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Exercise-Based Oncology Rehabilitation: Leveraging the Cardiac Rehabilitation Model

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Abstract

PURPOSE—The value of exercise and rehabilitative interventions for cancer survivors is increasingly clear and oncology rehabilitation programs could provide these important interventions. However, a pathway to create oncology rehabilitation has not been delineated. Community-based cardiac rehabilitation (CR) programs staffed by health care professionals with experience in providing rehabilitation and secondary prevention services to individuals with coronary heart disease are widely available and provide a potential model and location for oncology rehabilitation programs. Our purpose is to outline the rehabilitative needs of cancer survivors and demonstrate how oncology rehabilitation can be created using a cardiac rehabilitation model.

METHODS—We identify the impairments associated with cancer and its therapy that respond to rehabilitative interventions. Components of the CR model that would benefit cancer survivors are described. An example of an oncology rehabilitation program using a CR model is presented.

RESULTS—Cancer survivors have impairments associated with cancer and its therapy that improve with rehabilitation. Our experience demonstrates that effective rehabilitation services can be provided utilizing an existing CR infrastructure. Few adjustments to current cardiac rehabilitation models would be needed to provide oncology rehabilitation. Preliminary evidence suggests that cancer survivors participating in an oncology rehabilitation program experience improvements in psychological and physiologic parameters.

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CONCLUSIONS—Utilizing the CR model of rehabilitative services and disease management provides a much needed mechanism to bring oncology rehabilitation to larger numbers of cancer survivors.

Keywords

cardiac rehabilitation; cancer survivors; oncology rehabilitation

Currently there are over 13 million cancer survivors in the United States with 18 million expected by 2022.¹ Individuals who undergo cancer therapy experience declines in fitness², strength³, and physical function⁴. Cancer and associated therapies result in local symptoms, such as range of motion deficits and lymphedema, as well as systemic impacts including fatigue, deconditioning and pain syndromes.⁵ Survivors of some types of cancers are also at increased risk for the development of cardiovascular disease.^{6,7} The unintended consequences of cancer treatments can be ameliorated by rehabilitative interventions. Exercise interventions have documented improvements in aerobic fitness, strength and other persistent effects of cancer therapy. Additionally, epidemiologic evidence is accumulating that physical activity improves cancer related outcomes such as decreasing recurrence and increasing survival although randomized controlled trial data are lacking.^{8,9,10} Given the proportion of individuals living with a cancer diagnosis oncology rehabilitation programs should become a standard component of cancer survivor care.

Cardiac rehabilitation (CR) is standard of care for individuals after a cardiac event. Exercise is the cornerstone of CR but risk factor management, stress reduction, behavioral and nutritional counseling, and tobacco cessation are also core components.¹¹ CR professionals have the expertise required to provide monitored exercise, lifestyle interventions and other rehabilitative services to a wide variety of patients, including cancer survivors.¹² In addition to reductions in cardiac and overall mortality¹³ and a decreased rate of cardiac rehospitalizations, CR participation is associated with improvements in exercise capacity¹⁴ and measures of quality of life.¹⁵

Cardiac rehabilitation programs are widely available in the United States. With a focus on secondary disease prevention, decreasing mortality and morbidity, improving physical function and quality of life, CR provides an ideal framework for developing comprehensive oncology rehabilitation programs. The goal of this article is to outline the needs of cancer survivors which could be met by an oncology rehabilitation approach modeled after a successful CR program. Components of CR programs that provide the framework needed for oncology rehabilitation interventions are presented. We also describe a successful oncology rehabilitation program that uses a CR approach to chronic disease management.

REVIEW OF RELEVANT LITERATURE

Impact of Cancer and Cancer Treatment: Declines in Fitness, Strength, and Physical Function

The interplay of cancer and various cancer treatments results in physiologic decline and persistent side effects most of which can be improved with exercise and rehabilitation (Table 1).

Cardiorespiratory fitness is impaired in cancer survivors.¹⁶ In a recent meta-analysis by our group, we found fitness to be 25% lower among breast cancer patients in the post-adjuvant setting compared to healthy, sedentary women.¹⁷ Specifically, breast cancer patients 50 years of age had a similar fitness to sedentary, 60 year old women without a history of breast cancer. The decline in fitness appears sustained in breast cancer patients even 7 years after treatment compared to age-matched controls.¹⁸

Muscular strength is a key component of overall fitness. There is limited research evaluating the natural history of skeletal muscle strength among cancer survivors and the data we do have is gleaned from studies completed for other reasons. In a small prospective study of patients receiving an autologous transplant, upper extremity strength decreased by 24% and lower extremity strength decreased by 9% in 25 days from pre to post transplant.¹⁹ Recently reductions in the intrinsic function of skeletal muscle myofilaments has been identified in cancer patients and was associated with decreases in whole muscle strength and walking performance.²⁰

Strength and fitness decline could play an important role in limiting performance of activities of daily living and development of disability. Among individuals participating in the National Health Interview Survey almost 60% of those with a history of cancer report at least one functional limitation compared to 27% of the general population.²¹ Functional limitations identified include difficulty walking one-quarter of a mile, walking up stairs, and lifting or carrying. Cancer-related functional impairment is a particular concern for the 65% of cancer survivors age 65 or older that depend on function to maintain independence.

Impact of Cancer and Cancer Treatment: Persistent Side Effects

Surgery and radiation are common local treatment modalities that can impair mobility. Shoulder range of motion is limited in up to 45% of patients receiving sentinel lymph node evaluation and 86% of those receiving axillary dissections.²² Importantly, this dysfunction translated into limitations in activities such as household chores (44.2%) and lifting a gallon of milk (34.9%). Lymphedema can be acquired through disruption of lymphatic drainage resulting from cancer related surgery or radiation. Therapies to treat breast cancer are associated with a 21.4% incidence of lymphedema²³ and those with lymphedema experience strength and upper extremity impairment.²⁴ Lymphedema also occurs with treatment of melanoma, gynecologic malignancies, genitourinary, and sarcoma ranging in incidence from 10–30%.²⁵

The chemotherapeutic and targeted therapies used to treat cancer are associated with collateral damage that impacts the quality of life for many cancer survivors. Fatigue is the most commonly identified persistent effects of cancer therapy and is present in up to 80% of cancer survivors.²⁶ Cancer related fatigue is multifactorial and contributors include decreased activity, deconditioning, depression and sleep disturbance.^{27,28} Peripheral neuropathy results from several chemotherapeutic agents and is reported in up to a quarter of breast cancer survivors receiving paclitaxel²⁹ and is persistent in nearly half of colorectal cancer patients receiving oxaliplatin.³⁰ The most common anti-estrogen therapy for post-menopausal breast cancer survivors is aromatase inhibitors which are associated with joint pain and stiffness in over 40% of individuals.³¹

Depending on diagnosis and interventions, either weight gain or loss occurs with cancer therapy. Weight gain is more common for individuals receiving adjuvant therapy for breast and colon cancer.^{32,33} Results from the Nurses' Health Study revealed that a weight gain of 5–10 pounds after breast cancer diagnosis was associated with 50% higher rates of breast cancer recurrence and death.³⁴ Conversely, individuals with other malignancies such as lung, head/neck, pancreatic and upper gastrointestinal, frequently lose weight. This weight loss results in a reduction in skeletal muscle, is often not reversed by nutrition alone, and is accompanied by declines in strength.³⁵

Up to 35% of cancer survivors experience significant psychological distress,³⁶ twice the rate of the general population.³⁷ Even though anxiety and depression decline as individuals move beyond diagnosis, a significant percentage of breast cancer survivors experience severe anxiety and depression at 18 months.³⁸ Psychological factors appear to be associated with physical inactivity among cancer survivors.³⁹

Benefits of Exercise and Rehabilitation for Cancer Survivors

Exercise and rehabilitative interventions have proven beneficial for ameliorating impairments experienced by cancer survivors (Table 1). Aerobic interventions increase cardiopulmonary fitness in cancer survivors,⁴⁰ with increases ranging from 10–15%.¹⁶ Aerobic exercise benefits are found for survivors of several different cancers, including lung, breast, prostate, lymphoma, and hematologic malignancies.^{41,42} Muscle strength improves with resistance training interventions for cancer survivors with a variety of malignancies.⁴³ Increases in strength are also associated with improved physical function, including gait speed and ability to rise from a chair.⁴⁴

Exercise and rehabilitative interventions result in improvements in shoulder range of motion impairment in women treated for breast cancer.⁴⁵ Resistance training does not worsen lymphedema and, in fact, appears to decrease incidence of exacerbations and reduce symptoms.⁴⁶ A recent review of 56 studies with over 4000 participants identified benefits of exercise interventions for fatigue management delivered during and after cancer therapy.⁴⁷ Improvements have been reported in arthralgia pain associated with aromatase inhibitor use in post-menopausal women receiving an aerobic and resistance training intervention.⁴⁸ Resistance training also results in decreases in body fat percentage and increases in lean body mass among cancer survivors.⁴⁹ Exercise for cancer survivors results in decreased depression and improved quality of life.⁵⁰

While a randomized controlled trial is lacking, observational studies identify improved overall survival among cancer survivors who are more physically active. For breast cancer survivors, physical activity equivalent to 3 hours of moderate intensity activity is associated with a 34% reduction in breast cancer-specific mortality and a 41% reduction in all-case mortality.⁵¹ Two large observational studies have demonstrated that 6 hours per week of moderate intensity physical activity after a colon cancer diagnosis is associated with a reduction in colon cancer death and death from all causes compared to men or women who were physically inactive.^{9,10} Survival benefits with physical activity have also been identified for prostate cancer⁵² and glioblastoma.⁵³

Exercise Recommendations and Challenges for Cancer Survivors

The benefits cancer survivors derive from exercise and the number of deficits amenable to rehabilitation builds a strong case for establishing oncology rehabilitation programs. The American Cancer Society and the American College of Sports Medicine (ACSM) have recommended at least 150 minutes of moderate intensity aerobic physical activity weekly for cancer patients.^{54,55} However, survivors appear to decrease their activity after a cancer diagnosis, even in cases where no clear physical impairments are present. Direct measurement of physical activity using accelerometers in the NHANES 2003–2006 cohort indicates that 95.5% of cancer survivors do not meet physical activity recommendations.⁵⁶ This is a particular concern among those diagnosed with early stage cancers who are likely cured of their cancer, but are at increased risk for other chronic disease, such as diabetes and coronary heart disease.

Several barriers exist to improving exercise participation and rehabilitation. Cancer survivors note lack of facilities (25.5%), weakness (21.5%), and fear of falling (19.5%) as common barriers to exercise.⁵⁷ Fear of doing harm as a result of exercise is also a concern.⁵⁸ Cancer survivors may not exercise on their own. Adherence for a supervised intervention among lung cancer survivors was 73% compared to only 8.7% for those receiving a home-based intervention.⁴¹ Supervised exercise may be needed to support cancer survivor's transition to regular exercise. Referral patterns for rehabilitation are not established. Even among individuals with metastatic cancer, only 30% of those eligible for rehabilitative interventions obtain these services.⁵⁹

DISCUSSION AND PROGRAM EXAMPLE

Cardiac Rehabilitation as a Model for Oncologic Rehabilitation

An effective oncology rehabilitation program would improve fitness and address physical and psychological deficits. CR provides an ideal model for bringing oncology rehabilitation to cancer survivors at academic and community medical centers across the country. The CR program staff is trained to identify physical impairments and improve fitness. They are experienced dealing with a wide range of co-morbid medical conditions. CR programs have the necessary facilities, systems for referrals and integration into the medical system. Needs of cancer survivors vary across the trajectory of oncologic care. The phases within in CR can be used to address diverse needs (Table 2). Phase 1 oncology rehabilitation focuses on correcting severe deficits and deconditioning during oncologic treatment. Phase 2 oncology rehabilitation addresses ongoing deficits and focuses on improving fitness immediately post therapy. Cancer patients completing Phase 2 or those well beyond initial cancer treatment and who do not have significant deficits would enter Phase 3.

Multifactorial CR consists of exercise training, as well as lifestyle counseling and medical management interventions.^{11,60} The aerobic exercise component generally consists of 3 weekly ECG monitored exercise sessions for 8–12 weeks with frequency, duration, and intensity progressing over time and a plan for long-term exercise. Resistance training is typically provided with a goal to increase strength, skeletal muscle endurance, and consequently functional capacity.⁶¹ CR also includes cardiac risk factor reduction including

recommendations for smoking cessation, hypertension, dyslipidemia, diabetes, and weight management. Psychosocial management is a concern for cardiac patients with depression, anxiety, and denial which occurs in more than 20% of patients following a myocardial infarction.⁶²

A Phase 2 oncologic rehabilitation program would include many of the core components of CR (Table 3). Aerobic exercise and resistance training remain central interventions for oncology rehabilitation. Several of the supportive core modules currently provided in CR have similar value for cancer survivors, including weight management, stress reduction, and smoking cessation. In order for survivors to fully participate in exercise interventions, the common persistent effects of cancer therapy such as fatigue, deconditioning and mobility deficits need to be addressed. The impact of surgical and radiation interventions are unique to cancer survivors receiving these modalities and may require additional physical therapy. Occasionally exercise modalities may need to be modified based on deficits.

Lessons in Establishing an Oncology Rehabilitation Program

In 2011, we initiated an oncology rehabilitation program within the University of Vermont's CR facility. The focus was on a phase 2 model, however individuals beyond initial diagnosis were included. Few recommendations exist as to the baseline evaluations that might be appropriate for cancer survivors starting an exercise program. The ACSM guidelines recommend evaluation for musculoskeletal morbidities and peripheral neuropathies related to treatment regardless of time since treatment.⁵⁵ Prior to starting the oncology rehabilitation program, survivors are evaluated by a physician or mid-level provider to assess the appropriateness of participating in an exercise program and to identify persistent side effects that may need to be addressed. Previous and current therapeutic agents that contribute to deficits, such as cardiac impairment, fatigue, peripheral neuropathy, and arthralgias, are reviewed. Table 4 compares and contrasts the baseline evaluations completed in cardiac and oncology rehabilitation. A 6-minute walk test is completed to assess functional capacity for participating in aerobic exercise. If significant anxiety or depression is identified, participants are directed to our Cancer Patient Support Program if they are not already connected with a therapist.

Because of the frequency with which oncologic therapies result in musculoskeletal deficits, a physical therapist (PT) evaluates function prior to individuals entering the program. The PT evaluates for lymphedema, range of motion, and balance deficits. If sufficient deficit exists or severe deconditioning is identified, one-on-one physical therapy is provided. Alternatively, if physical limitations are found but participants are able to start the program, the PT instructs the exercise physiologist on the required modifications. With the assistance of a cardiologist specializing in onco-cardiology, participants entering oncology rehabilitation undergo cardiopulmonary exercise tolerance testing (ETT). The utility and safety of ETT testing was based on previous review of cardiorespiratory fitness testing in the cancer setting.⁶³

Data regarding fitness, strength, persistent impacts of cancer therapy, and quality of life are obtained at baseline and again at the end of the intervention. The data are used to evaluate the success of the intervention and to examine impacts of cancer treatment on fitness,

strength, and function. Participants sign an University of Vermont Institutional Review Board approved consent agreeing to have their data included in a research database.

The exercise intervention consists of twice weekly supervised aerobic and resistance training for 12 weeks with recommendations to perform aerobic activity on 2–3 additional days each week. The ACSM recommendations for exercise prescription for cancer survivors are followed.⁵⁵ Aerobic exercise training does not require ECG monitoring and exercise physiologists monitor the exercise sessions. The aerobic exercise intensity is 70–85% of peak heart rate as determined at the entry ETT. If an ETT is not completed, a rating of perceived exertion between 12 and 14 is used. Participants perform aerobic activity, generally brisk walking, for 20 minutes 3–4 times per week progressing to 50 minutes 4 or 5 times per week. The resistance training includes upper extremity and lower extremity exercise. Initial weight is set at 60–70% of one repetition maximum (1-RM). If a 1-RM is not available for a particular muscle group initial, the weight is set at a level participants can move using correct form for at least 8 repetitions. If a participant has lymphedema, they are instructed to exercise with their compression garment. Balance exercises are included because a significant number of cancer survivors have balance problems as determined by single leg stance. Cancer survivors enter the program in groups of 4–6. The first 3 sessions are conducted by exercise physiologists and they introduce the exercises and equipment to participants. Thereafter, individuals exercise in a less supervised fashion, with exercise physiologists available to help participants progress their aerobic and resistance training.

During the intervention, core education sessions focusing on nutrition and stress management are provided. Additional lectures on topics related to cancer side effects are available. If individuals are identified to have a particular need or interest in weight control or stress management, longer programs on each topic are available and can be completed either during or after the intervention. Each participant has a formal meeting with a staff member to discuss their plans for continuing to exercise. They can continue to attend oncology rehabilitation for a small fee. Recently we began sending a 3 month post-intervention survey to participants to assess their activity after completing the intervention.

Oncology Rehabilitation Program Results

Between January 2012 and December 2013, 280 cancer survivors were evaluated (Table 5). The majority were women with a diagnosis of breast cancer. Participants were approximately 2.5 years beyond diagnosis (range 2 months – 22 years). Twelve percent of those entering the program require additional physical therapy prior to starting the program. Of those who were evaluated, 221 (79%) started the program and 164 (74%) of these completed the program. Over 90% attended more than 15 exercise sessions. Of the participants completing the program, 6 (2%) died as a result of their malignancy.

Physiologic and Quality of Life Improvements

Table 6 describes changes resulting from the intervention for participants in oncology rehabilitation from January 2012 through December 2013.

Baseline exercise tolerance tests have been performed on 120 participants with an average peak oxygen uptake ($\dot{V}O_2$) of $23.4 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Over 70% of participants completing

baseline ETTs have a peak $\dot{V}O_2$ in the very poor category, with another 15% having peak $\dot{V}O_2$ measurements consider to be poor. Post-intervention ETTs are performed only for individuals who received chemotherapy (n = 18) and, for these individuals, peak $\dot{V}O_2$ increased but not significantly. The distance walked in 6 minutes increased significantly post-intervention. At baseline, the 1-RM chest press was 15th percentile (very poor) for 95% of breast cancer survivors at baseline compared to normal age matched individuals.⁶⁴ Leg press strength was <20th percentile for 68% of participants. Both chest press and leg press strength increased significantly as a result of the intervention. Fatigue scores, as measured by the Fatigue Symptom Inventory,⁶⁵ declined significantly after the intervention. Depression as measured by PHQ-9⁶⁶ and anxiety as measured by GAD-7⁶⁷ were also significantly lower after the program. The participants report that the social aspect of the intervention as important as the exercise.

APPLICATION TO PRACTICE

Disseminating Oncology Rehabilitation: Leveraging the Experience and Opportunities Provided by Cardiac Rehabilitation

CR programs and facilities provide an ideal framework for developing and disseminating oncology rehabilitation programs. Our experience demonstrates that a CR model can be used to provide exercise based oncology rehabilitation that can improve the physiologic and quality of life parameters of cancer survivors. Minimal changes are needed to provide oncology rehabilitation at CR sites. A cardiac rehabilitation staff has the expertise necessary to deal with multiple comorbidities. Education specific to cancer survivor medical challenges could be provided in 2–3 hours. Physical therapists often collaborate with CR and are available to address cancer related deficits as well as any orthopedic issues cancer survivors might experience. CR has the equipment and expertise to provide exercise interventions and on-site education and lifestyle management are often available.

CR has a wide “reach”. There are over 2,000 programs in the US in both academic and community settings. The majority of these locations have an affiliated or nearby cancer center. Many CR sites are underutilized and have the capacity to expand to include oncology rehabilitation programs. Using existing space that already has the equipment and staff necessary for rehabilitation is a cost effective way to provide oncology rehabilitation. Many CR sites have an infrastructure to collect data on the efficacy of their program and to conduct outcomes research. Oncology rehabilitation would also benefit from similar research strategies to identify the challenges cancer survivors experience before and during exercise and to provide outcomes assessment to support potential third-party insurance coverage in the future.

Challenges of Disseminating Oncology Rehabilitation

Several challenges remain with disseminating oncology rehabilitation to a wider population of cancer survivors (Table 7). There is a need to add to the limited research evaluating exercise-based oncology rehabilitation. Comparative effectiveness and dissemination research is needed to test whether rehabilitative programs result in improvements in patient, health care system, and cost outcomes. There is a surprising lack of research evaluating the

natural history of aerobic and strength decline associated with cancer and its therapy. Information gained from longitudinal studies on the impact of cancer therapy would provide valuable information for identifying the times of greatest decline and potential recovery. Focused recommendations about the mode, intensity, and frequency of exercise for many specific cancer diagnoses are lacking. Ideally oncology rehabilitation would start early (Phase 1) but there is limited research on the extent to which cancer survivors are willing or able to participate during challenging oncologic interventions. It is unclear which cancer survivors require a medically supervised intervention and who can start exercising on their own or in a community gym setting. Targeting rehabilitation to cancer survivors who would benefit most is important for determining the efficacy and cost effectiveness of these programs. Ideally a risk classification system would be created to determine who is at greatest need.

The impact of cancer therapy is often under recognized by oncology medical providers and the value of interventions to alleviate cancer related symptoms is often overlooked. At most cancer centers, there are minimal options for providing oncology rehabilitation. An infrastructure is needed to provide a seamless transition to rehabilitation and exercise opportunities and should be considered a standard part of oncologic care. Staff at rehabilitation sites may need reeducation about the unique challenges of cancer survivors, such as lymphedema, ROM deficits, and peripheral neuropathy.

There is a lack of insurance reimbursement for oncology rehabilitation. In our oncology rehabilitation program, components are reimbursed by insurance, but bundled insurance reimbursement is not available. As a result, some of the cost, in particular supervision in the gym and lifestyle education modules, must be supported by philanthropic funds. In our community, stakeholders and the public have been very supportive and finding funds to support this new program has not been a barrier. However, this is clearly not a long-term sustainable solution. The current changes in health care delivery may provide an opportunity to expand medically supervised rehabilitation programs to new populations such as cancer survivors.

SUMMARY

Oncology rehabilitation using a CR model is a promising intervention for cancer survivors. Fitness improves as does physical and psychological function. Implementation of oncologic rehabilitation on a wider scale awaits the collection of controlled data concerning the value of oncologic rehabilitation versus usual care in contemporary populations. As the cancer survivor population grows due to improved oncologic treatment, the importance of longer term functional outcomes will be accentuated.

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References

1. De Moor JS, Mariotto AB, Parry C, et al. Cancer survivors in the United States: prevalence across the survivorship trajectory and implications for care. *Cancer Epi Bio Markers Prev.* 2013; 22(4): 561–670.
2. Lakoski S, Eves ND, Douglas PS, Jones LW. Exercise rehabilitation in patients with cancer. *Nat Rev Clin Oncol.* 2012; 9(5):288–296. [PubMed: 22392097]
3. Merchant CR, Chapman T, Kilbreath SL, Refshauge KM, Krupa K. Decreased muscle strength following management of breast cancer. *Disabil Rehabil.* 2008; 30(15):1098–1105. [PubMed: 19230221]
4. Ness KK, Wall MM, Oakes JM, Robison LL, Burney JG. Physical performance limitations and participation restrictions among cancer survivors. A population-based study. *Ann Epidemiol.* 2006; 16:197–205. [PubMed: 16137893]
5. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors - a systematic review. *Int J Psychiatry Med.* 2010; 40(2): 163–181. [PubMed: 20848873]
6. Hoening MJ, Botma A, Aleman BM. Long-term risk of cardiovascular disease in 10-year survivors of breast cancer. *J Natl Cancer Inst.* 2007; 99(5):365–375. [PubMed: 17341728]
7. van den Belt-Dusebout AW, Nuver J, de Wit R, et al. Long-term risk of cardiovascular disease in 5-year survivors of testicular cancer. *J Clin Oncol.* 2006; 24(3):467–475. [PubMed: 16421423]
8. Holmes MD, Chen WY, Faskanich D, Kroenke C, Colditz GA. Physical activity and survival after breast cancer diagnosis. *JAMA.* 2005; 293:2479–2486. [PubMed: 15914748]
9. Meyerhardt JA, Giovannucci EL, Holmes MD, et al. Physical activity and survival after colorectal cancer diagnosis. *J Clin Oncol.* 2006; 24:3527–3534. [PubMed: 16822844]
10. Meyerhardt JA, Heseltine D, Niedzwiecki D, et al. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. *J Clin Oncol.* 2006; 24:3535–3541. [PubMed: 16822843]
11. Balady GJ, Williams MA, Ades PA, Bittner V, Comoss P, Foody JA, Franklin B, Sanderson B, Southard D. Core components of cardiac rehabilitation/secondary prevention programs: 2007 update: a scientific statement from the American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee, the Council on Clinical Cardiology; the Councils on Cardiovascular Nursing, Epidemiology and Prevention, and Nutrition, Physical Activity, and Metabolism; and the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation.* 2007; 115:2675–2682. [PubMed: 17513578]
12. Hamm LF, Sanderson BK, Ades PA, Berra K, Kaminsky LA, Roitman JL, et al. Core competencies for cardiac rehabilitation/secondary prevention professionals: 2010 update: position statement of the American Association of Cardiovascular and Pulmonary Rehabilitation. *J Cardiopulm Rehabil Prev.* 2011; 31(1):2–10. [PubMed: 21217254]
13. Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, Skidmore B, Stone JA, Thompson DR, Oldridge N. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med.* 2004; 116(10):682–692. [PubMed: 15121495]
14. Ades PA, Savage PD, Brawner CA, Lyon CE, Ehrman JK, Bunn JY, et al. Aerobic capacity in patients entering cardiac rehabilitation. *Circulation.* 2006; 113:2706–2712. [PubMed: 16754799]
15. Heran BS, Chen JM, Ebrahim S, et al. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev.* 2011; 6(7):1– 82.
16. Lakoski SG, Eves ND, Douglas PS, Jones LW. Exercise rehabilitation in patients with cancer. *Nat Rev Clin Oncol.* 2012; 9(5):288–296. [PubMed: 22392097]
17. Peel AB, Thomas SM, Dittus K, Jones LW, Lakoski SG. Cardiorespiratory fitness in breast cancer patients: a call for normative values. *J Am Heart Assoc.* 2014; 13:3(1):e000432.10.1161/JAHA.113.000432.10.1161/JAHA.113.000432 [PubMed: 24419734]
18. Lakoski SG, Barlow CE, Koelwyn GJ, et al. The influence of adjuvant therapy on cardiorespiratory fitness in early-stage breast cancer seven years after diagnosis: the Cooper Center Longitudinal Study. *Breast Cancer Res Treat.* 2013; 138(3):909–916. [PubMed: 23504137]

19. Hayes SC, Davies PS, Parker TW, Bashford J, Green A. Role of a mixed type, moderate intensity exercise programme after peripheral blood stem cell transplantation. *Br J Sports Med.* 2004; 38:304–309. [PubMed: 15155433]
20. Toth MJ, Miller MS, Callahan DM, et al. Molecular mechanisms underlying skeletal muscle weakness in human cancer: reduced myosin-actin cross-bridge formation and kinetics. *J Appl Physiol.* 2013; 114(7):858–868. [PubMed: 23412895]
21. Hewitt M, Rowland JH, Yancik R. Cancer survivors in the United States: age, health and disability. *J Gerontol A Biol Sci Med Sci.* 2003; 58(1):82–91.
22. Leidenius M, Leppänen E, Krogerus L, von Smitten K. Motion restriction and axillary web syndrome after sentinel node biopsy and axillary clearance in breast cancer. *Am J Surg.* 2003; 185(2):127–130. [PubMed: 12559441]
23. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol.* 2013; 14(6):500–515. [PubMed: 23540561]
24. Smoot B, Wong J, Cooper B, Wanek L, Topp K, Byl N, et al. Upper extremity impairments in women with or without lymphedema following breast cancer treatment. *J Cancer Surviv.* 2010; 4(2):167–178. [PubMed: 20373044]
25. Cormier JN, Askew RL, Muingovan KS, Xing Y, Ross MI, Armer JM. Lymphedema beyond breast cancer. *Cancer.* 2010; 116:5138–5149. [PubMed: 20665892]
26. Hofman M, Ryan JL, Figueroa-Moseley CD, Jean-Pierre P, Morrow GR. Cancer-related fatigue: the scale of the problem. *Oncologist.* 2007; 12 (Suppl 1):4–10. [PubMed: 17573451]
27. Meeske K, Smith AW, Alfano CM, McGregor BA, McTiernan A, Baumgartner KB, et al. Fatigue in breast cancer survivors two to five years post diagnosis: a HEAL Study report. *Qual Life Res.* 2007; 16(6):947–960. [PubMed: 17457697]
28. National Comprehensive Cancer Network. [Accessed February 6, 2014] Cancer-Related Fatigue (Version 1.2014). https://www.nccn.org/store/login/login.aspx?ReturnURL=http://www.nccn.org/professionals/physician_gls/pdf/fatigue.pdf
29. Seidman AD, Berry D, Cirincione C, et al. Randomized phase III trial of weekly compared with every-3-weeks paclitaxel for metastatic breast cancer, with trastuzumab for all HER-2 overexpressors and random assignment to trastuzumab or not in HER-2 nonoverexpressors: final results of Cancer and Leukemia Group B protocol 9840. *J Clin Oncol.* 2008; 26:1642–1649. [PubMed: 18375893]
30. Vincenzi B, Frezza AM, Schiavon G, Spoto C, Silvestris N, Addeo R, et al. Identification of clinical predictive factors of oxaliplatin-induced chronic peripheral neuropathy in colorectal cancer patients treated with adjuvant Folfox IV. *Support Care Cancer.* 2013; 21(5):1313–1319. [PubMed: 23196819]
31. Crew KD, Greenlee H, Capodice J, Raptis G, Brafman L, Fuentes D, et al. Prevalence of joint symptoms in postmenopausal women taking aromatase inhibitors for early-stage breast cancer. *J Clin Oncol.* 2007; 25(25):3877–3883. [PubMed: 17761973]
32. Vance V, Mourtzakis M, McCargar L, Hanning R. Weight gain in breast cancer survivors: prevalence, pattern and health consequences. *Obes Rev.* 2010; 12(4):282–294. [PubMed: 20880127]
33. Meyerhardt JA, Niedzwiecki D, Hollis D, Saltz LB, Mayer RJ, Nelson H, et al. Impact of body mass index and weight change after treatment on cancer recurrence and survival in patients with stage III colon cancer: findings from Cancer and Leukemia Group B 89803. *J Clin Oncol.* 2008; 26(25):4109–4115. [PubMed: 18757324]
34. Kroenke CH, Chen WY, Rosner B, et al. Weight, weight gain, and survival after breast cancer diagnoses. *J Clin Oncol.* 2005; 23(7):1370–1378. [PubMed: 15684320]
35. Gould DW, Lahart I, Carmichael AR, Koutedakis Y, Metsios GS. Cancer cachexia prevention via physical exercise: Molecular mechanisms. *J Cachexia Sarcopenia Muscle.* 2013; 4(2):111–124. [PubMed: 23239116]
36. Zabora J, Brintzenhofer K, Curbow B, Hooker C, Piantadosi S. The prevalence of psychological distress by cancer site. *Psychooncology.* 2001; 10(1):19–28. [PubMed: 11180574]

37. Hinz A, Krauss O, Haus JP, Hocke M, Kortmann RD, Stolzenburg JU, Schwarz R. Anxiety and depression cancer patients compared with the general population. *Eur J Cancer Care (Engl)*. 2010; 19(4):522–529. [PubMed: 20030697]
38. Vahdaninia M, Omidvari S, Montazeri A. What do predict anxiety and depression in breast cancer patients? A follow-up study. *Soc Psychiatry Psychiatr Epidemiol*. 2010; 45(3):355–361. [PubMed: 19458878]
39. Chambers SK, Lynch BM, Aitken J, Baade P. Relationship over time between psychological distress and physical activity in colorectal cancer survivors. *J Clin Oncol*. 2009; 27:1600–1606. [PubMed: 19255326]
40. Schmitz KH, Holtzman J, Courneya KS, Mâsse LC, Duval S, Kane R. Controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2005; 14(7):1588–1595. [PubMed: 16030088]
41. Quist M, Rørth M, Langer S, Jones LW, Laursen JH, Pappot H, et al. Safety and feasibility of a combined exercise intervention for inoperable lung cancer patients undergoing chemotherapy: a pilot study. *Lung Cancer*. 2012; 75(2):203–208. [PubMed: 21816503]
42. Persoon S, Kersten MJ, van der Weiden K, Buffart LM, Nollet F, Brug J, et al. Effects of exercise in patients treated with stem cell transplantation for a hematologic malignancy: a systematic review and meta-analysis. *Cancer Treat Rev*. 2013; 39(6):682–690. [PubMed: 23485478]
43. Strasser B, Steindorf K, Wiskemann J, Ulrich CM. Impact of resistance training in cancer survivors: a meta-analysis. *Med Sci Sports Exerc*. 2013; 45(11):2080–2090. [PubMed: 23669878]
44. Lønbro S, Dalgas U, Primdahl H, Johansen J, Nielsen JL, Overgaard J, et al. Lean body mass and muscle function in head and neck cancer patients and healthy individuals -results from the DAHANCA 25 study. *Acta Oncol*. 2013; 52(7):1543–1551. [PubMed: 23964657]
45. McNeely ML, Campbell K, Ospina M, Rowe BH, Dabbs K, Klassen TP, et al. Exercise interventions for upper-limb dysfunction due to breast cancer treatment. *Cochrane Database Syst Rev*. 2010; 16(6):1–48.
46. Schmitz KH, Ahmed RL, Troxel A, Cheville A, Smith R, Lewis-Grant L, Bryan CJ, Williams-Smith CT, Greene QP. Weight lifting in women with breast-cancer-related lymphedema. *N Engl J Med*. 2009; 361(7):664–73. [PubMed: 19675330]
47. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev*. 2012; 14:11:1–84.
48. Irwin, ML.; Cartmel, B.; Gross, C.; Ercolano, E.; Fiellin, M.; Capozza, S.; Rothbard, M., et al. Randomized trial of exercise vs. usual care on aromatase inhibitor-associated arthralgias in women with breast cancer: the hormones and physical exercise (HOPE) study. San Antonio. Breast Cancer Symposium; Thursday, December 12, 2013; Abstract #S3-03
49. Strasser B, Steindorf K, Wiskemann J, Ulrich CM. Impact of resistance training in cancer survivors: a meta-analysis. *Med Sci Sports Exerc*. 2013; 45(11):2080–2090. [PubMed: 23669878]
50. McClellan R. Exercise programs for patients with cancer improve physical functioning and quality of life. *J Physiother*. 2013; 59(1):57.10.1016/S1836-9553(13)70150-4 [PubMed: 23419919]
51. Ibrahim EM, Al-Homaidh A. Physical activity and survival after breast cancer diagnosis: meta-analysis of published studies. *Med Oncol*. 2011; 28(3):753–765. [PubMed: 20411366]
52. Kenfield SA, Stampfer MJ, Giovannucci E, Chan JM. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. *J Clin Oncol*. 2011; 29(6):726–732. [PubMed: 21205749]
53. Ruden E, Reardon DA, Coan AD, Herndon JE 2nd, Hornsby WE, West M, et al. Exercise behavior, functional capacity, and survival in adults with malignant recurrent glioma. *J Clin Oncol*. 2011; 29(21):2918–2923. [PubMed: 21690470]
54. Rock CL, Doyle C, Demark-Wahnefried W, Meyerhardt J, Courneya KS, Schwartz AL, et al. Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin*. 2012; 62(4):243–274. [PubMed: 22539238]
55. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine Roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc*. 2010; 42(7):1409–1426. [PubMed: 20559064]

56. Smith WA, Nolan VG, Robison LL, Hudson MM, Ness KK, Johansson K. Physical activity among cancer survivors and those with no history of cancer – a report from the National Health and Nutrition Examination Survey 2003–2006. *Am J Transl Res.* 2011; 15(3):352–350.
57. Blaney JM, Lowe-Strong A, Rankin-Watt J, Campbell A, Gracey JH. Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey. *Psychooncology.* 2013; 22(1):186–194. [PubMed: 23296635]
58. Larsson IL, Jonsson C, Olsson AC, Gard G, Johansson K. Women's experience of physical activity following breast cancer treatment. *Scan J Caring Sci.* 2008; 22(3):422–429.
59. Cheville AL, Kornblith AB, Basford JR. An examination of the causes for the under utilization of rehabilitation services among people with advanced cancer. *Am J Phys Med Rehabil.* 2008; 90(5 suppl):S27–S37. [PubMed: 21765261]
60. Ades PA. Cardiac rehabilitation and secondary prevention of coronary heart disease. *N Engl J Med.* 2001; 345(12):892–902. [PubMed: 11565523]
61. Williams MA, Haskell WL, Ades PA, Amsterdam EA, Bittner V, Franklin BA, et al. Resistance exercise in individuals with and without cardiovascular disease: 2007 update: a scientific statement from the American Heart Association Council on Clinical Cardiology and Council on Nutrition, Physical Activity, and Metabolism. *Circulation.* 2007; 116(5):572–584. [PubMed: 17638929]
62. Milani RV, Lavie CJ, Cassidy MM. Effects of cardiac rehabilitation and exercise training programs on depression in patients after major coronary events. *Am Heart J.* 1996; 132:726. [PubMed: 8831359]
63. Jones LW, Eves ND, Peppercorn J. Pre-exercise screening and prescription guidelines for cancer patients. *Lancet Oncol.* 2010; 11(10):914–916. [PubMed: 20708967]
64. Linda, S.; Pescatello, LS.; Arena, R.; Riebe, D.; Thompson, PD. ACSM's Guidelines for Exercise Testing and Prescription. 9. Philadelphia: Lippincott Williams and Wilkins; 2014. Health-related physical fitness testing and interpretation; p. 60-107.
65. Hann DM, Denniston MM, Baker F. Measurement of fatigue in cancer patients: further validation of the fatigue symptom inventory. *Qual Life Res.* 2000; 9(7):847–854. [PubMed: 11297027]
66. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001; 16(9):606–613. [PubMed: 11556941]
67. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch Intern Med.* 2006; 166(10):1092–1097. [PubMed: 16717171]

Table 1

Impairments Experienced By Cancer Survivors and Improvements with Exercise/Rehabilitation.

Impairments	Improvements with Rehabilitation
1. Reduced physiologic capacity: <ul style="list-style-type: none"> a. Reduced cardiorespiratory fitness b. Muscle weakness/atrophy c. Impaired function/disability 	1. Increased aerobic fitness and strength
2. Persistent impacts of cancer therapy: <ul style="list-style-type: none"> a. Range of motion deficits b. Lymphedema c. Fatigue d. Pain 	2. Decreased deficits and lymphedema symptoms: <ul style="list-style-type: none"> a. Less pain and fatigue
3. Weight management: <ul style="list-style-type: none"> a. Weight gain b. Loss of lean body mass and sarcopenia 	3. Weight loss/maintenance with exercise and lifestyle interventions; maintenance of lean body mass with exercise
4. Psychological issues: <ul style="list-style-type: none"> a. Depression b. Anxiety 	4. Improved quality of life; decreased depression and anxiety with exercise

Table 2

Phases of Cardiac and Oncology Rehabilitation.

Phases	Cardiac Rehabilitation	Oncology Rehabilitation
1	In-hospital interventions including: ROM; self-care progressing to walking and limited stair-climbing	Address ROM deficits after surgery Deconditioning during oncologic treatment; 1-on-1 physical therapy transitioning to independence and rehabilitative exercise
2	Outpatient structured medically supervised exercise ECG monitoring Exercise adjustment regularly by exercise physiologist Activity under supervision Risk factor reduction and lifestyle improvement	Structured medically supervised exercise immediately post oncologic therapy Address persistent side effects and deficits Supervised exercise progression Lifestyle improvement
3	Independent group exercise Monitoring own heart rate Lifestyle interventions to improve chronic disease management	Independent group exercise Improve fitness Lifestyle interventions to improve chronic disease management

Abbreviations: ECG, electrocardiogram; ROM, range of motion.

Table 3

Core Components of Phase 2 Cardiac and Oncology Rehabilitation Programs.

Cardiac Rehabilitation¹¹	Oncology Rehabilitation
Exercise training	Same
Physical activity counseling	Same
Nutrition counseling	Same
Psychosocial management	Same
Weight management	Same
Coronary risk factor management: <ul style="list-style-type: none"> • Management of hypertension and dyslipidemia • Diabetes management • Smoking cessation 	Persistent effects after oncology therapy: <ul style="list-style-type: none"> • Fatigue/sleep issues • Surgical/radiation related impairment • Pain syndromes, arthralgias • Deconditioning/weakness/balance issues

Table 4

Baseline Assessments of Participants in Oncology Rehabilitation at the University of Vermont (2011-present).

	Cardiac Rehabilitation	Oncology Rehabilitation
Medical history	Review of CV medical and surgical diagnoses and procedures Comorbidities Depression Musculoskeletal and neuromuscular disorders Symptoms of CV disease Medications CV risk profile	Review of oncologic history and interventions Comorbidities Depression and anxiety Musculoskeletal and neuromuscular disorders Medications Presence of and risk for late/lingering effects of oncologic therapy
Physical examination	Cardiopulmonary systems Blood pressure Auscultation of heart and lungs Inspection of lower extremities for edema Post-CV procedure wound sites Orthopedic and neuromuscular status Cognitive function	Cardiopulmonary systems Blood pressure Auscultation of heart and lungs Inspection of all extremities for lymphedema Treatment related ROM Orthopedic and neuromuscular status Cognitive function
Testing	12-lead ECG Health-related quality of life Treadmill test with ECG or 6-minute walk test	6-minute walk test Health-related quality of life Treadmill test offered

Abbreviations: CV, cardiovascular; ECG, electrocardiogram; ROM, range of motion.

Table 5

Baseline Characteristics of Participants in the University of Vermont Oncology Rehabilitation, January 2012 through December 2013.

Total Patients Evaluated (n = 280)	
Gender	
Male	40 (14%)
Female	240 (86%)
Age ^a , y	55.8 ± 12.1 years
Type of malignancy	
Breast	190 (68%)
Colo/Rectal	6 (2%)
Heme	8 (3%)
Lung	7 (3%)
Prostate	6 (2%)
Other	63 (22%)
Time since diagnosis ^a , y	2.36 ± 3.7
Oncologic Intervention	
Surgery	236 (84.3%)
Chemotherapy	190 (67.9%)
Radiation	204 (72.9%)

^aMean ± SD

Physiologic and Quality of Life Parameters of Participants in University of Vermont Oncology Rehabilitation, January 2012 through December 2013.

Table 6

	n	Baseline	Post-Training	% Change	P
6-minute walk, m	142	534.2 ± 171	582.7 ± 157.2	8.3%	.003
VO _{2peak} , mL·kg ⁻¹ · min ⁻¹	18 ^a	24.6 ± 6.53	25.8 ± 6.25	7.5%	.142
1-RM chest press, lbs	142	63.7 ± 41.2	81.3 ± 44.2	21.6%	.000
1-RM leg press, lbs	130	115.7 ± 40.7	147.4 ± 39.9	21.5%	.000
Fatigue Symptom Inventory	141	15.7 ± 12.2	10.0 ± 11.8	36.3%	.000
PHQ-9, depression score	152	5.34 ± 4.0	3.7 ± 3.5	25.1%	.000
GAD-7, anxiety score	154	2.87 ± 3.5	2.34 ± 3.2	18.5%	.042

Abbreviations: GAD-7, Generalized Anxiety Disorder; PHQ-9, Patient Health Questionnaire; 1-RM, 1 repetition maximum; VO_{2peak}, peak oxygen uptake;

^a Performed on a subset of participants.

Table 7**Future Directions for Implementing Oncology Rehabilitation Programs.**

1. Research needs
<ul style="list-style-type: none"> a. Controlled interventions to determine recommendations for specific malignancies and for specific times in the cancer survivor trajectory b. Information on the natural history of physiologic parameters of cancer survivors c. Dissemination studies for cancer survivors outside controlled trials
2. Increase awareness and identify oncology ‘champions’
3. Allocation of resources
<ul style="list-style-type: none"> a. Locations for interventions b. Acceptance from CR facilities c. Training to improve comfort level of CR staff d. Referral systems
4. Lobby for third-party reimbursement

Abbreviation: CR, cardiac rehabilitation.