmonary conditions. Whenever a patient with either of these conditions presents, a clinician should not only look to treat the underlying disease but also assess fatigue and seek to ameliorate the symptoms. Of great concern in cardiac and pulmonary disease is the issue of the role of central versus peripheral causes of fatigue. Clearly, the hypoperfusion, altered metabolism, hypoxemia, and hypercapnia seen in cardiopulmonary disease are obvious causes of peripheral fatigue, but the issue of central causes, although somewhat controversial, may need to be addressed as well. Depression, anxiety, and fear all play a role in the fatigue seen in patients with cardiopulmonary disease and need to be considered in treatment plans. The full discussion of the role of these central causes of fatigue is beyond the scope of this review, but it should be kept in mind whenever caring for patients with cardiopulmonary disease who have symptoms of fatigue.

The major direct causes of fatigue in cardiac and pulmonary patients fall into 3 areas, 2 of which are addressed closely in this review. The role of primary cardiac and pulmonary dysfunction as a cause of fatigue is critical to understand, as these conditions may be present in patients with other major conditions, such as stroke or peripheral vascular disease, and may further contribute to those disabilities. The role of medications is also important, especially in cardiac patients, as medications to prevent or reduce cardiac events often have side effects that cause fatigue. It is important for the clinician to be aware of these side effects and to instruct his or her patients about them. The third area, central causes of fatigue, also play an important role, but are not discussed here. Treatment modifications and exercise often help to ameliorate the limitations created by the fatigue and increase the patient's capacity

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to perform exercise with less functional limitations in the face of his or her disease and treatment limitations.

ASSESSMENT FOR FATIGUE IN THE CARDIOPULMONARY PATIENT

When a patient with cardiac or pulmonary disease presents, a common primary presenting complaint is fatigue. If a patient has dyspnea with exertion, he or she will also often disclose having a secondary symptom of fatigue if the clinician asks. These symptoms may actually be similar to depression, with a decrease in interest in usual activity, a feeling of exhaustion all the time, and a marked decline in overall activity. The decreased activity then accelerates the process of fatigue, and the patient progresses to immobility. The questions that a clinician needs to ask are rather straightforward during the examination.

1. Do you feel tired most of the time or all of the time?
2. Have you decreased participation in leisure activities or occupational activities due to exhaustion?
3. Have you had a decline in the level of activity that you do on a daily basis over the last 6 months?
4. Are there activities that you cannot perform at this time that you used to be able to do 6 months to a year ago, or before you fell ill, that you do not do now due to tiredness or exhaustion?
5. Do you go to bed earlier every day than you used to 6 months to a year ago or before you became ill?

If a patient answers yes to more than 1 of these questions, he or she is likely experiencing symptoms of fatigue.

Fatigue in Cardiac Disease

One of the most common causes of fatigue in cardiac disease is seen in association with myocardial infarction (MI). An unusual feature of the presentation of fatigue after acute MI is that it is much more common in women than in men. In a study of acute coronary syndromes, fatigue was a presenting complaint in 18% of women and 9% of men.[5] The post-infarct fatigue syndrome was also associated with more severe fatigue when present in women compared with that in men. The causes of this gender difference are not clear.[6] Still, it is important to recognize that fatigue and ''tiredness'' are atypical symptoms that are more common in women who are having an acute myocardial event, and if unexplained by other causes, they should make the practitioner consider evaluation for cardiac disease in individuals at risk.[7] Possible speculation on mechanisms includes depression and anxiety and effects of hormonal changes, but these have not yet been elucidated.

Chronically, after an acute myocardial event, fatigue is even more commonly seen than that during the acute onset of infarction. The hypothesized causes of this increase in fatigue are multifactorial and are still unknown in many cases. Likewise, fatigue is also more common in individuals with congestive heart failure (CHF) and is often a primary feature of the condition. Interestingly, the symptom of fatigue is often present even without overt cardiac dysfunction or evidence of either systolic or diastolic dysfunction in both patients with post-MI syndromes and in patients with CHF. This has led investigators to try to elucidate the possible causes of CHF-related fatigue but with little clear success. Since the symptoms of fatigue are often vague and can overlap with any other aspects of advanced cardiac disease, there is often a great deal of difficulty in distinguishing between physiologic effects of decreased cardiac

output, deconditioning, aging, and underlying mood disorders in specific cases.[8] Highlighting the central role of fatigue in CHF, several studies have defined CHF syndromes based on inclusion of at least 2 of the following: dyspnea, *fatigue,* orthopnea, paroxysmal nocturnal dyspnea, third heart sound, jugular venous distention, rales, and leg edema. The biological mechanisms of fatigue that may be a part of heart failure include the following possible areas.

A large component of fatigue in cardiac disease can come from depression, which is commonly seen in both CHF and after MI. As a correlation of psychological state and fatigue, for any patient with cardiac disease, the presence of depression greatly increases the likelihood of fatigue.[9–11] Additionally, the presence of depression increases mortality among all cardiac patients. It has been hypothesized that the mechanism for fatigue in depression and in cardiac disease may actually share several mechanisms. Some of the commonly shared abnormalities between patients with fatigue in cardiac disease (without depression) and patients with pure depression (without cardiac disease) include sympathoadrenal dysregulation, decreased heart rate variability, platelet dysfunction, and negative health behaviors. In addition to these changes, there also may be an attenuation of baroreflex control of heart rate and a contribution from immune system dysfunction.[12] Attenuation of the baroreceptor reflex and loss of heart rate variability are associated with premature death in patients with cardiac disease, highlighting the importance of treatment of the fatigue if at all possible, since this may be a treatable risk factor in cardiac disease. These studies also correlated the autonomic dysfunction seen in the depressed population with an increase in cardiovascular mortality, further strengthening the importance of efforts to improve the autonomic function.

Additionally, hypothalamic-pituitary-adrenal (HPA) axis abnormalities in purely cardiac and purely depressed patients can share similarities in the alterations seen in stress responses. To have a normal stress response, there needs to be a synthesis of corticotropin-releasing hormone (CRH) in the hypothalamus, which then causes an increase in adrenocorticotropic (ACTH) hormone via the hypothalamo-hypophyseal portal system. The ACTH in turn causes an increase in secretion of catecholamines and cortisol from the adrenal glands, which then regulate the HPA axis via a feedback mechanism. Depression and cardiac disease both cause an excess of cortisol secretion and alterations in CRH and ACTH concentrations—in a pattern that mimics stress. This leads to an excess of sympathetic tone, which in turn leads to a reflex increase in heart rate in the "stress mode," consistent with levels that are observed in untreated CHF and post-MI patients. In tandem with these findings is a decrease in heart rate variability in both depressed patients and in individuals with cardiac disease, which is known to be associated with increased risk of sudden death after MI.[13–16] Similar findings of alteration in baroreflex responses are also present in patients with cardiac disease and depression, most of whom also have symptoms of fatigue.[17]

Immune system dysfunction is also seen to have a role in fatigue in patients with cardiac disease. There is a role of alteration in cytokines and in the regulation of immune function that happens in both depression and with cardiac disease. Specifically, there is an association of excess of tumor necrosis factor alpha (TNF-α)[18] and interleukin 1-beta[19] (IL-1-β) and the symptoms of fatigue. A similar pattern of increased cytokines is also seen in patients after coronary surgery, after MI, and with heart failure. This alteration of cytokines and increased TNF-α may play a role in post-surgical or post-MI fatigue, which is seen in a great number of patients.[20,21] The final mechanism that the immune dysregulation may have on the control of fatigue in cardiac patients may be through the effects that dysregulation of immune function can have on the HPA axis with alteration of catecholamines and subsequent increased

circulating cortisol. It has been hypothesized that myocardial disease, specifically infarction, can lead to immune activation with the cascade or increased TNF-α and IL-1-β, leading to deregulation of the prefrontal cortex and producing limbic dysfunction with subsequent mood changes (depression) and direct increase in the humoral factors, which can lead to increased fatigue.[22,23] A side effect of this is also an increase in cardiac events, including arrhythmias and increased MI. Reversal of the fatigue has not been clearly shown to improve the cardiac events but has been associated with an improvement in the humoral markers discussed previously.

Another consideration in the relationship of fatigue and cardiac disease is the role that fatigue has as a risk factor for further cardiac events. In the Copenhagen Heart study, vital exhaustion—a marker of fatigue with associated depressive symptoms—was found to be an independent risk factor for ischemic heart disease.[24] Patients with depression were nearly twice as likely to develop subsequent cardiac events and had an increased overall mortality even for noncardiac events. The increased incidence of events and death was thought to be possibly mediated by the mechanisms mentioned already, including autonomic dysfunction, immune dysregulation, and altered platelet function. The same increase in events was found for patients who underwent percutaneous transluminal coronary angioplasty with an increased incidence in new cardiac events in patients who reported vital exhaustion.[25]

Fatigue in Pulmonary Disease

Just as in patients with cardiac disease, patients with chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), and other lung conditions often present with fatigue as a prominent symptom. In patients with COPD, fatigue is second only to breathlessness in incidence as a major symptom, being present in 68% to 80% of patients.[2,4] Fatigue is also commonly seen in ILD, and assessment for the presence of fatigue is an integral part of the assessment of quality of life in lung disease.[26,27] Although the exact cause of fatigue in these patients with chronic lung disease is not clearly understood, there are some aspects that overlap with other chronic diseases and some that are unique to lung disease.

The features of fatigue with COPD and ILD that are shared with other chronic diseases include muscle weakness, early fatigue (exhaustion with exercise), muscle wasting, and decreased muscle function. This is seen in the same way as in cardiac disease. There are thought to be several contributing factors to this constellation of fatigue symptoms, including semistarvation (both cardiac and pulmonary cachexia), reduced physical activity, and aging, along with the effects of lung failure. Additionally, patients with chronic lung disease often exist in a chronic catabolic state and have muscle changes that can resemble those seen in patients with anorexia and starvation.[28] Another factor that can further increase this catabolic state is the effects of medications and the effects of immobility imposed by frequent hospitalizations and the limitations on activity from the lung disease itself. Patients with lung disease will often enter a spiral of decreasing weight after a series of hospitalizations with intubations and periods of decreased nutrition, high-dose steroids, and courses of broad-spectrum antibiotics.

Another cause of the fatigue that is so often present in COPD may be related to dyspnea and the effort of breathing. Patients with severe COPD may have no relief from the effort of breathing and develop anxiety and depression, which compound their fatigue.[29] The mechanism of a large component of respiratory fatigue is related to the effort of breathing itself. The work of breathing is increased in COPD, because all aspects of the ventilatory cycle are active, since exhalation no longer is a passive activity due to air trapping. This increase in the work of breathing can increase resting

metabolic demand up to twice the normal level.[29] To further complicate this fatigue from increased work, there is a chronic increase in metabolic demand, which, coupled with the altered nutrition seen in patients with severe COPD, can lead to muscle wasting and malnourishment discussed previously. This leads to muscular weakness and increased perception of work, and a deadly downward spiral can ensue.

In addition to the increased metabolic demand, there are also limitations with appetite and changes in the ability to maintain lean body mass. The limitations to maintaining adequate dietary intake are multifactorial. Mechanical difficulty with eating comes from a combination of pressure on the diaphragm from a large meal, decreasing ventilatory reserve, and the increased metabolic demand of digestion, causing the patient to have more dyspnea.[29] Decreased appetite from medications and the effects of glucocorticoids increasing fat percentage with a loss of lean body mass also contribute. The result is a pulmonary cachexia, which cycles with progressively more lean body mass loss into a chronic and potentially lethal spiral. This progressive cachexia and loss of lean body mass also lead to weakness of the muscles of respiration (diaphragm and accessory muscles of ventilation, which are extensively used for patients with COPD), leading to a loss of ventilatory capacity, which in turn leads to increased symptoms of dyspnea and chronic fatigue.[30] Finally, it is hypothesized that there may also be biochemical pathways contributing to this chronic weight loss, but these are not clearly understood at this point.

Another factor in the development of fatigue in COPD is the possible presence of obstructive sleep apnea (OSA) along with lung disease.[31,32] This is a relatively common concurrence of conditions, and one of the most prominent effects of sleep deprivation from OSA is an increase in fatigue, above and beyond the effects of COPD itself. The most effective intervention for a patient who presents with both conditions is to treat both COPD and OSA simultaneously and aggressively. Nocturnal, noninvasive, bilevel ventilation is a hallmark of this treatment and will help with OSA directly and may provide nocturnal rest for the ventilatory muscles fatigued by the increased effort of ventilation with obstructive lung disease. As evidence of the relationship of the conditions, when appropriately treated, most patients experience a marked improvement in fatigue. An additional interesting finding in individuals with both OSA and COPD is that fatigue is increased in direct proportion to decreased activity and fatigue is not directly related to the severity of OSA.[31,32]

There is also an elevated incidence of depression in patients with OSA and COPD. This depression may be difficult to tease out from the physiologic effects of apnea.[33] Another common factor with both OSA and COPD is the effects of hypercarbia and hypoxemia on the individual, with both abnormalities causing fatigue.

For patients with ILD, the mechanism of fatigue may be due to depression, muscle wasting, medications, and associated collagen, vascular, or autoimmune diseases, along with the effects of immobility. Medications that are most often associated with fatigue include corticosteroids and chemotherapeutic agents, such as azathioprine (Imuran), cyclophosphamide (Cytoxan), and interferon. Just as in COPD, added to these effects is the extra effort of breathing, possible presence of hypoxemia, and the development of pulmonary hypertension with subsequent right heart failure. The constellation of problems can all be seen in a single patient as the disease progresses, and, in part, this is why aggressive treatment with oxygen may help. However, no matter what treatments are offered, the onset of fatigue is likely. Just as in COPD, the extra work of breathing, combined with weakened musculature, can contribute to the onset of fatigue. Unlike in COPD, the increased work of breathing in ILD is not due to the loss of elasticity and subsequent active exhalation but rather due to the loss of compliance of the lungs. As the disease progresses, the lungs become

very stiff and excessive force is needed to ventilate them, leading to smaller tidal volumes with increased inefficiency of breathing.

The effects of autoimmune conditions and collagen vascular diseases on fatigue are due to many mechanisms similar to those discussed in cardiac disease with increased cytokines and subsequent dysregulation of the immune system. High doses of glucocorticoid medications are also often used to treat concomitant collagen vascular disease, and these medications also have a role in causing fatigue. The underlying autoimmune disease can also directly damage muscles, causing direct muscle weakness and associated fatigue.[34] An example of this is connective tissue disease-associated pulmonary fibrosis, which is seen in up to 89% of patients with mixed connective tissue disease, whereas up to 69% of patients have pulmonary function test abnormalities.[34] The histopathology of lung involvement is similar to usual interstitial pneumonitis or nonspecific interstitial pneumonitis in most cases. In some rarer cases, ILD may be due to the treatment for the disease, most commonly when patients receive methotrexate as a part of the treatment of their autoimmune disorder.[35]

Just as in patients with cardiac disease, patients with pulmonary disease can develop fatigue after surgery. Additionally, there is the possibility of fatigue in the setting of lung cancer and after the treatments that are instituted for cancer—surgery, chemotherapy, and radiation therapy. These treatments are all known to contribute to fatigue but will not be discussed in detail here. Other sources are available to review the serious consequences of cancer on lung function and the effects of medications, and interested readers can find the details in specific texts that relate to these disorders.[35] The usual effect is one of ILD and the associated abnormalities discussed earlier.

ROLE OF DEPRESSION AND ANXIETY

Depression, anxiety, and fear underlie all of the cardiopulmonary conditions that may lead to the presence of fatigue, and these affective disorders may actually augment the symptoms of fatigue when they are present. As stated above, not only is depression well known to be associated with fatigue but also fatigue is often one of the cardinal presenting symptoms of depression. The major point to remember with patients affected by cardiopulmonary disease is that whenever fatigue seems to be out of proportion to the degree of underlying disease, an assessment for depression or anxiety should be considered. When it is present, treatment of depression can help to alleviate the symptoms of fatigue, allowing for an increase in physical activity, which will also improve fatigue.

ROLE OF MEDICATIONS IN FATIGUE IN CARDIOPULMONARY DISEASE

Among medications for the treatment of cardiac disease, historically, beta blockers and diuretics have been thought to be associated with the highest incidence of the side effect of fatigue. Evaluations of calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and antiarrhythmics have sporadic reports of fatigue, but the beta blockers are most often reported to be associated with fatigue.

Interestingly, recent re-evaluation of the side effects of beta blockers has come to dispute the ''commonly known'' association of beta blockade and fatigue. Several recent studies have shown that the physiologic benefits of the beta blockers actually decreased fatigue in patients with coronary artery disease (CAD) and heart failure when used appropriately.[36,37] Similarly, patients using diuretics that maintained euvolemia and normal electrolyte balance did not experience increased fatigue. This means that physicians treating patients with cardiac disease who are found to have fatigue

should not automatically attribute the symptoms of fatigue to the medications. Instead, improved treatment of their underlying condition or evaluation for depression or another cause of increased fatigue should be considered.

Pulmonary medications do not usually have an association with fatigue, with the exception of glucocorticoids. The effects of steroids on fatigue can be usually attributed to the effects on muscle catabolism, weight gain, and the changes on affect, particularly the onset of depression. Patients with high-dose steroid treatment are most likely to have these adverse effects, so minimizing the dosage is important. Similarly, patients with transplantation are also likely to be on high doses of prednisone and have these associated symptoms.

The effects of medications on fatigue are of particular interest in both pulmonary and cardiac transplant patients. A common symptom in this population of patients after transplantation is that they have continued fatigue long after their transplant and recovery, even with good graft function. This fatigue is never as severe as before their transplant, but the energy level and exercise capacity remain reduced.[38] In cardiac transplant patients, there is a decreased cardiac output due to denervation of the heart with resultant cardiac dysfunction that leads to a lower maximum cardiac output, with coincident reduction in exercise capacity.[40] Pulmonary transplant patients do not have cardiac limitation but have decreased exercise capacity.[35] In a large part, the transplant medications themselves contribute to the decreased capacity (ie, the effect of glucocorticoids from decreased muscle strength and muscle mass).

Another key contribution to decreased exercise capacity is the effect of calcineurin inhibitor (CI) medications. Practically all transplant patients are treated with a regimen that includes both glucocorticoids and CI. The most commonly used CIs are cyclosporine and tacrolimus. Although there are some differences, all of the CIs inhibit the function of calcineurin, which plays an important role in the regeneration of muscle, and the CIs thus inhibit the formation of type I muscle fibers.[39–41] Cyclosporin has also been associated with mitochondrial dysfunction and the developments of myopathy. The mechanisms appear to involve inhibition of mitochondrial respiration, and impairment of the enzyme function of succinate dehydrogenase has been found.[42,43] The fatigue may well be related to this effect on mitochondrial function and may explain the high prevalence of fatigue in these patients. Unfortunately, for the treatment of fatigue, reduction of the medications is not an option for these patients. The best compromise is to treat them symptomatically with exercise and encourage maintenance of lean body mass, while coordinating with the transplant service to try to minimize the immunosuppressive medications as much as possible. Fortunately, the levels of medications often decrease markedly in the first year after transplantation if there is no rejection, only to be boosted in times of possible rejection.

A summary of the potential effects of some commonly used cardiac and pulmonary medication classes is seen in **Table 1**.

Possible Therapeutic Interventions

Patients with cardiac and pulmonary disease commonly have fatigue for the reasons discussed earlier, some of which are directly due to their disease, some of which are due to metabolic and other effects of their condition, and some of which may be due to complications in the treatment of their disease. Fortunately, some of the causes of fatigue can be ameliorated through treatment. In the management of affective causes of fatigue, it is essential to treat depression, anxiety, and fear if they exist in all cardiopulmonary patients. This alone may help increase the patient's energy level to help facilitate involvement with other treatments such as exercise that will further improve the patient's fatigue. For depression and anxiety, treatment should include both

Table 1
Common medications used to treat cardiac and pulmonary disease that may cause fatigue

Cardiac Disease	Mechanism for Fatigue	Effect on Fatigue
Beta blocker	Decreased sympathetic activation	No clear evidence in recent studies
ACE inhibitors	Unclear mechanism	Sporadic reports
Diuretics	Metabolic disarray Dehydration	No effect as long as electrolytes and fluid balance normal
Antihypertensives	Lowered blood pressure Decreased ability to mount a sympathetic response	Direct effect of low blood pressure
Pulmonary disease		
Glucocorticoids	Muscle weakness Hyperglycemia Hypertension Weight gain Mood changes	Can clearly increase fatigue through a combination of physiologic effects
Interferon	Fever Malaise	May cause fatigue directly
Cytotoxic agents	Anemia Malaise Exhaustion	May cause fatigue directly
Post-transplant		
Glucocorticoids	Muscle weakness Hyperglycemia Hypertension Weight gain Mood changes	Can clearly increase fatigue
Calcineurin inhibitors	Decreased muscle contractility Decreased type 1 fiber generation Impaired function of succinate dehydrogenase	Associated with muscle weakness and fatigue
Cytotoxic agents	Anemia Malaise Exhaustion	May cause fatigue directly
Antihypertensive agents	Needed to counteract elevation of blood pressure from glucocorticoids and calcineurin inhibitors Lowered blood pressure	Direct effect of low blood pressure

pharmacologic therapy as well as psychotherapy. The issue is to try to relieve psychomotor retardation and the central effects of depression that cause fatigue. The full discussion of the effect of depression on fatigue and how to treat it is covered in other sources.

The treatment of muscle weakness and muscle fiber fatigue is possible and can assist in the relief of fatigue in cardiopulmonary disease. The muscle dysfunction that exists with lung disease responds to both the treatment of the underlying condition as well as to exercise to directly strengthen muscle and increase muscle fiber endurance. As an example, in COPD, leg fatigue is a prominent symptom and is

seen in up to one-third of patients. Associated with the leg fatigue there is also a decrease of up to 20% in muscle twitch force.[44,45] This loss of strength and endurance leads to an increase in symptoms of fatigue, as every activity is nearer the maximum strength of the individual. Treating bronchospasm and dyspnea alone does not resolve the issues of fatigue, and it is only with a combination of exercise that there is even more significant improvement.[46,47] For patients with COPD, treatment of the underlying COPD with lung volume reduction surgery (LVRS) can lead to an improvement in function but has no clear effect on the underlying symptoms of fatigue.[48] Exercise capacity with LVRS increased 10% to 15%, and pulmonary function testing showed improved forced expiratory volume in 1 second (from 59 to 71% predicted), but the perceived measures of fatigue with exertion were unchanged. However, this same population of patients experience a significant improvement in ratings of perceived fatigue with exertion when they exercise,[49] and they also had associated levels of improvements in exercise capacity without any improvements in pulmonary function. Similar findings exist for exercise with ILD.

The method of exercise for patients with pulmonary limitation should emphasize endurance training. The level of dyspnea that patients experience is such that they may not continue to exercise if the level of exertion is too high, and it is consistency in exercise with a dedication to increased endurance that yields the best benefits.[48,49] Additionally, the use of supplemental oxygen is essential to limit fatigue, both with exercise training and with activity. Chronic hypoxemia will lead to fatigue on its own, and the avoidance of this additional factor in fatigue is essential in the management of both dyspnea and the prevention of chronic hypoxemia with its associated fatigue.

For patients with cardiac disease, similar findings exist, and treatment of the underlying cardiac condition is important, as it will allow for better perfusion and improved function with decreased fatigue. This is especially true in ischemic disease and in CHF.

TREATMENT OF OBESITY

Finally, although it has not yet been mentioned, treatment of obesity, if present, is essential in helping to manage fatigue in cardiopulmonary patients. Deconditioning and excess weight are epidemic in our society and are the root cause of a great deal of fatigue, even without other underlying conditions. Cardiopulmonary patients are not immune to developing deconditioning and obesity. In fact, these groups of patients may actually have a higher degree of both due to inactivity from their cardiopulmonary limitations. With pulmonary disease, dyspnea is the usual limiting factor, and with cardiac disease, both dyspnea and chest pain will limit activity. Therefore, any program of therapy that is aimed to reduce fatigue in cardiopulmonary patients needs to address weight reduction to increase the likelihood of success.

The treatment approaches for weight reduction are outside of the scope of this review, but most of the common approaches used for healthy individuals will also work for patients with cardiopulmonary disease. Practitioners are urged to be familiar with local resources so that they can avail themselves of assistance in helping to manage weight loss.

PRINCIPLES OF EXERCISE FOR PATIENTS WITH FATIGUE IN CHRONIC CARDIAC AND PULMONARY DISEASE

A properly designed cardiac or pulmonary program will start with an assessment of the primary condition. For patients with cardiac disease, an evaluation of cardiac function and limitations is essential for safety and to maximize the effectiveness of the cardiac rehabilitation program. Control of CHF and ischemia is required, and the patient

should have an assessment of maximal exercise capacity to help with safety assessment and planning for the appropriate level of sustainable exercise. For pulmonary patients, the patient should be on an optimized regimen of bronchodilation and should be on an appropriate level of supplemental oxygen. It is also important to limit the amounts of systemic steroids as much as possible. When present, the patient's anxiety should also be controlled, because this can contribute to a limitation for exercise. Treatment of anxiety can include pharmaceutical measures, but a good rehabilitation program will also include stress management and education.[38,46,47] Guidelines for supplemental oxygen and hemodynamic parameters for the lung patients can also be directed with physiologic testing and pulmonary function testing.

Once the parameters for safe exercise are determined, patients are best placed in a supervised program initially to facilitate participation and to increase the maximal exercise that they can perform. There are several other issues that will affect the ability of the patients to participate in the exercise program.

For patients with cardiopulmonary disease, accessibility is important. This includes maintaining cost at a reasonable level and developing a continuing exercise program that is home based. Often there may need to be negotiation with insurers to assure coverage. For cardiac diseases, in situations where accessibility or insurance coverage may be difficult, home-based programs have proven effective in the maintenance of conditioning. Home-based programs also have the additional benefit of associated improvements in fatigue that are often better with home-based exercise than center-based exercise.[50] Placing exercise in community-based settings is also helpful and can be done at senior centers, community centers, schools, and residential facilities. Educational and motivational programs can also be included to maintain enthusiasm, and the socialization that occurs in the community-based settings may also help patients to overcome anxiety and depression, which contribute to their fatigue.[30]

Safety and effectiveness of the exercise program need to be assured through appropriate assessment and prescription of precautions. As discussed here, use of supplemental oxygen and appropriate monitoring for cardiac patients will help to reassure patients and allow them to exercise to an appropriate level. The effectiveness of the exercise program will also be maximized when an appropriate level of intensity and duration are achieved. Increased-duration exercise sessions that are more frequent are associated with more benefits. Additionally, exercise that is done with weight bearing and near the anaerobic threshold is more effective. A rough rule of thumb for intensity is to try to achieve sustained exercise for 30 minutes at an intensity of approximately 60% of peak performance 3 to 5 times a week.[51–53] Since upper-extremity activity causes more fatigue than that with similar-intensity leg exercise, there also needs to be a focus on arm exercise to improve upper-limb strength and endurance. A properly executed gentle exercise program for the upper body can achieve similar improvements to those with the exercise programs for lower extremities.[54]

For a complete exercise program, muscle-strengthening exercise needs to be incorporated in addition to the conditioning exercises. In patients with significant muscle weakness, such as lung disease patients who have been on long-term glucocorticoids, or in post-transplant patients, there is a need to focus on proximal and large muscle groups for strengthening. This also applies to cardiopulmonary patients who may have had prolonged hospitalizations and are in need of recovery from immobility. If possible, the exercises should include free weights as opposed to circuit training, since there is a better training effect.[55,56] For convenience and variety, effective strengthening programs can also include theraband or other forms of resistance exercises.[34,55,56]

Another element in maintaining the benefits of exercise include making sure that the patient adheres to the exercise program. Physician encouragement and patient motivation are also important.[57,58] It is essential for the fatigued cardiopulmonary patient not to have an overwhelming program that may seem too difficult to achieve. Rather than presenting a very intense and threatening series of overall goals, smaller short-term goals can be helpful and build a sense of accomplishment in the patient. Additionally, the types of exercise that the patient enjoys should be emphasized, and ones that are not comfortable should be avoided as a regular part of the program. Circuit training also introduces variety and may help to prevent injury from overuse or repetitive strain. When a patient has achieved a level of capacity, repeat exercise testing to demonstrate the new level of strength and conditioning may also help and can be in the form of a 6-minute walk test or cardiopulmonary exercise test. Some techniques that can make the actual exercise program more enjoyable include finding an exercise partner (spouse or friend), incorporating the exercise into a recreational sport, and using techniques for distraction during sustained exercise, such as television, music, or conversation. Patients who are enrolled in a formal program also often find camaraderie in the exercise program and so can increase their adherence by being more excited to come for the socialization that their exercise program provides.[38,55]

Once the cardiopulmonary patients have achieved a degree of conditioning with the associated improvement in fatigue, they should be encouraged to think of incorporating exercise as a part of their ongoing overall health care plan. The physician and other members of the health care team need to be unwavering in their support for exercise, and it is important to also enlist the patient's family as a support. Educating the patient on the role of exercise in treating the underlying cardiopulmonary disease and in combating the side effects of medications is also important. A summary of the effects of exercise on fatigue in chronic cardiopulmonary disease is presented in **Table 2**.

POTENTIAL AREAS FOR RESEARCH IN CARDIOPULMONARY FATIGUE

Since there are still numerous areas that have not been defined in the role of fatigue in cardiac and pulmonary diseases, ongoing research is needed. A special consideration is that even with the recent marked improvements in treatment for cardiac and pulmonary disease, fatigue is still a major presenting symptom or part of cardiopulmonary disease. Theoretically, recent advancements in treatment have allowed for the correction of the underlying pathophysiology or even eradication of the underlying disease, thus removing the cardiac or pulmonary cause of fatigue. However, even after these interventions, the symptoms of fatigue often continue to persist for patients.

The most successful examples of definitive treatment of underlying cardiac disorders include valve replacement for valvular heart disease and revascularization for early ischemic heart disease (before MI and onset of heart failure). In these patients, there is the best chance for definitive relief of fatigue. For patients who are on medications for restoration of exercise capacity (such as intravenous inotropic agents) or supplemental oxygen, the underlying fatigue often persists. In patients who receive transplantation, there is also persistence of fatigue due to the medication regimens for prevention of resection and side effects, effectively creating an exchange of the original cardiopulmonary condition for "transplant disease." Research efforts need to be focused on attempts to improve overall function and to enhance cardiac and pulmonary function to improve fatigue symptoms, while minimizing the side effects of the treatment that cause fatigue. This combination of searching for effective

Table 2
Benefits of exercise in chronic cardiopulmonary disease

Benefits	Effect on Physiology	Subsequent Effect on Fatigue
Decreases risk of CAD mortality	Decreased cardiac events	Unclear
Decreases risk of hypertension	Lowered incidence of hypertension	Decrease
Lowers blood pressure in individuals with hypertension	Lowered blood pressure	Decrease
Maintains muscle strength	Improved muscle strength	Unclear
Maintains bone mass	Improved bone density	Unclear
Improves glycemic control	Lower blood sugar	Decrease
Improved coordination	Decreases fall risk	Unclear
Improved sense of well-being	Relieves symptoms of anxiety and depression	Decrease
Improved health-related quality of life	Improves ability to function	Unclear to decrease
Reduced risk of cancer	Less neoplasm	Unclear
Improved lipid profile	Decreased cardiovascular risk	Unclear
Increased exercise capacity	Improved ability to function	Decrease
Decreased obesity	Lowers body weight	Decrease
Improved sleep quality	Less fatigue from sleep deprivation	Decrease
Improved self-image	Lowers chance of affective disorders	Decrease

treatments for a symptom while actually using treatments that may contribute to the symptom makes the study of fatigue and its treatments very challenging.

FUTURE PROSPECTS IN FATIGUE IN CARDIOPULMONARY DISEASE

The future challenges in defining fatigue in cardiopulmonary disease are numerous. Unfortunately, as mentioned above, the research in the area of fatigue in cardiac and pulmonary disease is limited, and much still needs to be done. There is a clear role for central versus peripheral factors, and this is true of research regarding all forms of fatigue not just fatigue seen in patients with heart or lung disease. Still, the best approach for a patient with fatigue in cardiopulmonary disease is to address multiple issues simultaneously. First, there needs to be attention to maximizing the treatment of the underlying condition and minimizing the physiologic disturbances from hypoxemia, hypercarbia, and decreased cardiac output or myocardial compromise. Then there needs to be attention to contributing conditions, such as obesity, deconditioning, depression, or anxiety. Finally, there needs to be consideration of the possible effects of the treatments themselves and minimizing the possibilities that the treatments cause fatigue. Through this multifaceted approach, the clinician will best be able to help patients with their fatigue.

In conclusion, the take-home message for health care practitioners working with cardiopulmonary patients with fatigue is to have a good understanding of the underlying conditions and the possible treatment options. In addition to maximizing medical management of the cardiac and pulmonary conditions, an appropriate exercise program needs to be done, along with appropriate medication management and

evaluation of and treatment for obesity, depression, anxiety, and other conditions associated with fatigue. It may not be possible to totally remove the symptom of fatigue, but with appropriate management, the symptom can be controlled sufficiently to allow patients to return to a higher level of functioning.

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