

# Assessment and Management of Cancer-Related Fatigue

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Cancer-related fatigue is one of the most common symptoms experienced by patients receiving chemotherapy and/or radiation therapy. It is subjective in nature; therefore, assessing the extent of its interference with the patient's quality of life and functional status is important. Assessment should also include contributing factors as well as underlying etiologies. Clinicians need to reassess and more than likely readjust the patient's fatigue management along the cancer continuum. Educating the patient to effectively manage other symptoms such as pain in addition to proper nutrition and hydration, exercise, and energy conservation will help empower patients to manage their fatigue.

## KEY WORDS

fatigue, quality of life, treatment side effects

The 2012 National Comprehensive Cancer Network defines cancer-related fatigue (CRF) as “a distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning.”<sup>1</sup> Fatigue is one of the most common symptoms that cancer patients experience when receiving treatment with chemotherapy and/or radiation. Percentages of patients who experience CRF vary across studies from 25% to 100% depending on the type of treatment and the type and stage of cancer.<sup>2-5</sup> Curt and colleagues<sup>6</sup> telephone surveyed 379 patients who had received chemotherapy and found that 76% experienced fatigue at least a few days during the last course of chemotherapy and 30% experienced fatigue every day. Cancer-related fatigue has been experienced by patients from time of diagnosis to clinical remission and, for breast cancer survivors in particular, 5 to 10 years after diagnosis.<sup>4,7-11</sup> As treatment for cancer advances, there are more survivors with CRF years after treatment has ended.

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Fatigue also affects patients with other diseases. Solano and colleagues<sup>12</sup> conducted a systematic search of medical databases and textbooks and, from 64 original studies, identified 11 common symptoms among patients with terminal cancer, acquired immunodeficiency syndrome, heart disease, chronic obstructive pulmonary disease, or renal disease. Pain, breathlessness, and fatigue were experienced by more than 50% of the patients across all 5 diseases, suggesting the possibility of a common pathway that patients with terminal diseases face. Thus, palliative care is appropriate for noncancer patients as well.

## CLINICAL CHARACTERISTICS

The pathophysiology of CRF is not well understood even today. Since the late 1800s, basic scientists and clinicians have been attempting to explain the causes of CRF.<sup>13</sup> Given the similar constructs of the models, Mitchell<sup>10</sup> organized them into 4 themes: energy balance/energy analysis, fatigue as a stress response, neuroendocrine-based regulatory fatigue, and hybrid models. Energy balance/energy analysis posits an imbalance of energy intake, metabolism, and expenditure, thus facilitating the development of fatigue. Fatigue as a stress response suggests that there is a continued adaptation along a continuum that is differentiated in both behavioral and symptom characteristics. Neuroendocrine-based regulatory fatigue theorizes that the multidimensionality of fatigue is due to a dysregulation of the neuroimmunoendocrine system, which is interrelated both anatomically and functionally and includes the hypothalamic-pituitary-adrenal axis, cytokines, circadian rhythms, and neurotransmitters.<sup>10,14,15</sup> Hybrid models include those that suggest that stressors caused by cancer and cancer treatments generate a decline in 4 particular areas (cognitive function, nutrition, muscle endurance, and quality of sleep), which impedes ability to adapt, as well as those that propose that biological, psychological, and functional variables induce CRF.<sup>10</sup>

Fatigue can be peripheral or central.<sup>16</sup> Peripheral fatigue can be referred to as muscle fatigability caused by muscle and neuromuscular disorders. It occurs when there is a lack of neuromuscular system response after central stimulation. Central fatigue results when transmission of motor impulses has failed or there is an inability to perform voluntary activities.<sup>17</sup> It affects not only the physical body but

also cognition such that patients find it difficult to concentrate mentally.<sup>16</sup>

Contributing factors to fatigue, sometimes referred to as secondary fatigue, include age, physical symptoms, psychological symptoms, comorbidities, advanced disease, treatment side effects, and abnormal laboratory values (Table 1).<sup>1,13,18-21</sup> With advanced cancer, the impact of each factor contributing to fatigue will vary throughout the disease trajectory.<sup>21</sup>

## EFFECTS OF FATIGUE ON QUALITY OF LIFE

Both CRF and non-CRF greatly affect the patient's quality of life (QOL) physically, mentally, emotionally, socially, and spiritually.<sup>11,22-25</sup> Studies have shown that CRF interferes with performing activities of daily living, decreases functional status, and limits QOL especially for elderly individuals. In addition, CRF is associated with decreased survival and interferes with employment, enjoyment of life, relationships, and motivation to battle the cancer.<sup>4,26,27</sup> Cancer-related fatigue has been linked to increased depression, anxiety, and mood disturbance and can impact the family's financial status.<sup>4</sup> Similarly, noncancer patients experiencing fatigue describe it as feeling tired, weak, and having little energy and perceive it as one of their worst symptoms.<sup>21,28,29</sup> For many patients, fatigue can be demoralizing as it robs them of who they used to be. They grieve the loss of their usual roles and responsibilities.<sup>28</sup>

The literature is replete with data confirming the effects of fatigue on QOL, except in the area of spirituality.

A small phenomenological study conducted by Potter<sup>25</sup> revealed that most participants described feelings of hopelessness about their situation. Six patients with advanced cancer in a palliative day care unit who, unprompted, expressed suffering from fatigue were interviewed for the study. Fatigue was discussed in relation to their cancer and dying. For these patients, fatigue was used as a measurement of where they were in the illness trajectory. Inability to control fatigue and the limitations it forced on them were constant battles for these patients. Those who placed more importance on spiritual and religious beliefs were more accepting of their fatigue. The effects on spirituality of non-CRF are much the same. Benzein and Berg<sup>24</sup> looked at the relationship between hope, hopelessness, and fatigue in 40 patients receiving palliative care, along with 45 family members. Results showed that family members actually had less hope than the patients did, and patients found this very difficult to deal with while dying. Authors suggest that if patients experience hope as hoping *for* something (eg, cure), fatigue poses a bigger obstacle to hope than if the patient is living *in* hope (reconciliation with life and death) because hopelessness is seen as loss of control.<sup>24,30</sup> A sense of hopelessness—feelings of no control to change a situation—is common among both populations experiencing profound fatigue.

## ASSESSMENT OF CRF

Given that fatigue is a subjective experience, the patient's self-report using the 0 (no fatigue) to 10 (severe fatigue) scale is suggested by the National Comprehensive Cancer Network (NCCN).<sup>1</sup> However, patient, professional, and system barriers exist that hinder effective fatigue assessment and management. Studies have revealed that patients do not report fatigue for several reasons, including a belief that fatigue is inevitable, untreatable, and unimportant.<sup>31</sup> Patients fear that CRF can negatively affect medical treatment if reported, such as needing to reduce or stop treatment, or the belief that fatigue means that the disease is not responding to treatment and/or getting worse.<sup>32</sup> Professional barriers include a lack of knowledge about the underlying causes of fatigue; lack of assessment, leading to underreporting, underdiagnosing, and undertreatment; an unwillingness to initiate discussion if unaware of available treatment; or a belief that little can be done to manage the symptom.<sup>1,32,33</sup> Documentation of fatigue in the medical record is not common practice nor required by the Joint Commission, thus creating a systems barrier. As a result, CRF assessment and management are not viewed as priorities, and clinicians are not reminded to document its occurrence.<sup>34,35</sup> Obtaining a referral to physical or occupational therapy can be burdensome, thus preventing some patients from being referred.<sup>36</sup> Unfortunately, interventions are provided to patients when the fatigue is already severe and

**TABLE 1** Contributing Factors to Fatigue<sup>1,13-16</sup>

Patient-reported symptoms
Physical: pain, shortness of breath, generalized tiredness, inability to perform daily tasks, heart palpitations, insomnia, lack of appetite, immobility
Psychological: depressed mood, anxiety, emotional distress
Comorbidities
Cardiac, renal, pulmonary, neurological, gastrointestinal, hepatic, endocrine, organ failure
Treatment related
Therapies: chemotherapy including targeted therapies, radiation, surgery
Medications: side effects, changes in taste, polypharmacy
Other
Abnormal laboratory values from cancer, treatment, or infection



thus less likely to implement or benefit from them.<sup>36</sup> Type of health care coverage/reimbursement for medications/treatment/therapies can also be a barrier.<sup>34,36,37</sup>

In addition to the patient's self-report, using a multidimensional approach to elicit more information will enable the clinician to better manage the fatigue. Descriptors beyond severity, such as onset, duration, interference in daily activities, exacerbating and palliative factors, and treatments tried, are helpful. In addition, there are several single-item, multi-item, and multidimensional tools that have been developed to measure fatigue, and they have been reviewed by Piper and colleagues<sup>34</sup> (Table 2). Some of these measures include single-item tools such as the NCCN Intensity Scale,<sup>38</sup> Fatigue Intensity Scale,<sup>36</sup> and the Visual Analogue Scale.<sup>39,40</sup> Multi-item tools include the Brief Fatigue Inventory<sup>41</sup> and the Cancer-Related Fatigue Distress Scale.<sup>42-44</sup> Multidimensional measures include the Cancer Fatigue Scale,<sup>44,45</sup> Fatigue Assessment Questionnaire,<sup>44,46</sup> and the Revised Piper Fatigue Scale.<sup>47-49</sup> Single- and multi-item measures embedded in other scales include the Profile of Mood States Fatigue and Vigor subscales,<sup>50</sup> the Symptom Distress Scale,<sup>41,51</sup> and the Edmonton Symptom Assessment System.<sup>52,53</sup> These tools can be used both in research and in the clinical area.

## MANAGEMENT OF FATIGUE

The goal of fatigue management is palliation, that is, to help the patient mitigate the effects of fatigue and, as much as possible, maximize existing energy levels. Patients should be screened for underlying treatable etiologies such as those mentioned under the "Clinical Characteristics" section.

### Nonpharmacologic Interventions

General education should be provided to the patient with regard to treatment-related fatigue from chemotherapy and radiation therapy. General strategies include conserving energy; balancing rest and activity; optimizing nutrition; preventing weight loss; and using distraction such as listening to music, reading, enjoying nature, and taking 1-hour naps if needed.<sup>1,10,54</sup> Teaching patients to use a diary to self-monitor their fatigue lets them see when their energy levels peak and diminish. It also provides the opportunity to plan their day accordingly.<sup>55</sup> Other fatigue management interventions can be categorized into either nonpharmacologic (Table 3) or pharmacologic approaches. Nonpharmacologic interventions for CRF include patient education, exercise, energy conservation, proper nutrition and hydration, and complementary therapies such as acupuncture, cognitive behavior, and relaxation breathing.<sup>1,10,13,18,54</sup> The NCCN guidelines organize the nonpharmacologic interventions into 3 categories: activity enhancement (eg, exercise), physical therapies (eg,

massage), and psychosocial interventions (eg, cognitive behavioral therapy).<sup>1</sup>

### Activity Enhancement

Research has shown exercise to be the most effective approach for managing CRF.<sup>18,55-59</sup> Based on the patient's performance status and preference, there are several exercise activities that may be beneficial, such as walking, swimming, biking, resistive exercise, aerobics, or a combination of exercises. Although studies on exercise range in frequency, intensity, and duration, empirical evidence is lacking for guidelines.<sup>10</sup> Exercise should be tailored to the patient's needs to maximize its benefits. McMillan and Newhouse<sup>59</sup> conducted a meta-analysis to look at the effects of exercise interventions on CRF as well as to shed light on prescriptive exercise guidelines. Electronic databases, journals, and articles were systematically searched, resulting in 16 studies representing 1426 participants (exercise = 759; control = 667). Study eligibility criteria included subjects 18 years or older, diagnosis of or treatment for cancer, exercise used to treat CRF, quantitative evaluation of the intervention, and adequate statistical data. Results showed that exercise significantly reduced CRF ( $P < .001$ ). The subgroup analysis on different types of exercise demonstrated that aerobic, resistance, and mixed training interventions improved CRF, with aerobic exercise having the most significant effects ( $P < .001$ ). Furthermore, exercise conducted in a supervised setting showed significant reduction in CRF as compared with unsupervised settings.

Puetz and Herring<sup>60</sup> also conducted a meta-analysis to look at the effects of exercise on CRF in patients both during and after treatment to assess how much the effect is differentiated over the time of treatment and recovery. Electronic databases were systematically searched, resulting in 70 randomized control trials (43 active treatment; 27 posttreatment). Study eligibility criteria included cancer patients in active treatment or posttreatment, randomized to an exercise or nonexercise evaluation, and CRF outcome measured before, during, and/or after exercise training. Results support other studies that exercise reduces CRF in patients both during and after treatment. The overall mean effect was similar to the effects of exercise on other cancer-related outcomes such as QOL, depression, and anxiety; individual/group therapy; and pharmacotherapy. Over time during active treatment, CRF improvement varied based on the patient's baseline fatigue scores and adherence to the exercise regimen. Those with a higher adherence to exercise experienced the most improvement, even when baseline fatigue scores were low. For posttreatment, the effects of exercise on CRF were greater when the interval between the end of treatment and starting an exercise program was longer, when the exercise program was shorter in length, and when trials used a wait-list comparison. Results revealed

**TABLE 2 Sample Fatigue Assessment Tools**

Instrument	Reference	Description
Single-item tools		
NCCN Intensity Tool	Mock et al (2007) <sup>38</sup>	Single item Assesses severity 0-10 scale (0 = no fatigue, 10 = worst fatigue)
Fatigue Intensity Scale	Borneman et al (2007) <sup>36</sup>	Single item Assesses intensity 0-10 scale (0 = no fatigue, 10 = overwhelming fatigue)
VAS for Fatigue	Glaus (1993) <sup>39</sup> Hauser and Walsh (2008) <sup>40</sup>	Single item Assesses severity Uses a 10-cm, 0-to-100-mm horizontal line 0 = does not feel tired, 100 = feels totally exhausted
Multi-item tools		
Brief Fatigue Inventory	Jean-Pierre et al (2007) <sup>41</sup>	9 items Measures intensity or severity (present, usual, worst fatigue during past 24 h) 0-10 scale (0 = no fatigue, 10 = fatigue as bad as one can imagine) Average of 9 items provides a global fatigue severity score (1-3, mild; 4-6, moderate; 7-10, severe)
Cancer-Related Fatigue Distress Scale	Holley (2000) <sup>42</sup> Holley (2000) <sup>43</sup> Piper (2004) <sup>44</sup>	20 items Measures distress 0-10 Likert scale Assesses fatigue over past 7 d
Multidimensional cancer-related fatigue tools		
Cancer Fatigue Scale	Piper (2004) <sup>44</sup> Okuyama et al (2000) <sup>45</sup>	15 items Assesses physical, cognitive, affective dimensions of fatigue 1-5 scale (1 = not at all, 5 = very much) Maximum score is 60 (physical, 1-28; affective, 0-16; cognitive, 0-16)
Fatigue Assessment Questionnaire	Piper (2004) <sup>44</sup> Beutel et al (2006) <sup>46</sup>	20 items Assesses physical, affective, cognitive dimensions of fatigue over past week and month 0-3 scale (0 = not at all, 3 = strongly; +3 indicates addition of VAS to measure fatigue and distress)
Revised Piper Fatigue Scale	Berger et al (2007) <sup>47</sup> de Jong et al (2006) <sup>48</sup> Piper et al (1998) <sup>49</sup>	22 items plus 5 open-ended items not included in the scoring Assesses behavioral/severity, affective meaning, sensory, and cognitive/mood 0-10 scale
Single-item and multi-item cancer-related fatigue measures within other scales		
Profile of Mood States Fatigue and Vigor subscales	Meek et al (2000) <sup>50</sup>	5- to 7-item subscale 8-item vigor subscale Both measure intensity 5-point Likert scale over past week

(continues)

**TABLE 2** Sample Fatigue Assessment Tools, Continued

Instrument	Reference	Description
Symptom Distress Scale	Jean-Pierre et al (2007) <sup>41</sup> Boehmke (2004) <sup>51</sup>	Single item Measures distress 5-point Likert scale
Edmonton Symptom Assessment System	Bruera et al (2007) <sup>52</sup> Reddy et al (2007) <sup>53</sup>	Single item Measures intensity 0-10 scale (0 = no fatigue, 10 = worst fatigue)

Adapted from Piper et al.<sup>34</sup>

Abbreviations: NCCN, National Comprehensive Cancer Network; VAN, Visual Analogue Scale.

that CRF for posttreatment patients was a predictor of exercise adherence and was more restorative, whereas for patients in active treatment, exercise was more palliative. All exercise interventions should be tailored to the patient's need, accounting for performance and physical status, and modified over the disease trajectory.

Physical therapy consultations are warranted when patients have comorbidities (eg, heart disease and chronic obstructive pulmonary disease), recent major surgery, functional/anatomic deficits, or substantial deconditioning.<sup>1(pMS-9)</sup> Use caution with patients who have bone metastasis, low platelets, anemia, fever/infection, or limitations due to metastasis or other illnesses.<sup>1(pMS-9)</sup> Occupational therapists (OTs) can be invaluable in assessing and analyzing functional problems. Specific to CRF, OTs can provide practical advice concerning energy conservation and lifestyle management.<sup>61,62</sup> Some of the most common interventions include assessing and addressing educational needs, mobility, self-care skills, home management skills, need for assistive devices, and upper extremity strength and function.<sup>61-63</sup> As CRF affects the patient's functional capacity, OTs can facilitate adapting activities that are meaningful yet in line with patient's current capabilities. Making sure that they have the proper equipment helps to increase the patient's independence, which, in turn, empowers them to continue making their own health care decisions and preserves their dignity as they cope with CRF.<sup>61,62</sup>

### Physical Therapies

Physical therapies include interventions such as acupuncture and massage therapy.<sup>1</sup> Several studies looking at the efficacy of acupuncture for CRF have demonstrated clinical significance, but more randomized control studies are needed with larger sample sizes to demonstrate statistical significance.<sup>64-67</sup> A recent study conducted by Johnston et al<sup>65</sup> looked at patient education with acupuncture for relief of CRF. This was a randomized controlled feasibility study. Thirteen participants (7 control, 6 treatment) were women, were considered free of breast cancer (after treatment), and had a fatigue rating of 4 or higher on the Brief

Fatigue Inventory. Part 1 of the intervention entailed educating patients to improve self-care through exercise, nutrition, and cognitive behavioral techniques (4 weekly 50-minute sessions of stress management). In the second part of the intervention, patients received 8 weekly 50-minute acupuncture sessions. Results showed positive but not statistically significant results. Mean (SD) CRF scores at baseline were 6.33 (1.39) for the treatment group and 6.00 (1.09) for the control group. After 10 weeks of treatment, scores were 2.13 (1.23) and 4.38 (2.53) for the treatment and control groups, respectively. The treatment group experienced a 2.38-point decline (66%) in CRF as compared with the control group. Although the results of this study were not statistically significant, they were clinically significant.

Several massage studies show clinical significance, but similar to acupuncture, more large-scale randomized control trials are needed for statistical significance to confirm efficacy.<sup>10,68-70</sup> One randomized control study (N = 86) looked at the efficacy of classical massage treatment for reducing symptoms related to breast cancer and improving mood.<sup>70</sup> Women with primary breast cancer were randomized into either the massage group or the waiting list. The intervention group received biweekly 30-minute classical massages in the back and neck area twice a week for 5 weeks. The control group did not receive additional treatment beyond usual care. Each intervention participant completed questionnaires at baseline (T1), at the end of intervention (T2), and at 11 weeks follow-up (T3). Results showed a reduction in fatigue at the end of the intervention, which was sustained over time and was statistically significant compared with the control group at week 11. If massage can be proven in larger studies to be effective for reducing CRF, it could be used as an additional intervention to medication and physical activity.<sup>10</sup>

### Psychosocial Therapy

Cognitive behavioral therapy teaches patients to understand how thoughts can influence their feelings and behavior. They are taught to recognize and identify thought patterns and behaviors when they occur and to use cognitive coping



skills to modify them.<sup>71</sup> Unlike cognitive behavioral therapy, which teaches patients to modify the meaning or content of negative thoughts, mindfulness-based cognitive therapy teaches patients to use a detached perspective to avoid the escalation of negative thought patterns.<sup>72</sup> A recent study (N = 100) looked at the effectiveness of mindfulness-based cognitive therapy in reducing CRF in cancer survivors of mixed diagnoses.<sup>72</sup> Patients were randomized to either the inter-

vention (n = 59) or the wait-list (n = 24) group. Fatigue severity was determined using the subscale of the Checklist Individual Strength tool. Questionnaires were completed at baseline and at the end of the 9-week intervention. The intervention group received a 6-month follow-up. The intervention group received 9 weeks of a protocolized group therapy that included 8 weekly sessions lasting 2.5 hours, one 6-hour session, and one 2.5-hour follow-up session

**TABLE 3** Nonpharmacologic Interventions

Nonpharmacologic Interventions	Explanation
Patient education	
Description of fatigue	Fatigue is a sense of feeling tired that impacts one physically, psychologically, and cognitively. It is different than being tired which gets better with rest.
Common causes of fatigue	Anemia, uncontrolled symptoms such as pain, lack of appetite, or sleep problems, comorbidities, infection.
Use of the 0-10 scale to rate fatigue	1-3, mild; 4-6, moderate; 7-10, severe.
When to call physician	Call if fatigue is getting worse and prevents patient from carrying out ADLs.
What to tell the physician	When it started, what makes it better/worse, description of interference with ADLs (due to the subjective nature of fatigue, this helps clinician better understand the extent of fatigue impact).
Exercise	
Importance of exercising	Heart, lungs, and muscles require exercise to stay healthy. Exercise should be tailored to the patient's needs and capabilities and disease status. Exercise should be initiated slowly and increased over time. Safety should always be assessed before initiating exercise. Where warranted, refer to physical/occupational therapy.
Energy conservation	
Energy conservation can help to reduce the burden of fatigue and use energy more effectively	Prioritize activities. Ask for help or delegate tasks. Balance rest and activities, performing activities during times of higher energy. Adhere to a regular bedtime. Sit instead of standing.
Nutrition and hydration	
Importance of maintaining good nutrition and hydration Monitor weight	Will help increase energy levels. Preserves lean body mass. Better tolerate treatment. Refer to nutritionist when warranted.
Complementary therapies to improve fatigue	
Acupuncture Cognitive behavioral therapy Hypnosis Massage therapy Reiki Relaxation breathing	

Adapted from Berger<sup>2</sup>, Mitchell,<sup>10</sup> Anderson et al,<sup>13</sup> Eaton and Tipton,<sup>18</sup> and Portenoy and Itri.<sup>54</sup>  
Abbreviation: ADLs, activities of daily life.



2 months after the ninth session, for a total of 28.5 hours. Results revealed a positive effect on CRF as the primary outcome variable. The mean fatigue score at postmeasurement was significantly lower in the intervention group (95% confidence interval, 33.2-37.9) than in the wait-list group (95% confidence interval, 40.0-47.4), controlling for pretreatment fatigue levels. Kwekkeboom and colleagues<sup>71</sup> found similar positive results in a review of 43 studies on mind-body interventions. Along with coping skills training and imagery/hypnosis, cognitive behavioral therapy has improved the cancer-related symptoms of pain, fatigue, and sleep disturbance.

### Nutritional Consultation

It is beyond the scope of this article to address the many issues that cancer patients experience affecting their nutrition which, in turn, adds to their CRF. Nutrition consults are needed to deal with the complexities interfering with dietary and fluid intake resulting from the cancer itself, treatments, and adverse effects of treatment.

### Pharmacologic Interventions

Although several medications have been used to reduce CRF, larger randomized control trials are needed to rigorously evaluate their effectiveness in patients with CRF.<sup>10,54</sup> The most commonly used medications in treating CRF are psychostimulants (methylphenidate and modafinil), antidepressants (paroxetine and bupropion), and cholinesterase inhibitors (donepezil).<sup>10,54</sup> Less commonly used medications include corticosteroids and hematopoietic growth factors.<sup>13,73</sup> Methylphenidate has been reported to improve QOL, reduce CRF, and along with exercise, increase functional capacity.<sup>21,10,74-76</sup> Appropriate adult dosing for this drug is 10 to 60 mg daily in 2 to 3 divided doses preferably 30 to 45 minutes before meals. Maximum dose is 60 mg/d. Dose may be limited by adverse effects. Modafinil was originally approved for the treatment of narcolepsy and is currently the drug of choice for multiple sclerosis.<sup>76</sup> It works in the central nervous system by facilitating release of the neurotransmitters dopamine, norepinephrine, and serotonin, promoting wakefulness.<sup>21</sup> The starting dose of this drug for adults is 200 mg daily in the morning. The maximum dose is 400 mg/d.

Antidepressants such as paroxetine and sertraline (selective serotonin reuptake inhibitor) have not shown to be effective in relieving CRF.<sup>1,10,13,76</sup> Bupropion is a norepinephrine dopamine reuptake inhibitor that may act as a stimulant and has provided significant improvement for depression and CRF.<sup>76</sup> The starting dose for adults is 100 mg daily for 3 days, then the dose is increased to 100 mg 3 times daily at least 6 hours apart. Maximum dose is 450 mg/d in 3 divided doses. Donepezil, a reversible acetylcholinesterase inhibitor used in treating patients with Alzheimer disease, has shown promise for CRF.<sup>76</sup> The half-life is prolonged at 70 hours with a plasma protein binding of

96%. Starting dose is 5 mg daily at bedtime, with dose increased to 10 mg daily after 4 to 6 weeks. Maximum dose is 23 mg daily after 3 months. Corticosteroids have been used to treat CRF and increase energy levels on a short-term basis.<sup>1,21,76</sup> The NCCN<sup>1</sup> also recommends using corticosteroids for patients at the end of life but only after ruling out other causes of CRF. Another medication that has been used for CRF is hematopoietic growth factors. However, due to the higher mortality rates and propensity for thromboembolic events, they are not frequently used and have been pulled from drug trials due to safety concerns.<sup>13</sup> Other medications have been used to treat CRF without consistent efficacy, but the NCCN has now included the consideration of psychostimulants for CRF after other causes have been ruled out.<sup>1</sup>

### CASE PRESENTATION

David is a 57-year-old white man with stage IV lung cancer with no comorbidities. He was a typical example of advanced lung cancer with multiple symptoms. He had a 30-pack-year history of smoking and was currently smoking. Ultrasound-guided biopsy revealed several abnormally enlarged right cervical lymph nodes. Initial magnetic resonance imaging showed no evidence for mass, and positron emission tomography/computed tomography revealed widespread metastatic disease, including areas of the neck, mediastinum, retroperitoneum, mesenteric, and pelvis; right pleural effusion; as well as extrinsic compression on the superior vena cava. In addition to generalized tiredness, the patient experienced pain related to the apical mass, causing a Pancoast syndrome, for which he was placed on a Duragesic patch 50 µg. This dose was gradually reduced to 12.5 µg with good pain control. He rated his fatigue as a "15 of 10" and was dyspneic. David took Marinol to help stimulate his appetite and compazine to help with nausea. Because of severe anemia, he received blood transfusions twice. David received 35 palliative radiation treatments along with concurrent carboplatin and Taxol, of which he completed 5 treatments. The chemotherapy and radiation took just about all the energy he had. He was barely able to make his appointments and he travelled more than an hour to get to the clinic. According to David, his QOL was almost nonexistent. His family members rallied around him, providing encouragement, but he was close to giving up. Two months later, the cancer spread to the frontal lobe of the brain, causing him to have seizures, for which he received additional 14 radiation treatments. Consolidation therapy of carboplatin and paclitaxel was then considered, but David refused due to profound fatigue. He just could not take any more. It was important at this point for all those involved in David's care to support his decision. Helping him to realize he was not giving up on himself was critical and to understand that it was the treatment that was no longer working helped to allay his feelings

of guilt and to begin the process of reestablishing some sense of control through the decision-making process. He also began to interject comments about spiritual issues but was not open to a chaplain visit. He did allow the research nurse to pray with him.

The health care providers were aggressive in assessing David's many symptoms because in this case, treating fatigue was complicated. The underlying etiologies and contributing factors to his fatigue, such as pain, nausea, and anemia, were treated. These factors have an even greater impact on fatigue toward the end of life.<sup>1</sup> In addition to the Marinol, David was seen by the nutritionist regarding his lack of appetite and was educated on foods that would be of most benefit. He was asked to rate his fatigue on the 0-to-10 scale at every visit. Although David's fatigue levels never decreased to the point that he would have liked, it did improve from a 15 of 10 to a 4 of 10, allowing him to enjoy a somewhat better QOL for a short while. Maintaining effective pain control was key in alleviating one aspect of his fatigue. David was educated on the necessity to include some kind of exercise every day to the ability that he could and was encouraged to participate in as many family activities as possible. During this time, different family members would take him for rides to the beach, where he would take very short walks in the sand. Not only did David greatly enjoy these trips but they also provided positive memories for the family. David's lung cancer eventually progressed to the point where hospice was initiated. The entire health care team was vital to David's care. He presented with widely metastatic lung cancer and lived 4 months after diagnosis.

## IMPLICATIONS FOR NURSING PRACTICE

Fatigue is one of the most common symptoms experienced by patients with cancer treated with chemotherapy and/or radiation. In fact, it is the most common symptom experienced by breast and lung cancer patients who are alive for more than 5 years.<sup>4,7-11,77</sup> It is multidimensional and multi-causal; therefore, clinicians need to assess and readjust the management of fatigue along the patient's cancer experience. Assessment needs to go beyond the 0-to-10 scale to include how fatigue is interfering with the patient's QOL and functional capacity. Patient and family education in the areas of pain control, proper nutrition and hydration, exercise, and energy conservation is crucial to empowering the patient with a sense of control over fatigue.

In addition to the many physical and functional issues related to CRF, it is vital for the health care team to remember that the patient is still a whole person. As shared in the case study, David's QOL was affected psychosocially and spiritually as well as physically. As the cancer progresses and symptoms increase, it is sometimes difficult to not fall

prey to the "tyranny of the urgent," thereby objectifying the patient's experience to things that can be measured and fixed. Studies by Krishnasamy<sup>1,78</sup> reported that fatigue produced significant regret, a sense of loss at gradually giving up things that are enjoyed, and sadness. It is important that patients feel heard and acknowledged when they share their feelings. Validating feelings is not a new intervention but can be easily overlooked when dealing with time constraints and multiple issues. Mystakidou and colleagues<sup>1,79</sup> found that fatigue, pain, lack of appetite, and feeling sad were predictors for patient's desire for a hastened death. Cancer-related fatigue continues to present many challenges to helping patients maintain or improve their QOL.

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