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2. Review evidence regarding the outcomes of rehabilitation interventions for cancer survivors before, during, and after treatment.

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# Impairment-Driven Cancer Rehabilitation: An Essential Component of Quality Care and Survivorship

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Adult cancer survivors suffer an extremely diverse and complex set of impairments, affecting virtually every organ system. Both physical and psychological impairments may contribute to a decreased health-related quality of life and should be identified throughout the care continuum. Recent evidence suggests that more cancer survivors have a reduced health-related quality of life as a result of physical impairments than due to psychological ones. Research has also demonstrated that the majority of cancer survivors will have significant impairments and that these often go undetected and/or untreated, and consequently may result in disability. Furthermore, physical disability is a leading cause of distress in this population. The scientific literature has shown that rehabilitation improves pain, function, and quality of life in cancer survivors. In fact, rehabilitation efforts can ameliorate physical (including cognitive) impairments at every stage along the course of treatment. This includes prehabilitation before cancer treatment commences and multimodal interdisciplinary rehabilitation during and after acute cancer treatment. Rehabilitation appears to be cost-effective and may reduce both direct and indirect health care costs, thereby reducing the enormous financial burden of cancer. Therefore, it is critical that survivors are screened for both psychological and physical impairments and then referred appropriately to trained rehabilitation health care professionals. This review suggests an impairment-driven cancer rehabilitation model that includes screening and treating impairments all along the care continuum in order to minimize disability and maximize quality of life. *CA Cancer J Clin* 2013;000:000-000. ©2013 American Cancer Society.

**Keywords:** cancer rehabilitation, prehabilitation, physiatry, physical therapy, occupational therapy, speech therapy, survivorship, disability, impairment, impairment-driven, long-term effects, side effects



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## Introduction

Cancer is one of the most prevalent, disabling, and costly health care conditions affecting people living in the United States and other developed countries. More than 40% of those born today will develop some type of cancer during their lifetime.<sup>1</sup> Due to advances in diagnosis, treatment, and supportive care for cancer, the 5-year relative survival rate for all cancers diagnosed has increased from 49% (1975-1977) to 67% (2001-2007).<sup>2</sup> The majority (64%) of cancer survivors were diagnosed five or more years ago. Siegel et al projected the number of cancer survivors in the United States will increase from 13.6 million to 18 million by 2022.<sup>3</sup> However, the survival rates alone do not reflect the significant burden of treatment toxicity. Oncologists have

the dual concern of increasing survival rates while simultaneously trying to decrease treatment toxicity. Therefore, identifying and addressing treatment-induced physical impairments that can lead to considerable disability is an important part of cancer care.

The cost of cancer is enormous. In 2011, Mariotto et al reported that health care costs for approximately 13.8 million cancer survivors was estimated to be \$124.57 billion and, based on current growing incidence and improved survival rates, the number of cancer survivors in the United States will increase by 2020 to at least 18.1 million, generating an annual cost of \$157.77 billion that year.<sup>4</sup> It is difficult to quantify the indirect costs of cancer survivorship in the United States (eg, lost wages, caregiver burdens,

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transportation, and adaptive equipment), although they are obviously enormous. Other countries, however, have attempted to quantify these costs. Polish health economists have estimated that work loss due to cancer accounts for 0.8% of its gross domestic product.<sup>5</sup> If the United States had a similar work loss due to cancer (with a gross domestic product of approximately \$15 trillion), the equivalent cost would be \$120 billion. Although it is challenging to estimate the profound direct and indirect health care costs of cancer and its sequelae, 2 recent systematic reviews suggested that cancer rehabilitation is cost-effective.<sup>6,7</sup> In addition, a 2013 Scandinavian study reported that of the approximately 1100 participants who were consecutively recruited an average of 11 months after diagnosis and assessed at the beginning and end of rehabilitation, 76% returned to work within a mean of 6 weeks.<sup>8</sup>

An important study published in 2012 compared the health-related quality of life (HRQOL) in cancer survivors with that of others.<sup>9</sup> Cancer survivors reported a much worse HRQOL for both physical and emotional health compared with population norms. Weaver et al<sup>9</sup> assessed HRQOL in 1822 adults with a history of cancer and 24,804 individuals who had never been diagnosed with cancer. Poor physical health was reported by 24.5% of cancer survivors but by only 10.2% of those without a history of cancer. Poor mental health was reported by 10.1% of cancer survivors compared with 5.9% of adults without a cancer diagnosis. When extrapolated, this study suggests that 3.3 million cancer survivors in the United States may have poor physical health and 1.4 million may have poor mental health.

This study demonstrated that cancer survivors' HRQOL is more often influenced by physical issues than emotional problems. Approximately 1 of 4 cancer survivors reported poor physical health whereas only 1 of 10 reported poor mental health. Although the physical and emotional components were reported distinctly in this study, in reality there is considerable overlap and influence of one upon the other.

Evidence suggests that patients, in fact, have many unmet needs.<sup>10</sup> For example, Cheville et al found that in 163 women with metastatic breast cancer, 92% had at least one physical impairment, with a total of 530 impairments identified overall; 484 of these impairments (91%) required a physical rehabilitation intervention and 469 (88%) required physical and/or occupational therapy.<sup>11</sup> Despite more than 90% of the participants needing cancer rehabilitation services, fewer than 30% received this care. With the exception of lymphedema, less than 2% of the impairments that were not detected during hospitalization and required physical or occupational therapy received treatment. Thorsen et al evaluated 1325 survivors of the 10 most prevalent cancers and found that 63% reported the need for at least one rehabilitation service, with physical therapy being the most frequently reported need (43%).<sup>12</sup>

They also reported that patients were often not referred for services; 40% of the participants reported unmet rehabilitation needs. A study by Schmitz et al found that at least 60% of breast cancer survivors had one or more treatment-related impairments at each checkpoint over a 6-year follow-up period.<sup>13</sup> Cheville et al evaluated the detection and treatment of functional problems in cancer survivors and concluded that "Functional problems are prevalent among outpatients with cancer and are rarely documented by oncology clinicians."<sup>14</sup>

A leading cause or perhaps even *the* leading cause of emotional distress in cancer survivors is physical disability. Banks et al investigated distress in cancer survivors and found that the major cause was disability.<sup>15</sup> They concluded, "The risk of psychological distress in individuals with cancer relates much more strongly to their level of disability than it does to the cancer diagnosis itself."<sup>15</sup> Ponto et al observed that, in women living with ovarian cancer, a predictor of distress was poor performance status.<sup>16</sup> A study of 112 Jordanian patients receiving chemotherapy found that lower scores in emotional and physical functioning were associated with higher reports of distress.<sup>17</sup> In fact, the link between physical and psychological function is becoming so important that, in a recent study of screening in an inpatient setting, researchers advised, "...routinely screening for psychological and physical distress should become a first step in the assessment of the biopsychosocial needs of people receiving inpatient treatment for cancer."<sup>18</sup>

There is a need to better understand and clarify the field of cancer rehabilitation, including the selection of appropriate screening for impairments and subsequent disability as well as the identification of health care professionals who are qualified to treat patients for their rehabilitation needs. Rehabilitation health care professionals should be focused on functional outcomes that include activities of daily living (eg, dressing or bathing). However, effectively completing activities of daily living indicates a very low level of function and most cancer survivors accomplish them without any problems. Other functional outcomes that include instrumental activities of daily living, such as performing household chores or going to the grocery store to get food, should also be evaluated. However, even focusing on instrumental activities of daily living is not enough as functional problems may be subtle, but cause significant disability and reduced QOL. For example, rehabilitation professionals who treat patients with head and neck cancer know that subtle swallowing impairments may lead to significant functional problems and subsequent disability for many individuals.<sup>19</sup> Consider the head and neck cancer survivor who continues to have subtle swallowing issues and wants to return to work but has no privacy during lunch to eat without being observed. He may elect to stay on disability rather than risk embarrassment or, even worse, choking or aspirating when rushing through lunch even though his

**TABLE 1. Examples of Functional Assessment Tools<sup>a</sup>**

<b>General performance</b>
Functional Independence Measure (FIM)
Short-Form 36 (SF-36)
Karnofsky Performance Status Scale
Eastern Cooperative Oncology Group (ECOG)
National Institutes of Health Rehabilitation Medicine Department Performance Scale (NIH-RMDPS)
<b>Mobility/balance</b>
Timed Up and Go (TUG) Test
6-Minute Walk Test
Tinetti Balance and Gait Assessment Tools
<b>Pain</b>
Visual analog scales
Brief Pain Inventory
<b>Fatigue</b>
Visual analog scales
Piper Fatigue Scale
Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F)
<b>Distress</b>
Distress Thermometer
Hospital Anxiety and Depression Scale

<sup>a</sup>This is not intended to be a complete list.

family needs his former income and he can perform all functions of his job.

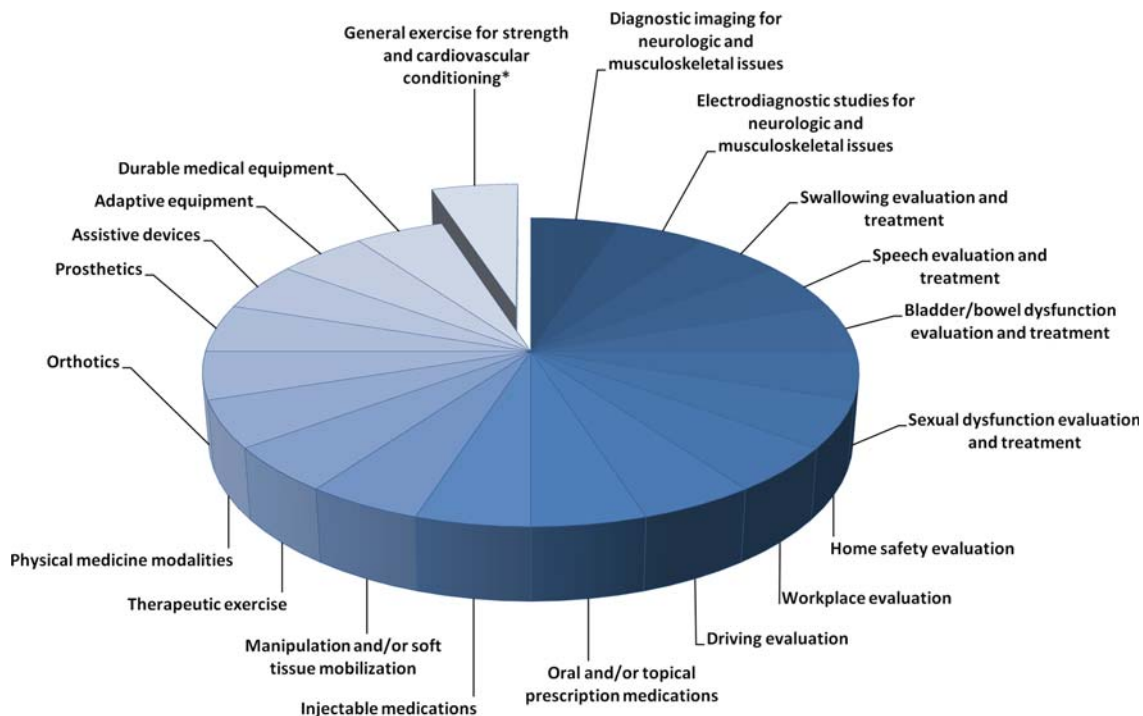
It is important to: 1) focus on screening for physical impairments (from mild to severe) as they need to be identified and treated to improve survivors' physical and psychological outcomes (Table 1); and 2) refer cancer survivors who have problems amenable to rehabilitation interventions to the appropriate health care professionals who have the expertise to evaluate and treat their physical impairments and maximize functional status (Fig. 1). It takes years of training in rehabilitation medicine to appropriately evaluate and treat this diverse and medically complicated patient population; therefore, rehabilitation interventions to treat physical impairments should be performed only by health care professionals who are trained in rehabilitation. Physiatrists should ideally be part of the cancer care team and would be instrumental in diagnostic evaluations as well as provide unique expertise in prescribing pain medications to treat nonmalignant conditions that are a result of cancer treatments, perform injections, and prescribe appropriate splints and other devices. A physiatrist, a specialist in the nonoperative treatment of musculoskeletal problems, might serve as the attending physician on the inpatient rehabilitation unit.

Fitness professionals are an important part of the rehabilitation team as well; however, as they are not trained to treat physical impairments, their scope of practice is limited to providing general exercise recommendations. Patients should only be triaged for general exercise instruction after they have been screened and treated for impairments by trained rehabilitation professionals. Safety is a significant concern in this medically complex population, and lack of appropriate screening or treatment may result in further injury or other medical complications.<sup>20-22</sup>

The following 3 examples highlight the value of screening for and treating physical impairments in a best practices cancer rehabilitation model of care as well as demonstrate the relationship between cancer treatment-related impairments and disability. Because driving is a critical factor in many cancer survivors' lives, enabling them to be independent and functional in the community and at work and avoid significant disability, driving will be the impairment of focus in each example.<sup>23,24</sup> This functional outcome (ie, driving) will remain static while the diagnosis, impairment, and disability vary depending on the case.

The first case is a young man with an osteosarcoma and a right-sided below-the-knee amputation who was unable to drive. Interdisciplinary rehabilitation interventions included medications (physiatrist), a prosthesis (prosthetist), gait training and therapeutic exercise (physical therapist), and a driving evaluation with adaptive equipment recommendations including a left accelerator pedal (occupational therapist). While this patient's impairment was unchanged (amputation), his level of disability significantly improved. The second case is a middle-aged man who had head and neck cancer and had stopped driving during treatment. Discontinuation of driving during treatment is a relatively common occurrence in this population.<sup>25,26</sup> Loss of cervical range of motion, an impairment, made driving unsafe. Care included physiatry (medications to decrease pain and muscle spasms), physical therapy (soft-tissue mobilization and therapeutic exercise), and occupational therapy (adaptive equipment including larger mirrors and sensors that were activated when backing up or changing lanes). This patient's impairment improved but never returned to his premorbid baseline; however, his driving disability resolved. A third case involves a middle-aged woman treated for breast cancer who subsequently developed lymphedema and pain with paresthesias in her hand on the affected side while driving for more than a few minutes. Rehabilitation interventions included physiatry (nerve conduction studies indicated median nerve compression at the wrist for which surgical decompression was recommended), physical therapy (reduction of lymphatic congestion both preoperatively and postoperatively), and occupational therapy (custom hand splint and adaptive equipment including voice-activated computer software that would allow her to send emails without using the keyboard





**FIGURE 1.** Rehabilitation Interventions Focused on Improving Physical Health and Decreasing Disability. Psychosocial, nutrition, and integrative therapies were not included. \*This is the only intervention that is not typically reimbursable by third party payors in the United States.

while healing). Her driving disability was completely resolved, and she was able to return to work.

Impairments and disability are related, but not the same. Mild impairments may cause significant disability and, conversely, rather severe impairments may only cause minor disability. Therefore, in order to alleviate disability, it is important to screen for impairments and then determine how they are related to current function. The prospective surveillance model has been suggested for breast cancer survivors and is focused on the early identification and treatment of physical impairments in this population.<sup>27</sup> Unfortunately, a significant barrier that contributes to patients not being triaged appropriately for rehabilitation medicine services is a lack of understanding about and/or implementation of screening questions, tools, and procedures that help to identify physical impairments in survivors. Psychological screening (distress screening) is an important part of cancer care as well. In fact, every facility that provides cancer care should be implementing screening procedures for both physical and psychological impairments. While this review is primarily focused on screening for and treating physical impairments, both are of paramount importance and influence each other for better or worse. Therefore, a recommended rehabilitation approach is to focus on impairment-driven cancer rehabilitation, which should include screening for and treating psychological and physical impairments simultaneously. Table 2 highlights some of the different strategies included in this approach that might be deployed by an interdisciplinary rehabilitation team.

The prospective surveillance model, recently described for a female breast cancer population in a supplement to the journal *Cancer*, has much to offer in the early identification of impairments and is complementary to impairment-driven cancer rehabilitation care.<sup>28</sup> In the prospective surveillance model, the focus is on surveillance at various junctures throughout the care continuum and into long-term survivorship with the goal of the early identification of impairments followed by appropriate referrals to rehabilitation professionals. In this model, there is the theoretical risk of overdiagnosing impairments in cancer survivors that may not affect their ability to function or QOL. While this is a concern, the practical reality today is one of underdiagnosis and an all-too-common scenario in which cancer survivors are left to their own devices to either “accept a new normal” or to self-identify impairments that are causing them considerable pain, functional loss, disability, and reduced QOL to their health care providers. Diagnosing malignancies often follows a similar pattern in that screening tests may detect cancers at an earlier stage than when patients present with a self-identified “lump” or other symptom. Impairments that may be relatively easily addressed by rehabilitation interventions if detected early can become very difficult to treat if they have progressed over weeks, months, or years. If both the diagnosis of the initial malignancy and the subsequent treatment-related impairments are allowed to progress to the point where the patient self-identifies the condition, the diagnosis is likely to be at a more advanced stage and may require more

**TABLE 2. Common Interdisciplinary Rehabilitation Team Strategies**

SERVICE	PURPOSE	EXAMPLES
Diagnostic imaging	Diagnose etiology of impairment	MRI for diagnosis of adhesive capsulitis or “frozen shoulder” in a patient with breast cancer
Electrodiagnosis	Diagnosis of neuropathy or myopathy	Diagnose long thoracic nerve palsy or “winging scapula” in a patient with lung cancer
Cardiovascular conditioning	Mitigate fatigue	Treat postchemotherapy fatigue
Therapeutic exercise	Address specific muscle imbalances	Address shoulder dysfunction in a patient with head and neck cancer
Manipulation and soft-tissue mobilization	Improve range of motion	Address sequelae associated with radiation fibrosis syndrome
Thermal and electrical modalities	Control pain	TENS for neuropathic pain
Oral and topical analgesics	Control pain	Lidocaine patch for postthoracotomy pain
Injections and implantable pumps	Control pain	Phenol injection of splanchnic nerve for pancreatic cancer pain
Swallowing evaluation	Identify and improve swallowing impairments and avoid or reduce aspiration	Recommend dietary modifications in a patient with laryngeal cancer
Speech evaluation	Identify and improve speech and language impairments	Improve speech in a patient with brain metastasis in the left hemisphere
Assistive devices	Enhance function	Prescribe a reacher for a patient with loss of lumbar motion from metastasis
Orthotics	Compensate for weakness or limited range of motion to improve ambulation and avoid falls	Prescribe an ankle-foot orthosis for a patient with foot drop from neuropathy
Prosthetics	Replace amputated limb	Prescribe prosthesis for a patient with osteosarcoma of the radius
Home evaluation	Assess and improve safety of home environment	Assess functional mobility in the home, including stairs, for a patient with fixation after metastasis to femur
Work evaluation	Evaluate and improve ability to perform essential job functions	Facilitate return to work after resection for a brain tumor
Driving evaluation	Assess and improve safe driving	Recommend adaptive equipment such as larger mirrors and sensors for a patient with head and neck cancer with limited cervical range of motion
Mental health counseling	Evaluate and improve psychological well-being	Recommend specific coping strategies for decreasing anxiety around returning to work
Neuropsychological testing	Evaluate cognitive deficits in “chemo brain”	Recommend rehabilitation interventions that focus on adaptive strategies to improve memory and concentration as well as functional organization in daily life

MRI indicates magnetic resonance imaging; TENS, transcutaneous electrical nerve stimulation.

medical services with perhaps a worse outcome. Notably, the anticipated outcome with impairments that were not addressed early would likely be increased morbidity, whereas the anticipated outcome with cancer that is not addressed early may be increased morbidity and/or mortality. While a recent review of studies on the cost-effectiveness of cancer rehabilitation was positive, there is a lack of data to date on the financial benefits of the prospective surveillance model.<sup>6</sup>

While rehabilitation in its totality encompasses much more than physical impairments, without a clear and concise focus on identifying and treating physical impairments (including cognitive dysfunction) in cancer survivors, there is little hope of improving their care. The contention,

supported in the literature cited previously,<sup>14</sup> is that if health care professionals focused on routinely screening patients with cancer for physical impairments, in addition to distress and other issues, and then referred appropriately to trained rehabilitation professionals, significant improvement in function, reduced disability, lower direct and indirect healthcare costs, and increased physical and psychological HRQOL would result (Table 1) (Fig. 1).<sup>29</sup> Therefore, this review is written from the standpoint of impairment-driven cancer rehabilitation. Admittedly, the rehabilitation literature often does not make the distinction between physical and psychological health outcomes clear, but where distinction does exist, attempts were made to highlight it.

## Identifying Physical Impairments in Patients With Cancer

Table 3 lists the myriad impairments that may occur in patients with cancer, impacting virtually every organ system, and Table 1 lists some examples of validated tools that may be used to identify physical impairments in this population. These impairments can be due to tumor compression, treatment side effects, or paraneoplastic phenomena. While they can be sudden, catastrophic events such as spinal cord compression, Chevillat et al noted that in patients with metastatic breast cancer, disablement is more frequently “driven by the accrual of multiple physical impairments, adverse symptoms, and their interactions rather than by discrete and functionally catastrophic impairments.”<sup>30</sup> In order to limit the scope of this review, several common impairments will be presented as examples. This article focuses on rehabilitation interventions; the reader should refer to specific treatment guidelines for the medical and surgical management of these conditions.

### Pain

Most cancer patients experience pain during the course of their illness, often debilitating pain.<sup>31</sup> Pain is also one of the most common issues that cancer rehabilitation health care professionals routinely address. It is estimated that 30% to 50% of patients undergoing acute cancer treatment will experience pain and up to 70% of those with metastatic disease will have pain.<sup>32</sup>

Chronic pain in cancer survivors is relatively common as well. Postmastectomy, postamputation, and postthoracotomy pain syndromes have all been described previously. The prevalence of chronic postmastectomy and postthoracotomy pain may be as high as 50%.<sup>33-35</sup> In another recent study, researchers found that approximately 2 of 3 women undergoing surgery for breast cancer developed pain.<sup>36</sup> Other studies of chronic pain in patients undergoing limb amputation and thoracotomy report incidences of up to 70% to 80%.<sup>37</sup> Head and neck cancer survivors have a reported incidence of chronic pain of approximately 50%.<sup>38-40</sup>

In a Danish study, researchers evaluated more than 3000 female breast cancer survivors who were on average just over 2 years after surgery.<sup>33</sup> This study found that approximately 50% of the women reported pain. Of the women who complained of pain, 20% had contacted a physician within the past 3 months for reports of pain in the surgical area, despite having had the surgery on average more than 2 years earlier. Interestingly, in this study, women were more likely to report persistent pain if they were younger (aged younger than 40 years), had received radiation treatment, had undergone an axillary lymph node dissection rather than a sentinel lymph node biopsy, or had experienced pain in other parts of their body as well.

Barriers to managing pain have been described in the literature, and chronic pain is such a significant issue in

cancer survivors that physicians at The University of Texas M. D. Anderson Cancer Center in Houston suggested, “Promotion of wellness behaviors and the use of physical therapy and physical medicine techniques early in cancer recovery may help to diminish the intensity and incidence of chronic pain in long-term survivors. For example, perhaps all mastectomy or radical neck dissection patients should be put through a course of physical therapy as a part of routine care.”<sup>37,41</sup>

Pain affects QOL in cancer survivors and may be due to the malignancy itself, side effects or aftereffects of the treatment, or other unrelated comorbidities.<sup>42</sup> Fear of pain may be the cause of functional limitations rather than the pain itself, and in a study comparing patients with advanced cancer with those with chronic noncancer pain, the fear of pain predicted limitations in function only in those patients with advanced cancer.<sup>43</sup> Pain severity correlates closely with function, and in a study of Chinese patients with cancer, those with more severe pain had poorer function while those with mild, well-controlled pain functioned similarly to individuals without pain.<sup>44</sup> Thus, it is critical to identify the pain generator(s) as specific interventions can frequently ameliorate pain, sometimes without medications. It is also important to note that pain often occurs in “clusters,” with other symptoms such as sleep or mood disturbance.<sup>45</sup> Table 4 lists some common examples and associated characteristics of cancer treatment-related pain.

### Fatigue

Cancer-related fatigue (CRF) is defined as an “overwhelming and sustained exhaustion and decreased capacity for physical and mental work...not relieved by rest.”<sup>46</sup> In addition, fatigue has been shown to impact negatively one’s economic, social, and emotional status.<sup>47,48</sup> Furthermore, CRF is correlated with treatment intensity and can last well past the completion of treatment.<sup>49</sup> As many as 75% of patients with cancer have CRF and the likelihood of developing fatigue is increased with any cancer-related treatment and is also more likely to occur with comorbidities (eg, hepatic, cardiac, renal, and pulmonary) and other conditions (eg, insomnia, inactivity, chronic pain, and mood disorders).<sup>50,51</sup> Fatigue often persists beyond the treatment period.<sup>52</sup>

It has been shown that improving quality of sleep is helpful, but increasing the amount of “rest” is not effective in reducing the symptoms of CRF.<sup>53</sup> Careful attention to comorbidities and their treatment will reduce CRF. Treatment of depression and chronic pain has also been shown to improve symptoms.<sup>54</sup> Exercise has been shown to mitigate fatigue and this is even true while patients are receiving active treatment of their cancer.<sup>55-57</sup>

### Neurologic Impairments

A wide variety of impairments of nervous system function may result from cancer, either by direct effect at the primary

**TABLE 3. Common Impairments in Cancer Patients<sup>a</sup>**

IMPAIRMENT CATEGORY	REASON TO REFER TO REHABILITATION	CANCER DIAGNOSIS														
		LUNG	BREAST	PROSTATE	COLORECTAL	CNS	HEAD/NECK	MELANOMA	LYMPHOMA	OSTEOSARCOMA	OVARIAN	TESTICULAR	ADVANCED			
General physical	Difficulty returning to premorbid activities	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Fatigue	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Joint pain, diffuse (eg, arthralgias)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Musculoskeletal pain (eg, myalgias, myofascial pain)	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Neuropathic pain	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Somatic pain	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Visceral pain	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Weakness	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Deconditioning <sup>b</sup>	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Autonomic dysfunction	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Back pain	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
	Balance dysfunction	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Bowel dysfunction			■	■	■											
Cervical range-of-motion limitations			■			■										
Chemotherapy-induced peripheral neuropathy	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Chest/thoracic pain	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Cognitive impairment	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Compression neuropathy	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Dystonia		■														
Gait dysfunction	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Graft-versus-host disease								■								
Headaches					■											
History of falls		■		■	■	■	■	■	■	■	■	■	■	■	■	
Jaw excursion, limited			■													
Joint pain, localized	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Joint range-of-motion limitations	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	



TABLE 3. (Continued)

IMPAIRMENT CATEGORY	REASON TO REFER TO REHABILITATION	CANCER DIAGNOSIS											
		LUNG	BREAST	PROSTATE	COLORECTAL	CNS	HEAD/NECK	MELANOMA	LYMPHOMA	OSTEOSARCOMA	OVARIAN	TESTICULAR	ADVANCED
	Lumbosacral plexopathy												
	Lymphedema												
	Muscular asymmetry												
	Neck pain												
	Osteopenia/osteoporosis												
	Paralysis												
	Plexopathy												
	Radiation fibrosis syndrome												
	Radiculopathy												
	Scapular winging												
	Scar adhesions												
	Sensory deficits												
	Sexual dysfunction												
	Shoulder pain												
	Speech impairment												
	Swallowing impairment												
	Trismus												
	Urinary dysfunction												
	Visuospatial and/or proprioception dysfunction												
Psychosocial	Psychosocial dysfunction												
Functional	Difficulty with ADLs (dressing/bathing, etc)												
	Difficulty with IADLs (chores/shopping, etc)												
	Orthotics												
	Prosthetics												
	Assistive devices (cane, reacher, etc)												

TABLE 3. (Continued)

IMPAIRMENT CATEGORY	REASON TO REFER TO REHABILITATION	CANCER DIAGNOSIS											
		LUNG	BREAST	PROSTATE	COLORECTAL	CNS	HEAD/NECK	MELANOMA	LYMPHOMA	OSTEOSARCOMA	OVARIAN	TESTICULAR	ADVANCED
	Adaptive equipment needs	■	■	■	■	■	■	■	■	■	■	■	■
	Durable medical equipment needs	■	■	■	■	■	■	■	■	■	■	■	■
	Home safety evaluation	■	■	■	■	■	■	■	■	■	■	■	■
	Workplace evaluation	■	■	■	■	■	■	■	■	■	■	■	■
	Driving evaluation	■	■	■	■	■	■	■	■	■	■	■	■

ADLs indicates activities of daily living; CNS, central nervous system; IADLs, instrumental activities of daily living.

<sup>a</sup>This is not meant to be a comprehensive list of cancer diagnoses or impairments.

<sup>b</sup>In need of instruction about a safe and therapeutic exercise program.

Modified from the "When to Refer to Rehab" template with permission from Oncology Rehab Partners, LLC, Northborough, Massachusetts.

or metastatic tumor site or secondarily as a consequence of surgery, chemotherapy, or radiation treatments. Neurologic impairments, regardless of whether they are due to the malignancy or the cancer treatment, may significantly impact the individual's physical, social, vocational, and emotional capabilities. Rehabilitation strategies need to factor in progressive, sometimes rapid, functional decline; the toxic effects of cancer treatments; tumor recurrence; CRF; medical fragility; and the psychological and family issues associated with an often terminal disease. The interdisciplinary rehabilitation team is best equipped to handle the complexities of restorative care in these situations, and meet the patient's and family's goals of maximizing functional recovery and preserving QOL.

Chemotherapy-induced peripheral neuropathy, a possible side effect of some chemotherapy drugs, is the most prevalent neurologic complication of cancer.<sup>58</sup> It is estimated that peripheral neuropathy may develop in 50% to 60% of patients treated with taxanes and can result from paraneoplastic phenomena as well.<sup>59,60</sup> Neuropathy symptoms may be subtle and functional losses in sensation, proprioception, and motor function can accrue almost imperceptibly over time. For example, Wampler et al screened patients with breast cancer after treatment with taxanes and found significant postural instability.<sup>61</sup> Interventions include balance training, an emphasis on using visual compensation for proprioception, and orthotics. Patients need education about foot care and environmental hazards such as throw rugs.

The term "chemo brain" refers to a patient's report of mild cognitive impairment (MCI) during or following chemotherapy. Although this term is widely used by patients, it is somewhat controversial in the medical literature as not all experts agree on the use of the term, the etiology of the symptoms, and/or whether this is a legitimate diagnosis.<sup>62,63</sup> Many chemotherapeutic drugs cause neurotoxicity, and the brain may be affected. There are numerous proposed mechanisms behind chemotherapy-induced MCI<sup>64,65</sup> and subsequent impairments, although subtle, may cause significantly decreased function and disability in cancer survivors.<sup>63,66,67</sup> Neurocognitive interventions to improve function are an important part of rehabilitation care and often involve psychiatry and occupational and speech therapy consultations. Although the pathophysiology of MCI in cancer survivors is different than in patients with traumatic brain injury, the rehabilitation interventions used are often similar and focus on strategies that improve memory, attention, and organizational skills. In fact, it is not uncommon for patients with mild traumatic brain injuries (concussions), such as military personnel exposed to blasts,<sup>68</sup> to have impairments and functional problems that are similar to those in patients who have undergone chemotherapy. Neuropsychological testing may be performed prior to consultations to identify specific deficits.

**TABLE 4. Examples of Nonmalignant Pain Due to Cancer Treatment**

PRIMARY CANCER	SYMPTOM	PAIN GENERATOR	TREATMENTS
Lung cancer	Chest wall pain	Postthoracotomy pain	TENS, lidocaine patch, intercostal block
Breast cancer	Hand pain	Carpal tunnel syndrome from lymphedema	Lymphedema therapy, splinting, injection, surgical release
Laryngeal cancer	Shoulder pain	Scapular winging from accessory nerve palsy	Taping, manual mobilization, scapular stabilization exercises

TENS indicates transcutaneous electrical nerve stimulation.

Brain tumors often cause neurologic sequelae. Despite increases in the survival rates of patients with primary brain tumors and advances in treatment, survival is limited for many individuals and this feature needs to be factored into the timing, duration, and types of rehabilitation interventions offered. Nevertheless, rehabilitation after brain tumor resection has been shown to result in better outcomes, including gains in functional status and discharge to home.<sup>69</sup> In fact, patients with brain tumors have been found in some studies to have shorter lengths of stay on acute rehabilitation units compared with those with other noncancerous brain disorders, possibly as a result of higher initial levels of functional independence on admission, fewer behavioral issues, better social support, and expedited discharge planning due to cancer-related prognostic factors.<sup>70</sup>

Most patients with brain tumors have multiple impairments depending on tumor location and size and, in those who have undergone surgery, the volume of tissue excised. In a study of patients with brain tumors undergoing acute rehabilitation, the most common neurologic deficits included impaired cognition (80%), weakness (78%), and visual-perceptual dysfunction (53%).<sup>71</sup> In a more recent study of 106 patients, the most common impairments reported were pain (56%; which included a 42% incidence of headaches), ataxia (44%), seizures (43%), paresis (37%), cognitive dysfunction (36%), and visual impairment (35%).<sup>72</sup>

Specific rehabilitation measures for patients with brain tumor-related disability emphasize early attention to mobilization, including bed mobility, transfer training, and ambulation or wheelchair skills. Those patients presenting with unilateral leg weakness will benefit from a physical therapist assisting with progressive gait and balance training and, when necessary, using an assistive device appropriate for the degree of stability required (single-point cane, 4-pronged cane, or walker). Provision of an ankle-foot orthosis to control weakness and/or spasticity of the ankle musculature is often needed. The risk of limb contracture, especially in ankle plantar flexion, wrist and finger flexion, and shoulder adduction and internal rotation is increased in patients with weakness, particularly spastic hemiplegia. Early and regular stretching programs, along with appropriate limb positioning and supportive devices such as Multi Podus boots, are critical. Glenohumeral support and position in bed

and wheelchair, the latter involving a lap table or arm trough, is key to preventing hemiparetic shoulder pain. A flaccid or significantly subluxed glenohumeral joint may require a humeral cuff or sling-type arm support that is used judiciously so as to not promote a contracture in internal rotation and adduction. For individuals limited by unilateral arm weakness, an occupational therapist can provide adaptive equipment such as reachers, sock donners, or elastic shoelaces.

Injuries to the spinal cord may be secondary to either traumatic or nontraumatic causes. Cancer-related spinal cord injury (SCI) incidence may actually exceed that from trauma and represents the most frequent type of nontraumatic SCI.<sup>73</sup> Symptoms consistent with SCI occur as a result of metastasis in up to 5% of all patients with cancer.<sup>74</sup> Weakness is present in 74% to 76% of patients, autonomic dysfunction in 52% to 57% of patients, and sensory loss in 51% to 53% of patients.<sup>75</sup> Pain alone may persist for a month or more (average, 6 weeks) before significant neurological changes develop. The acute onset of back or neck pain in a patient with cancer should be considered to be spinal metastasis until proven otherwise. It is critical, therefore, to rule out metastasis prior to sending the patient for an exercise program as spinal metastases may result in pathologic fracture and even cord compression if proper precautions are not instituted.

Positive results have been demonstrated following rehabilitation in individuals with disability from spinal cord tumors, with significant functional gains measured after inpatient rehabilitation.<sup>76</sup> For patients with incomplete injury, those with the greatest number of neurological deficits were found to benefit the most from inpatient rehabilitation. Factors that have been identified as better prognostic indicators of survival after inpatient rehabilitation include lymphoma, multiple myeloma, breast and kidney cancer types; SCI as the presenting symptom; slow progression rate of neurologic symptoms; combined surgical and radiation treatments; partial bowel control; and partial independence with transfers from bed to chair on admission to the rehabilitation unit.<sup>77</sup> In a more recent retrospective study from Australia, patients with primary spinal cord tumors and those without pain had significantly better functional outcomes than those with

metastatic disease and those with pain. However, all groups made substantial progress on average.<sup>78</sup>

Medical complications associated with recent SCI are common, potentially life-threatening, and require a vigilant and knowledgeable hospital staff. Comprehensive care for SCI includes the management of pain, autonomic dysreflexia, pulmonary and urinary tract infections, thromboembolic disease, bowel and bladder dysfunction, decubitus ulcers, limb contractures, and spasticity as well as attention to ventilatory ability in those with high spinal levels of injury. Certain measures instituted immediately after the onset of spinal cord dysfunction remain standards of acute care in this patient population. Prophylaxis for lower extremity venous thromboses with low-molecular-weight heparin should be initiated immediately unless otherwise medically contraindicated and continued for at least the duration of the rehabilitation phase (eg, for a total of 3 months in cases of plegia or severe paresis). Other areas of management that should be instituted early in patients with loss of thoracic musculature include incentive spirometry and chest physiotherapy. The initiation of intermittent bladder catheterization every 4 to 6 hours when daily bladder volumes are less than 2 liters should be routine treatment, as well as the institution of a bowel program with daily or every-other-day suppository or digital stimulation. Other key measures in early spinal cord care include the prevention of skin breakdown in body areas commonly at risk (occiput, sacrum, greater trochanter, heels, and ischial tuberosities) by the patient turning in bed every 2 hours, as well as the use of a specialized pressure relief bed and wheelchair mattresses, and heel protectors. In addition, at least daily limb range of motion should be initiated immediately after the onset of the SCI. Of note, as a result of vasoconstriction from splanchnic sympathetic nerve stimulation by noxious stimuli below the level of the spinal lesion, patients with severe spinal cord dysfunction above the T6 level are prone to developing autonomic dysreflexia, which includes a significant increase in blood pressure above baseline. If blood pressure remains significantly elevated, pharmacological measures and intensive monitoring may be needed.<sup>79</sup>

### Bony Metastases

The vast majority of cases of skeletal cancer are of metastatic origin. Bone metastases are a frequent source of cancer-related physical impairment that require the active involvement of the rehabilitation team. Challenges for the treating team arise when metastatic bone lesions produce severe pain that limits function or increases the risk of fracture during therapeutic exercise or mobility. Rehabilitation for this patient population focuses on decreasing the stress or immobilizing compromised bone through the provision of assistive devices and orthoses, strength and balance training, and modification of the patient's environment. Whenever possible, bed rest should be avoided as it adds

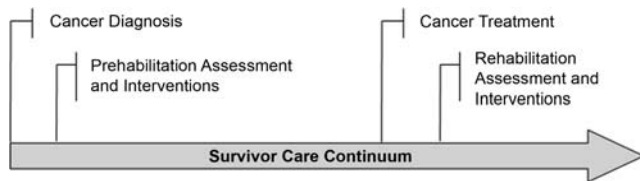
to general debility and further functional loss, as well as increases the risks of hypercalcemia and thromboembolic disease. Depending on the severity and location of the lesion, mobility restrictions can range from non-weight-bearing to weight-bearing as tolerated. For complete non-weight-bearing restrictions, assistive devices in the form of walkers or bilateral crutches are typically necessary. If the condition is bilateral, wheelchair mobility may become the safest option. Single-point canes are used for patients with minimal balance deficits and smaller lesion size, but patients with larger, more symptomatic lesions should be advanced to a forearm-type crutch, which permits a greater degree of weight support.

It is critical to first rule out the coexistence of upper extremity lytic lesions before prescribing assistive devices that require weight support through the arms. Bracing may reduce the risk or symptoms of a pathologic fracture involving the upper extremities and can facilitate use of the arms in functional activities. Those individuals with upper limb lesions should be taught to minimize torsion and weight-loading and may benefit from an arm sling or humeral cuff support. In the spine, use of a Jewett brace to prevent spinal flexion or a custom-molded clamshell design to give stability in all directions can be prescribed. When more rigid bracing is not tolerated secondary to poor skin tolerance or discomfort, a thoracolumbar corset provides limited support and pain relief. Spinal bracing needs to extend several segments above and below the involved area of the spine.

Cancer patients with pathological fractures and associated functional deficits have been shown to make significant gains when admitted to an inpatient rehabilitation hospital unit.<sup>80</sup> It should be recognized that the rehabilitation of patients with skeletal metastases has multiple inherent risks, and strategies to exercise these patients remain largely theoretical due to a lack of empiric data. However, the alternative to rehabilitation therapies is often bed rest, which carries its own set of potential complications, including muscle contractures, weakness and atrophy, osteoporosis, orthostatic hypotension, pressure sores, pulmonary infection, and an increased risk of thromboembolic disease.

### Soft-Tissue Impairments Associated With Cancer Diagnoses

Cancer and/or its treatments can cause significant soft-tissue abnormalities. One of the most frequently observed is lymphedema, which is extremity swelling resulting from disruption of the lymphatics following axillary or groin lymph node dissection. The prevalence of lymphedema in patients with breast cancer has been generally reported to be between 15% and 30%.<sup>81</sup> Complete decongestive therapy, which includes the use of manual lymph drainage and compression garments, is effective in controlling edema. When applied early in the course of treatment, before the development of a significant volume increase (eg, a greater



**FIGURE 2.** Timeline of Prehabilitation and Rehabilitation Assessments and Interventions.

than 250-cc increase in the arm), lymphedema can almost be reversed.<sup>82,83</sup> Weight lifting, traditionally believed to be contraindicated in patients with lymphedema, has subsequently been shown to be beneficial.<sup>84</sup>

Another frequently seen soft-tissue complication of cancer treatment is radiation fibrosis. Long-term sequelae include contracture and loss of muscle mass. Conservative management with manual release techniques, stretching exercises, and corticosteroid injections to the shoulder (used judiciously) may help to improve range of motion. The use of antifibrotic agents, such as pentoxifylline, in the treatment of this problem has shown promise.<sup>85</sup> Botulinum toxin injections have also been used successfully.<sup>86</sup>

## Cancer Rehabilitation and the Care Continuum

Opportunities to screen for and treat impairments in cancer survivors may begin shortly after diagnosis and continue even years after the completion of cancer treatment (Fig. 2). The care continuum includes prehabilitation (interventions designed to increase one's function in anticipation of an upcoming stressor),<sup>87,88</sup> rehabilitation during acute cancer care, rehabilitation after acute cancer care, and rehabilitation of patients with cancer as a chronic condition (that may or may not ultimately be the cause of their mortality). Prehabilitation is a process on the cancer continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment and includes physical and psychological assessments that establish a baseline functional level, identify impairments, and provide interventions that promote physical and psychological health to reduce the incidence and/or severity of future impairments. Rehabilitation professionals who treat physical impairments, including cognitive dysfunction, typically include but are not limited to physiatrists, physical therapists, occupational therapists, speech-language pathologists, and rehabilitation nurses.

### Prehabilitation

Prehabilitation is the precursor to rehabilitation and may involve a single or multiple interventions in anticipation of upcoming cancer treatment; interventions may be considered prior to virtually any type of cancer treatment.<sup>89</sup> A prehabilitation program usually begins with an initial assessment to identify any postdiagnosis, but pretreatment, impairments. If these exist, then appropriate triage

**TABLE 5.** Improving the Oncology-Rehabilitation Interface

- Include trained rehabilitation professionals in the formal cancer care programming, including survivorship programming.
- Educate all staff involved in the care of oncology patients about impairment-driven cancer rehabilitation care.
- Establish a multidisciplinary cancer rehabilitation program/service line or, alternately, create a referral process for rehabilitation services within the geographic area.
- Use screening tools to identify impairments.
- Identify screening opportunities and integrate with appropriate on-site and/or local referral resources.
- Map patient flow through the organization.
- Require documentation of the navigation process, including cancer rehabilitation referrals.
- Track patient functional outcomes across the continuum of care beginning with a baseline assessment.
- Include reassessments to identify new or ongoing rehabilitation needs.
- Include the patient as a partner in his/her rehabilitation care.
- Use patient education materials to complement rehabilitation care.

measures should be considered, which may include referrals to physiatrists and/or physical, occupational, or speech therapists (Table 5). If impairments are not identified, then the goal is to prevent or limit future impairments, especially focusing on those that may occur with upcoming cancer treatment (Table 6). Courneya and Friedenreich described the Physical Exercise Across the Cancer Experience (PEACE) Framework that recommended “buffering” prior to cancer treatment, which is one type of prehabilitation intervention (exercise).<sup>88</sup> Patients awaiting resection can be offered supervised preoperative strength and endurance exercises to buffer the potentially detrimental effects of postsurgical immobility. Multimodal prehabilitation, or the use of more than one intervention at a time (such as concurrent physical therapy and nutrition counseling), may be more successful than unimodal treatment. Interval reassessments are, of course, necessary to maximize the efficacy of interventions and coordinate with upcoming cancer treatment(s).

Preoperative physical therapy is effective in reducing the length of hospital stay and postoperative complication rates in patients undergoing surgery. Examples include lung, colorectal, and esophageal cancer.<sup>87,90-97</sup> Morano et al formulated a 4-week prehabilitation program that did not delay the “usual workup” for lung cancer and subsequent resection surgery.<sup>97</sup> This trial of 24 patients randomized to pulmonary prehabilitation or breathing exercises only demonstrated that patients in the pulmonary prehabilitation subset had a shorter hospital stay and a shorter duration of chest tube necessity.



**TABLE 6. Examples of Prehabilitation Goals**

- Improve cardiovascular, pulmonary, and/or musculoskeletal function.
- Improve balance and reduce the risk of falls.
- Reduce anxiety and improve coping with specific cognitive behavioral strategies.
- Improve quality of sleep with sleep hygiene education.
- Optimize surgical outcomes with smoking cessation interventions.
- Optimize diet with nutrition counseling.
- Begin preoperative pelvic floor muscle strengthening to improve continence outcomes.
- Begin pretreatment swallowing exercises to improve swallowing outcomes.
- Implement home safety strategies to avoid falls.
- Facilitate return to work with adaptive equipment.

An Italian study demonstrated improved function in patients with stage I or II non-small cell lung cancer and chronic obstructive pulmonary disease who underwent an extensive prehabilitation program, including supervised aerobic exercises and strength training.<sup>90</sup> Eleven patients underwent a 4-week physical therapy program prior to lobectomy, with medical evaluation occurring prior to and on completion of the program. Later, Divisi et al observed 27 patients in a 4-week to 6-week prehabilitation program of physical therapist-supervised breathing exercises, cycle ergometry with telemetry monitoring, smoking cessation, and nutrition optimization.<sup>91</sup> All patients achieved functional improvement as measured by peak oxygen consumption and pulmonary function tests.

A Japanese study used historical controls to avoid depriving any of their patients of the benefits of prehabilitation.<sup>92</sup> Twenty-two patients with lung cancer and chronic obstructive pulmonary disease underwent supervised hospital-based respiratory therapy and an independent walking program for 2 weeks prior to undergoing lobectomy. These patients were compared with 60 patients with lung cancer who received care at the same institution before the prehabilitation program. Despite greater impairments in lung function being noted in the prehabilitation group, the prehabilitation patients had fewer postoperative complications and a shorter hospital stay.

Timing and availability of potentially curative treatment are important considerations when designing a prehabilitation program. Benzo et al followed 9 control patients and 10 study patients to demonstrate the efficacy of physical therapy prior to lung resection surgery in a randomized controlled trial (RCT).<sup>93</sup> The study patients required a chest tube for a shorter duration of time, had lower postoperative respiratory morbidity, and needed fewer days in the hospital after surgery.

Of note, in a prior study, the same authors tried to randomize patients to 4 weeks of prehabilitation or usual care before lung resection, but neither providers nor patients were willing to wait the 4 weeks before the potentially curative surgery. As such, Benzo et al recommended the shorter-duration prehabilitation program, tailored to meet the surgery date.<sup>93</sup> Although the timing of cancer treatments remains of utmost importance, even short-duration prehabilitation may provide significant benefit. Rehabilitation can potentially affect mortality, as functional capacity may predict survival in patients with non-small cell lung cancer.<sup>98</sup>

Kim et al and Carli et al experimented with different options in order to determine best practices for prehabilitation in patients prior to colorectal surgery. The pilot study by Kim et al randomized 21 patients scheduled to undergo bowel resection to physical therapy or control groups.<sup>94</sup> The physical therapy group underwent 2 to 5 weeks of aerobic exercise of increasing intensity. Although the distance walked improved in both the study group and the control group, heart rate and oxygen uptake during submaximal exercise as well as peak power output were found to be improved in the study group only.

In their following study, Carli et al randomized 112 patients to an intervention group of participants who took part in a structured cycling and strengthening program with interval supervision or to a control group.<sup>95</sup> Remarkably, there were no significant differences in outcomes noted between the groups. As such, the authors tried to address nutritional, psychological, and exercise compliance issues in the design of a subsequent study.<sup>87,99</sup> The patients who underwent trimodal prehabilitation with optimization of nutrition, anxiety reduction, and moderate aerobic exercise combined with resistance training had a better postoperative walking capacity at 4 weeks and 8 weeks after surgery as compared with historical controls. As noted in a Canadian study, resistance training is particularly important in this population as only 25% of colorectal cancer survivors may be meeting strength exercise guidelines.<sup>100</sup>

A Japanese retrospective cohort study reviewed the outcomes of prehabilitation in 100 patients with esophageal cancer who underwent esophagectomy.<sup>96</sup> The prehabilitation group received preoperative respiratory rehabilitation for greater than 7 days prior to surgery while a control group received insufficient or no breathing training. The prehabilitation group had fewer postoperative pulmonary complications than controls.

Prehabilitation also plays a role in other operable cancers, such as prostate cancer. Perioperative unimodal rehabilitation provides a significant benefit in patients with prostate cancer.<sup>101</sup> Goode reviewed studies evaluating the role of

pelvic floor therapy on continence after prostatectomy.<sup>101</sup> Of the studies that included preoperative pelvic floor muscle training with a physical therapist, 2 showed a clinically significant benefit and one did not. Taken in the context of the 5 of 6 studies that showed a benefit of unimodal rehabilitation in patients with prostate cancer at different times on the care continuum, prehabilitation appears to be helpful for these patients overall. Physical therapists are particularly important in treating this population.

Speech-language pathologists may also offer targeted unimodal exercise interventions that improve outcomes prior to the treatment of head and neck cancer. Patients with head and neck cancer often experience physical and psychological impairments due to the potential for changes in their speaking and swallowing abilities.<sup>102</sup> The current Johns Hopkins protocol for the treatment of patients with head and neck cancer includes prehabilitation with a speech-language pathologist for education, baseline assessment of swallowing, nutrition, and prophylactic oral motor exercises.<sup>103</sup> In this protocol, Tippett and Webster advocate for pretreatment intervention before surgery, chemotherapy, or radiation to achieve the best outcomes in patients with head and neck cancer.<sup>103</sup>

Further evidence for prehabilitation is provided by a RCT of the initiation of swallowing exercises prior to and during chemoradiation treatment for patients with head and neck cancer.<sup>104</sup> Patients who underwent the swallowing therapy intervention had better function at 3 and 6 months after treatment of their cancer than controls. Of note, nearly 70% of patients assigned to the swallowing therapy intervention stopped doing their home program by the fifth week of radiation treatment. Remarkably, they still had improvement 3 to 6 months later, although no significant difference was noted subsequently.

The studies cited herein demonstrate the efficacy of some prehabilitation interventions in the treatment of patients with cancer. Further research is needed to better understand the role of prehabilitation in the treatment of newly diagnosed patients.

### Rehabilitation During Acute Cancer Care

Historically, preoperative and postoperative care were provided by surgeons. However, research suggests that a multidisciplinary approach may result in better outcomes. A variety of terms have been used to describe these approaches, such as “fast-track rehabilitation” or “enhanced recovery” or “accelerated rehabilitation,” and they have been studied in different cancer populations including, but not limited to, patients with colorectal,<sup>105</sup> ovarian,<sup>106</sup> gastric,<sup>107</sup> pancreatic,<sup>108</sup> and lung cancer.<sup>109</sup> In a 2013 retrospective study on patients undergoing an esophagectomy with a fast-track rehabilitation that included early mobilization, epidural analgesia control, fluid infusion volume

control, and enteral nutrition for early discharge (compared with a group receiving conventional care), Cao et al found that the intervention group had fewer complications, less postoperative pain, a reduction in the length of their hospital stay, and a faster return to work and normal activities.<sup>110</sup> In a 2013 review of fast-track rehabilitation articles published between 1966 and 2012, Adamina et al concluded, “Multidisciplinary management of perioperative patient care has improved outcomes.”<sup>111</sup>

During active cancer treatment, rehabilitation interventions may be helpful in preventing the predicted decline in QOL related to the disease and treatment side effects; however, lifestyle factors and comorbid diagnoses cannot be ignored. Brown et al observed that patients did not experience reduced fatigue during radiation treatment despite a multimodal rehabilitation program.<sup>112</sup> Participants in the failed intervention suggested that addressing alcohol and tobacco abuse, mood disorders, sleep disorders, and sleep hygiene in any subsequent group sessions might reduce fatigue.<sup>113</sup> They also recommended that caregivers be included, but not for every session. According to these survey data, it appears that patients prefer a multimodal program that includes counseling services.

Although reported separately, a study of the same group of patients with cancer undergoing radiation treatment at the Mayo Clinic found that their QOL was maintained in the multimodal rehabilitation intervention group at one month of follow-up, but declined significantly in the control group of patients who were receiving the usual radiation oncology care without rehabilitation.<sup>114</sup> At 6 months, intervention patients maintained their QOL, while controls gradually returned to baseline. Of note, the strength training was well-tolerated.<sup>115</sup> In addition, aerobic activities were not included in the sessions, which may be one explanation for the lack of improvement in fatigue. Regardless, the higher QOL in the intervention group demonstrated a significant benefit of multimodal rehabilitation.

A subsequent study by Clark et al did show that a shorter, 6-session, multimodal rehabilitation program could also maintain QOL during the intense period of radiation treatment.<sup>113</sup> A total of 131 patients with cancer undergoing radiation were randomized to a multimodal rehabilitation program or to standard medical care without rehabilitation. The multimodal team included a physical therapist, psychologist/psychiatrist, advanced practice nurse, clinical social worker, and certified hospital chaplain. At one month of follow-up, the QOL was significantly better in the intervention group than the control group. There was no significant difference at 6 months, despite a follow-up telephone intervention.

Another study demonstrated improved QOL after a unimodal rehabilitation intervention specific to patients with prostate cancer undergoing radiation treatment.<sup>116</sup> Monga et al randomized 30 patients with prostate cancer to a physical therapy intervention or to radiation treatment without aerobic exercise. The intervention patients demonstrated improved QOL and less fatigue.<sup>116</sup> A recent review by McNeely and Courneya endorsed both aerobic and resistance training as effective evidence-based treatment for CRF, but cautioned that training may be more effective during the survivorship phase of care.<sup>117</sup> Further study will be helpful in determining the best way to prevent and treat fatigue during radiation, but it seems reasonable to consider that supervised aerobic conditioning plays an important role.

Multimodal rehabilitation has also been studied in patients with cancer during chemotherapy. Adamsen et al randomized 269 patients to an intervention set or a control set.<sup>118</sup> Of note, patients had 21 different types of cancer diagnoses, including solid tumors and hematologic malignancies. Patients in the intervention set received high-intensity and low-intensity supervised physical training, relaxation techniques, and manipulation. Supervision was performed by a physical therapist or trained nurse specialist. Those in the control set received standard medical care and were permitted to perform unsupervised physical activity as tolerated. After 6 weeks, patients in the intervention set demonstrated less fatigue, improved aerobic capacity, greater strength, improved vitality, and better emotional well-being.<sup>118</sup> The intervention resulted in a significant improvement in depression, but not in anxiety.<sup>119</sup>

A more recent study by Andersen et al evaluated 213 patients with cancer undergoing chemotherapy who were randomized to their multimodal intervention of high-intensity and low-intensity supervised physical training, relaxation techniques, and manipulation for 6 weeks or a wait-list control group.<sup>120</sup> The control group could participate in the intervention after their first 6 weeks of standard medical care and observation only. CRF was significantly reduced in the intervention group, but there was no statistically significant effect on QOL. Of note, this study did include aerobic exercise, which may be the key physical rehabilitative tool for fatigue treatment.

Inpatient rehabilitation is an important option for patients undergoing acute treatment but who are unable to leave the hospital. A review of the efficacy of inpatient rehabilitation found that patients with cancer who undergo this care may have a higher rate of transfer back to acute care and a shorter life expectancy overall than patients with other diagnoses (such as stroke, traumatic brain injury, or SCI).<sup>121</sup> Functional gains after rehabilitation were not only significant, but similar to the gains made by noncancer patients. These authors did recommend that life expectancy

be considered in determining the length of stay in acute inpatient rehabilitation, but the presence of metastatic disease did not adversely affect functional gains.

Many of the studies discussed demonstrate the efficacy of physical therapy. However, in many cases, isolated physical therapy may not be enough to overcome an impairment. A multidisciplinary team approach may reasonably be recommended, especially for patients with neuromuscular impairments.<sup>122</sup> One example of this type of impairment is a gait or balance abnormality from chemotherapy-induced peripheral neuropathy. Patients can be screened for potential risk factors for peripheral neuropathy during the prehabilitation phase and offered rehabilitation services at any point during the care continuum if they develop significant impairment.

Another example of a multidisciplinary approach to acute care rehabilitation involves patients with trismus as a complication of head and neck cancer. These patients may not be able to open their mouths fully due to pain and physical limitations despite aggressive speech and/or physical therapy. The adjunct use of botulinum toxin injections, pain medications, and a dynamic jaw-opening device has been shown to improve trismus in a pilot study.<sup>123</sup> Botulinum toxin injections have been successfully used by physiatrists to treat spasticity and dystonia in patients with many different types of cancer, even while the patient is undergoing chemotherapy.<sup>124</sup> There may be a role for similar injections in the treatment of dystonia, neuralgia, or migraine associated with radiation fibrosis syndrome.<sup>86</sup>

Patient-centered care involves encouraging survivors to continue to implement the strategies and techniques that they learned from their rehabilitation caregivers. They will hopefully continue to perform therapeutic exercises and other physical activity on their own. A large study that addressed self-rated health in older patients with cancer found that 46% of those studied who were older than 65 years of age and 41% of participants who were older than 80 years of age reported engaging in physical activity independently during cancer treatment.<sup>125</sup> In this study, patients older than 65 years of age who exercised during treatment experienced less shortness of breath during treatment and better self-rated health both during and after treatment. The oldest patients (those older than 80 years of age) who were physically active during treatment reported better self-rated health and less memory loss during treatment and better self-rated health and less fatigue after treatment. Overall, cancer patients receiving acute care, even elderly patients, exhibit a favorable risk-to-benefit profile for rehabilitative training, and some experience a significant improvement in outcomes.



A 2013 meta-analysis focused on the psychological impact of exercise interventions delivered during adjuvant treatment of breast cancer in an attempt to assess the “optimal dose.”<sup>126</sup> Seventeen studies were included and revealed improvements for all outcomes including fatigue, depression, and QOL. Interestingly, relatively low doses of exercise (fewer than 12 metabolic equivalent for task [MET] hours/week) consisting of approximately 90 minutes to 120 minutes of weekly moderate exercise were more efficacious in improving fatigue and QOL than higher doses. This study serves as an important reminder that there are many factors to consider when prescribing exercise in order to optimize a cancer survivor’s health, including the current health status of the patient, comorbidities, and past and current cancer treatment, as well as the exercise mode, frequency, duration, and intensity.

### Rehabilitation After Cancer Care in Survivors

The rehabilitation of survivors after acute cancer treatment is a broad topic and one that has been studied in some cancer populations (eg, individuals with breast and lung cancer) more than others (eg, those with hematologic<sup>127</sup> or bladder<sup>128</sup> malignancies). It is beyond the scope of this article to review all interventions in all cancer diagnoses or populations (such as adult survivors of childhood cancers)<sup>129</sup>; therefore, key studies will be highlighted as examples.

A recent Cochrane Database Review of exercise interventions that were initiated after the completion of active cancer treatment included 40 trials with 3694 participants (1927 participants in an exercise group and 1764 in a comparison group).<sup>56</sup> This review concluded that exercise may have beneficial effects on HRQOL and certain HRQOL domains for cancer-specific concerns such as body image and self-esteem, fatigue, and anxiety in survivors of breast cancer. The authors noted that the results must be interpreted cautiously due to several factors, including the heterogeneity of exercise programs, cancer types, and cancer treatments. In another 2012 meta-analysis on physical activity in cancer survivors after the completion of “main treatment,” Fong et al reviewed 34 RCTs (22 or 65% of which were breast cancer studies),<sup>130</sup> and concluded that in breast cancer survivors who had finished acute treatments, physical activity had positive effects on physiology, body composition, physical functions, psychological outcomes, and QOL. When patients with other types of cancers were also included, exercise was associated with reduced body mass index and body weight, increased peak oxygen consumption and peak power output, and improved QOL.

In survivors of prostate cancer, a recent review found that incontinence, fitness, fatigue, body constitution, and QOL can be improved by “clinical exercise” during and after acute cancer treatments.<sup>131</sup> Of note in this systematic

review, the authors concluded that “supervised exercise” is more effective than “nonsupervised exercise.”

CRF is a common impairment even after treatment is completed. A German study randomized 63 patients with cancer who were participating in a multimodal rehabilitation program including physical therapy, patient education, group exercise, and psychooncologic counseling to either an intervention group that received additional structured strength training and aerobic exercises or to a control group that received the standard rehabilitation program.<sup>132</sup> After rehabilitation, both groups showed improvement in muscle strength, QOL, physical well-being, and functionality. At 3 months after rehabilitation, only the intervention group demonstrated persistent improvements in QOL and function. Furthermore, the intervention group demonstrated a significant improvement in CRF that was not seen in the control group.

A smaller RCT of patients who had been successfully treated for gynecologic cancer demonstrated improvement in CRF after 12 weeks of supervised aerobic and strength training exercises.<sup>133</sup> The intervention group demonstrated improvement immediately after the intervention as well as 6 months later. The persistence of improvement in fatigue may be related to the enrollment of patients who were sedentary prior to the study. These patients likely made the successful transition from supervised to unsupervised training, which is beneficial to nearly all aspects of health in previously sedentary patients. A meta-analysis published in 2012 found that exercise reduced fatigue in patients with cancer both during and after acute treatments.<sup>134</sup> Of note is that the authors of this review concluded that the effect was palliative during treatment and recuperative after treatment.

Therapeutic exercise directed at specific impairments may reduce musculoskeletal pain and improve function. For example, survivors of head and neck cancer may experience pain and weakness in the shoulder, related to spinal accessory nerve damage or irritation. McNeely et al randomized 52 survivors of head and neck cancer to a control group that received a standard, supervised, therapeutic exercise program or to an intervention group that received a supervised progressive resistance program that was tailored to treat their individual needs associated with cancer-related impairment of the shoulder.<sup>135</sup> Outcomes were measured at baseline and at the end of the 12-week intervention. The patients who underwent the progressive resistance exercise that was tailored to their needs demonstrated reduced pain and improved upper extremity muscular strength and endurance compared with the control subset. A 2012 review led by Carvalho et al found 3 trials, including the study by McNeely et al,<sup>135</sup> involving 104 participants that evaluated therapeutic exercise interventions for shoulder dysfunction in individuals treated for head and neck cancer.<sup>136</sup> In this review, 2 RCTs demonstrated that progressive resistance training combined with range-of-motion exercises and stretching was more

effective than “standard physiotherapy.” Of note is that other exercise regimens were not shown to be effective compared with postoperative physical therapy.

Patients who undergo stem cell transplantation as part of their treatment often experience impairments in strength and endurance. Knols et al evaluated the efficacy of a 12-week supervised aerobic and strength training program on physical functioning in patients within 6 months of stem cell transplantation.<sup>137</sup> Sixty-seven patients in the control group did not receive any formal rehabilitation, but did receive usual medical care as needed. Sixty-four participants in the intervention group demonstrated improved physical performance both immediately after the intervention and at the 3-month follow-up.

Supervised exercise in patients with lymphoma appears particularly motivating for long-term exercise (up to 6 months).<sup>138</sup> However, it would be helpful to know if rehabilitation makes a difference after a year or more. A trial to investigate long-term return-to-work in cancer survivors followed cancer patients for 3 years after diagnosis.<sup>139</sup> Seventy-two patients in the intervention group underwent a high-intensity physical rehabilitation program. Thirty-eight age-matched controls received usual medical care for cancer survivors. All subjects were evaluated by telephone at 3 years. Of note, all subjects had been working at the time of their cancer diagnosis. Approximately 78% of the patients in the intervention group returned to working the same number of hours as they did prior to their cancer diagnosis, compared with 66% of patients from the control group. The authors concluded that strength and interval training is useful in maximizing return-to-work in cancer survivors.

A 2011 study published by Korstjens et al evaluated the effects of cancer rehabilitation on psychological functioning and compared a usual-care comparison group, a group that received physical training, and a group that underwent both physical training and cognitive behavioral problem-solving training.<sup>140</sup> The researchers expected that the group that underwent both physical training and cognitive behavioral problem-solving training would outperform the other groups; however, they found that the 2 intervention groups performed similarly and only had additional benefits over the usual-care comparison group with regard to anxiety. The authors concluded that physical training was “feasible and sufficient” to reduce cancer survivors’ anxiety. A recent meta-analysis that included 56 studies evaluated the effectiveness of physical exercise on psychosocial functioning and HRQOL in breast cancer survivors and found that both physical exercise and behavioral techniques improve psychosocial functioning and HRQOL; however, more research is needed to understand the combined effect of these interventions.<sup>141</sup>

## Rehabilitation of Patients With Cancer as a Chronic Condition

An early review of rehabilitation interventions for patients with advanced cancer was reported by Cheville in 2001.<sup>142</sup> Since then, Cheville et al have contributed much to the literature on the evidence-based needs, often unmet, of patients with advanced cancer. For example, as noted in the introduction to this review, Cheville et al found that of 163 women with metastatic breast cancer, 92% had at least one physical impairment, with 530 impairments identified overall, and that fewer than 30% of the participants received the appropriate care.<sup>11</sup> In 2011, Cheville et al reviewed the causes of underuse of rehabilitation services for individuals with advanced cancer.<sup>30</sup> In this review, the authors suggested that much of the disability associated with advanced cancer may be avoided and stated that this is “an important public health issue.”<sup>30</sup> One of the central questions in this review was, “Why does functional loss in patients with cancer fail to trigger rehabilitation referrals?”<sup>30</sup> Cheville et al explored several reasons, including that cancer-related disability is often insidious and that cancer care delivery systems are not conducive to the early detection of functional problems. In this particularly fragile population, the authors encouraged health care professionals to avoid underestimating the functional loss that may occur with minor impairments and stated, “Even seemingly benign impairments warrant attention, given their capacity to erode diminishing functional reserve.”<sup>30</sup> International studies have demonstrated the need for rehabilitation and its underuse as well.<sup>143-146</sup> Indeed, the burden of impairments directly related to cancer and/or cancer treatments can be profound when considered as a whole rather than the sum of each part.

Although palliative care may be offered at any stage of cancer, some of the published literature regarding rehabilitation in patients with advanced cancer has focused on palliative care populations. For example, in an editorial addressing this issue, Eyigor wrote, “In palliative care, improvement of physical function is more than control of symptoms. Despite this, most palliative care and hospice programs disregard physical performance while evaluating quality of life (QOL).”<sup>147</sup> Eyigor suggested several possible reasons for this deficit, including a lack of knowledge or education about the benefits of rehabilitation in this population, a limited supply of physiatrists familiar with patients with advanced cancer, and oncologists not directing patients to rehabilitation. Eyigor recommended, “Including physiatrists in the overall plan for palliative care is likely to increase the success of general treatment in addition to patient-family satisfaction.”<sup>147</sup> In a survey study by Spill et al evaluating oncologists’ and physiatrists’ attitudes regarding rehabilitation for patients with advanced cancer, the researchers mailed out 820 surveys and received responses from 395 physicians (response rate



of 48%).<sup>148</sup> Both groups had similar attitudes about care in many respects, but one area where they differed was with regard to rehabilitation services for patients with advanced cancer regardless of prognosis. When it came to the physicians' willingness to refer/accept a patient with advanced cancer regardless of estimated prognosis, only 8.4% of the oncologists were willing to refer in contrast to 15.1% of the physiatrists reported as 35% willing to accept the referral. The authors concluded that oncologists view prognosis as a more significant barrier to rehabilitation services than do physiatrists.

Certainly, the rehabilitation of patients with cancer as a serious chronic condition involves careful assessment of the individual's goals and life expectancy. If there is an anticipated short life expectancy, rehabilitation goals should take this into account and focus on improving function and QOL for the patient as well as reducing the burden of care. All interventions, including but not limited to physiatry and physical, occupational, and speech therapies, should be tailored to meet the goals of the patient and modified in the case of declining health. One of the more robust areas of rehabilitation research in patients with advanced cancer has focused on physical activity, and there is increasing evidence that therapeutic exercise may be beneficial in individuals living with cancer as a chronic condition, even when the disease has progressed considerably. For example, studies in individuals with cachexia have demonstrated that even with advanced disease, skeletal muscles have the capacity to respond to exercise training.<sup>149</sup>

Albrecht and Taylor reviewed 16 articles published between 1994 and 2010 to determine the effect of physical activity in patients with advanced-stage cancer.<sup>150</sup> They found that even patients with advanced-stage cancer can benefit from rehabilitation in terms of improvements in mood, pain, fatigue, shortness of breath, constipation, and insomnia. Preference for the location of their aerobic and strength training program varied greatly; consequently, the ideal location (home vs hospital) could not be determined. Of note, most participants in the studies were willing and able to complete physical activity despite having an advanced stage of disease.

Authors of a subsequent pilot study of 24 patients with terminal cancer randomized the patients to a control group with a sham therapy intervention (local touch to the area of pain) or a physical therapy intervention for 2 weeks.<sup>151</sup> The physical therapy intervention included massage as well as formal rehabilitative exercises. They found results similar to those of Albrecht and Taylor,<sup>150</sup> namely that the patients who received legitimate physical therapy demonstrated improved mood and decreased pain compared with the patients who received the sham touch intervention.

A prospective, single-arm intervention study of patients with stage III or IV inoperable lung cancer evaluated the effect of a hospital-based strength training and aerobic

exercise program.<sup>152</sup> Twenty-three patients completed the training during chemotherapy. There was significant improvement in physiologic and emotional HRQOL at the 6-week follow-up. The authors concluded that exercise training is appropriate for patients with inoperable lung cancer, even while they are undergoing treatment.

A RCT of 36 patients in the United Kingdom with advanced breast or hematologic cancer evaluated the unmet needs of these patients using the Supportive Care Needs Survey.<sup>153</sup> The intervention group received personalized multimodal rehabilitation care in a hospice daycare unit that could include any or all of the following services: physiotherapy, complementary therapy (ie, acupuncture, Reiki, etc), and counseling or social services. The control group received usual care with access to the medical team, but no specific multidisciplinary intervention. The intervention group demonstrated significantly fewer unmet needs, and meeting these needs appeared to be cost-effective.

Cherville et al randomized 66 adult patients with stage IV lung or colorectal cancer to a home-based walking and strengthening program or usual care.<sup>154</sup> Unlike the previously described studies, patients currently in hospice care were excluded. At 8 weeks, the intervention group reported improved mobility, fatigue, and sleep quality compared with the usual-care group.

A larger RCT of patients with advanced cancer in Norway that was published in 2011 evaluated fatigue and physical performance in these patients.<sup>155</sup> A total of 121 patients were randomized to the physical exercise group and 110 patients were randomized to the usual-care group. Patients in the physical exercise group performed circuit training, incorporating both aerobic and strength training exercises with postexercise stretching. After 8 weeks of physical exercise, fatigue was not reduced, but physical performance was significantly improved in the exercise group. The authors theorized that fatigue was not improved because many of these patients with incurable disease experienced disease progression over the 8-week intervention period. Of note, since patients were recruited from daycare palliative care units, hospice patients were not excluded. The inclusion of patients with a greater illness burden may be part of the reason that these findings differ from those of other smaller studies that demonstrated improvements in fatigue with 8 weeks of exercise.

Physical activity has been an important area of research in patients with advanced cancer, but there are many other issues that need to be addressed in this population including, but not limited to, voice and speech outcomes in survivors of advanced head and neck cancer that may improve with speech-language pathologist consultations,<sup>156</sup> breathlessness in patients with advanced lung cancer who may benefit from nursing interventions,<sup>157</sup> and the rehabilitation of survivors with metastatic bone disease.<sup>158</sup> The scope of this article

precludes an exhaustive discussion of impairments and rehabilitation interventions, but before leaving this topic in patients with advanced cancer, it is essential to consider the cognitive issues that may significantly compromise the QOL of these individuals and the considerable strain that this may place on caregivers and the health care system. For example, cognitive impairments in individuals with brain tumors are typically more severe as the disease progresses, and more research to identify the efficacy of specific rehabilitation interventions is needed.<sup>159</sup> Patients with advanced cancer may also experience delirium, and in a 2013 narrative review, Kang et al noted that approximately one-half of these cases may be reversed with a comprehensive approach to management.<sup>160</sup>

## Conclusions

Delivering quality, patient-centered care requires that all cancer patients and survivors be screened for psychological and physical impairments throughout the care continuum in order to preserve and/or improve their functioning and QOL. Impairments, from subtle to profound, should be identified and treated by trained health care professionals. Because many survivors present with multiple impairments,

treatment often requires an interdisciplinary team approach that can offer multimodal interventions. General exercise referrals, whether they involve advice in the office setting or referrals to skilled fitness professionals, while an important component of the rehabilitation care continuum, should be offered to survivors only after their impairments have been identified, treated optimally by rehabilitation health care professionals, and safety precautions and contraindications identified and documented. Although all oncology health care professionals should be knowledgeable about impairment-driven cancer rehabilitation in order to make appropriate and timely referrals to rehabilitation professionals, it is particularly important that oncologists, nurse practitioners, physician assistants, patient navigators, and mental health professionals be able to quickly identify impairments and refer patients for their rehabilitation needs. Primary care physicians also play an important role in facilitating referrals. As impairment-driven cancer rehabilitation can significantly improve physical and psychological health outcomes in survivors as well as reduce direct and indirect health care costs, future research efforts should be focused on building on the current evidence in order to provide quality integration of this care into oncology clinical practice. ■

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