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Exercise Recommendations for the Management of Symptoms Clusters Resulting from Cancer and Cancer Treatments

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Abstract

Objective—To review existing exercise guidelines for cancer patients and survivors for the management of symptom clusters.

Data source—Review of Pubmed literature and published exercise guidelines.

Conclusion—Cancer and its treatments are responsible for a copious number of incapacitating symptoms that markedly impair quality of life (QOL). The exercise oncology literature provides consistent support for the safety and efficacy of exercise interventions in managing cancer- and treatment-related symptoms as well as improving quality of life in cancer patients and survivors.

Implications for Nursing Practice—Effective management of symptoms enhances recovery, resumption of normal life activities and QOL for patients and survivors. Exercise is a safe, appropriate and effective therapeutic option before, during, and after the completion of treatment for alleviating symptoms and symptom clusters.

Keywords

Exercise; Physical Activity; Cancer; Symptoms; Quality of Life; Yoga; Tai Chi; Aerobic Exercise; Resistance Exercise; Cancer-Related Fatigue; Fatigue; Cognition; Distress; Sarcopenia; Cachexia; Bone Loss

Over 1.6 million new cases of cancer will be diagnosed in America in 2016, bolstering the number of Americans who are currently affected by the disease.¹ A large percentage of individuals diagnosed with cancer are undergoing or have completed treatment for the disease. Due to advances in screening and treatment, the mortality rate for all types of cancer was reduced by 23% from 1991 to 2000.¹ Consequently, many Americans diagnosed with this disease are living beyond the once designated life expectancy of 5 years. As screening

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and treatment continue to get better, the overall number of cancer survivors will increase. Although mortality rates are being reduced, many cancer survivors still suffer from acute, chronic, and late symptoms brought about by cancer and treatments for cancer. Acute symptoms are those which develop before or during treatment, but have a short duration (days, weeks, or months); chronic symptoms may continue for months or years; and late symptoms develop months or years after treatments are complete. All three types of symptoms at any stage of the cancer trajectory have significantly adverse effects on cancer patients and survivors.

Cancer treatment most often includes surgery, chemotherapy, radiation therapy, hormone therapy, immune therapy and/or a combination of these therapies. These therapies may cause an array of physical and psychological symptoms that hinder a cancer patient's ability to comply with treatment protocols, perform activities of daily living (ADL), and maintain a conventional standard of living.² Some of the most commonly reported symptoms stemming from cancer and its treatments are loss of physical function, sarcopenia, cachexia, bone loss, cancer-related fatigue, cognitive impairment and distress.²⁻⁴ Although these symptoms can occur in isolation, most cancer patients and survivors report being effected by several of these symptoms concomitantly.⁵ The clustering effect of these symptoms is not simply additive but can be multiplicative in terms of the negative consequence they portend—significantly impairing a patient's ability to successfully complete treatment and a survivor's ability to thrive post-treatment.⁶ Treatments that efficaciously target several symptoms at once are optimal in these situations. Exercise is an effective treatment modality that successfully remediates several symptoms that frequently cluster together.

UNDERREPRESENTED POPULATIONS

Minority and underrepresented populations in the United States (e.g., racial and ethnic minorities, individuals living below the poverty line, sexual and gender minorities) bear a disproportionate burden of cancer. Some minority and underserved populations experience higher rates of cancer incidence and prevalence⁷ while others experience higher risk of cancer mortality.⁸ The American Cancer Society indicated that some minority populations are more likely to develop and die from cancer than the United States population in general.⁹ Disparities in cancer care also extend into supportive care and symptom management, with lower engagement in rehabilitation, follow-up care, and survivorship care among some minority groups.⁸ Research suggests that these health disparities exist because individuals from minority and underserved populations are more likely than their counterparts to report health risk behaviors, including less time spent exercising, more psychological distress, more current alcohol use, more current smoking, and a lifetime history of smoking.⁷ Minority and underserved patients may also be more likely to receive a late stage diagnosis due to socioeconomic disparities and lack of access to healthcare⁹. Some of these disparities in health risk behavior persist into post-cancer diagnosis and survivorship⁷. Exercise is also an effective treatment option for symptoms among these populations.

EXERCISE AND BIOLOGICAL MECHANISMS FOR SYMPTOM CLUSTERS

Exercise may be effective in mitigating several symptoms that cluster together because it is a treatment capable of influencing biological pathways that may be involved in the etiology of several symptoms and because it is a treatment capable of influencing multiple biological pathways simultaneously. Examples of biological pathways hypothesized to be involved in the pathophysiology of commonly co-occurring symptoms include inflammatory immune responses, metabolic and neuroendocrine adaptations, and genetic and epigenetic influences.^{10,11} For example, inflammatory immune responses that are involved in cell differentiation, proliferation, and apoptosis are associated with several symptoms.¹¹ Higher resting levels of certain sympathetic hormones have been implicated in fatigue and predict a clustering of pain, depression and fatigue.¹⁰ The polymorphism of certain genetic strands have also been linked to fatigue. Research suggests that these mutations in genotype are directly related to increases in fatigue in response to hormone therapy and radiation therapy among cancer patients.¹⁰ To date a growing body of research strongly suggests that exercise is an effective treatment for a myriad of symptoms stemming from cancer and its treatments. Exercise is known to positively influence immune, metabolic, neuroendocrine, genetic and epigenetic function in individuals without cancer. Because exercise can directly influence these pathways individually and simultaneously, it is a promising treatment for symptoms that cluster together.¹²

PATIENT-REPORTED SYMPTOMS

Sleep Problems, Depression, Pain, Anxiety, Fatigue and Cognitive Impairment

Sleep disruption is reported by 30% to 50% of cancer patients.¹³ Cancer patients and survivors commonly experience poor sleep quality and it is several times more prevalent in this population than in the general population.^{13,14} Those who nap frequently report higher incidences of sleep problems.¹⁵ While depression,¹⁶ pain¹⁷ and anxiety are reported by a large majority of cancer patients and survivors,¹⁸ the mixed depression/anxiety phenotype occurs in two-thirds of depressed cancer patients and has been associated with more severe depressive symptoms, with less improvement after treatment, worse quality of life, poorer adherence to treatment, slower recovery, greater suicide risk, and higher cost-utilization.¹⁹

Cancer-related fatigue (CRF) is a dose-limiting toxicity and one of the most common and distressing symptoms of cancer and its treatments.²⁰ CRF can linger for years after treatments are completed in otherwise healthy survivors.²¹ Reports by patients suggest that cancer-related-fatigue is more severe, more persistent, and more incapacitating than fatigue caused by lack of sleep or overexertion and is not alleviated by sufficient sleep or rest.^{22–25} Cancer-related-fatigue adversely impacts all facets of quality of life and may be a factor in reducing survival.²¹ Most patients who are undergoing cancer treatment report CRF, and nearly half report their condition as severe.^{26–29} Research on long-term cancer survivors suggest that approximately one-quarter to one-third experience persistent fatigue for up to 10 years after cancer diagnosis.^{30,31} Cancer-related-fatigue is more common, more severe, and more persistent in patients who undergo more than one treatment type.^{26–29} It is multi-faceted and may have physical, mental, and emotional manifestations and is associated with a variety of co-occurring symptoms, such as sleep problems, depression, pain, anxiety and

physical inactivity.^{26–29} CRF is often described by patients as the most distressing side effect of treatment, even more so than nausea and vomiting due to its impact on their ability to perform activities of daily living and their quality of life.^{26–29}

Adverse cognitive changes associated with cancer and cancer treatments have become an increasing concern. Approximately 75% of cancer patients experience some form of cognitive impairment after a cancer diagnosis and/or during cancer treatments (e.g. chemotherapy, radiation, surgery, hormone therapy), and this impairment continues for months or years in 20% to 35% of survivors.^{32–40} Common cognitive impairments include diminished memory, executive function, attention, and concentration.^{41–43} Cognitive problems of this nature can have a severe negative impact on the mental and physical well-being of patients, ultimately resulting in decreased quality of life. For example, research has shown that 57% of breast cancer patients were unable to do their jobs as effectively, maintain the same job, or work at all following chemotherapy due to difficulty with memory and attention.^{37,44} In addition to the effect that cognitive impairments have on the ability of cancer patients to do their jobs, they also result in reductions in social engagements, and interference with compliance of cancer treatments.^{45–47} These negative consequences are exacerbated when cognitive impairment co-occurs with sleep problems, depression, pain, anxiety, fatigue and physical inactivity as is often the case.

PHYSIOLOGICAL SYMPTOMS

Physical dysfunction, Cachexia, Sarcopenia and Bone Loss

Decreased physical function is associated with increased toxicity and mortality among oncology patients.⁴⁸ Chemotherapy and radiation treatments lead to reductions in cardiac and pulmonary function.^{26,49,50} Treatment with anthracyclines, taxanes and/or trastuzumab can cause acute or chronic cardiac dysfunction in patients and, in some cases, the potential for the development of cardiomyopathies limits the amount that these agents can be used to treat the cancer, ultimately, affecting prognosis.^{51,52} These cardiotoxicities can develop during treatment or years after treatment is complete.^{53,54} Patients treated with methotrexate and bleomycin can develop pulmonary toxicities.^{55–58}

Muscle dysfunction is a prevalent occurrence in the oncology setting, cancer and its related treatments lead to impaired muscle function through atrophy and loss of strength.^{59,60} The sarcopenia and malaise experienced by cancer patients may impair their ability to perform activities of daily living and remain independent during and following treatment.^{61–63} Cancer cachexia can be defined as a significant reduction in body weight resulting primarily from loss of skeletal muscle and adipose tissue. Cachexia leads to a reduction in cancer treatment tolerance, quality of life and increased mortality.⁶⁴ In fact, emergent evidence suggest that muscle wasting⁶⁵ and weight loss⁶⁶ are effective predictors of mortality in cancer patients. Cancer cachexia is a multifactorial syndrome that cannot be fully reversed by conventional nutritional interventions and eventually leads to progressive functional impairment.⁶⁷ Although research is not conclusive on the efficacy of exercise on cachexia⁶⁸, it has demonstrated the ability of exercise (specifically resistance training) to increase skeletal muscle mass in cancer patients and survivors.^{69,70,71}

A large percentage of patients who are diagnosed with cancer experience cancer-treatment-induced bone loss.⁷² In some cases patients receiving treatment for cancer more than triple the average bone loss seen with normal aging.⁷³ This reduction in bone mineral density is accompanied by a 1.3–5-fold increase in fracture rate when compared to individuals not undergoing treatment.⁷⁴ Female patients treated with chemotherapy, oophorectomy, and aromatase inhibitors often experience a decrease in the production of endogenous estrogens and develop premature menopause that may lead to reduced bone mineral density which increases the risk of fracture.^{75–77} Increasing evidence demonstrates that weight-bearing aerobic and resistance exercise may benefit bone metabolism⁷⁸ and maintain bone mineral density,⁷⁹ and the two combined could offer a valuable intervention for moderating bone loss among cancer patients⁸⁰.

EXERCISE AS THERAPY FOR SYMPTOMS

Exercise improves a wide array of psychological and physical symptoms including muscle atrophy and weakness, fatigue, obesity, immune function, insomnia, anxiety, cognitive decline and impaired quality of life, among others.^{5,81–104} In addition, epidemiological data also suggest that increased physical activity via regular exercise reduces the risk of cancer recurrence and cancer mortality.^{105–107} While exercise is an effective intervention for improving symptoms, such as sleep problems, depression, pain, anxiety, fatigue, cognitive impairment, physical dysfunction, cachexia, sarcopenia and bone loss that occur in isolation, research has shown that exercise is also effective for the treatment of symptoms that occur in a cluster.^{5,108,109} Exercise can be uniquely designed for the specific needs of each cancer patient or survivor based on age, health status and ability.^{27–29,81,97,110–151}

The American College of Sports Medicine (ACSM) published public health recommendations for exercise among cancer patients and survivors.¹³⁷ Cancer patients and survivors should start low and progress to 150 minutes of moderate intensity or 75 minutes of vigorous intensity aerobic exercise per week accompanied by 20–30 minutes of strength training across all the major muscle groups 2 to 3 times per week and regular stretching daily each week.^{137,152–154} Despite these published public health guidelines, it is estimated up to 70% of cancer survivors do not meet these ACSM public health recommendations.¹⁵⁵ This lack of regular exercise is especially problematic for cancer patients and survivors when combined with the considerable physical and psychological symptoms they experience.

Despite the numerous benefits of exercise, the majority of cancer survivors report that they do not discuss exercise with their oncology care team throughout their cancer treatment and recovery.^{27,156,157} However, research shows that cancer survivors of all ages want their oncology providers to initiate discussions about exercise and make appropriate referrals.¹⁵⁷ Survivors prefer to receive information on exercise early in the treatment trajectory and throughout the post-treatment period.¹⁵⁸ Given the benefits of exercise during and after cancer treatments, routine discussions about exercise between oncology nurses and their patients and survivors along with appropriate referrals to a qualified exercise physiologist could significantly improve prognosis, recovery, symptom burden and multiple domains of quality of life in these individuals.

Managing Risk and Contraindications for Exercise in an Oncology Setting

It is always essential to identify an individual's level of risk and address potential contraindications (e.g., orthopedic, cardiopulmonary, oncologic) that might affect exercise safety and tolerance when beginning exercise therapy.¹⁵⁹ Contraindications do not mean that a cancer patient or survivor cannot exercise at all. Managing risk and contraindications simply require specific modifications to the exercise regimen so that the individual can exercise safely and still achieve the desired physical and mental health benefits.¹⁵⁹ Although active exercisers or those at low to moderate risk based on the ACSM guidelines are not required to obtain medical clearance to continue or begin a low to moderate exercise program, most oncology patients and survivors will need and benefit from further medical assessment because their exercise risk will be moderate to high.¹⁵⁹ These patients and survivors will benefit from additional medical assessment by qualified medical professionals including oncologists, surgeons, cardiologists, orthopedists, and neurologists among others because these consultations will provide important information required by exercise physiologists to appropriately modify an exercise prescription and account for cancer-specific, cardiovascular, pulmonary, metabolic, orthopedic, neurologic or other co-morbidities.¹⁵⁹ These additional medical evaluations should be conducted prior to the initiation of any baseline exercise testing which precedes developing an exercise prescription and, subsequent, exercise participation.¹⁵⁹

Exercise Prescription for Cancer Patients and Survivors

Exercise testing, exercise prescription and exercise monitoring should be done by qualified exercise professionals, especially for patients and survivors experiencing a high symptom burden and those at moderate risk beginning or continuing vigorous exercise and those at high risk commencing or continuing any level of exercise.¹⁵⁹ Exercise prescriptions for patients and survivors should be individualized and tailored based on the individual's health status, disease trajectory, previous and/or current treatment, symptom burden, current fitness level, past and present exercise participation and individual preferences in order to be safe and effective.^{137,152} Moderately intense aerobic exercise prescriptions (55%–75% of heart rate maximum¹⁶⁰) scheduled over as little as 10 minutes and no more than 90 minutes a day 3–7 days per week are effective at reducing symptom burden as well as improving quality of life among cancer patients and survivors.^{28,97,116,161} Accumulating 30 minutes of daily activity through short bouts of aerobic exercise (3–10 minutes each), with rest in between, can also significantly reduce symptoms in these patients.¹³⁷ Moderate-to-vigorously intense anaerobic resistance exercise prescriptions schedule 3 times per week and progressively increasing up to as few as 2 sets and no more than 4 sets of 8–15 repetitions are effective at reducing symptoms.^{110,115,136,139,162} Combination exercise prescriptions including both aerobic and anaerobic exercise are safe and very effective for most oncology patients and survivors. Low to moderately intense mindfulness-based exercise prescriptions including Yoga and Tai Chi Chuan scheduled 1–3 times a week for 60–90 minutes are also highly effective in reducing symptom burden among cancer patients and survivors.^{3,4,6,96,163,164} Additionally, those with advance disease can safely perform, tolerate and benefit from low intensity exercise.^{165–170}

Exercise Professionals

Research has shown that patients are more likely to comply with exercise prescriptions during and following cancer treatments at the advisement of their treatment physician or nurse.¹⁷¹ Most prefer a direct referral to a qualified exercise specialist.¹³⁷ The minimum qualifications for a certified exercised specialist include a bachelor's degree or higher in an accredited exercise science or kinesiology program. A certification from the American College of Sports Medicine (ACSM) as a Cancer Exercise Trainer confirms that the exercise professional has obtained the minimum education required to safely and effectively prescribe exercise for cancer patients and survivors.¹³⁷ This certification, which can be obtained by individuals with varied educational backgrounds (e.g., exercise physiologists, physical therapists, nurses), requires specific training in the domain of cancer-specific issues that must be addressed when a patient or survivor plans to begin or maintain an exercise program during primary treatment and beyond. The certification also provides a very useful professional competency benchmark for oncology professionals who are looking for exercise referral options in their local communities.^{137,172,173}

CONCLUSION

The exercise oncology literature provides consistent support for the safety and efficacy of exercise interventions in managing cancer- and treatment-related symptoms as well as improving quality of life in cancer patients and survivors. Notwithstanding limitations, the evidence suggest that physical activity is safe and efficacious for cancer patients and survivors as a therapy for multiple symptoms that occur in isolation and occur together in symptom clusters. Globally, research suggests that aerobic exercise, resistance training, a combination of both, and mindfulness forms of exercise, such as Yoga and Tai Chi Chuan are effective in reducing symptom burden, helping cancer patients cope with their disease, improve recovery, and increase overall QOL. Exercise should be recommended for all patients and survivors experiencing symptoms and, especially for those with a clustering of multiple symptoms.

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